NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Medical technology consultation: MTG35 Memokath-051 stent for ureteric obstruction

Supporting documentation – Committee papers

The enclosed documents were considered by the NICE medical technologies advisory committee (MTAC) when making their draft recommendations:

1. **Medical technology consultation document –** draft guideline
2. **EAC assessment report** – an independent report produced by an external assessment centre who have reviewed and critiqued the available evidence.
3. **Assessment report overview** – an overview produced by the NICE technical lead which highlights the key issues and uncertainties in the company's submission and assessment report.
4. **Adoption scoping report** – produced by the adoption team at NICE to provide a summary of levers and barriers to adoption of the technology within the NHS in England.
5. **Consultation comments** – comments received from consultees during the consultation period.

Please use the above links and bookmarks included in this PDF file to navigate to each of the above documents.

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Medical technology consultation document

Memokath-051 stent for the treatment of ureteric obstruction

The National Institute for Health and Care Excellence (NICE) is producing guidance on using the Memokath-051 stent for the treatment of ureteric obstruction in the NHS in England. The medical technologies advisory committee has considered the evidence submitted and the views of expert advisers.

This document has been prepared for public consultation. It summarises the evidence and views that have been considered, and sets out the draft recommendations made by the committee. NICE invites comments from the public. A more detailed description of the issues considered by the committee and the evidence base can be found in the assessment report and overview.

The advisory committee is interested in receiving comments on the following:

- Has all of the relevant evidence been taken into account?
- Are the summaries of clinical effectiveness and resource savings reasonable interpretations of the evidence?
- Are the provisional recommendations sound, and a suitable basis for guidance to the NHS?
- Are there any equality issues that need special consideration and are not covered in the medical technology consultation document?

Note that this document is not NICE's final guidance on the Memokath-051 stent for the treatment of ureteric obstruction. The recommendations in section 1 may change after consultation. After consultation the committee will meet again to consider the evidence, this document and comments from public consultation. After considering these comments, the committee will prepare its final recommendations which will be the basis for NICE's guidance on the use of the technology in the NHS in England.

For further details, see the Medical Technologies Evaluation Programme process guide and Medical Technologies Evaluation Programme methods guide.

Key dates:

- Closing time and date for comments: 17:00 on 09 November 2017
- Second medical technologies advisory committee meeting: 17 November 2017

NICE medical technologies guidance addresses specific technologies notified to NICE by sponsors. The 'case for adoption' is based on the claimed advantages of introducing the specific technology compared with current management of the condition. This case is reviewed against the evidence submitted and expert advice. If the case for adopting the technology is supported, then the technology has been found to offer advantages to patients and the NHS. The specific recommendations on individual technologies are not intended to limit use of other relevant technologies which may offer similar advantages.

1 Draft recommendations

1.1 The case for adopting Memokath-051 stents for the treatment of ureteric obstruction is partially supported by the evidence. There is limited clinical, procedural and outcomes evidence, and clinicians using ureteric stents including Memokath-051 stents should therefore submit data to a national registry (see section 4.7).

1.2 Memokath-051 stents when implanted by trained and experienced surgeons (see section 4.7) and in appropriate patients are associated with equivalent success rates to double-J stents and a better patient experience. Compared with double-J, using Memokath-051 stents may also reduce the number of stent replacements needed. Memokath-051 stents for the treatment of ureteric obstruction should be considered as an option in patients with:

- malignant ureteric obstruction and anticipated medium- or long-term survival after adjunctive therapy or
- benign ureteric obstruction who cannot have reconstructive surgery or
- ureteric obstruction of any kind who cannot have a double-J stent or other stent or who need to avoid repeat procedures.

1.3 The cost consequences of adopting Memokath-051 stents in current pathways are uncertain. However, when used in the

populations described in section 1.2 and by experts trained in its use, it may be cost neutral or cost saving compared with standard treatment because of reduced need for repeat procedures.

2 The technology

Description of the technology

2.1 The Memokath-051 stent (PNN Medical) is a thermo-expandable, nickel-titanium alloy ureteric stent. It is intended as an alternative to conventional ureteric stents for people with malignant or benign ureteric obstruction. The nickel-titanium alloy has a shape memory effect which is designed to allow the stent to be more easily inserted and anchored in position. A spiral coil design aims to prevent endothelial ingrowth of the tumour or stricture into the stent so that it can be easily removed. Four different versions of Memokath-051 stents are available (single or double cone, for either antegrade or retrograde insertion), each in several different lengths. Memokath-051 stents can be used to treat obstructions elsewhere in the urinary tract, but this is outside the scope of this evaluation.

2.2 The cost of a Memokath-051 stent used in the company's submission is £1,690 (excluding VAT). This includes the Memokath-051 stent, a guidewire and a dilator-insertion sheath.

2.3 The company claims in the case for adoption that the Memokath-051 stent is a safe, simple and reliable ureteric stent with several advantages over other stents:

- it is better tolerated by the patient, with fewer stent-related symptoms and complications
- it avoids the need for stent replacement every 6 months, which saves costs
- it restores dignity and improves quality of life

- it reduces the risk of tissue ingrowth
- it can easily be removed with no side effects
- it uses theatre time more efficiently by avoiding the need for major surgery.

Current management

2.4 Ureteric obstruction must be treated quickly to avoid the development of obstructive renal failure. Obstructions can be treated by stenting the ureter, creating a nephrostomy or through reconstructive surgery. The NICE guideline on acute kidney injury states that people with upper urinary tract obstruction should be referred to a urologist. If appropriate, nephrostomy or stenting should be done as soon as possible (at least within 12 hours of diagnosis).

2.5 NICE has produced more specific guidance for malignant ureteric obstruction as a result of prostate or bladder cancer. The NICE guideline on prostate cancer recommends decompression of the upper urinary tract by nephrostomy or inserting a double-J stent. The NICE guideline for bladder cancer recommends nephrostomy or retrograde stenting (if technically feasible) for people with locally advanced or metastatic bladder cancer.

3 Evidence

Summary of clinical evidence

3.1 The evidence for Memokath-051 stents comprises 16 studies in adults with benign or malignant ureteric obstruction. Six of these were comparative observational studies: 2 full papers, 3 conference abstracts and 1 clinical trial record and abstract. The other 10 studies were single-arm observational studies published as full texts. For full details of the clinical evidence see section 3 of the assessment report.

Main points from the EAC's analysis of the clinical evidence

3.2 The external assessment centre (EAC) considered all of the comparative studies and 8 of the 10 single-arm studies to provide results which were relevant to the decision problem. The other 2 single-arm studies (Bach et al. 2013 and Boyvat et al. 2005) had less relevance to the decision problem because they did not have acceptable levels of internal or external validity, so they were not included in the analysis.

3.3 The quality of reporting across all the studies was generally poor. None of the studies provided adequate details on patient characteristics, stent insertion procedures, follow-up, statistical analyses and uncertainty around the results. Migration rates and clinical success were the most commonly reported outcomes but definitions of clinical success varied, so statistical pooling could not be done.

3.4 The 6 comparative studies compared Memokath-051 stents with:

- Allium stents (Bolton et al. 2015)
- UVENTA stents (Kim et al. 2014)
- double-J stents (Granberg et al. 2010, Maan et al. 2010)
- Resonance stents (Nam et al. 2015)
- ileal ureteral replacement surgery (Akbarov et al., 2017).

Memokath-051 stents had lower clinical success rates compared with Allium stents, UVENTA stents and ileal ureteral replacement surgery, but was comparable to double-J and Resonance stents. In a pooled analysis of migration rates, Memokath-051 stents had the highest rates compared with Allium, double-J and UVENTA stents. However, the EAC advised that the results should be treated with caution, because the rates for the comparators are informed by fewer studies and patients than those for Memokath-051 stents.

3.5 None of the studies provided comparative data for stent removal and replacement. A pooled analysis of the Memokath-051 stent treatment arms showed that 16.0% were removed and replaced, 17.7% migrated and 6.3% were encrusted. There was not enough evidence for a subgroup analysis of patients who could not have surgery or antegrade or retrograde insertion. Clinical success rates for Memokath-051 stents ranged from 50% to 64% in people with benign ureteric obstruction and from 33% to 100% in people with malignant ureteric obstruction. In Kim et al. (2014), Memokath-051 stents had similar clinical success rates to UVENTA in the benign population but was statistically significantly inferior to UVENTA in the malignant population.

3.6 The EAC concluded that the evidence for Memokath-051 stents came mainly from small, poorly reported observational studies. It considered that only 2 comparative studies (Maan et al. 2010 and Kim et al. 2014) and 1 single-arm study (Zaman et al. 2011) had acceptable internal and external validity.

Summary of economic evidence

3.7 The company submitted 3 economic studies, 2 of which were excluded by the EAC. The EAC identified 2 other relevant studies (Gonzalez et al. 2011 and Zaman et al. 2012). It considered that although the studies were poorly reported and in a heterogeneous group of patients, the results indicated that Memokath-051 is likely to be cost saving compared with double-J stents.

3.8 The model submitted by the company was based on an unpublished analysis comparing Memokath-051 with double-J stents. The EAC replicated the company's model, making it fully executable, and modified it to improve its usefulness for decision-making. The EAC's main changes included:

- extending the time horizon to 5 years

- including reconstructive surgery and other metallic stents as comparators
- adding the ability to report a break-even time point between Memokath-051 and the comparators
- including the risk of urinary tract infections
- adding scenario analyses to model the risk of unplanned Memokath-051 replacement in 4 scenarios
- introducing deterministic sensitivity analyses.

In the cost modelling, there is planned replacement of double-J stents after 6 months and no planned replacement of Memokath-051 over the 5-year time horizon. The EAC model also included a monthly risk of unplanned replacement for both technologies based on clinical data. Further details are in section 4.2.2 and 4.5 of the assessment report.

EAC's analysis of the economic evidence

3.9 The company's base-case results showed that compared with double-J stents, using Memokath-051 could save £4,156 per patient over 2.5 years. After the EAC revisions to the model, this saving fell to £1,619 per patient over 5 years.

3.10 Compared with reconstructive surgery, Memokath-051 stents are only cost saving if no planned replacement is needed. The incremental cost per patient after 5 years ranged from £467 to –£1,009, depending on the extrapolation of unplanned replacements.

3.11 Planned stent replacement is the main cost driver for Memokath-051 compared with other metallic stents:

- compared with UVENTA and Allium stents, Memokath-051 is cost neutral in the worst case but may generate cost savings with more positive assumptions

- compared with Resonance stents, Memokath-05 is cost saving after 12 months.

The EAC advised that the comparisons with Allium and Resonance stents should be interpreted with caution, because they are based on assumptions instead of comparative clinical data.

3.12 The EAC concluded that Memokath-051 stents appears to be a plausible cost-saving treatment option for ureteric obstruction in people who cannot have reconstructive surgery and who are expected to need a ureteral stent for at least 30 months.

4 Committee discussion

Clinical effectiveness

4.1 Having noted the EAC's comments on the limited evidence, the committee concluded that there was sufficient evidence to partially support the claimed patient benefits of Memokath-051 compared with double-J stents. It considered, however, that the claimed patient benefits compared with other metallic stents were not substantiated by the limited evidence available. The clinical experts commented that although the level of evidence was disappointing for a technology that has been commercially available for over 15 years, possible explanations include both the relatively rare circumstances under which Memokath-051 stents are used and the technically demanding nature of its insertion.

Care pathway

4.2 The clinical experts explained that double-J stents are the most commonly used stent for ureteric obstruction. They stated that the primary objective for patients who present with acute ureteric obstruction is to stabilise the patient by relieving the obstruction and treating any infection present. This is usually done by first creating a nephrostomy and or inserting a double-J stent (or

sometimes both). Once the patient is stable, a decision can be made about longer-term management. Options that are routinely considered include reconstructive surgery or inserting a metallic stent (such as Memokath-051). Important factors that influence this decision include the nature of the underlying disease process (benign or malignant) and patient prognosis. The clinical experts emphasised the need for careful patient selection by specialists with sufficient expertise and experience of the different technologies and procedures.

Patient selection with benign ureteric obstruction

4.3 The clinical experts explained that there is a heterogeneous group of benign conditions that may present with ureteric obstruction, for which reconstructive surgery is considered the standard of care. However, they explained that surgery may be unsuitable for some patients because of procedural risk or other co-morbidities. In these circumstances, inserting a metallic stent (such as Memokath-051) may be a reasonable alternative. The committee heard that Memokath-051 stents should not be used in patients with bladder stones because of an increased risk of stent encrustation, or in patients with pelvi-ureteric junction obstruction because of an increased risk of stent migration. One expert provided anecdotal evidence that they had successfully used a Memokath-051 stent in patients with vascular ureteral strictures. The committee concluded that Memokath-051 stents should be considered as a treatment option in patients with benign ureteric obstruction who cannot have reconstructive surgery.

Patient selection with malignant ureteric obstruction

4.4 Some ureteric obstructions have malignant causes; treatments for such malignancies may result in medium- or even sometimes long-term survival. The clinical experts explained that in these cases, the life expectancy of the patient is often the most important factor in determining how long stent treatment will be needed. The

committee recalled from the evidence that using Memokath-051 reduces the need for stent replacements compared with double-J stents, so it may be of particular value in patients with malignant ureteric obstruction with medium- or long-term life expectancy after adjunctive treatment. The committee also concluded that Memokath-051 stents may be a useful option for people who cannot have a double-J stent, or for those for whom repeat procedures are a high risk.

Quality of life benefits

4.5 The committee concluded from the published evidence and expert advice that Memokath-051 stents are usually well tolerated, and associated with fewer adverse symptoms than double-J stents.

Complications

4.6 Stent migration is the most common complication with Memokath-051. The clinical experts explained that this may be for several reasons, including the obstruction being resolved, stents placed too close to the pelvi-ureteric junction, or using a stent that is too long. They suggested that migration may be reduced as long as Memokath-051 stents are selected and inserted by experienced clinicians.

Future data collection

4.7 Given the limited evidence available, the committee recommended that clinical, procedural and outcomes data on the use of ureteric stents (including Memokath-051) be collected and published through a national register. On the basis of clinical experts' advice, the committee considered that the British Association of Urological Surgeons was likely to be the most appropriate organisation to establish and oversee such a register.

NHS and system impact considerations

4.8 The committee considered that the decision to use Memokath-051 should only be made by a multidisciplinary team that includes endo-urologists and interventional radiologists.

4.9 The clinical experts explained that the training and experience of the clinician were important factors when using Memokath-051 stents. They stated that there are important technical challenges and decisions which include ensuring the correct stent size is selected, that appropriate dilation of the ureter is undertaken and that placement of the stent is optimal. The company confirmed that it offers training, workshops and proctorships within the acquisition cost of the Memokath-051 stents. The clinical experts confirmed that the company's training had been helpful, but they felt there was a need to further formalise this training process (such as defining the number of stents inserted before competency is achieved).

Cost savings

4.10 The committee considered that any cost savings were uncertain because of the lack of good quality supportive evidence, the heterogeneous patient group and the complicated care pathway. It preferred the EAC's revised cost model to the company's model. The clinical experts explained that double-J stents may need to be replaced after just a few weeks; the model assumed double-J stent replacement at 6 months, so the estimated cost savings from using Memokath-051 instead may be conservative. The committee concluded that when used in appropriate patients by experts trained in its use, Memokath-051 is most likely to be cost neutral or cost saving compared with standard treatment.

Peter Groves
Chair, medical technologies advisory committee
October 2017

5 Committee members and NICE project team

Committee members

This topic was considered by the medical technology advisory committee which is a standing advisory committee of NICE.

Committee members are asked to declare any interests in the technology to be appraised. If it is considered there is a conflict of interest, the member is excluded from participating further in that evaluation.

The minutes of each committee meeting, which include the names of the members who attended and their declarations of interests, are posted on the NICE website.

NICE project team

Each medical technologies guidance topic is assigned to a team consisting of 1 or more health technology analysts (who act as technical leads for the topic) and a technical adviser or senior technical analyst.

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Technical analyst

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ISBN:

The Memokath-051 Stent for the Treatment of Ureteric Obstruction

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Declared interests of the authors

Description of any pecuniary relationship with the company, both personal and of the EAC. Please refer to NICE's Code of Practice for declaring and dealing with conflicts of interests.
http://www.nice.org.uk/niceMedia/pdf/Guidanceondeclarationsofinterest.pdf

None

Acknowledgements

The authors would like to thank the following expert advisers who were appointed by NICE and provided advice about the treatment of ureteral strictures:

- Mr Ranan Das Gupta, Consultant Urologist;
- Mr Matthew Shaw, Consultant Urologist;
- Ms Daniela Andrich, Consultant Urological Surgeon;
- Mr Mahmoud Elfar, Consultant Urologist.

The authors are also grateful to Helen Cole at The Newcastle upon Tyne Hospitals NHS Foundation Trust for assisting with deriving supply costs of surgical consumables.

Rider on responsibility for report

The views expressed in this report are those of the authors and not those of NICE. Any errors are the responsibility of the authors.

Contents

ABBREVIATIONS

Term	Definition
AKI	Acute kidney injury
AUH	Aintree University Hospital
BNF	British National Formulary
CBA	Cost-benefit analysis
CT	Computed tomography
EAC	External Assessment Centre
FDA	Food and Drug Administration
GHTF	Global Harmonization Task Force
HES	Hospital Episode Statistics
IFU	Instructions for use
IVU	Intravenous urography
MAUDE	Manufacturer and User Facility Device Experience
MHRA	Medicines & Healthcare products Regulatory Agency
MTEP	Medical Technologies Evaluation Programme
N/A	Not applicable
NHS	National Health Service
NICE	National Institute for Health and Care Excellence
NR	Not reported
OECD	Organisation for Economic Co-operation and Development
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PSS	Personal social services
PSSRU	Personal social services research unit
PUJ	Pelvi-ureteric junction
RCT	Randomised Controlled Trial
SD	Standard deviation
TCC	Transitional cell carcinoma
USSQ	Ureteral stent symptom questionnaire
UTI	Urinary tract infection
vs	Versus

1 Executive Summary

The company undertook a literature review to identify clinical evidence on Memokath-051 (single-arm studies, or compared with double-J stents), identifying 5 studies. The External Assessment Centre (EAC) expanded the selection criteria to include other comparators and identified 16 studies, including all those used by the company. These were 6 comparative studies, including 3 abstracts and 1 clinical trial record, comparing Memokath-051 to 1 of 5 comparators (reconstructive surgery, double-J stents, UVENTA stents, Allium stents and Resonance stents) and 10 single-arm, observational studies.

The studies were judged low quality evidence, primarily because of inadequate reporting of study design, patient characteristics and outcomes. Overall, Memokath-051 had similar success rates compared with double-J stents and Resonance stents but had worse outcomes than the Allium, UVENTA and reconstructive surgery. The most commonly reported adverse event associated with Memokath-051 was stent migration which occurred more frequently in Memokath-051 than in any of the comparators.

The company included 3 economic studies, 2 of which were excluded by the EAC as they were not deemed full economic evaluations. The EAC's literature review identified the remaining study plus 2 new studies. All were poor quality but indicated that Memokath-051 was cost saving versus double-J stents provided it remained in situ for sufficient time. The company submitted a model comparing Memokath-051 to double-J stents only. It reported Memokath-051 generated savings of £4,156 per patient over 30 months compared with double-J stents. No sensitivity analyses were conducted.

The company's model captured the key cost elements (initial procedure, planned replacement of double-J stents and unplanned replacements of Memokath-051). The EAC modified several inputs and its structure, to include reconstructive surgery and other metallic stents as comparators. The EAC's model reported savings of at least £1,619 over 5 years with Memoakth-051 compared to double-J stents. Across all scenarios, in patients who require a stent for at least 30 months, Memokath-051 is cost saving versus double-J stents.

Memokath-051 is estimated to be cost neutral compared with other metallic stents. It is cost saving compared with surgery up to month 53. The results of all analyses are limited by the poor quality of clinical and resource use data informing them and no assessment against nephrostomy could be made.

To conclude, Memokath-051 is likely to be a cost-effective treatment option in patients who are not indicated for reconstructive surgery and who are expected to require a ureteral stent for at least 30 months.

2 Background

Throughout this report, the EAC makes reference to specific sections within the company's submission as: (Section X.X, Submission). Where the EAC cites clinical experts, further information can be obtained from the correspondence log.

2.1 Overview and critique of company's description of clinical context

The company provided a comprehensive description of the Memokath-051 (Section 2.2, Submission). The description benefitted from diagrams, but the presentation of the information was poorly structured as the text did not always align with what was required within the submission template. The company referred to the relevant National Institute for Health and Care Excellence (NICE) guidelines as given in the final scope for the topic (Section 3.2, Submission).

The EAC developed the description submitted by the company to provide a more comprehensive description of the technology as well as providing information on the comparators and the clinical care pathway. The EAC reports on further potentially relevant NICE guidelines associated with this topic in Section 2.1.2.

2.1.2 EAC overview of the condition, technology, comparators, clinical pathway and relevant clinical guidelines

Patients with ureteric obstruction as a result of malignant or benign strictures

The ureter is a narrow muscular tube that urine flows through from the kidney to the bladder (NHS North Bristol Trust, 2014). The adult ureter is typically between 28 and 32 cm in length and has an outer and inner diameter of 4 to 6 mm and 2 to 4 mm, respectively (Claudon et al., 2003). Ureteric stricture is characterised by a narrowing of the ureter and can have malignant or benign causes. When the ureter is obstructed, the normal flow of urine from the kidney to the bladder is disrupted which can lead to complications associated with the kidney and urinary tract. Irrespective of the cause of the stricture it is necessary to relieve the obstruction in the ureter (NHS North Bristol Trust, 2014). Therefore, the patient population receiving treatment for ureteric stricture is heterogeneous (i.e. differing degrees of disease severity and patient condition and life years remaining). This is highlighted by the breadth of the notified indications for Memokath-051 as given in the topic briefing (NICE, 2017b). The notified indication is for people with ureteral strictures including:

- All benign anatomical strictures, including those due to: trauma; infection; ureteral anastomosis strictures; post-irradiation; iatrogenic and retro-peritoneal fibrosis;

- All malignant anatomical strictures, including those due to: cancer of the pelvic organs; cervical cancer; prostate cancer or bladder cancer.

A clinical expert advised that the life expectancy of those with a ureteric obstruction resulting from a malignant stricture varies depending upon the type of cancer. He highlighted that some cancers are very sensitive to treatment so some patients with a malignant stricture may live for many years. The EAC understands from this that the required functional lifetime of the stent depends upon the life expectancy of the patient rather than the degree of the stricture. For patients with a benign stricture, the clinical expert advised that life expectancy would not be limited by the aetiology of the stricture and so is expected to be normal for this patient group. Little information has been identified from the literature by the EAC on the life expectancy of those requiring ureteric stenting. One source reported that for patients with metastatic cancer that causes ureteral obstruction, the median life expectancy is generally less than 1 year (Chow et al., 2015) whilst another source reported those with a malignant ureteral obstruction have a median survival rate of 3.7 to 15.3 months (Pavlovic et al., 2016).

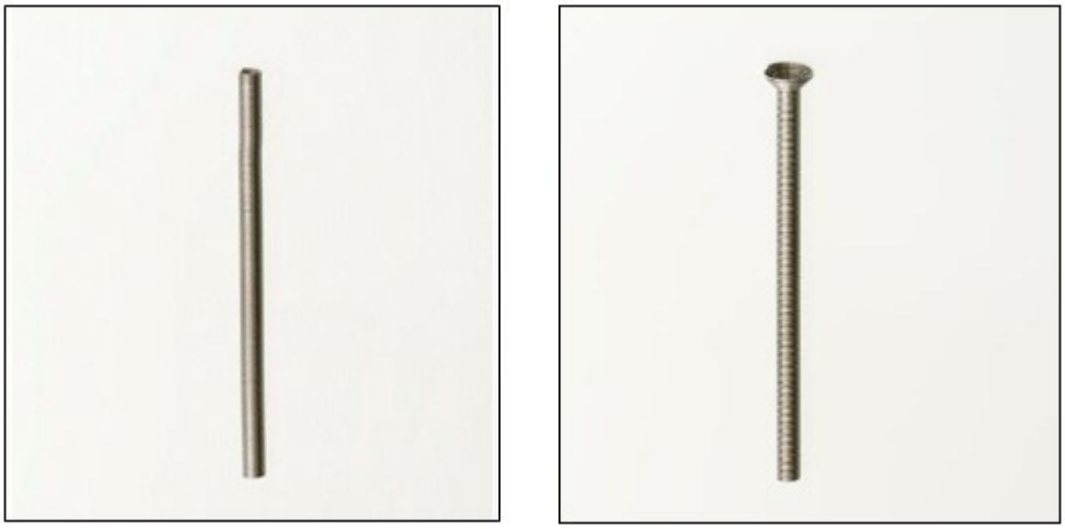
As highlighted in the topic briefing (NICE, 2017b), estimating the number of people who require a long-term ureteric stent as a result of malignant or benign ureteric strictures is difficult. Data from the Hospital Episode Statistics (HES) for England show that in 2014-15 there were: 7,674 retrograde insertions; 2,733 retrograde removals of ureteric stents; 80 cases of percutaneous insertions (i.e. antegrade insertions) and 22 replacements of ureteric metallic stents (Health and Social Care Information Centre, 2015). No additional information on the type of stent (plastic or metallic) or the reason for insertion was given in the topic briefing nor is freely available on HES online. These data incorporate all of the available stent types.

Technology: Memokath-051

Memokath-051 is a thermo-expandable nickel-titanium alloy spiral stent (Kulkarni and Bellamy, 1999). The nickel-titanium material can be either soft or rigid, depending upon temperature. This property allows for the material to have thermo-sensitive ‘shape memory’. The stent is soft in the pre-insertion state (i.e. at low temperatures, between 7 ^{o}C and 13 ^{o}C) but once inserted into the ureter the temperature of the stent is increased by flushing with sterile fluid at temperatures between 60 ^{o}C and 65 ^{o}C which results in either 1 end of the stent (single cone design) or both ends of the stent (double cone design) returning to its preformed cone shape (Maan et al., 2010).

The stent remains in the cone shape at normal body temperatures, with the cone-shaped end of Memokath-051 anchoring the stent into position (Abdallah et al., 2013). Figure 2.1 shows the Memokath-051 stent prior to insertion (left) and the expanded cone-shaped end following instillation of warm sterile fluid (right) and was included in the company's submission (Section 2.2, Submission).

Figure 2.1: The Memokath-051 ureteral stent. Pre-insertion (left), with expanded cone following instillation of warm water (right)



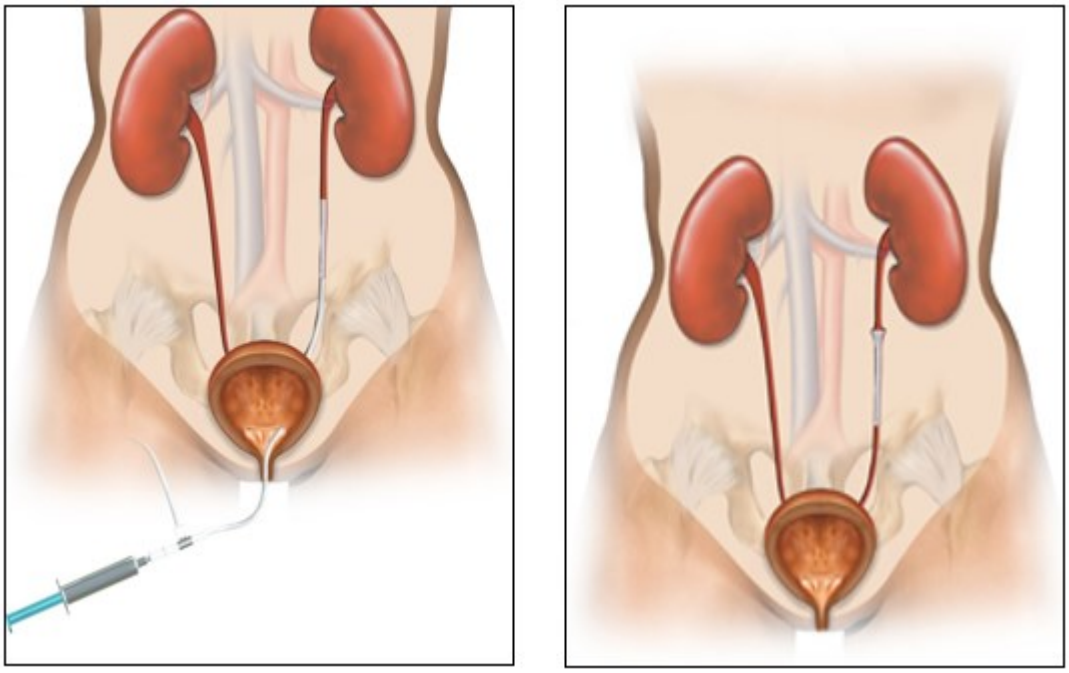
Memokath-051 is 1 of 4 versions of the device (Memokath-051, Memokath-028, Memokath-044 and Memokath-045) with the other versions being outside the scope of this assessment. Memokath-051 is available in 6 lengths (30, 60, 100, 150, 200, 250 mm) in the single cone design and in 4 lengths (60, 80, 100 and 120 mm) in the double cone design. The double cone design is used when the stricture is at the pelvi-ureteric junction (PUJ) (PNN Medical). The current version of Memokath-051 is 10.5 Fr in shaft diameter (whereby Fr refers to the French catheter scale and 1 Fr is equal to 1/3mm). This is larger than the previous version of Memokath-051 which was 9.5 Fr in shaft diameter (Talyor et al., 2013). Further, the cone size has increased from10.5 Fr to 22.5 Fr (Talyor et al., 2013). The company advised the EAC that the latest version has been on the market since around 2001 (correspondence log).

Memokath-051 can be inserted either antegrade (direction of the kidney to the bladder) or retrograde (from the direction of the bladder to the kidney) (PNN Medical). The insertion of the Memokath-051 stent involves the insertion of a guidewire through the stricture followed by the insertion of a dilator-insertion sheath (both provided with the device). Memokath-051 is then inserted into the sheath, positioned just above the proximal end of the stricture, prior to the sheath being removed and exposure of the full stent to the stricture (Maan et al., 2010). The company's instructions for use report that the stent is correctly

placed using contrast study to visualise the position of the stricture and radiopaque markers placed on patient's skin with adhesive tape (PNN Medical, 2016).

Error! Not a valid bookmark self-reference. Figure 2.2 shows the retrograde insertion of Memokath-051 (left) and the Memokath-051 stent in situ (right) and was included in the company's submission (Section 2.2, Submission).

Figure 2.2 The Memokath-051 ureteral stent: retrograde insertion (left), in situ (right)



The company advised that Memokath-051 has been on the market since 1996 and that sales figures suggest that more than 10,000 patients have had exposure to the device (Section 2.2, Submission). This is assumed to be worldwide. Two clinical experts advised that they undertake at least 5 and usually around 20 procedures involving the insertion or replacement of the Memokath-051 stent per year.

Indications for the Memokath-051 are ureteric obstruction, which may occur after medical procedures, and ureteral compression caused by benign or malignant disease. The stent may be used in connection with ureter dilatation and/or ureterotomy. Contraindications are: febrile patients (temperature above 38ºC); paediatric patients; impaired renal function in the kidney on the same side; active urinary tract infection (UTI); present urinary calculi, PUJ obstruction without obvious stricture or fibrosis; and known pathological processes that might require insertion of instruments larger than the internal diameter of the stent (PNN Medical, 2016).

Information provided by the company indicates that Memokath-051 is used in both tertiary and district general hospitals (correspondence log). Experts advised that the following barriers to uptake for Memokath-051 exist compared with double-J stents (NICE, 2017a):

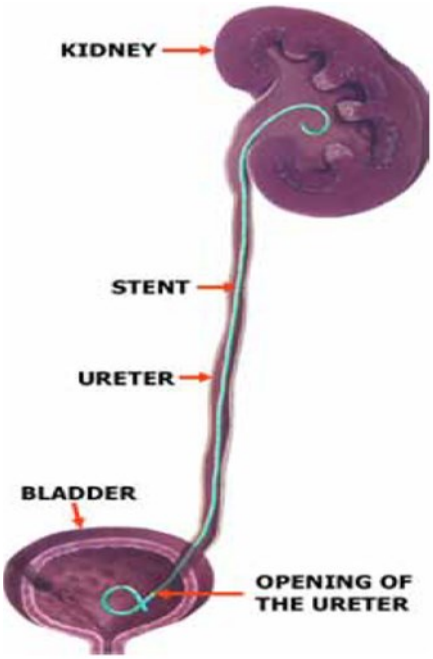
- Training and experience: inserting and removing Memokath-051 is deemed more technically challenging than double-J stents. Further, most urologists are experienced in using double-J stents.
- Patient selection: patients considered eligible for treatment with Memokath-051 are usually those with more complex conditions. Memokath-051 may be used in patients who require a stent for longer than a year, but not as a very long term solution.
- The initial cost of Memokath-051 is higher than double-J stents.
- Urologists will not know which length of Memokath-051 will be needed until they are performing the insertion procedure. A variety of sizes need to be kept in stock and most of the experts consulted kept 2 of each length. The upfront cost of this may act as an adoption challenge due to limited resources.
- Clinician confidence: issues around stent failure (including migration) may put clinicians off using Memokath-051.
- Lack of awareness: Memokath-051 has not been widely marketed although awareness is growing.

Comparator: Double-J stents

Double-J stents are designed as a slender plastic tube with a 'J' shaped hook at each end. The stent spans the full length of the ureter and the anchoring hook ends are positioned in the kidney and in the bladder to hold the stent in position (Lehmann, 2002). Double-J stents are available in various lengths, between 24 and 30cm for adult patients, and have a diameter of 2-3mm (Dartford and Gravesham NHS Trust, 2014). They are made from polyurethane, silicone or various polymers (Pavlovic et al., 2016).

Figure ***2.3*** shows a double-J stent in situ.

Figure 2.3: Double-J stent in situ (Dartford and Gravesham NHS Trust)



Double-J stents can be inserted either antegrade or retrograde. Some patients undergoing the antegrade stenting procedure will have already undergone a percutaneous nephrostomy allowing the stent to be inserted into the kidney through the existing tube. Where this is not the case, a radiologist will use X-ray or ultrasound to determine where to insert the stent into the kidney. This is commonly in the patient's back. Under local anaesthetic a needle is placed through the skin and into the kidney. To insert the stent, the radiologist then places a guidewire down the needle or tube firstly into the kidney then into the ureter, through the stricture and on into the bladder before passing the stent over the guidewire. The guidewire is then removed. The stent is left in place spanning the entire ureter (University Hospital Southampton NHS Foundation Trust, 2000). Some patients may have a separate catheter inserted temporarily to allow the urine in the kidney to drain externally. The catheter will be removed but the stent will remain in place (University Hospital Southampton NHS Foundation Trust, 2000). This level of detail on antegrade stenting could not be identified for other stent types but may apply.

Retrograde stenting involves a similar set-up to antegrade stenting with the procedure differing in the direction of insertion into the body. Retrograde insertion appears to be the more common technique used for stenting given the HES data for England (7,674 retrograde insertions and 80 antegrade insertions) (Health and Social Care Information Centre, 2015). A cystoscope is passed

through the patient's urethra into the bladder to identify the opening of the ureters. Using X-ray, a guidewire is passed through the urethra and bladder and into the ureter and finally into the kidney. The stent is then passed over the guidewire and the distal end lodged in the kidney. The positioning of the stent is checked before the guidewire is removed (Barts Health NHS Trust, 2012b).

The time that the stent remains in place is dependent on the needs of the patient but it can remain in the body for up to 6 months as indicated in the topic briefing (NICE, 2017b). Clinical experts have reported that routine replacement of double-J stents occurs within 6 months of insertion. One expert advised that double-J stents are typically replaced at 3 months following insertion of the 1st stent, but may be replaced less frequently should double-J stents be proven to work in a particular patient. The interval between replacements rarely exceeds 6 months.

Comparator: Nephrostomy

Nephrostomy is recommended as a treatment option in various NICE guidelines for people with ureteric strictures (NICE, 2013, NICE, 2014). A nephrostomy involves inserting a catheter into the skin under local anaesthetic using a guidewire into the kidney. The tube is held in place with stitches and allows for urine to drain from the kidney into a bag situated outside of the body (Macmillan, 2014, University Hospital Southampton NHS Foundation Trust, 2016).

A nephrostomy is typically seen as a temporary solution to a blockage prior to a more permanent solution such as stenting or surgery. A catheter has a lifespan of around 3 months and some patients may require exchange of their catheter should nephrostomy be required for longer than 3 months (Guy's and St Thomas' NHS Foundation Trust, 2013).

Comparator: Reconstructive surgery

Reconstructive surgery is a curative treatment option for patients with ureteric strictures. Experts judged that where patients can tolerate reconstructive surgery, typically those with benign strictures, they should be referred to a tertiary centre for this (NICE, 2017a). The experts highlighted the following surgical options that are available to patients with ureter strictures: ureteric re-implantation into the bladder; balloon dilation; laser endopyelotomy, extra-anatomical bypass. An expert informed that as part of reconstructive surgery patients have a double-J stent inserted. This is removed a few weeks after surgery once healing has occurred. A further type of reconstructive surgery is ileal ureter replacement. A brief description of each procedure is given below:

- Ureteric re-implantation (also known as ureteroneocystostomy) involves the re-implantation of the ureter into the bladder and is

generally used when the issue with the ureter is within 3 to 4 cm of the bladder (Ellsworth et al., 2016).

- Balloon dilation involves inserting a balloon catheter into the upper urinary tract and inflating the balloon to widen the ureter.
- Laser endopyelotomy is typically used to treat an obstruction of the PUJ (where the kidney joins the ureter). A laser is used to cut the ureter at the point of the obstruction and a balloon may be used to dilate the ureter.
- Extra-anatomical bypass is used as a treatment option when surgical reconstruction of the ureter is not possible, or is contra-indicated, and when stenting has failed. The procedure involves replacement of the full ureter with a prosthetic stent which extends from the kidney and into the bladder beneath the skin thus allowing the urine to leave the kidney, bypassing the obstruction in the ureter (Pavlovic et al., 2016). This is outside of the scope as it is not a type of reconstructive surgery.
- Ileal ureter replacement has been described as an alternative procedure to Memokath-051 for patients with ureteric obstruction (Akbarov et al., 2017). The procedure involves using a section of the ileum (small intestine) to substitute the ureter (Armatys et al., 2009).

Comparator: Metallic and alloy stents (including nitinol stents)

The company comments on metallic stents with reference to the Wallstent in their background section (Section 2.2, Submission) but does not comment on any other metal stents that are available. Examples of metal stents available on the market in England include:

- 'Resonance' by Cook Medical (Cook Medical) which is composed of nickel-cobalt-chromium-molybdenum alloy;
- 'Allium' by Allium Medical (Allium Medical) which is composed of nickel-titanium alloy;
- 'UVENTA' (TaeWoong Medical) by TaeWoong Medical, composed of a single layer of polytetrafluoroethylene between 2 superlastic nitinol layers.

A freedom of information request from NHS supply chain indicated that 131 Resonance stents have been sold through NHS supply chain over the past 5 financial years (correspondence log). However, these stents are likely sold through other sources too.

Metal stents can take on different designs such as a tightly wound coil (e.g. Resonance) (Rao et al., 2011) or a mesh (e.g. Allium and UVENTA) (Kachrilas

et al., 2013) but all aim to preserve long-term urinary drainage whilst not needing to be frequently exchanged (Al Aown et al., 2010).

Unlike Memokath-051, both the Allium and UVENTA stents do not have a thermo-expandable mechanism and are instead are 'self-expandable', meaning that the stents are packed in a small shape that is easy to insert into the ureter where they then expand independently (Kulkarni, 2014). The Allium and UVENTA stents are similar in design, featuring a nickel-titanium alloy mesh between thin polyester membranes, which help to prevent tissue ingrowth (Kulkarni, 2014). The Allium stent has a distal coil that is retained in the bladder in order to anchor the stent and prevent migration (Moskovitz et al., 2012). Both stents are inserted using a similar procedure to the Memokath-051, with the UVENTA stent delivered through a sheath and the Allium stent through a delivery catheter. As noted in the topic briefing, the UVENTA and Allium stents can be used for up to 18 months and 3 years, respectively (NICE, 2017b).

The Allium stent is indicated for long-term stenting of malignant or benign ureteral occlusions (i.e. patients indicated for insertion of a double-J stent for 6 months or longer). Contraindications are: UTI, fever or chills; hematuria; patients who cannot tolerate antibiotic treatment or iodine preparations; patients on anticoagulation therapy or with post-surgical anatomy that precludes cystoscopic or percutaneous approach; and patients with a history of illness, medication or surgery that may affect the efficacy of the stent (Allium Medical).

The UVENTA stent is indicated for malignant ureteral obstruction. No information about contraindications is given on the manufacturer's website (TaeWoong Medical, 2016).

The principal differences between the UVENTA and Allium stents and the Memokath-051 stent are the shape (a metallic mesh, rather than the coil shaped used in Memokath-051) and mechanism (self-expandable, rather than thermo-expandable). Further, Memokath-051 and UVENTA stents do not feature a distal coil for anchoring in the bladder as seen in the Allium stent.

The Resonance stent is a non-expandable coiled metallic stent. It does not have a lumen like the Memokath-051, Allium and UVENTA stents, and urine is expected to drain by the side of the stent (Kulkarni, 2014). Similarly to a double-J stent, the Resonance stent features curled ends which are positioned in the kidney and bladder to prevent migration (Rao et al., 2011). The stent is inserted either antegrade or retrograde and requires the use of a guidewire, catheter and sheath to insert the catheter under fluoroscopic guidance or direct vision (Cook Medical, 2012) under a similar procedure to the insertion of Memokath-051. The Resonance stent is indicated for adult patients with extrinsic ureteral obstruction. The manufacturers state that there are no known contraindications

(Cook Medical, 2012). It is more similar to a double-J stent than the Memokath-051, Allium and UVENTA stents, but can remain in the body for a longer indwelling time than double-J stents, up to 12 months (Cook Medical).

Clinical care pathway

The clinical care pathway for ureteric stricture involves the obstruction in the ureter to be relieved to allow the kidney to decompress. The most appropriate treatment option is selected based patient characteristics (i.e. the clinical condition of the patient, morbidities) (Kulkarni, 2014).

The company advised that Memokath-051 should be considered as the first line treatment for all cases of chronic ureteric strictures due to benign or malignant diseases. However, it is understood that patient characteristics determine the possible use of Memokath-051 (NICE, 2017a). Under the following conditions, patients would be treated with the Memokath-051 stent as the preferred option:

- Patients with malignant terminal illness who have a life expectancy of 1 year or over;
- Those with benign or malignant strictures who have a life expectancy of less than a year and cannot tolerate a double-J stent or where the risk of repeated procedures using general anaesthetic needs reducing;
- Those with benign strictures who are unsuitable for reconstructive surgery and/or require a stent for longer than 1 year.

Further, Memokath-051 may not be the treatment option of choice for patients with the following characteristics:

- Those with benign ureteric strictures where reconstructive surgery would be curative should be referred to a tertiary centre for corrective surgery;
- Those requiring a short term stent;
- Those with progressive malignant disease where the ureter may become blocked above or below the stent (the EAC notes that the company does not agree with this criterion);
- People with malignant disease who are close to the end of their lives;
- One expert reported that they would not use Memokath-051 for a stricture at the proximal part of the ureter (close to junction with the kidney) as they have experience of these migrating.

Table 2.1 gives an indication of the differences across technologies relating to the procedure, their pre-operative requirements, peri-operative issues and post-operative requirements.

Table 2.1: Summary of the procedure, resource use and follow-up for each intervention

	Memokath-051	Double-J stents	Metallic stents	Nephrostomy	Reconstructive surgery
Indication	Ureteric obstruction, which may occur after medical procedures, and ureteral compression caused by benign or malignant disease (PNN Medical, 2016)	Many brands of double-J stents are available. As an example, Percuflex Ureteral Stent is intended to facilitate drainage from the kidney to the bladder via placement endoscopically or fluoroscopically by a trained physician (Boston Scientific, 2014).	Resonance: Adult patients with extrinsic ureteral obstruction (Cook Medical, 2012) Allium: Long-term stenting of malignant or benign ureteral occlusions (Allium Medical, 2016) UVENTA: Malignant ureteral obstruction (TaeWoong Medical, 2016)	To relieve urinary obstruction of benign or malignant nature, or urinary fistulas (Hausegger and Portugaller, 2006)	Ureteric re-implantation: Obstruction or fistula in the lower third of the ureter (Ellsworth et al., 2016) Balloon dilation: ureteral stricture (Yu et al., 2016) Laser endopyelotomy: PUJ obstruction (NICE, 2009) Ileal ureter replacement: ureteral stricture or injury (Armatys et al., 2009)
Type of procedure	Either antegrade or retrograde insertion (PNN Medical). Clinical experts: Method selected based on ureteric anatomy, reconstruction and tolerability of bladder component stent, and on failure to gain retrograde access, would use antegrade method	Antegrade insertion as an inpatient procedure (University Hospital Southampton NHS Foundation Trust, 2000). Retrograde procedure as an outpatient procedure (McFarlane et al., 2001). Clinical experts: Method selected based on same criteria as stated for Memokath-051	Either antegrade or retrograde insertion (Kachrilas et al., 2013). Clinical experts: Method selected based on same criteria as stated for Memokath-051	Insertion of catheter into the kidney under local anaesthetic (University Hospital Southampton NHS Foundation Trust, 2016)	Ureteric re-implantation: Either by open surgery or minimally invasive laparoscopic approach (Ellsworth et al., 2016) Balloon dilation: retrograde (non-UK source) (Yu et al., 2016) Laser endopyelotomy: either antegrade or retrograde (Barts Health NHS Trust, 2012a) Ileal ureter replacement: Not reported (NR) if open or laparoscopic surgery
Who conducts the procedure	Urologist (2 present) with an anaesthetist also present (non-UK source) (Gonzalez et al., 2011)	Radiologist (University Hospital Southampton NHS Foundation Trust, 2000) and assumed to	Assumed same as Memokath-051	Radiologist (University Hospital Southampton NHS Foundation Trust, 2016) and assumed to	Assumed to be a surgical team

	Memokath-051	Double-J stents	Metallic stents	Nephrostomy	Reconstructive surgery
		be accompanied by a surgical team.		be accompanied by a surgical team	
Anaesthesia for insertion and follow-up medication	Intraoperative: General anaesthetic (Agrawal et al., 2009). Clinical experts: general anaesthetic. Post-operative: 5 days of norfloxacin (Agrawal et al., 2009)	Local anaesthetic (University Hospital Southampton NHS Foundation Trust, 2000). Clinical experts: General anaesthetic mostly. Note that it can be done under local anaesthetic	Resonance: General anaesthesia (Patel et al., 2017) Allium: General or local anaesthesia (non-UK source) (Moskovitz et al., 2012) UVENTA: No information identified. Assumed to be similar to other metal stents Clinical experts: general anaesthetic	Local anaesthetic (Macmillan, 2014, Guy's and St Thomas' NHS Foundation Trust, 2013)	Ureteric re-implantation: General anaesthetic (Ellsworth et al., 2016). Balloon dilation: spinal anaesthesia (non-UK source) (Yu et al., 2016). Laser endopyelotomy: general anaesthetic (Barts Health NHS Trust, 2012a) Ileal ureter replacement: assumed to be general anaesthetic as open surgery
Setting	Operating theatre. Although not routine, placement can also theoretically be performed in outpatient clinics (NICE, 2017b) Clinical experts: operating theatre	X-ray department or operating theatre (University Hospital Southampton NHS Foundation Trust, 2000) Clinical experts: operating theatre	No information identified. Assumed to be similar to other metal stents Clinical experts: operating theatre	Either in an X-ray department or an operating theatre using portable X-ray equipment or ultrasound devices (University Hospital Southampton NHS Foundation Trust, 2016)	Assumed to be an operating theatre
Duration of procedure	On average, <30 minutes, but could be up to 1 hour in some cases (Zaman et al., 2011, Papatsoris and Buchholz, 2010) Clinical experts: average 45 minutes	About 1 hour (University Hospital Southampton NHS Foundation Trust, 2000) Clinical experts: Average 22.5 minutes	Resonance: About 30 minutes (Patel et al., 2017) Allium & UVENTA: No information identified. Clinical experts: average 40 minutes	Up to an hour (Macmillan, 2014)	NR

	Memokath-051	Double-J stents	Metallic stents	Nephrostomy	Reconstructive surgery
Examinations and medication (perioperative)	Pre-operative: renal function and mid-stream urine sample testing. Evaluate the stricture characteristics; intravenous urography (IVU) or retrograde study (Agrawal et al., 2009) Clinical experts: Computed tomography (CT) scan and nuclear medicine imaging. Intra-operative: Clinical experts: confirmation of stent placement using fluoroscopy and image intensifier Post-operative: IVU and mid-stream sample testing at 6 weeks (Agrawal et al., 2009) Clinical experts: analgesia given if required Serial follow-up imaging, reported specifically as 3 follow- up visits with X-ray in first year. (Zaman et al., 2011) Clinical experts: x-ray, renogram and clinical assessment	Pre-operative: 20 minute medical consultation (grade of medical staff NR and non-UK source). (Gonzalez et al., 2011). Clinical experts: CT scan. Intra-operative: Clinical expert: pyelogram at time of insertion. Confirmation of stent placement using fluoroscopy and image intensifier. Post-operative: Clinical experts: analgesia given if required. Cystogram every 3 months (Lehmann, 2002). Alternative source reported, 2 out-patient follow-ups with X-ray per year. (Zaman et al., 2011). Clinical experts: X-ray or ultrasound and clinical assessment.	Resonance: No information identified. Assumed to be similar to other metal stents. Allium: imaging (renography/CT urography) 6 weeks post-insertion (Moskovitz et al., 2012). UVENTA: No information identified. Assumed to be similar to other metal stents. Clinical experts did not distinguish between make of stent. Same diagnostic tests used as with Memokath-051. Intra-operative: Clinical expert: Confirmation of stent placement using fluoroscopy and image intensifier. Post-operative: Clinical experts: Analgesia if required. X-ray, renogram and clinical assessment	Intraoperative: intravenous fluids, sedatives and prophylactic antibiotics (Macmillan, 2014).	Ureteric re-implantation: cystoscopy may be performed pre-operatively (Ellsworth et al., 2016) Balloon dilation: pre-operative: uroflowmetry, cystoscopy, retrograde urethrogram, cystourethrogram intra-operative: retrograde urethrogram, Post-operative: uroflowmetry performed at every 3-month follow-up visit for 3 years (non-UK source) (Yu et al., 2016) Laser endopyelotomy: NR. Assumed to be similar to other surgeries Ileal ureter replacement: NR. Assumed to be similar to other surgeries

	Memokath-051	Double-J stents	Metallic stents	Nephrostomy	Reconstructive surgery
Hospital length of stay	Average of around 1.5 days but could be up to 1 week (Agrawal et al., 2009, Papatsoris and Buchholz, 2010)	Observation on a ward (Barts Health NHS Trust, 2012b, University Hospital Southampton NHS Foundation Trust, 2000)	No information identified. Assumed to be similar to Memokath-051	4-6 hours to ensure nephrostomy is functioning correctly. Some may require an overnight stay (Macmillan, 2014, Guy's and St Thomas' NHS Foundation Trust, 2013)	Ureteric re-implantation & Balloon dilation: NR. Assumed to be similar to other surgeries Laser endopyelotomy: 2-3 days (Barts Health NHS Trust, 2012a) Ileal ureter replacement: 7 days (Armatys et al., 2009)
Indwelling time	Mean indwelling time is generally greater than 1 year and some studies report stent indwelling times of up to 4 years (Granberg et al., 2010, Bach et al., 2013)	Up to 6 months (NICE, 2017b)	Resonance: Up to 12 months (Cook Medical, 2012) Allium: Up to 3 years (NICE, 2017b) UVENTA: Up to 18 months (NICE, 2017b)	Around 3 months (Guy's and St Thomas' NHS Foundation Trust, 2013)	Not applicable (N/A)
Removal and replacement	Removal performed under local anaesthetic and fluoroscopy, using a cystoscope. Fluid below 10ºC is used to soften stent, which can then be grasped using biopsy/grasping forceps and uncoiled for removal. (Agrawal et al., 2009, NICE, 2017b) Alternative source: stent can be removed using a balloon catheter (Papatsoris and Buchholz, 2010)	Performed under local anaesthetic using a cystoscope. Forceps are used to remove the stent. Some stents feature an extraction string, allowing removal by pulling on the string. The frequency of using the different methods for removal were NR (NHS North Bristol Trust, 2014) Stents can be replaced as an outpatient procedure using fluoroscopy and conscious sedation. The	Resonance: removed using cystoscopic techniques with forceps (Cook Medical, 2012) Allium: removed using cystoscopic techniques with forceps, the stent unravels (Allium Medical, 2012) UVENTA: NR Clinical experts: gave the same response as for Memokath-051	Catheter removal or replacement at around 3 months post-surgery (Guy's and St Thomas' NHS Foundation Trust, 2013)	Ureteric re-implantation: Catheter removal 1-2 days following surgery (Ellsworth et al., 2016). Balloon dilation: catheter removed 2-3 weeks post-surgery (Yu et al., 2016) Laser endopyelotomy: catheter usually removed 1 day post-surgery. Ureteric stent usually removed after 4–6 weeks post-surgery (Barts Health NHS Trust, 2012a) Ileal ureter replacement: Stent removed 11 days post-

	Memokath-051	Double-J stents	Metallic stents	Nephrostomy	Reconstructive surgery
	Clinical experts: replacement and removal require GA and an ureteroscopy is likely necessary. A CT scan is not needed for stent replacement	old stent is partially pulled out of the patient and a guide wire is passed through, allowing the old stent to be fully removed and the new stent inserted over the guide wire (Lehmann, 2002) Clinical experts: no differences reported between the insertion and replacement procedures			operatively (Armatys et al., 2009)

Overview of relevant clinical guidelines

The company correctly noted that there is no specific recommendation for stricture ureter disease. The company reproduced the 3 NICE guidelines included in the final scope which indicate the current management of patients with ureteric strictures due to various causes. The 3 NICE guidelines are summarised below:

- Acute kidney injury (AKI) (CG169) (NICE, 2013): all people with upper urinary tract obstruction should be referred to an urologist, and that when nephrostomy or stenting is undertaken, it should be done as soon as possible and certainly within 12 hours of diagnosis;

- Prostate cancer (CG175) (NICE, 2014): offer decompression of the upper urinary tract by percutaneous nephrostomy or by insertion of a double-J stent to men with obstructive uropathy secondary to hormone-relapsed prostate cancer;

- Bladder cancer (NG2) (NICE, 2015): consider percutaneous nephrostomy or retrograde stenting (if technically feasible) for people with locally advanced or metastatic bladder cancer and ureteric obstruction who need treatment to relieve pain, treat AKI or improve renal function before further treatment.

In addition, the company included information on other endourologic options for intervention of strictures sourced from a urology textbook (Wein et al., 2011). Although this provided useful background information, the textbook is not an evidence-based clinical guideline.

The company did not identify a potentially relevant guideline, the NICE interventional procedures guidance (IPG46) on laparoscopic pyeloplasty, where a listed indication is obstruction of the PUJ (NICE, 2004).

2.2 Critique of company's definition of the decision problem

The EAC have completed Table 2.2 to critique the company's definition of the decision problem. During correspondence with the company following submission they confirmed that that Table A1 in the company's submission was based on the draft scope published by NICE (correspondence log). The company was given the opportunity to update Table A1 based on the final scope and provided an updated table (correspondence log) which the EAC has used for its critique of the company's definition of the decision problem.

Table 2.2: Critique of company's definition of the decision problem

Decision problem	Company submission	Matches decision problem? (Y/N/partially)	EAC comment
Population	***Reported action in Table A1:*** Patients with ureteric obstruction, specifically as a result of malignant or benign strictures ***Action taken in the submission:*** Limited to adults Excluded studies with only malignant or only benign strictures	***Reported action in Table A1:*** Y ***Action taken in the submission:*** N	The EAC did not limit to adults when conducting their literature review to accurately reflect the NICE scope, however, no studies in children were identified and the EAC notes that the company state Memokath-051 is contraindicated in children hence their decision on this criteria is valid. The EAC included studies that made reference to either malignant or benign stricture
Intervention	***Reported action in Table A1:*** Memokath-051 ***Action taken in the submission:*** Memokath-051	***Reported action in Table A1:*** Y ***Action taken in the submission:*** Y	Company submission matched the final scope
Comparator(s)	***Reported action in Table A1:*** Double-J stents Nephrostomy Reconstructive surgery Metal including nitinol stents ***Action taken in the submission:*** Comparison with double-J stents in chronic cases only	***Reported action in Table A1:*** Y ***Action taken in the submission:*** N	The company did not provide justification for not including all comparators listed in the final scope in their submission. The company later provided justification via communication with the EAC. They omitted surgery as a comparator given their decision to "reflect reality and practicality on the ground…focus on the value of Memokath-051 in the nearest indicated cases." The EAC considered all comparators in its review of the clinical evidence
Outcomes	***Reported action in Table A1:*** NR ***Action taken in the submission:*** All outcomes reported in the included studies were extracted	***Reported action in Table A1:*** N ***Action taken in the submission:*** Partially	The EAC considered all outcomes listed in the final scope in its review of the clinical evidence
Cost analysis	***Reported action in Table A1:*** Nothing reported ***Action taken in the submission:***	***Reported action in Table A1:*** N	The company included Double-J stents as its sole comparator, whilst the EAC considered other comparator

Decision problem	Company submission	Matches decision problem? (Y/N/partially)	EAC comment
	Only comparator was double-J stents. Costs were considered from a hospital perspective over a 2.5 year time horizon No sensitivity analyses were undertaken	***Action taken in the submission:*** Partially	for which there was clinical evidence. Nephrostomy was excluded on this ground.
Subgroups	***Reported action in Table A1:*** Nothing reported ***Action taken in the submission:*** No subgroups	***Reported action in Table A1:*** N ***Action taken in the submission****:* N	The EAC identified evidence in relation to 1 of the subgroups detailed in the scope (malignant versus (vs) benign). There was no evidence in relation to the other subgroups

Special considerations, including issues related to equality

The final scope identified the following special consideration relating to equality: "Some ureteric obstructions are a result of malignancy - all people with cancer are protected under the Equality Act from the point of diagnosis. People with ureteric strictures may benefit from Memokath-051 as an alternative to double-J stents, as it may be associated with a reduced number of replacement procedures and reduced adverse events, which would improve their quality of life. Memokath-051 may also provide an alternative treatment for people with ureteric strictures who cannot tolerate or who have had failed conventional stents, who would otherwise be nephrostomy-dependent and are likely to be classed as disabled under the Equality Act."

The company did not provide any information on equality issues associated with the technology and did not consider the malignant population independently, hence did not address this consideration. The EAC has identified no further equality issues and notes that although some cancers are specific to males and others to females, the overall ratio of patients included within the clinical evidence reported in Section 3 is approximately equal.

3 Clinical Evidence

3.1 Critique of and revisions to the company's search strategy

Section 7.1 of the company submission contains a description of the search methodology used to identify clinical evidence, but this is very limited and is not sufficient to accurately replicate or evaluate the company's search. The full search strategies, exactly as run in each resource, are not provided. Section 10, Appendix 1 of the submission, where it is expected that they are recorded, is blank. The EAC requested clarification of the search methods from the company (correspondence log). Whilst some information that was omitted from the original submission (specifically the number of records retrieved per resource) was provided in this document, exact search strategies for each resource were still missing. Moreover, rather than providing clarification, the additional information contradicted the original submission in terms of the resources searched and the search concepts used. The EAC was unable to rerun the company's search and therefore undertook a *de novo* literature search to identify clinical evidence on Memokath-051. The strategy was constructed to search for records containing the name of the device or the manufacturer, in addition to studies where Memokath was not explicitly mentioned in the title or abstract of the record and instead referenced a unique feature of the device such as thermo-expansion or shape memory. The search was conducted in a range of resources containing both published and unpublished research. The EAC search retrieved 2,061 records, 1,274 remained after deduplication and were assessed for relevance. A full critique of

the company search strategy and a description of the EAC search methods and results is provided in Appendix A.

3.2 Critique of the company's study selection

The company identified 56 studies from their literature search of which 23 were identified for further evaluation through full retrieval of the papers.

The company sifted the studies identified by the literature search according to the criteria reported in Table B1 of the submission. The company does not report whether single or double independent study selection was undertaken. Two sets of criteria are presented, 1 for identifying single-arm studies and 1 for comparative studies.

The eligibility criteria reported by the company were not in alignment with the scope.

- Population: The company limited the population to adults and ureteric obstruction due to both benign and malignant reasons. Studies assessing populations of either benign causes or malignant causes were excluded;

- Comparators: The company limited eligible comparators to double-J stents and did not look for evidence in relation to the other comparators listed in the scope; nephrostomy, reconstructive surgery and other metallic and alloy stents;

- Outcomes: The outcomes listed by the company in Table B1 of the submission were limited to relief of back pressure, and/or improvement of QOL which does not reflect the scope. However, the company does not seem to have applied this criteria and has extracted data on other outcomes reported in the studies too;

- Publication type: The company noted conference abstracts would only be included in "*exceptional circumstances*". No information was provided on the additional criteria applied to abstracts. The EAC requested clarification from the company who reported that as only 1 abstract met its selection criteria it was included (correspondence log);

- Additional limits: The company limited eligible studies to English language and studies published from 1992 onwards. It stated studies with less than 10 patients would not be eligible but in the eligibility tables state studies with less than 20 patients would not be eligible. Based on the excluded studies list the EAC understands excluding studies of less

than 20 patients to be the criteria used. No justification was provided for these limits.

After sifting of the full papers, the company identified a total of 6 separate publications (describing 5 studies (Agrawal et al., 2009, NCT00166361, 2014, Kulkarni and Bellamy, 2001, Kulkarni and Bellamy, 1999, Papatsoris et al., 2007, Patel et al., 2011)) for inclusion in the submission. One study that was reported as a clinical trial record only was included (NCT00166361, 2014).

On request, the company provided the included and excluded studies list to the EAC (correspondence log). Based on this list 18 studies were excluded at full text review rather than 17 as listed in the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flow diagram. Ten studies were excluded because they were abstracts only and the company could not obtain the full paper (Bach et al., 2013, Bach et al., 2011, Franke et al., 2010, Kim et al., 2014, Klarskov et al., 2005, Lee et al., 2005, Liatsikos et al., 2005, Moraitis et al., 2010, Papadopoulos et al., 2010, Papatsoris and Buchholz, 2010). Of these, 4 appear to be conference abstracts (Bach et al., 2011, Franke et al., 2010, Lee et al., 2005, Moraitis et al., 2010) but the remaining 6 full text articles are available. Two studies with less than 20 patients (Arya et al., 2001, Azizi et al., 2012) were excluded, 1 of which is published in French (Azizi et al., 2012). Three studies were excluded because they assessed malignant populations only (Allen et al., 2010, Sountoulides et al., 2010, Zaman et al., 2011), of which 2 are review articles (Allen et al., 2010, Sountoulides et al., 2010), 2 studies were published in German (Schenck et al., 2010, Schenck et al., 2008) and 1 further study including retroperitoneal fibrosis cases only was excluded (Bourdoumis et al., 2014).

A further discrepancy was noted in relation to 1 of the company's included studies. Based on the included and excluded studies list, Maan 2010 (Maan et al., 2010) was identified by the search however, based on the information provided within the submission, it appears that Patel 2011 (Patel et al., 2011) was retrieved and reviewed instead of the Maan 2010 paper. Both papers report on the same study. Patel 2011 (Patel et al., 2011) reports data for the subgroup of patients that received Memokath-051 whilst Maan 2010 (Maan et al., 2010) also reported data for the double-J comparator arm.

The company used the PRISMA methodology to report on the studies identified and presented a separate diagram for the review of single-arm studies and comparative studies (Section 7.2.2, Submission).

The company's selection criteria were not deemed appropriate to identify all the studies that are relevant to the scope, therefore the EAC have revised the selection criteria in line with the scope. The updated criteria are shown in

Table ***3.1***. Due to the number of studies identified by the EAC selection criteria, an additional limit was imposed to exclude abstracts reporting single-arm studies. Only abstracts reporting comparative studies were eligible for inclusion due to the paucity of published comparative evidence.

Table 3.1: Updated EAC selection criteria

	Inclusion criteria	**Exclusion criteria**
Population	Patients with ureteric obstruction as a result of malignant or benign strictures	Patients with ureteric obstruction due to any other reason
Intervention	Memokath-051	Other Memokath devices (028, 044 and 045)
Comparators	• Double-J stents; • Nephrostomy; • Reconstructive surgery; • Metallic and alloy stents (including nitinol stents); • No comparator.	Any other device

Outcomes	• Clinical success rate (e.g. improved renal function, no obstruction);
	• Quality of life including:
	  ○ Tolerability and comfort;
	  ○ Pain scores including from subsequent bladder irritation.
	• Frequency of follow-up visits;
	• Length of time stent remains in situ;
	• Frequency of stent removal/reversal;
	• Number and rate of replacement stents;
	• Number and rate of repeat procedures requiring anaesthesia and surgery;
	• Theatre time and hospital stay;
	• Device-related adverse events including procedure related complications.	

Study design	Randomised controlled trials (RCTs) of any size and duration Prospective and retrospective, non-randomised comparative and uncontrolled studies will be eligible for inclusion if they report relevant clinical effectiveness or safety data for Memokath-051 and a relevant comparator Non comparative or single-arm studies will be eligible if they provide relevant data for Memokath-051	News articles, letters, editorial, commentaries and single case reports
Limits	No date limit English language only *Abstracts reporting comparative studies only**	Studies published in languages other than English *Abstracts reporting single-arm studies**

* *Additional criteria applied due to high number of eligible studies*

3.3 Included and excluded studies

The EAC identified 16 studies (reported in 22 records) as eligible for inclusion in the review (see PRIMSA diagram in Appendix B and excluded studies table in Appendix C). Of these:

- 12 studies are reported as full text publications: 2 comparative studies (Kim et al., 2014, Maan et al., 2010) and 10 single-arm studies (Agrawal et al., 2009, Arya et al., 2001, Bach et al., 2013, Bourdoumis et al., 2014, Boyvat et al., 2005, Klarskov et al., 2005, Kulkarni and Bellamy, 2001, Papadopoulos et al., 2010, Papatsoris and Buchholz, 2010, Zaman et al., 2011);

- 3 comparative studies were identified as conference abstracts only (Akbarov et al., 2017, Bolton et al., 2015, Nam et al., 2015);

- 1 comparative study was identified as a clinical trial record and an abstract only (NCT00166361, 2014, Granberg et al., 2010). Where outcomes were reported in both sources, those from the clinical trial record were used given that more information was typically provided and the record was quality assessed.

All of the studies included by the company were identified and included in the EAC review with the exception of 1, Papatsoris (2007) (Papatsoris et al., 2007). This record was not identified in any of the databases searched and is not listed on the journal website so it is unclear how this was identified by the company. However, an updated version of this study, Papatsoris (2010) (Papatsoris and Buchholz, 2010), was identified from the search and included in the EAC review.

Eight studies that were excluded by the company were subsequently included in the EAC review (Arya et al., 2001, Bach et al., 2013, Bourdoumis et al., 2013, Kim et al., 2014, Klarskov et al., 2005, Papadopoulos et al., 2010, Papatsoris and Buchholz, 2010, Zaman et al., 2011) and a further 4 studies that do not appear to have been identified in the company submission have been included in the EAC review (Akbarov et al., 2017, Bolton et al., 2015, Boyvat et al., 2005, Nam et al., 2015). Reasons for any disagreements in the company and EAC selections are presented in Table 3.2.

Table 3.2: Comparison of the studies (and associated publications) included in the company review and the EAC review

Study	Associated publications	Included in company review?	Included in EAC review?	Reason for disagreement
Agrawal 2009 (Agrawal et al., 2009)	**NA**	**Y**	**Y**	Not applicable- this study was identified in both reviews
Akbarov 2017 (Akbarov et al., 2017)	**NA**	**N**	**Y**	This record does not seem to have been identified by the company
Arya 2001 (Arya et al., 2001)	**NA**	**N**	**Y**	Less than 20 patients therefore did not meet the company's eligibility criteria but did meet the revised EAC criteria
Bach 2013 (Bach et al., 2013)	**NA**	**N**	**Y**	Excluded by the company because they could not obtain the full paper
Bolton 2015 (Bolton et al., 2015)	**NA**	**N**	**Y**	This record does not seem to have been identified by the company
Bourdoumis 2014 (Bourdoumis et al., 2014)	Bourdoumis 2013 (Bourdoumis et al., 2013)	**N**	**Y**	Excluded by the company because it includes retroperitoneal fibrosis patients. However all patients are have benign or malignant ureteral strictures so the EAC have included this study
Boyvat 2005 (Boyvat et al., 2005)	**NA**	**N**	**Y**	This record does not seem to have been identified by the company
Kim 2014 (Kim et al., 2014)	Kim 2013 (Kim et al., 2013)	**N**	**Y**	Excluded by the company because they could not obtain the full paper
Klarskov 2005 (Klarskov et al., 2005)	**NA**	**N**	**Y**	Excluded by the company because they could not obtain the full paper
Kulkarni 2001 (Kulkarni and Bellamy, 2001)	Kulkarni 1999 (Kulkarni and Bellamy, 1999)	**Y**	**Y**	Not applicable- this study was identified in both reviews
Maan 2010 (Maan et al., 2010)	Patel 2011 (Patel et al., 2011)	**Y**	**Y**	Based on the included and excluded studies list shared by the company, this record appears to have been identified by the company searches but excluded at first sift; however, the associated Patel 2011 paper was retrieved and reviewed Maan 2010 has been used as the primary publication in the EAC review
Nam 2015 (Nam et al., 2015)	**NA**	**N**	**Y**	This record does not seem to have been identified by the company

Study	Associated publications	Included in company review?	Included in EAC review?	Reason for disagreement
NCT00166361 (NCT00166361, 2014)	Granberg 2010 (Granberg et al., 2010)	**Y**	**Y**	The clinical trial record was identified by the company. An additional abstract for the same study was identified in the EAC review.
Papadopoulos 2010 (Papadopoulos et al., 2010)	**NA**	**N**	**Y**	Excluded by the company because they could not obtain the full paper
Papatsoris 2010 (Papatsoris and Buchholz, 2010)	Papatsoris 2007 (Papatsoris et al., 2007)	**Y**	**Y**	Papatsoris 2010: Excluded by the company because they could not obtain the full paper Papatsoris 2007: This record was not identified in any of the databases searched by the EAC and is not listed on the journal website. It is unclear how this was identified by the company. An updated version of this study (Papatsoris 2010) was identified and included in the EAC review
Zaman 2011 (Zaman et al., 2011)	**NA**	**N**	**Y**	Malignant patients only, therefore did not meet the company's eligibility criteria but did meet the revised EAC criteria

Further details of the included studies identified by the EAC are presented in Table 3.3. Studies reported as conference abstracts or clinical trial records only are highlighted in grey throughout the report. The colour coding in the table relates to whether the study matches the scope fully (green dots), partially (yellow dots) or not at all (red dots).

Table 3.3: Overview of EAC's included studies

Study name (acronym)	Design and intervention(s)	Participants and setting*	Follow-up	Outcomes	Withdrawals	Comments
Comparative studies						
Akbarov 2017 (Akbarov et al., 2017) (abstract only)	Observational study (retrospective) investigating Memokath-051 and Ileal Ureteral Replacement (IUR)	**Patients:** Patients with ureteral strictures (benign or malignant) **Memokath-051 group:** 27 renal units in 17 patients. Mean age 59 years **IUR group:** 27 patients. Mean age 55 years **Indication for stent placement:** NR **Details of stent placement:** NR **Setting**: NR, but authors based in Germany	Assessment included examination of serum creatinine, renal ultrasound, retrograde pyelography and isotopic renography Mean follow-up period was 42 months	Technical success, clinical success and complications	NA- retrospective review	Abstract only- limited information Authors conclude that IUR is preferable and describe Memokath-051 as an "alternative niche solution" Study partially matches the scope and provides limited non-UK comparative data
Bolton 2015 (Bolton et al., 2015) (abstract only)	Observational study (case series) investigating Memokath-051 and Allium stents Patients completed the ureteral stent symptom questionnaire (USSQ)	**Patients:** 30 patients with benign (n=24) and malignant (n=6) strictures **Allium group:** 9 patients **Memokath-051group:** 21 patients **Indication for stent placement:** NR **Details of stent placement**: NR **Setting**: NR, but authors based in Ireland	NA- data collected from a one-off survey	Clinical success and complications	All 30 patients that provided data were included	Abstract only- limited information Authors report that data collected on 30 patients was reported. Unclear whether this is the full sample size Study partially matches the scope and provides limited non-UK comparative data
Kim 2014 (Kim et al., 2014)	Observational study (retrospective) comparing efficacy and safety of Memokath-051 and UVENTA stents	**Patients:** 27 patients (males: 11, females: 16) between November 2011 and May 2013 **Memokath-051group:** 10 patients (males: 4, females: 6) with 14 ureter units treated. Mean age 60 (±19 standard deviation (SD)) years **Indication for stent placement:** benign: 8, (idiopathic: 4, tuberculosis: 1, retroperitoneal fibrosis: 2, benign ureteral mass: 1); malignant: 6 (43%) (stomach cancer: 2,	All patients underwent radiography of the kidneys, ureters, and bladder after the stents were placed to confirm their position All patients were scheduled for follow-up at the outpatient clinic at week 1 and at 3, 6 and 12 months after stent	Technical success, clinical success, length of time the stent remains in situ and complications	2 patients died due to their original malignancy	Authors suggest that careful patient selection and delicate insertion procedure are important to achieve better outcomes and fewer cases of stent migration with the Memokath-051 stent Study partially matches the scope and provides non-UK comparative data

Study name (acronym)	Design and intervention(s)	Participants and setting*	Follow-up	Outcomes	Withdrawals	Comments
		colorectal cancer: 2, gynecological cancer: 2) **UVENTA group:** 17 patients (males: 7, females: 10) with 17 ureter units treated. Mean age was 56 (± 15.9) years **Indication for stent placement:** benign: 8 (57%) (idiopathic: 1, tuberculosis: 1, retroperitoneal fibrosis: 1, vesicoureteral anastomosis stricture in transplanted kidney: 2); malignant: 12 (71%) (stomach cancer: 4, colorectal cancer: 3, gynecological cancer: 2, retroperitoneal cancer: 1, pancreatic cancer: 1) **Details of stent placement:** All patients were initially treated with a double-J stent. Both the Memokath-051and UVENTA stents were inserted retrograde in all patients. Stents were inserted by 2 experienced endourological surgeons at the institution **Setting**: Korea ●	insertion. Urinalysis, urine culture, serum creatinine level, IV urography, and computed tomography were performed, and, if necessary, diuretic renography was performed at follow-up examination of relevant patients **Memokath-051group:** Mean follow-up of 13.6 (±4.6) months. 1 patient died during follow-up. **UVENTA group:** Mean follow-up of 12.0 (±2.6) months. 1 patient died during follow-up No statistically significant difference between the 2 groups (p=0.244)			
Maan 2010 (Maan et al., 2010)	Observational study (questionnaire survey) comparing QoL between double-J and Memokath-051 stents using the USSQ ●	Over a 1-year period (January 2008 - 2009), a cohort of 70 consecutive patients who underwent insertion of a conventional (double-J) or metal ureteral stent (Memokath-051) for the management of a ureteral stricture were mailed the USSQ 4 weeks after stent placement **Patients:** 41 patients (males: 22, females:19) completed and returned the USSQ (response rate: 58.5%): **Double-J:** n=23 (males: 11, females: 12, mean age: 51.19 (SD: 13.67)), **Memokath-051**: n=18 (males: 11, females: 7, mean age: 59 (SD: 16.37))	NA- data collected from a one-off survey	QoL measured using the USSQ, pain, stent removal/replacement ●	NA	Study partially matches the scope and provides UK comparative data a small number of outcomes

Study name (acronym)	Design and intervention(s)	Participants and setting*	Follow-up	Outcomes	Withdrawals	Comments
		Indications for stent placement: **Memokath-051group**: malignant strictures: 9 (prostate cancer: 5, gynecological malignancy: 3, bowel malignancy:1), benign strictures: 9 (idiopathic: 4, iatrogenic from instrumentation: 2, retroperitoneal fibrosis: 3) **Double-J group:** NR **Details of stent placement:** Double-J stents were inserted retrograde **Setting**: UK ●				
Nam 2015 (Nam et al., 2015)	Observational study (case series) comparing Memokath-051 and Resonance stents ●	**Patients:** **Memokath-051**: 6 (6 ureteral units) patients, mean age: 69.8 ± 11.4 (52 - 82); **Resonance**: 14 (17 ureteral units) patients, mean age: 52.5 ± 15.6 (29 - 76) **Indications for stent placement:** NR- all malignant **Details of stent placement:** NR **Setting**: Not reported (NR) but authors based in Korea ●	**Memokath-051**: mean follow-up: 16 (range: 4 - 98) months; **Resonance**: mean follow-up: 15.7 ± 2.1 (13 - 20)	Clinical success, theatre time and QoL ●	NR	Study partially matches the scope and provides comparative data for a small number of outcomes
NCT00166361 2014 (NCT00166361, 2014) (clinical trial record)	Non-randomised, open-label, clinical study investigating Memokath-051 vs double-J ●	Adults with presence of extrinsic ureteral obstruction secondary to inoperable pelvic or abdominal malignancy or secondary to changes caused by surgery, chemotherapy, or radiation for pelvic and/or abdominal malignancies who have had >2 standard double-J stent exchanges with no prospect of being stent-free) were recruited from Feb 2004 - May 2011 **Patients:** 24 patients. **Memokath-051:** 14 patients; 5 >= 65 years; female: 11, male: 3 **Double-J:** 10 patients (retrograde placed); 10 >= 65 years; female: 7, male: 3	Monitoring continued for as long as the stent was in place Patients with retrograde placed double-J stents were followed every 3 to 4 months	Length of time stent remains in situ and complications Clinical success reported in Granberg 2010 (Granberg et al., 2010) ●	5 patients: 4 patients were screen failures and were not treated; 1 patient was treated as a compassionate use patient with a smaller Memokath-051stent	Low number of subjects in each cohort Clinical trial record only Study partially matches the scope and provides non-UK comparative data

Study name (acronym)	Design and intervention(s)	Participants and setting*	Follow-up	Outcomes	Withdrawals	Comments
		Indication for stent placement: NR **Details of stent placement:** Double-J stents were inserted retrograde **Setting**: United States ●				
Single-arm studies						
Agrawal 2009 (Agrawal et al., 2009)	Observational study (case series) investigating Memokath-051 ●	Patients who had a Memokath-051 inserted between November 1996 - November 2007 **Patients** 74 stents inserted into 55 patients (benign: 27, malignant: 28). Mean age: 60 (range: 11 - 90) **Indications for stent placement** Benign strictures: ileal conduit: 4, radiation induced: 8, iatrogenic: 5, PUJ obstruction: 2, endometriosis: 2, retroperitoneal fibrosis:2, transplant: 1, idiopathic: 1, After abdominal aortic aneurysm: 2 Malignant strictures: colorectal cancer: 10, cancer of the anal canal: 2, prostate cancer: 2, transitional cell carcinoma (TCC) bladder: 2, cervical cancer: 3, vaginal cancer: 1, vulva cancer: 1, uteral cancer: 1, breast cancer: 2, pancreatic cancer: 2, lymphoma: 2, TCC ureter: 1 Indications for metallic stenting included primary stenting for malignancy, failed conventional open and endoscopic techniques, palliation, and where significant comorbidity limited repetitive stent changes **Details of stent placement:** All stents were inserted by 1 surgeon in the UK and internationally following a standard protocol **Setting**: UK ●	Mean follow-up: 16 (range: 4 - 98) months	Clinical success, hospital stay, stent removal/replacement and complications ●	NR	Study partially matches the scope and provides single-arm data specific to UK

Study name (acronym)	Design and intervention(s)	Participants and setting*	Follow-up	Outcomes	Withdrawals	Comments
Arya 2001 (Arya et al., 2001)	Observational study (case series) investigating Memokath-051 ●	**Patients** Patients with benign lower ureteric obstruction managed using the Memokath-051 stent 13 stents placed in 11 patients (to treat 12 ureteric strictures). Mean age 58 (range: 35-85) years **Indications for stent placement:** NR **Details of stent placement** 7 stents were inserted retrograde. 6 stents were inserted antegrade **Setting**: UK ●	Before discharge and at the follow-up all patients were assessed for baseline urea, electrolytes, creatinine, urine microscopy and culture. Contrast-medium studies (nephrostogram/IVU) were undertaken immediately after insertion to confirm the stent position and ureteric patency. Other follow-up investigations included isotope renography and an abdominal X-ray at 6-monthly intervals for the first year, and then annually Mean follow-up period was 18 (1.5-33) months	Clinical success, length of time the stent remains in situ, stent removal/replacement and complications ●	NR	Study partially matches the scope and provides single-arm data specific to UK
Bach 2013 (Bach et al., 2013)	Observational study (case series) investigating Memokath-051 ●	**Patients** 8 stents in 8 male renal transplant patients. Mean age 49 (29-77) years. 1 patient presented with a previously inserted, completely encrusted metal mesh stent. The Memokath-051stent was inserted through the previous stent after it had been cleared of encrustations **Indications for stent placement:** NR **Details of stent placement:** 7 stents were inserted retrograde and 1 antegrade Memokath-051 was inserted under general anaesthesia on a day-case procedure with prophylactic gentamycin.	In addition to their regular follow-up with a nephrologist, all patients were followed up in the investigator's own specialised endourology outpatient clinic with clinical examination, serum urea, creatinine and electrolytes levels, radiography of the kidneys, ureters and bladder to confirm stent position and ultrasonography of the kidneys	Technical success, clinical success, stent removal/replacement and length of time the stent remains in situ ●	NA	Study partially matches the scope and provides single-arm data specific to UK

Study name (acronym)	Design and intervention(s)	Participants and setting*	Follow-up	Outcomes	Withdrawals	Comments
		All patients received additional oral antibiotics 1 week postoperatively **Setting**: Unclear, but appears to be UK ●	Follow-up was at 6 weeks, 3 months, and every 6 months thereafter. Mean follow-up period was 55 months			
Bourdoumis 2014 (Bourdoumis et al., 2014)	Observational study (case series) investigating Memokath-051 ●	**Patients** 14 patients (males: 6, females: 8) treated for retroperitoneal fibrosis of benign and malignant aetiologies across 23 renal units. Mean age 60.2 (±8.4 SD) years. All patients were initially treated with a double-J stent **Indication for stent placement:** benign (idiopathic restrictive filling pattern: 12 patients (85.7%)); malignant (breast carcinoma and lymphoma): 2 **Details of stent placement:** NR **Setting**: UK ●	Follow-up visits involved a brief clinical examination and symptomatic assessment, serum electrolyte, urea, and creatinine measurement and radiographic control of stent position (plain radiograph) Follow-up was at 6 weeks, 3 months, 6 months, and annually thereafter. Mean follow-up period was 22.5 (3-56) months	Clinical success, stent removal/replacement and complications ●	NA.	Study authors note possible procedural issues with stent insertion, which could lead to migration: balloon dilation of stricture to a greater extent than necessary; inappropriate stent placement in terms of length/location
Boyvat 2005	Observational study (case series) investigating Memokath-051 ●	**Patients** 4 patients (males: 3, females: 1) who underwent renal transplant and had a Memokath-051 placed in the transplant ureter due to recurrent ureteral stenosis (n=3) or complete occlusion (n=1). The interval between transplantation and stenosis ranged from 5-24 months. Average age 37 (range: 22-47) years Interval between transplantation and stenosis/obstruction: 11 months for patient 1, 18 months for patient 2, 5 months for patient 3, 24 months for patient 4 All 4 patients presented to the hospital with elevated serum creatinine and blood	Patients were followed up by ultrasonography and serum creatinine levels on the first and tenth days, then at monthly intervals for the first 3 months and every 3 months thereafter Mean follow-up period was 20 (18-21) months	Technical success, clinical success, stent removal/replacement and complications ●	NA	Authors offer explanations for both instances of complications observed, and conclude that insertion of Memokath-051 is safe and feasible in this population Study partially matches the scope and provides single-arm data non- UK

Study name (acronym)	Design and intervention(s)	Participants and setting*	Follow-up	Outcomes	Withdrawals	Comments
		area nitrogen levels. Ultrasonography (US) at their admission demonstrated hydroureteronephrosis in all 4 patients, and nephrostomy was performed in each case. Pyelography 2 days after nephrostomy catheter placement showed distal stenosis in 3 patients and obstruction in 1 patient All 4 patients underwent nephrostomy previous to stent insertion **Indication for stent placement:** NR **Details of stent placement:** All stents were inserted antegrade **Setting**: Turkey ●				
Klarskov 2005 (Klarskov et al., 2005)	Multi-centre, observational study (case series) investigating Memokath-051 ●	**Patients** 37 stents placed in 33 patients (males: 15, females: 18) with ureteral obstruction at 7 Danish centres. Median age: 57 years (range: 35 - 87). The stricture was unilateral in 29 patients and bilateral in 4. 4 patients did not have a prior double-J stent or had not undergone nephrostomy prior to inclusion **Indication for stent placement:** benign: 21, post-irradiation: 5; malignant: 7 **Details of stent placement:** 1 patient had the stent inserted via nephrostomy, and 1 had the procedure performed under spinal analgesia. The rest of the patients had the procedure performed under general anaesthesia and endoscopically **Setting**: Denmark ●	Patients were scheduled to be followed up after 1 month and thereafter every 3 months for at least 1 year Patients were assessed clinically and by means of urine and blood tests at all visits. Urography was done at Month 1, and plain X-ray and renography at months 3 and 12 or when indicated, together with clearance in a number of patients	Clinical success, stent removal/replacement and complications ●	NR	Study in Denmark
Kulkarni 2001 (Kulkarni and Bellamy, 2001)	Observational study (case series) investigating Memokath-051	**Patients:** Patients with ureteral strictures caused by malignant and benign disease. 37 stents placed in 28 patients (males: 10, females: 18). Mean age was 59	Excretory urography was performed at 6 weeks with renal function tests, and urine microscopy and culture.	Stent removal/replacement, clinical success and complications	NA	Study in UK

Study name (acronym)	Design and intervention(s)	Participants and setting*	Follow-up	Outcomes	Withdrawals	Comments
	●	(range: 29-86) years. In 17 patients a Double-J stent had been placed previously. In the remaining 11 patients there was no prior stenting **Indications for stent insertion:** Malignant total: 18; recurrent colorectal/anal cancer: 6, prostate cancer retroperitoneal spread: 1, breast cancer retroperitoneal spread: 2, bladder transitional cell cancer: 2, lymphoma: 1, vaginal cancer pelvic extension: 1, vulval cancer pelvic extension: 1, cervical cancer: 3, uterine body cancer: 1 Benign total: 10; ischemic (ureteroileal): 2, post-radiotherapy: 2, Iatrogenic: 1, benign retroperitoneal fibrosis: 1, post-transplant stricture: 1, ureteropelvic junction obstruction: 1, endometriosis: 1, idiopathic: 1 **Details of stent placement:** 27 stents were inserted retrograde, 1 antegrade, and 3 bilaterally. IV antibiotic prophylaxis was given at anaesthesia induction (120 mg gentamicin) and Norfloxacillin was given orally for 5 days thereafter. Patients were discharged the next day after x-ray of the kidneys, ureters and bladder **Setting**: UK ●	These studies were repeated at 3-month intervals thereafter. Diaminetriaminepentaacetic acid renography was done in relevant cases. Ultrasound has been used for follow-up more recently after upper tract decompression has been achieved Mean follow-up period was 19.3 (3-35) months	●		
Papadopoulos 2010 (Papadopoulos et al., 2010)	Observational study (case series) investigating Memokath-051 ●	**Patients** During a 5-year period (2003 - 2008), 19 Memokath-051 stents (15 retrograde, 4 antegrade) were placed in 13 patients Mean age: 60.7 (range 36 - 81). Male: 8 (61.5%), female: 5 (38.5%). All patients had been unsuccessfully treated previously using temporary double-J stents or dilation **Indications for stent insertion:** benign:	Follow-up defined as the period during which the stent functioned properly. Patients were reviewed in the outpatient clinic 3 months post stent insertion and then 6 monthly for 3 years and annually thereafter	Clinical success, stent removal/replacement and complications ●	3 patients (including the 2 with malignant strictures) died during follow-up	Authors conclude that Memokath-051 may represent an alternative treatment in the management of patients with ureteral strictures, but that they still carry a significant risk of complications including

Study name (acronym)	Design and intervention(s)	Participants and setting*	Follow-up	Outcomes	Withdrawals	Comments
		11, malignant: 2, no further details reported **Details of stent placement:** All patients received prophylactic antibiotics and underwent an abdominal X-ray on first postoperative day to ensure correct position **Setting**: UK ●	Mean follow-up period was 14.3 (0 - 54 months) (0 represents cases where the stent did not work postoperatively)			stent migration and encrustation Study in UK
Papatsoris 2010 (Papatsoris and Buchholz, 2010)	Observational study (case series) investigating Memokath-051 ●	**Patients:** Patients with ureteral strictures who underwent insertion of a Memokath-051 from April 2004 - March 2009 were studied. 73 patients (male: 34, female: 39) with 86 ureteral strictures (benign: 55, malignant: 31). 13 patients underwent insertion of bilateral stents. Mean age 57.5 years (range: 23 - 84) **Indications for stent placement:** Benign strictures: idiopathic: 22, iatrogenic: 10, retroperitoneal fibrosis: 14, vesicoureteral anastomosis stricture: 5, pelvic inflammatory disease: 2, pelvic endometriosis: 1, Crohn disease: 1 Malignant strictures: cervix cancer: 11, prostate cancer: 6, bowel cancer: 7, breast cancer: 2, bladder cancer: 2, gastric cancer: 2, lymphoma: 1 **Details of stent placement:** In all cases, stents were inserted retrograde. All patients received intravenous antibiotics at induction, followed by a week of oral antibiotics **Setting**: UK ●	Follow-up protocol includes clinical examination, serum urea, creatinine, electrolyte levels, radiography of the kidneys, ureters, and bladder and ultrasonography of the kidneys at 2 weeks, 3 months, and every 6 months thereafter Mean follow-up period of 17.1 months (range: 1 - 55 months)	Theatre time, hospital stay, length of time the stent remained in situ, clinical success, stent removal/replacement and complications ●	NR	Study in UK
Zaman 2011 (Zaman et al., 2011)	Observational study (case series)	**Patients:** Patients with malignant ureteric strictures with or without prior double-J stents referred to the NHS clinic over a 4 year	All patients were followed up in the clinic at 12 weeks with renal biochemistry, renal	Theatre time, clinical success, stent removal/replac	At the latest follow-up, 3 (8%) patients had died with	Authors report that they did not formally assess QOL in this study, but that patients tolerated the stents well

Study name (acronym)	Design and intervention(s)	Participants and setting*	Follow-up	Outcomes	Withdrawals	Comments
	investigating Memokath-051 ●	period. Active kidney stone formers and pregnant females were not included. 42 stents were inserted in 37 patients (males: 17, females: 20), mean age: 64 years (range: 32-83) **Indications for stent placement:** Bowel cancer: 9, cervix carcinoma: 11, uterine cancer: 3, ovarian cancer: 3, post radiation: 6, prostate cancer: 6, gastric cancer: 2, breast cancer: 1 and lymphoma:1 **Details of stent placement:** Stents inserted by 1 of 3 experienced surgeons in the same hospital Prophylactic gentamicin was given at induction unless contraindicated and patients were discharged on 3 days of oral broad spectrum antibiotics **Setting**: UK ●	ultrasonography and IVU if clinically indicated. Thereafter, follow-up was at 3 months, then 6-monthly for 1 year and then yearly with renal biochemistry and renal ultrasonography Mean follow-up period was 22 months (range 5 - 60 months) 5 (13%) patients were followed up for over 2 years, 18 (19%) patients between 1 and 2 years and 14 (38%) for less than 1 year	ement and complications ●	a functioning Memokath-051 stent in situ	with minimal or no lower urinary tract symptoms Study in UK

* Gender was not consistently reported in the studies. Where data were reported, details of gender have been included. Grey shading indicates that the paper is available as an abstract only.

Colour coding relates to whether the study matches the scope fully, partially, or not at all: ● ● ●

3.4 Overview of methodologies of all included studies

The company completed table B6 of its submission (Section 7.4, Submission) including limited information in relation to each of their included studies. The EAC has extracted additional information for these studies and for the additional studies identified in the EAC review which is summarised below and provided in detail in Table 3.3.

Comparative evidence identified by EAC

Six comparative observational studies were identified; 2 of which were published as full papers (Kim et al., 2014, Maan et al., 2010) 3 of which are only available as conference abstracts (Akbarov et al., 2017, Bolton et al., 2015, Nam et al., 2015) and 1 as a clinical trial record and abstract (NCT00166361, 2014, Granberg et al., 2010). The studies compared Memokath-051 with Ileal Ureteral Replacement (IUR) (Akbarov et al., 2017), Allium stents (Bolton et al., 2015), UVENTA stents (Kim et al., 2014), Resonance stents (Nam et al., 2015) and double-J stents (Maan et al., 2010, NCT00166361, 2014). The studies ranged in size from 9 patients (Bolton et al., 2015) to 27 patients (Akbarov et al., 2017) in each treatment arm.

Details of patient characteristics were poorly reported across the studies. Four studies (Akbarov et al., 2017, Kim et al., 2014, Maan et al., 2010, Nam et al., 2015) reported the mean age of patients which ranged from 51 (Kim et al., 2014) to 70 (Nam et al., 2015) years. A further study reported that 15 of 24 patients were over the age of 65 years (NCT00166361, 2014).

Two studies included only patients with malignant strictures (NCT00166361, 2014, Nam et al., 2015), 3 studies included patients with both benign and malignant strictures due to a wide range of causes (Bolton et al., 2015, Kim et al., 2014, Maan et al., 2010, Akbarov et al., 2017). Follow-up times varied across the studies from a mean of 12 months (Kim et al., 2014) to 42 months (Akbarov et al., 2017). The NCT00166361 trial stated that patients were monitored for as long as the stent was in place (NCT00166361, 2014).

One study reported that the stents were inserted by 2 experienced endourological surgeons at the institution (Kim et al., 2014). None of the other comparative studies identified provided information on the number and level of experience of the clinician(s) inserting the stent. Two studies report some details of whether stents were inserted antegrade or retrograde. One study specified that double-J stents were retrograde placed but this information was not provided for the Memokath-051 stents (NCT00166361, 2014) and another specified that both Memokath-051 and UVENTA stents were inserted retrograde (Kim et al., 2014).

In 3 studies patients completed the USSQ to compare the QoL scored between Memokath-051 and double-J stents (Bolton et al., 2015), Allium stents (Bolton et al., 2015) or Resonance stents (Nam et al., 2015).

Common outcomes reported across the studies include clinical success, time stent was in situ and complications.

All of the studies except 2 (Bolton et al., 2015, Nam et al., 2015) reported on their funding status. Of these, 3 received no funding or declared no competing financial interests (Akbarov et al., 2017, Kim et al., 2014, Maan et al., 2010). The remaining study was funded by both the Mayo Clinic and PNN Medical (i.e. the company) (NCT00166361, 2014).

None of the comparative studies reported conducting sample size calculations to ensure that the study was adequately powered. There was 1 prospective study (NCT00166361, 2014) and 3 retrospective studies (Akbarov et al., 2017, Kim et al., 2014, Maan et al., 2010). Two studies did not report whether patients were recruited prospectively or retrospectively (Bolton et al., 2015, Nam et al., 2015).

Single-arm evidence

Ten single-arm studies, published as full papers, were identified in the EAC's review, and they were all observational case series studies investigating Memokath-051 (Agrawal et al., 2009, Arya et al., 2001, Bach et al., 2013, Bourdoumis et al., 2014, Boyvat et al., 2005, Klarskov et al., 2005, Kulkarni and Bellamy, 2001, Papadopoulos et al., 2010, Papatsoris and Buchholz, 2010, Zaman et al., 2011). The studies ranged in size from 4 patients (Boyvat et al., 2005) to 73 patients (Papatsoris and Buchholz, 2010). The details provided in relation to the patients, indications for stent placement and details of stent placement varied considerably across the studies.

Two of the studies included only patients that had undergone renal transplant (Bach et al., 2013, Boyvat et al., 2005). These patients are a subgroup of the eligible population defined in the scope. The sample sizes were small in both trials (n=4 (Boyvat et al., 2005) and n=8 (Bach et al., 2013)). Patients were followed up at regular intervals with a mean follow-up time of 20 (Boyvat et al., 2005) to 55 months (Bach et al., 2013). Both studies reported data in relation to technical success, clinical success and stent removal/replacement.

One study included only patients with malignant strictures (Zaman et al., 2011), 1 included patients with benign strictures only (Arya et al., 2001) while the remaining 6 studies included patients with both benign, malignant or both types of strictures due to a wide range of causes (Agrawal et al., 2009, Bourdoumis et al., 2014, Klarskov et al., 2005, Kulkarni and Bellamy, 2001, Papadopoulos et al., 2010, Papatsoris and Buchholz, 2010). Patients were followed up for a mean of 14.3 months (Papadopoulos et al., 2010) to 22.5 months (Bourdoumis et al., 2014) across the trials.

Four of the studies reported on their funding status and stated that they received no funding or declared no competing financial interests (Agrawal et al., 2009, Bach et al., 2013, Bourdoumis et al., 2014, Papatsoris and Buchholz, 2010). The remaining 6 studies did not report any information on their funding status (Arya et al., 2001, Boyvat et al., 2005, Klarskov et al., 2005, Kulkarni and Bellamy, 2001, Papadopoulos et al., 2010, Zaman et al., 2011).

3.5 Overview and critique of the company's critical appraisal

3.5.1 Critique of the company's critical appraisal

The company critically appraised its included studies using Global Harmonization Task Force (GHTF) guideline for critical appraisal which rates the appropriateness of the device, application, patient group and data collection study design on a 3 point scale and required yes/no responses to the appropriateness of outcome measures, follow-up and whether statistical and clinical significance were reached.

The company did not provide justifications for the ratings given. Based on the company's ratings (Table B8.3, Submission), all of the studies met the majority of the criteria adequately. However, the company notes the descriptive nature (Kulkarni and Bellamy, 2001, Papatsoris et al., 2007) and lack of comparators (Agrawal et al., 2009, Kulkarni and Bellamy, 2001, Papatsoris et al., 2007) in some studies as limitations.

3.5.2 EAC's critical appraisal

The EAC undertook its own critical appraisal for all studies identified based on criteria proposed by the Centre for Reviews and Dissemination (Centre for Reviews and Dissemination, 2009). Critical appraisal was not carried out for the studies published as conference abstracts or clinical trial records due to the limited information available. A summary of the critical appraisal focusing on the internal and external validity of studies in relation to the decision problem is presented in Table 3.4. The fully completed checklist is provided in Appendix D.

Table 3.4: Summary of critical appraisal in relation to decision problem

Study	Internal validity[1]	External validity[2]
Comparative studies		
Maan 2010 (Maan et al., 2010)	**Acceptable** Cohort recruitment was acceptable. A validated primary outcome measure was used (USSQ). Unclear/limited reporting about measuring the exposure, identification of confounding factors and precision of results. Patient follow-up was not applicable for critical appraisal due to the design of the study	**Acceptable** Patients and procedure in line with scope. Relevant for some outcomes reported in the scope; including, QoL, stent removal/replacement and complications/AEs. Eligible comparator (double-J). UK setting
Kim 2014 (Kim et al., 2014).	**Acceptable** Cohort recruitment, measurement of exposure and patient follow-up were acceptable. Unclear/limited reporting about outcome measurement, confounding factors, and precision of results. Highest quality study based on critical appraisal results	**Acceptable** Patients and procedure in line with scope. Relevant for some outcomes reported in the scope; including, clinical and technical success, length of time stent remains in situ and complications/AEs. Eligible comparator (UVENTA). Non-UK setting (Korea)
NCT00166361 2014 (NCT00166361, 2014)	**Low** All patients followed up. Unclear/limited reporting about cohort recruitment, exposure and outcome measurement, identification of confounding factors and precision of results	**Acceptable** Patients and procedure in-line with scope. Relevant for some outcomes reported in the scope; including, length of time stent remains in situ and complications/AEs. Eligible comparator (double-J). UK setting
Single-arm studies		
Agrawal 2009 (Agrawal et al., 2009)	**Low** Unclear/limited reporting about patient recruitment, exposure and outcome measurement, identification of confounding factors, patient follow-up and precision of results	**Acceptable** Patients and procedure in line with scope. Relevant for some outcomes reported in the scope; including, clinical success, hospital stay, stent removal/replacement and complications/AEs outcomes. No comparator. UK setting
Arya 2001 (Arya et al., 2001)	**Low** Unclear/limited reporting about patient recruitment, exposure and outcome measurement, identification of confounding factors, patient follow-up and precision of results	**Acceptable** Patients and procedure in line with scope. Relevant for some outcomes reported in the scope; including, clinical success, length of time stent remains in situ, stent removal/replacement and complications/AEs. No comparator. UK setting
Bach 2013 (Bach et al., 2013)	**Low** All patients were followed up. Unclear/limited reporting about cohort recruitment, exposure and outcome measurement, confounding factors and precision of results. Stent insertion was carried out differently in some of the patients	**Not acceptable** Inconsistent population, which comprised of 8 renal transplant patients receiving varying stent insertion procedures. No comparator. UK setting
Bourdoumis 2014	**Low**	**Acceptable**

Study	Internal validity[1]	External validity[2]
(Bourdoumis et al., 2014)	All patients were followed up. Unclear/limited information reported about cohort recruitment, exposure and outcome measurement, confounding factors, and precision of results	Patients and procedure in line with scope. Relevant for some outcomes reported in the scope; including, clinical success, stent removal/replacement and complications/AEs. No comparator. UK setting
Boyvat 2005 (Boyvat et al., 2005)	**Low** All patients were followed up. Unclear/limited information reported about cohort recruitment, exposure and outcome measurement, confounding factors, and precision of results	**Not acceptable** Inconsistent population, which comprised of 4 patients who developed recurrent renal transplant ureter obstruction. Low number of patients. Non-UK setting (Turkey)
Klarskov 2005 (Klarskov et al., 2005)	**Low** Unclear/limited reporting about patient recruitment, exposure and outcome measurement, identification of confounding factors, patient follow-up and precision of results	**Acceptable** Patients in line with the scope. Relevant for some outcomes reported in the scope; including, clinical success, hospital stay, stent removal/replacement and complications/AEs outcomes in scope. No comparator. Non UK setting (Denmark)
Kulkarni 2001 (Kulkarni and Bellamy, 1999)	**Low** All patients were followed up. Unclear/limited information reported about cohort recruitment, exposure and outcome measurement, confounding factors, and precision of results	**Acceptable** Patients and procedure in line with scope. Relevant for some outcomes reported in the scope; including, clinical success, stent removal/replacement and complications/AEs outcomes in scope. No comparator. UK setting
Papadopoulos 2010 (Papadopoulos et al., 2010)	**Low** Unclear/limited reporting about patient recruitment, exposure and outcome measurement, identification of confounding factors, patient follow-up and precision of results	**Acceptable** Patients and procedure in line with scope. Relevant for some outcomes; including, clinical success, stent removal/replacement, complications/AEs outcomes in scope. No comparator. UK setting
Papatsoris 2010 (Papatsoris and Buchholz, 2010)	**Low** All patients were followed up. Unclear/limited information reported about cohort recruitment, exposure and outcome measurement, confounding factors, and precision of results. Highest number of patients investigated (73)	**Acceptable** Patients and procedure in line with scope. Relevant for some outcomes reported in the scope; including, clinical success, stent removal/replacement, theatre time, hospital stay, length of time stent remains in situ, complications/AEs outcomes in scope. No comparator. UK setting
Zaman 2010 (Zaman et al., 2011)	**Acceptable** The exposure was considered accurately measured and all patients were followed up. Limited/unclear information was reported about cohort recruitment, outcome measurements, confounding factors and precision of results	**Acceptable** Patients and procedure in line with scope. Relevant for some outcomes reported in the scope; including, clinical success, stent removal/replacement and complications/AEs outcomes in scope. No comparator. UK setting

1: Overall internal validity for each study has been assessed as 'High', 'Acceptable' or 'Low'; 2: Overall external validity for each study has been assessed as 'Acceptable' or 'Not acceptable'

Three comparative studies and 10 single-arm studies have been critically appraised by the EAC. Two comparative studies (reported across 2 abstracts (Akbarov et al., 2017, Bolton et al., 2015)) were not critically appraised as there was insufficient information reported to carry out an adequate assessment.

Two of the comparative studies received no funding or declared no competing financial interests (Kim et al., 2014, Maan et al., 2010) while the remaining study was funded by both the Mayo Clinic and PNN Medical (i.e. the company) (NCT00166361, 2014), increasing the potential for bias as the operators cannot be blinded to the procedures.

Of the single-arm studies, 4 stated that they received no funding or declared no competing financial interests (Agrawal et al., 2009, Bach et al., 2013, Bourdoumis et al., 2014, Papatsoris and Buchholz, 2010) while the remaining 6 studies did not report any information on their funding status (Arya et al., 2001, Boyvat et al., 2005, Klarskov et al., 2005, Kulkarni and Bellamy, 2001, Papadopoulos et al., 2010, Zaman et al., 2011), therefore, it is not possible to make a judgement on potential bias due to funding in these studies.

Cohort recruitment was considered acceptable in all 3 comparative studies (Kim et al., 2014, Maan et al., 2010, NCT00166361, 2014) and 7 single-arm studies. Three single-arm studies (Arya et al., 2001, Bourdoumis et al., 2014, Papadopoulos et al., 2010) reported limited information about how their cohort was recruited. In particular, it was unclear to the EAC in these studies as to whether the cohort comprised of the total number of patients receiving stents within the reported time frame, or whether patients had been specifically selected. Patient characteristics at baseline between the Memokath-051 and comparator group were considered similar in both of the comparative studies ((Maan et al., 2010), (Kim et al., 2014)) with no statistically significant differences reported. In the single-arm studies, however, limited/unclear information was reported by authors concerning the similarity of patients included in the studies. As a result, there is insufficient information available to assess heterogeneity across all of the studies in terms of the patient characteristics.

In the comparative study reported by Kim *et al.* (Kim et al., 2014), the EAC considered the exposure to be accurately measured. In this study, a full description of the insertion procedure, which was carried out for all patients by 1 of 2 experienced surgeons, was reported by the authors. In another comparative study conducted by Maan *et al.* (Maan et al., 2010), a detailed description of how Memokath-051 was inserted is provided; however, insufficient information was reported for the EAC to accurately assess whether there was any variation across patient procedures. For the third comparative study (NCT00166361, 2014), no details about the stent insertion procedure were provided in the clinical trial record.

Regarding the single-arm studies, in Bach 2013 (Bach et al., 2013) some of the patients underwent different insertion procedures and therefore did not accurately

measure the exposure. The remaining single-arm studies reported unclear/limited information about the exposure to permit judgement by the EAC.

In 1 of the comparative studies (Maan et al., 2010), the outcome was considered to be accurately measured by the EAC. In this study, the authors report the use of the validated USSQ as their primary outcome measurement to evaluate patient symptoms and impact on quality of life following stent (i.e. Memokath-051 and double-J) insertion. In the second comparative study (Kim et al., 2014), the outcomes, measurement methods and follow-up intervals are well defined. However, the authors do not report whether the outcome assessors were blinded to the device. In the final comparative study (NCT00166361, 2014), the outcomes were well defined, but there was insufficient detail reported in the clinical trial record for the EAC to permit an overall judgement. Across the single-arm studies, information relating to the definition of outcomes, measurement methods, follow-up intervals or blinding of outcome assessors was deemed too limited / unclear to inform an assessment by the EAC.

Potential confounding factors and their possible impact on outcomes were not well reported in any study. In 2 of the comparative studies (Kim et al., 2014, Maan et al., 2010), the authors report that patients were well matched for age and gender, but no other confounding variables were identified and/or taken into account. In the third comparative study (NCT00166361, 2014), and amongst the single-arm studies, insufficient information about any confounding factors was reported for the EAC to permit judgement.

Regarding the comparative studies, Maan 2010 (Maan et al., 2010) was not appraised in relation to patient follow-up as the study design did not involve following up patients. In the second comparative study patients were followed-up completely and the 2 patients who were lost to follow-up (death) are clearly reported by the authors (Kim et al., 2014). In the third comparative study, the clinical trial record indicates that all patients were followed until the stent needed to be removed due to failure (NCT00166361, 2014). In 7 of the 10 single-arm studies, patient follow-up was considered satisfactory by the EAC. Amongst these studies, and in the context of their aims and objectives, the follow-up period was deemed appropriate and well defined. Where losses to follow-up occurred (such as the patient deaths (Kim et al., 2014, Kulkarni and Bellamy, 2001, Papadopoulos et al., 2010, Zaman et al., 2011)), these were clearly stated by the authors.

The presentation and precision of the results was limited across all studies. In 1 of the comparative studies (Maan et al., 2010), the scores for each domain of the USSQ were presented and compared for both groups (i.e. Memokath-051 and double-J). In this study, the authors present median values and p-values; however, no standard deviations or confidence intervals are reported. Similarly, in the second comparative study (Kim et al., 2014), the authors report p-values and standard deviations as part of their results, but do not present confidence intervals. Statistical analysis was also

lacking across the single-arm studies, where the majority of authors focused on providing a narrative synthesis and simple descriptive statistics.

All 3 comparative studies provided acceptable levels of external validity are therefore considered applicable to the scope and acceptable in terms of generalisability (see Table 3.4). In Maan 2010 (Maan et al., 2010), the patients and procedure are in line with the scope and data for a number of relevant outcomes have been reported. Similarly; in Kim 2014 (Kim et al., 2014) and NCT00166361 2015, the patients, procedure and outcomes presented in the study are also relevant. However, it is noted that the comparative study reported by Kim 2014 (Kim et al., 2014) was conducted in a non-UK setting (Korea), which may potentially limit its overall usefulness.

The single-arm studies generally had low levels of internal validity; however, their external validity was enhanced by the fact they were observational studies and therefore may reflect clinical practice better than a strictly protocol driven trial.

Two studies (Bach et al., 2013), (Boyvat et al., 2005) were considered to have limited value in relation to the decision problem and neither study provided acceptable levels of internal or external validity. In Bach 2013 (Bach et al., 2013), the study investigated a small and inconsistent selection of renal transplant patients who received varying stent insertion procedures. In Boyvat 2005 (Boyvat et al., 2005), a similarly small (only 4 patients) and inconsistent population is reported, and the study was also conducted in a non-UK setting. Due to these factors, these studies will be excluded from further discussion.

3.6 Results

3.6.1 Critique of company's report of results

The company has partially completed table B9 for each study along with screenshots of results tables from the publications. The company presented data in relation to all of the outcomes reported in the studies rather than those relevant to the decision problem. The company did not attempt to provide any description or summary of the outcomes reported across the trials and did not identify any data in relation to the subgroups of interest to the scope.

3.6.2 EAC's report of results

The results of the studies included by the EAC and deemed to have acceptable levels of external validity are summarised in the following sections. Throughout this section, studies reported as conference abstracts or clinical trial records only are shaded in grey in the tables.

Technical success

Technical success, i.e. successful stenting of the ureteral stricture was not reported consistently across the studies. Two studies, 1 comparative and 1 single-arm studies, noted that stent insertion was technically successful in all cases (Kim et al., 2014, Zaman et al., 2011). Both studies were deemed to be well conducted with acceptable generalisability. The remaining studies did not explicitly report on this outcome.

Table 3.5: Results of the EAC's included studies: Technical success

Study	Patients	Mean follow- up (months)	Technical success
Kim 2014 (Kim et al., 2014)	**Memokath-051:** 10 patients with 14 ureter units treated **UVENTA:** 17 patients	**Memokath-051:** 13.6 (±4.6) **UVENTA group:** 12.0 (±2.6) months	Stent insertion technically successful in all cases
Zaman 2011 (Zaman et al., 2011)	42 stents were inserted in 37 patients	22 (range: 5 - 60)	Insertion was successful in all cases without technical difficulty

Clinical success

Clinical success was reported in 13 of the 16 studies (Agrawal et al., 2009, Akbarov et al., 2017, Arya et al., 2001, Bolton et al., 2015, Bourdoumis et al., 2014, Kim et al., 2014, Klarskov et al., 2005, Kulkarni and Bellamy, 2001, Papadopoulos et al., 2010, Papatsoris and Buchholz, 2010, Zaman et al., 2011, Nam et al., 2015), data for clinical success for the NCT00166361 study was reported in the associated abstract (Granberg et al., 2010). Clinical success rates ranged from 43% (Kim et al., 2014) to 100% (Granberg et al., 2010, Zaman et al., 2011) in the Memokath-051 treatment arms.

In the comparative studies, Memokath-051 had a lower clinical success rate compared to Allium stents (81% vs 100%) (Bolton et al., 2015), UVENTA (43% vs 82%) (Kim et al., 2014) and IUR (35% vs 89%) (Akbarov et al., 2017) but was found to be comparable to double-J stents (100% success rate in both arms) (Granberg et al., 2010) and Resonance stents (82% and 86% for Memokath-051 and Resonance stents respectively) (Nam et al., 2015).

What constitutes clinical success and the approach to measuring and reporting it has not been consistently defined in the studies, therefore, it is difficult to determine the validity of this outcome and its relevance to decision making. Definitions refer to 1 or more of the following: stent patency or functioning, successful tract decompression, improved renal function and lack of obstruction. Unsuccessful procedures seem to be those requiring stent removal or replacement, but these criteria are not consistently reported so it is not possible to make a judgement on how similar or comparable this outcome is across the studies. In particular, it is not clear how long a stent must remain

functioning and in place before it is classified as a clinical success in each trial. The frequency and duration of follow-up varies across the studies so the point at which clinical success is being measured varies. For these reasons we would could not pool the data statistically. A summary of the evidence for this outcome is presented below in Table 3.6.

Table 3.6: Results of the EAC's included studies: Clinical success

Study	Follow-up	Patients	As described in publication	Proportion
Comparative studies				
Akbarov 2017 (Akbarov et al., 2017)	42 (range: NR)	**Memokath-051:** 27 renal units in 17 patients **IUR group:** 27 patients	Successful upper tract decompression	**Memokath-051:** 35% **IUR**: 89%
Bolton 2015 (Bolton et al., 2015)	NR.	**Allium:** 9 **Memokath-051**: 21	Primary patency rate	**Memokath-051**: 81% **Allium**: 100%
NCT00166361 2014 Data from Granberg 2010 (Granberg et al., 2010)	NR.	**Memokath-051:** 18 stents in 15 patients **Double-J group:** 10 patients	Upper tract decompression	**Memokath-051:** 100% **Double-J**: 100%
Kim 2014 (Kim et al., 2014)	**Memokath-051:** 13.6 (±4.6) **UVENTA group:** 12.0 (±2.6) months	**Memokath-051:** 10 patients with 14 ureter units treated. **UVENTA:** 17 patients	Success was defined as improved renal function and no obstruction	**Memokath-051**: 43% Benign: 50% Malignant: 33% **UVENTA**: 82% (p=0.31) Benign: 60% (p=1.0) Malignant: 92% (p=0.022) **Memokath-051 vs UVENTA** Overall: p=0.31 Benign: p=1.00 Malignant: p=0.022
Nam 2015 (Nam et al., 2015)	**Memokath-051:** 16 (range: 4 - 98); **Resonance** 15.7 (range: 13 - 20)	**Memokath-051:** 6 patients (6 ureteral units) patients **Resonance:** 14 patients (17 ureteral units)	Inverse of 'early failure rates''	**Memokath-051:** 82% **Resonance:** 86%
Single-arm studies				
Agrawal 2009 (Agrawal et al., 2009)	16 (range: 4 - 98)	74 stents inserted into 55 patients	Normal or improved functional drainage	95%
Arya 2001 (Arya et al., 2001)	18 (range: 1.5-33)	13 stents placed in 11 patients	Ureteric obstruction relieved	64%
Bourdoumis 2014	22.5 (range: 3-56)	23 renal units stented in 14 patients	Improved renal function and lack of	79%

Study	Follow-up	Patients	As described in publication	Proportion
(Bourdoumis et al., 2014)			complications after placement	
Klarskov 2005 (Klarskov et al., 2005)	Median: 14 (range: 3-30)	37 stents placed in 33 patients	Functional stents at death or last follow-up with no or minimal complications	47%
Kulkarni 2001 (Kulkarni and Bellamy, 2001)	19.3 (range: 3-35)	37 stents placed in 28 patients	Functional stents at follow-up	75%
Papadopoulos 2010 (Papadopoulos et al., 2010)	14.3 (range: 0 - 54)	13 patients	Satisfactory result (symptom-free patients and non-obstructive MAG-3 renogram curves) after initial insertion	46% after initial insertion, 77% after final insertion
Papatsoris 2010 (Papatsoris and Buchholz, 2010)	17.1 (range: 1 - 55)	86 ureteral strictures in 73 patients	Overall success rate	93%
Zaman 2011 (Zaman et al., 2011)	22 (range: 5 - 60)	42 stents were inserted in 37 patients	Improved or maintained renal function	100%

P-values and variance estimated have been extracted where reported

Details of stents removal, replacement, length of time in situ and rates of migration and encrustation

Limited data were reported in the comparative trials in relation to the length of time the stent remained in situ. In the 2 studies reporting these data, Memokath-051 remained in place longer than UVENTA (14 months vs 12 months) (Kim et al., 2014) and considerably longer than double-J stents (17 months vs 4 months) (NCT00166361, 2014). One study was published in full (Kim et al., 2014) while the other was only reported as a clinical trial record, however, both studies had an acceptable level of external validity and findings are likely to be generalisable. In the 1 single-arm trial reporting this data (Papatsoris and Buchholz, 2010), Memokath-051 remained in situ for a mean of 11 months (Papatsoris and Buchholz, 2010).

The most common reasons for stent removal and/or replacement were due to migration or encrustation. In the comparative trials, rates of stent migration were higher in the Memokath-051 arms compared to IUR (19% vs 0%) (Akbarov et al., 2017), UVENTA (43% vs 6%) (Kim et al., 2014) and double-J (11% vs 0%) (Maan et al., 2010). No data were available for Allium or Resonance. In the single-arm trials, rates of stent migration were between 8% (Arya et al., 2001) and 46% (Papadopoulos et al., 2010).

One single-arm study (Agrawal et al., 2009) reported migration rates by different versions of Memokath-051 (normal- 9.5 Fr outer diameter, wide- 10.5 Fr outer

diameter and dual expansion). Rates of migration were 10%, 21% and 14% for normal, wide and dual expansion Memokath-051 stents respectively.

Comparative data for the rates of encrustation were not available for IUR, UVENTA or Resonance. Memokath-051 had higher rates of encrustation compared to Allium (19% vs 0%) (Bolton et al., 2015) and double-J stents in 1 study (29% vs 0) (NCT00166361, 2014). In the single-arm trials, rates of encrustation ranged from 0% (Zaman et al., 2011) to 23% (Arya et al., 2001). In Zaman 2011 (Zaman et al., 2011) authors report that known stone formers were excluded from their trial which could account for why none of their patients experienced encrustation.

There was no comparative evidence in relation to the rate of stent removal and replacement. In the single-arm studies, it appears to be that the majority of stents were removed (but not replaced) due to encrustation (Arya et al., 2001, Bourdoumis et al., 2014, Papatsoris and Buchholz, 2010), resolution of stricture (Maan et al., 2010) or progressive disease (Papatsoris and Buchholz, 2010) and it is unclear whether or not they were replaced by another stent. In comparison, stents replacement was usually due to migration (Agrawal et al., 2009, Arya et al., 2001, Bourdoumis et al., 2014, Kulkarni and Bellamy, 2001, Maan et al., 2010, Papadopoulos et al., 2010, Zaman et al., 2011), suboptimal positioning (Kulkarni and Bellamy, 2001) and in a few cases encrustation (Agrawal et al., 2009) or progressive disease (Agrawal et al., 2009, Kulkarni and Bellamy, 2001). Papatsoris 2010 reported that 15 stents were replaced after a mean indwelling time of 18 months but the reason for this is unclear (Papatsoris and Buchholz, 2010).

Table 3.7: Results of the EAC's included studies: Stent removal, replacement, length of time in situ and rates of migration and encrustation

Study	Patients	Mean follow- up (months)	Length of time in situ (months)	Stents removed*	Stent replacement*	Stent migration*	Encrustation*
Comparative studies							
Akbarov 2017 (Akbarov et al., 2017)	**Memokath-051:** 27 renal units in 17 patients **IUR group:** 27 patients	42 (range: NR)	NR	NR	NR	**Memokath-051:** 5 (19%). **IUR:** 0 as not applicable	NR
Bolton 2015 (Bolton et al., 2015)	**Allium:** 9 **Memokath-051**: 21	NR	NR	NR	NR	**Allium:** 0 **Memokath-051**: 4 patients (19%).	NR
Kim 2014 (Kim et al., 2014).	**Memokath-051:** 10 patients with 14 ureter units treated. **UVENTA:** 17 patients	**Memokath-051:** 13.6 (±4.6) **UVENTA group:** 12.0 (±2.6) months	**Memokath-051:** 13.6 (7-21) **UVENTA**: 12 (9-16) (p=0.244)	**NR**	NR- authors report that 6 migrating stents were replaced by Memokath-051 or UVENTA but treatment groups unclear	**Memokath-051**: 6 stents (43%); **UVENTA**: 1 stent (6%), p=0.004	NR
Nam 2015 (Nam et al., 2015)	**Memokath-051:** 6 patients (6 ureteral units) patients **Resonance:** 14 patients (17 ureteral units)	**Memokath-051:** 16 (range: 4 - 98); **Resonance** 15.7 (range: 13 - 20)	NR	NR	NR	NR	NR
Maan 2010 (Maan et al., 2010)	**Double-J:** 23 patients **Memokath-051**: 18 patients	NA- one-off survey.	NR	**Memokath-051:** 2 due to resolution of stricture (11%)	**Memokath-051:** 17% 1 stent replaced with a longer stent 2 stents due to migration	Memokath-051: 2 (11%) Double-J: 0	NR

Study	Patients	Mean follow- up (months)	Length of time in situ (months)	Stents removed*	Stent replacement*	Stent migration*	Encrustation*
NCT00166361 2014 (NCT00166361, 2014)	**Memokath-051:** 14 patients **Double-J:** 10 patients	NR	**Memokath-051:** 17 (1 - 59) **Double-J**: 3.97 (2.56 - 5.36)	NR	NR	**Memokath-051:** 1 (7%) (2 events), **Double-J:** 0 (0%)	**Memokath-051:** 4 (29%) **Double-J:** 0 (0%);
Single-arm studies							
Agrawal 2009 (Agrawal et al., 2009)	74 stents inserted into 55 patients	16 (range: 4 - 98)	NR	NR	14 (19%) replaced due to: -migration: 8, - encrustation: 2, - stricture progression: 3, - incorrect length: 1	13 (18%) Benign: 7 (26%) Malignant: 6 (21%) Version of Memokath-051 Normal: 2 (10%) Wide: 10 (21%) Dual expansion: 1 (14%)	2 (3%)
Arya 2001 (Arya et al., 2001)	13 stents placed in 11 patients	18 (range: 1.5-33)	NR	3 stents due to encrustation (23%)	1 stent due to migration (8%)	1 (8%)	3 (23%)
Bourdoumis 2014 (Bourdoumis et al., 2014)	23 renal units stented in 14 patients	22.5 (range: 3-56)	NR	1 stent due to encrustation (4%)	2 stents due to migration (9%)	2 (9%)	1 (4%)
Klarskov 2005 (Klarskov et al., 2005)	37 stents placed in 33 patients	Median: 14 (range: 3-30)	NR	21 out of the original 37 stents (57%) 4 of the 7 replacement stents (57%)	NR	10 (27%)	5 (14%)
Kulkarni 2001 (Kulkarni and Bellamy, 2001)	37 stents placed in 28 patients	19.3 (range: 3-35)	NR	1 stent due to demand by a patient with a psychiatric problem (3%)	6 overall (16%) -2 due to sub-optimal positioning -3 due to migration	4 (11%)	NR

Study	Patients	Mean follow- up (months)	Length of time in situ (months)	Stents removed*	Stent replacement*	Stent migration*	Encrustation*
					-1 following progression of underlying malignancy		
Papadopoulos 2010 (Papadopoulos et al., 2010)	13 patients	14.3 (range: 0 - 54)	NR	3 stents migrated and were not replaced (23%)	3 stents due to migration (23%)	6 (46%)	1 (8%)
Papatsoris 2010 (Papatsoris and Buchholz, 2010)	86 ureteral strictures in 73 patients	17.1 (range: 1 - 55)	11.2 months (range: 1 - 39 months)	6 stents overall (7%) 4 due to encrustation 2 due to progressive malignant obstruction- these stents replaced with double-J or reconstructive surgery	15 stents were exchanged after a mean indwelling time of 18 months. (17%)	15 (17%)	4 (5%)
Zaman 2011 (Zaman et al., 2011)	42 stents were inserted in 37 patients	22 (range: 5 - 60)	NR	NR	5 stents due to migration (12%)	5 (12%)	0 (stone formers were excluded)

* Percentages have been calculated with the number of stents rather than patients as the denominator to account for the fact some patients may have had more than 1 stent.

P-values and variance estimated have been extracted where reported

Operative time and hospital stay

The mean operative time was reported in 1 comparative abstract and 2 single-arm studies (Nam et al., 2015, Papatsoris and Buchholz, 2010, Zaman et al., 2011). The Memokath-051 procedure took significantly longer than for Resonance stents (118 minutes vs 44 minutes, p=0.006) (Nam et al., 2015). Nam 2015 was reported as a conference abstract only so it was not possible to assess the external validity of this study based on such limited information (Nam et al., 2015).

Data were consistent in the 2 single-arm studies with a mean operative time of 23 (Papatsoris and Buchholz, 2010) to 26 (Zaman et al., 2011) minutes. External validity was deemed to be acceptable the two single-arm trials. We note that the Nam 2015 study was carried out in Korea while the 2 single-arm studies were carried out in the UK so the differences in operative time may be indicative of differences in the procedures or differences in the definition of operative time in these countries.

Mean hospital stay was also reported in 2 single-arm studies with a mean stay of 1.43 days (Agrawal et al., 2009) to 1.5 days (Papatsoris and Buchholz, 2010).

Table 3.8: Results of the EAC's included studies: Operative time and hospital stay

Study	Patients	Operative time	Hospital stay
Nam 2015 (Nam et al., 2015)	**Memokath-051:** 6 patients (6 ureteral units) patients **Resonance:** 14 patients (17 ureteral units)	**Memokath-051:** 117.7 ± 99.1 minutes; **Resonance:** 43.6 ± 14.1 minutes (p=0.006)	NR
Agrawal 2009 (Agrawal et al., 2009)	74 stents inserted into 55 patients	NR	1.43 (0 - 7) days
Papatsoris 2010 (Papatsoris and Buchholz, 2010)	86 ureteral strictures in 73 patients	23 mins (range: 17 - 52 mins)	1.5 days (range: 1 - 5 days)
Zaman 2011 (Zaman et al., 2011)	42 stents were inserted in 37 patients	26 mins (range: 20 - 34 mins)	NR

P-values and variance estimated have been extracted where reported

Quality of life

Three comparative studies reported results of the USSQ. Memokath-051 had favourable results compared to double-J stents in relation to pain, urinary frequency, symptom bother and living with current symptoms (Maan et al., 2010). Actual outcome data were not reported in the other 2 studies but authors did report that similar results were found between Memokath-051 and Resonance stents. There was insufficient comparative data to inform a comparison with Allium stents.

Table 3.9: Results of the EAC's included studies: Quality of life

Study	Comparator	Patients	Mean follow- up (months)	Quality of life
Bolton 2015 (Bolton et al., 2015)	ALLIUM	**Allium:** 9 **Memokath-051**: 21	NA- one-off survey	Results from the USSQ showed that patients noted mild flank pain following stent insertion and self-limiting hematuria
Maan 2010 (Maan et al., 2010)	Double-J	**Double-J:** 23 patients **Memokath-051**: 18 patients	NA- one-off survey	Patients that responded 'yes' to pain: **Memokath-051:** 7 (39%) **Double-J:** 18 (78%), p=0.009 Urine frequency every 2 hours: **Memokath-051:** 70%, **Double-J:** 47% Extremely bothered by urinary symptoms: **Memokath-051**: 5.6%, **Double-J:** 31.8% Had a negative view toward living with their current urinary symptoms: **Memokath-051:** 35.3%, **Double-J:** 66.7%
Nam 2015 (Nam et al., 2015)	Resonance	Memokath-051: 6 patients (6 ureteral units) patients Resonance: 14 patients (17 ureteral units)	Memokath-051: 16 (range: 4 - 98); Resonance 15.7 (range: 13 - 20)	Authors report that differences in USSQ scores were not statistically significant between stents; each produced similar scores

P-values and variance estimated have been extracted where reported

Complications and adverse events

Stent migration and encrustation were the most commonly reported complications following placement of Memokath-051 stents; incidence of these have been discussed. The other most commonly reported adverse events included UTI (Akbarov et al., 2017, Klarskov et al., 2005, Papatsoris and Buchholz, 2010, Zaman et al., 2011) and blockage or obstruction (Akbarov et al., 2017, Kim et al., 2014, Klarskov et al., 2005, NCT00166361, 2014, Zaman et al., 2011). There was a higher incidence of UTI in the Memokath-051 groups compared with IUR (41% vs 7%) (Akbarov et al., 2017). Data for UTI were not reported for the other comparisons. There was a higher rate of blockage with double-J stents compared with Memokath-051 in 1 study (33% vs 0) (Maan et al., 2010).

Table 3.10: Results of the EAC's included studies: Complications and adverse events

Study	Comparator	Patients	Mean follow-up (months)	Complications/Adverse events
Akbarov 2017 (Akbarov et al., 2017)	IUR	**Memokath-051:** 27 renal units in 17 patients **IUR group:** 27 patients	42 (range: NR)	**Memokath-051:** UTI: 7 patients (41%) Early total obstruction due to insufficient dilatation effect of the stent: 1 patient (4%) Gross haematuria, irritative voiding, urinary retention, and ureteroenteric fistula: 1 patient (4%) **IUR:** UTI: 2 patients (7%) Wound infection: 1 patient (4%) Pelvic vein thrombosis: 1 patient (4%)
Bolton 2015 (Bolton et al., 2015)	ALLIUM	**Allium:** 9 patients **Memokath-051**: 21 patients	NR	Ureteric perforation in 1 patient- unclear which treatment arm
Kim 2014 (Kim et al., 2014)	UVENTA	**Memokath-051:** 10 patients with 14 ureter units treated **UVENTA:** 17 patients	**Memokath-051:** 13.6 (±4.6) **UVENTA:** 12.0 (±2.6) months	Intermittent flank pain, intermittent gross hematuria, or acute pyelonephritis: **Memokath-051**: 2 patients (14%), **UVENTA**: 3 patients (18%) Obstruction by tumour progression: **Memokath-051:** 2 cases (14%), **UVENTA**: 0 Mucosal hyperplasia: **Memokath-051:** 0, **UVENTA:** 2 cases (12%)
Maan 2010 (Maan et al., 2010)	Double-J	**Double-J:** 23 patients	NA- one-off survey	Stent blockage **Memokath-051:** 0, **Double-J:** 6 (26%)

Study	Comparator	Patients	Mean follow-up (months)	Complications/Adverse events
		Memokath-051: 18 patients		
NCT00166361 2014 (NCT00166361, 2014)	Double-J	**Memokath-051:** 14 patients **Double-J:** 10 patients	NR	Serious adverse events reported by more than 1 patient in a treatment arm: Total: **Memokath-051:** 12 (86%), **Double-J:** 2 (20%) Bowel obstruction: **Memokath-051:** 4 (29%), **Double-J**: 0 (0%); Hospitalisation for sepsis: **Memokath-051:** 0 (0%), **Double-J**: 2 (20%); Stent encrustation/ obstruction: **Memokath-051:** 4 (29%), **Double-J**: 0 (0%); Hospital for disease progression: **Memokath-051:** 3 (21%), **Double-J**: 0 (0%); Edema of ureter: **Memokath-051:** 2 (14%), **Double-J**: 0 (0%); Hydroureteronephrosis: **Memokath-051:** 3 (21%), **Double-J**: 0 (0%); Other adverse events: **Memokath-051:** 10 (71%), **Double-J**: 8 (80%)
Agrawal 2009 (Agrawal et al., 2009)	None	74 stents inserted into 55 patients	16 (range: 4 - 98)	**Immediate complications:** Urinary extravasation: 1 (1%) Poor thermo-expansion: 1 (1%) Equipment failure (locking assembly): 1 (1%) **Late complications:** Fungal infections: 3 (6%)
Arya 2001 (Arya et al., 2001)	None	13 stents placed in 11 patients	18 (range: 1.5-33)	NR
Klarskov 2005 (Klarskov et al., 2005)	None	37 stents placed in 33 patients	Median: 14 (range: 3-30)	Complications during insertion procedure: 7 (19%) Malfunction: 9 patients, 12 ureters (27%); - *stent too short: 4, ureteric obstruction: 3, stent occluded by stones: 1, reason unknown: 4* UTI: 11 patients (33%)
Papadopoulos 2010 (Papadopoulos et al., 2010)	None	13 patients	14.3 (range: 0 - 54)	Ureteral strictures: 2 (15%)
Papatsoris 2010 (Papatsoris and Buchholz, 2010)	None	86 ureteral strictures in 73 patients	17.1 (range: 1 - 55)	No perioperative of immediate post-operative complications were recorded UTI: 6 (7%) 1 patient went into renal failure because of a blocked stent

Study	Comparator	Patients	Mean follow-up (months)	Complications/Adverse events
Zaman 2011 (Zaman et al., 2011)	None	42 stents were inserted in 37 patients	22 (range: 5 - 60)	UTI: 3 (7%); Blockage: 2 (5%)

P-values and variance estimated have been extracted where reported

Subgroup data

Data to support subgroup analyses were not available for patients unfit for surgery or antegrade or retrograde insertion.

Benign vs malignant stricture

Clinical success

There were limited data reported in relation to benign and malignant populations. One single-arm study reported data for a benign population (Arya et al., 2001) and a comparative study reported data for the benign subgroup of a mixed population (Kim et al., 2014). Clinical success rates for Memokath-051 in these studies were 50% and 64% in small samples of 8 (Arya et al., 2001) and 11 (Kim et al., 2014) patients respectively.

Three studies reported data for a malignant population (NCT00166361, 2014, Nam et al., 2015, Zaman et al., 2011) and another reported data for the malignant subgroup of a mixed population (Kim et al., 2014). The clinical success rate in the 3 studies of malignant patients only was 82% (Nam et al., 2015) or 100% (Granberg et al., 2010, Zaman et al., 2011) (data for clinical success in the NCT00166361 study were reported in Granberg 2010). However, in the subgroup analysis (Kim et al., 2014) Memokath-051 had a success rate of 33% in this population compared to 92% of patients receiving UVENTA. This difference may reflect differences in how clinical success was defined and at what point it was measured in the trials.

Table 3.11: Subgroup analysis: Clinical success

	Follow-up	Patients	As described in publication	Proportion
Benign populations				
Arya 2001 (Arya et al., 2001)	18 (range: 1.5-33)	13 stents placed in 11 patients	Ureteric obstruction relieved	64%
Kim 2014 (Kim et al., 2014). (subgroup)	**Memokath-051:** 13.6 (±4.6) **UVENTA group:** 12.0 (±2.6) months	**Memokath-051:** 8 ureters **UVENTA:** 5 ureters	Success was defined as improved renal function and no obstruction	**Memokath-051**: 50% **UVENTA**: 60% p=1.00
Malignant populations				
NCT00166361 2014 Data reported in Granberg 2010 (Granberg et al., 2010)	NR	**Memokath-051:** 18 stents in 15 patients **Double-J group:** 10 patients	Upper tract decompression	**Memokath-051:** 100% **Double-J**: 100%
Kim 2014 (Kim et al., 2014). (subgroup)	**Memokath-051:** 13.6 (±4.6) **UVENTA group:** 12.0 (±2.6) months	**Memokath-051:** 6 ureters **UVENTA:** 12 ureters	Success was defined as improved renal function and no obstruction	**Memokath-051**: 33% **UVENTA**: 92% p=0.022
Nam 2015 (Nam et al., 2015)	**Memokath-051:** 16 (range: 4 - 98); **Resonance** 15.7 (range: 13 - 20)	**Memokath-051:** 6 patients (6 ureteral units) patients **Resonance:** 14 patients (17 ureteral units)	Inverse of 'early failure rates''	**Memokath-051:** 82% **Resonance:** 86%
Zaman 2011 (Zaman et al., 2011)	22 (range: 5 - 60)	42 stents were inserted in 37 patients	Improved or maintained renal function	100%

P-values and variance estimated have been extracted where reported

Insufficient data were identified in the included studies for these subgroups to make any reasonable comparisons in relation to stents removal, replacement, length of time in situ, rates of migration and encrustation, operative time and duration of hospital stay, quality of life and other complications.

Table 3.12: Subgroup analysis: Stent removal, replacement, length of time in situ and rates of migration and encrustation

	Patients	Mean follow- up (months)	Length of time in situ (months)	Stents removed	Stent replacement	Stent migration	Encrustation
Benign populations							
Arya 2001 (Arya et al., 2001)	13 stents placed in 11 patients	18 (range: 1.5-33)	NR	3 stents due to encrustation	1 stent due to migration	1 (9%)	3 (27%)
Malignant populations							
Nam 2015 (Nam et al., 2015)	**Memokath-051**: 6 patients (6 ureteral units) patients **Resonance**: 14 patients (17 ureteral units)	Memokath-051: 16 (range: 4 - 98); Resonance 15.7 (range: 13 - 20)	NR	NR	NR	NR	NR
NCT00166361 2014 (NCT00166361, 2014)	**Memokath-051:** 14 patients **Double-J:** 10 patients	NR	**Memokath-051:** 17 (1 - 59) **Double-J**: 3.97 (2.56 - 5.36)	NR	NR	**Memokath-051:** 1 (7%) (2 events), **Double-J:** 0 (0%)	**Memokath-051:** 4 (29%) **Double-J:** 0 (0%);
Zaman 2011 (Zaman et al., 2011)	42 stents were inserted in 37 patients	22 (range: 5 - 60)	NR	NR	5 stents due to migration.	5 (12%)	0 (stone formers were excluded)

P-values and variance estimated have been extracted where reported

3.7 Description of the adverse events

Data for all outcomes, including those relating to complications, have been reported in Section 3.6. Within the expert questionnaires conducted by NICE, 1 expert report that Memokath-051 can block or migrate. Information pertaining to these events is reported, for all devices, in Section 3.6.

The company reported that no data were available from Medicines and Healthcare products Regulatory Agency (MHRA) or US Food and Drug Administration (FDA) Manufacturer and User Facility Device Experience (MAUDE) (Section 7.7.3, Submission). The EAC conducted a search of the FDA MAUDE database for the terms “Memokath” and “Memokath-051” from 01/01/1990 to 26/04/2017 and identified no reports. The EAC also conducted a search of MHRA freedom of information releases for the terms “Memokath” and “Memokath-051” on 26/04/2017, which identified no reports.

3.8 Description and critique of evidence synthesis and meta-analysis

The company did not attempt to synthesise data using meta-analysis and did not justify this decision.

In order to determine whether or not it is appropriate to pool the studies identified, the EAC considered a number of factors including the patient characteristics and details of the strictures, duration of follow-up, details of prior stenting and the experience of the clinician placing the stent (Table 3.13). However, the information for the majority of these factors to accurately conclude on their similarity was too limited.

Table 3.13: Key characteristics of the EAC's included studies: patient characteristics, details of the strictures, duration of follow-up, details of prior stenting and the experience of the clinician placing the stent

	Comparator	Patients	Gender (% male)	Mean age (years)	Type of stricture (benign/malignant)	Details of stent placing	Details of prior stenting	Details of the clinician placing the stent	Mean follow- up (months)
Comparative Studies									
Akbarov 2017 (Akbarov et al., 2017).	IUR	**Memokath-051:** 27 units in 17 patients **IUR group:** 27 patients	NR	**Memokath-051:** 59 **IUR group:** 55	Benign or malignant- proportions not reported	NR	NR	NR	42 (range: NR)
Bolton 2015 (Bolton et al., 2015)	ALLIUM	**Allium:** 9 patients **Memokath-051**: 21 patients	NR	NR	Benign: 24, malignant: 6	NR	NR	NR	NR
Kim 2014 (Kim et al., 2014).	UVENTA	**Memokath-051:** 10 patients with 14 ureter units treated **UVENTA:** 17 patients	**Memokath-051:** 40% **UVENTA:** 41%	**Memokath-051:** 60 (±19 SD) **UVENTA:** 6 (± 15.9).	**Memokath-051**: benign: 8, malignant: 6 **UVENTA:** benign: 5, malignant: 12	All stents were inserted retrograde	All patients were initially treated with a double-J stent.	Stents were inserted by 2 experienced endourological surgeons at the institution	**Memokath-051:** 13.6 (±4.6) **UVENTA group:** 12.0 (±2.6) months
Maan 2010 (Maan et al., 2010)	Double-J	**Double-J:** 23 patients **Memokath-051**: 18 patients	**Double-J:** 48% **Memokath-051**: 61%	**Double-J:** 51.19 (SD: 13.67) **Memokath-051**: 59 (SD: 16.37)	**Memokath-051:** benign: 9, malignant: 9 **Double-J:** NR	NR	NR	NR	NA- one-off survey

	Comparator	Patients	Gender (% male)	Mean age (years)	Type of stricture (benign/malignant)	Details of stent placing	Details of prior stenting	Details of the clinician placing the stent	Mean follow- up (months)
Nam 2015 (Nam et al., 2015)	Resonance	**Memokath-051:** 6 patients (6 ureteral units) **Resonance:** 14 patients (17 ureteral units)	NR	**Memokath-051:** 69.8± 11.4 (range: 52 - 82); **Resonance:** 52.5 ± 15.6 (range: 29 - 76)	All malignant	NR	NR	NR	**Memokath-051:** 16 (range: 4 - 98); **Resonance** 15.7 (range: 13 - 20)
NCT00166361 2014 (NCT00166361, 2014)	Double-J	**Memokath-051:** 14 patients **Double-J:** 10 patients	**Memokath-051:** 21% **Double-J:** 30%	**Memokath-051:** 5 >= 65 years **Double-J:** 10 >= 65 years	All malignant	**Double-J**: all placed retrograde. **Memokath-051**: NR	NR	NR	Up to 58 months
Single-arm studies									
Agrawal 2009 (Agrawal et al., 2009)	None	74 stents inserted into 55 patients	NR	60 (range: 11 - 90)	Benign: 27, malignant: 28	NR	NR	All stents were inserted by 1 surgeon in the UK and internationally following a standard protocol	16 (range: 4 - 98)
Arya 2001 (Arya et al., 2001)	None	13 stents placed in 11 patients	NR	58 (range: 35-85)	All benign	7 stents were inserted retrograde. 6	NR	NR	18 (range: 1.5-33)

	Comparator	Patients	Gender (% male)	Mean age (years)	Type of stricture (benign/malignant)	Details of stent placing	Details of prior stenting	Details of the clinician placing the stent	Mean follow- up (months)
						stents were inserted antegrade			
Bourdoumis 2014 (Bourdoumis et al., 2014)	None	23 renal units stented in 14 patients	43%	60.2 (±8.4 SD)	Benign: 12 , malignant: 2	NR	All patients were initially treated with a double-J stent	NR	22.5 (range: 3-56)
Klarskov 2005 (Klarskov et al., 2005)	None	37 stents placed in 33 patients	45%	57 (range: 35 - 87)	Benign: 21 , post-irradiation: 5; malignant: 7	NR	4 patients did not have a prior double-J stent or had not undergone nephrostomy prior to inclusion	NR	Median: 14 (range: 3-30)
Kulkarni 2001 (Kulkarni and Bellamy, 2001)	None	37 stents placed in 28 patients	36%	59 (range: 29-86)	Benign: 10, malignant: 18	27 stents were inserted retrograde, 1 antegrade, and 3 bilaterally	In 17 patients a Double-J stent had been placed previously. In the remaining 11 patients there was no prior stenting	NR	19.3 (range: 3-35)
Papadopoulos 2010 (Papadopoulos et al., 2010)	None	13 patients	62%	60.7 (range: 36 - 81)	Benign: 11, malignant: 2	NR	All patients had been unsuccessfully treated previously using temporary double-J stents or dilation	NR	14.3 (range: 0 - 54)

	Comparator	Patients	Gender (% male)	Mean age (years)	Type of stricture (benign/malignant)	Details of stent placing	Details of prior stenting	Details of the clinician placing the stent	Mean follow- up (months)
Papatsoris 2010 (Papatsoris and Buchholz, 2010)	None	86 ureteral strictures in 73 patients	47%	57.5 (range: 23 - 84)	Benign: 55, malignant: 31	In all cases, stents were inserted retrograde	NR	NR	17.1 (range: 1 - 55)
Zaman 2011 (Zaman et al., 2011)	None	42 stents were inserted in 37 patients	46%	64 (range: 32-83)	All malignant	NR	Eligibility criteria- with or without prior stenting	Stents inserted by 1 of 3 experienced surgeons in the same hospital	22 (range: 5 - 60)

For clinical success, the EAC concluded that definitions were too inconsistent across the trials and it is not clear how long a stent must remain functioning and in place before it is classified as a clinical success in each trial. The frequency and duration of follow-up varies across the studies meaning the point at which clinical success is being measured varies.

The only outcomes the EAC considered appropriate for pooling were stent removal, replacement, and rates of migration and encrustation.

Definitions of stent removal, replacement, migration and encrustation were considered to be more consistent across studies, however, the EAC notes that the rates are likely to be affected by the duration of follow-up in each study. A summary of the data pooled across the trials in the Memokath-051 treatment arms is reported below in Table 3.14.

Table 3.14: Pooled analysis: Memokath-051 stents removed, replaced, migrated and encrusted

	Number of studies	Number of patients	Number of stents inserted	Number of events	% of stents with events
Removed	7	190	227	37	16.3%
Replaced	8	249	306	49	16.0%
Migrated	13	344	419	74	17.7%
Encrusted	8	250	302	20	6.3%

There were no data available for any of the comparator stents in relation to stent removal and replacement. One study of double-J stents reported that none of the stents became encrusted. No data further data were available for rates of encrustation for Allium, UVENTA or Resonance stents. Rates of migration were reported in 1 study of Allium and UVENTA and 2 studies of double-J stents. There was no migration reported with double-J stents and Allium stents based on the studies identified. One stent (5.9%) in the UVENTA group migrated. We note that the rates for the comparator arms are informed by fewer trials and smaller patient numbers compared to Memokath-051 so direct comparisons cannot be made reliably.

Table 3.15: Pooled analysis: Rates of migration

Stent	Number of studies	Number of patients	Number of stents inserted	Number of events	% of stents with events
Memokath-051	13	344	419	74	17.7%
Allium	1	9	9	0	0
Double-J	2	33	33	0	0
UVENTA	1	17	17	1	5.9%

Length of time in situ was only reported in 4 studies and ranged from 11 months to 47 months in the Memokath-051 treatment arms. The EAC concluded that this outcome would be impacted by the duration of follow-up and would therefore not be suitable for pooling.

Mean operative time was reported in 3 studies. Two of the studies reported comparable times (23-26 mins), which is also in keeping with clinical expert opinion, while the third study reported an operative time of 118 minutes. The EAC does not consider it to be appropriate to pool these data.

Quality of life was reported in 3 studies, however, the actual change in scores have not been reported so pooling is not feasible.

Adverse events were reported inconsistently across the trials. Incidence of adverse events are likely to be affected by the duration of follow-up and so it was not considered appropriate to pool the data.

3.9 Ongoing studies

No ongoing studies within the scope of this decision problem were identified by either the company or the EAC. The steps taken by the EAC to identify ongoing studies are reported in Appendix A as part of the search strategy.

4 Economic Evidence

4.1 Published economic evidence

4.1.1 Critique of the company's search strategy

Section 8.1.1 of the company submission contains a description of the search methodology used to identify economic evidence, but this is very limited and is not sufficient to accurately replicate or evaluate the company's search. The full search strategies, exactly as run in each resource, are not provided. Section 10, Appendix 3 of the submission, where it is expected that they are recorded, is blank. The company do specify the resources that they searched for economic evidence (MEDLINE, PubMed, Embase, ClinicalTrials.gov, Google and in-house sources) but these do not include any resources specifically covering economic literature such as EconLit, NHS EED, CEA Registry, or the HTA Database. The company do not report the number of records identified per database or the time period covered by the search. The search's lack of reproducibility, and the failure to search economic resources, resulted in the EAC undertaking a *de novo* literature search.

The searches carried out by the EAC to identify clinical effectiveness evidence (reported in Section 3.1 and Appendix A) were not restricted by study design and were prospectively designed to retrieve both clinical effectiveness and

economic evidence. The sources searched were extensive, covered sources for both published and unpublished evidence, and included those required as a minimum by NICE for the search on economic evidence, as specified in the submission template (MEDLINE, MEDLINE In-Process, Embase). The additional search for economic evidence carried out by the EAC consisted of searches of the economic-specific resources required as a minimum by NICE in the submission template (EconLit and NHS EED), in addition to the CEA Registry.

The EAC's economic evidence searches identified 9 records, with 1 additional record supplied by NICE's expert advisors. 9 records remained after deduplication against the results already identified by the searches for clinical evidence. When added to the clinical evidence search results this provided a total of 2,071 records, with 1,283 remaining after deduplication which were assessed for relevance. Full details of the EAC economic searches, including full search strategies and result numbers by database, are provided in Appendix E.

4.1.2 Critique of the company's study selection

Company's study selection

During study selection the company adopted a PICO framework, in line with the approach taken to select clinical studies. However, the PICO criteria (Table C1, Submission) adopted for the economic selection was amended such that the outcomes were 'health economics', 'cost-effective analysis' and 'cost analysis'. These criteria are confusing, as the terms reported relate to study design rather than outcomes. Thus, it is unclear what outcomes were deemed relevant for inclusion by the company.

The selection criteria appropriately excluded those studies published before 1992 and those in non-English language. The population criteria were subject to the same limitations reported in Section 3.2.

EAC's study selection

The selection criteria adopted by the EAC, to select relevant economic studies, are summarised in Table 4.1. These are consistent with the scope.

Table 4.1: Selection criteria adopted by the EAC for economic study selection

	Inclusion criteria	Exclusion criteria
Population	Patients with ureteric obstruction as a result of malignant or benign strictures	Patients with ureteric obstruction due to any other reason
Intervention	Memokath-051	Other Memokath devices (028, 044 and 045)
Comparators	• Double-J stents; • Nephrostomy; • Reconstructive surgery; • Metallic and alloy stents (including nitinol stents); • No comparator.	Any other device
Outcomes	Not specified to maximise sensitivity.	
Study design	Heath economic studies (Memokath-051 v. comparator): • Cost-effectiveness; • Cost-utility; • Cost-benefit; • Cost-minimisation; • Cost-consequence.	Non-comparative cost analyses including cost of illness studies. Clinical studies reporting on cost of treatment in the discussion only without more formal analyses
Limits	Date = 1992 English language only	Studies published in languages other than English

The EAC applied the selection criteria listed in Table 4.1, to the literature search reported in Section 4.1.1.

4.1.3 Included and excluded studies

Company's selected studies

Of the 54 unique records identified, the company reported that 5 studies met its selection criteria (Section 8.1.3, Submission). However, only 3 studies were included within the remainder of the review (Agrawal et al., 2009, AUH, Papatsoris et al., 2007). These studies are summarised in Table 4.2. The EAC could not replicate the company's search strategy and therefore could not confirm whether the company had identified and excluded any relevant studies.

Table 4.2: Summary of company's included economic studies

Study and setting	Design	Population	Intervention	Comparator	EAC's judgement on inclusion
Agrawal 2009 (Agrawal et al., 2009) UK	Clinical study	Patients with malignant or benign ureteric strictures	Memokath-051	Double-J stents	Although this study reported on the price of the devices within its discussion, the EAC does not judge this to be an economic evaluation
Aintree University Hospital (AUH) 2012 (AUH)	Cost-minimisation analysis	Patients with malignant or benign ureteric strictures	Memokath-051	Double-J stents	The EAC agrees with the inclusion of this study
Papatsoris 2007 (Papatsoris et al., 2007)	Clinical study	Patients with malignant or benign ureteric strictures	Memokath-051	Double-J stents	Although this study reported on the price of the devices within its discussion, the EAC does not judge this to be an economic evaluation

The company did not report the results from any of its included studies, but critically appraised 2 of the 3 (Agrawal et al., 2009, Papatsoris et al., 2007). The 2 studies that the EAC judged to be out of scope are not discussed further in this report.

EAC's selected studies

Those records identified during the clinical searches (reported in Section 3.1) were sifted in addition to those identified through searching economic databases. In total, 1,283 records were screened. Three studies met the EAC's inclusion criteria as shown in the PRISMA diagram in Appendix F (AUH, Gonzalez et al., 2011, Zaman et al., 2012). Of the 3, 1 was identified through information provided to NICE by a clinical expert (AUH) and the remaining 2 were identified via the clinical effectiveness review reported in Section 3 (Gonzalez et al., 2011, Zaman et al., 2012). These are reported in Table 4.3. One study included within the clinical review (Section 3) reports on cost savings resulting from the avoidance of double-J stent exchanges (Granberg et al., 2010). However, this study does not provide any information pertaining to the costs of Memokath-051 and was thus excluded from this cost-effectiveness review.

Table 4.3: Summary of EAC's included economic studies

Study and Setting	Design	Population	Intervention	Comparator
AUH (AUH) UK	Cost-consequence analysis	Patients with malignant or benign ureteric strictures	Memokath-051	Double-J stents
Gonzalez 2011 (Gonzalez et al., 2011) Spain	Cost-consequence analysis	Patients with chronic obstructive uropathy	Memokath-051	Double-J stents
Zaman 2012 (Zaman et al., 2012) UK	Cost-consequence analysis	Patients with malignant ureteric strictures	Memokath-051	Double-J stents

4.1.4 Overview of methodologies of all included economic studies

The company did not report any methods (except a high level overview in Table C2, Submission) or results from its 3 included studies. The results of the EAC's included studies are presented in Table 4.4.

AUH presented a cost-consequence analysis specific to in the UK presenting the costs associated with the use of Memokath-051 compared to double-J stents. Costs were reported over a 1, 2 and 3 year time horizon for 24 patients requiring 32 stents. Patients required long term stenting of malignant and benign ureteric strictures (AUH).

Gonzalez *et al* (2011) report on a cost-consequence analysis comparing Memokath-051 with double-J stents whereby costs are reported on a per patient basis. The analysis uses costs from a Spanish hospital and reports total costs over an unspecified time horizon. Costs of stent insertion were included and "collateral effects" (i.e. catheter pain) at no additional cost was reported (Gonzalez et al., 2011).

Zaman *et al*. (2012) report on a cost- consequence analysis specific to patients undergoing surgery within Barts and The London National Health Service (NHS) Trust, UK. Costs were initially calculated per patient following a pre-defined patient pathway and then applied to the 37 patients who received 41 Memokath-051 stents. Costs were reported over a 22 month time frame (Zaman et al., 2012).

Table 4.4: Results of EAC's included economic studies

Study	Costs	Patient outcome	Results
AUH (AUH) UK	The following costs were included: • Hospital services; • Materials; • Theatre; • Recovery; • Consumables; • 6 monthly exchange for double-J stents; • Follow-up.	Authors identify QoL as the key outcome, but this is not measured.	**1st year:** Memokath-051 = £3,326 Double-J stent = £3,353 Cost saving = £27 **2nd Year:** Memokath-051 = £258 Double-J stent = £3,353 Cost saving = £3,095 **Cohort of patients** at AUH = £156,163 over 3 years
Gonzalez 2011 (Gonzalez et al., 2011) Spain	The following costs were included: • Consultations; • Theatre; • Recovery (admission); • Follow-up; • Exchange of double-J stents but frequency not specified.	Authors identify pain as an outcome, but this is not measured	**Cost per insertion:** Day case Double-J stents = £1,107 (€1,275) Day case Memokath-051 = £4,222 (€4,865) 1 day admission Double-J stents = £1,237 (€1,425) 1 day admission Memokath-051 = £4,351 (€5,014) Costs were converted using the 2011 OECD (Organisation for Economic Co-operation and Development) exchange rate
Zaman 2012 (Zaman et al., 2012) UK	The following costs were included: • Materials; • Theatre; • Recovery; • Follow-up; • 6 monthly exchange for double-J stents; • Replacement Memokath-051 as necessitated in practice.	Stent exchange (resulting from blockage or migration): Memokath-051 = 4.7% Double-J stent = 11.7% Replacements are included in costs	**Per cohort of patients over 22 month time frame:** Memokath-051 = £398,839 (€490,200) Double-J stent = £235,382 (€289,300) Cost saving = £ 163,457 (€200,900) Costs were converted using the 2012 OECD exchange rate

4.1.5 Overview and critique of the company's critical appraisal for each study

The company critically appraised 2 of its 3 included studies using GHTF guideline checklist for observational studies (Table 8.1-8.3, Submission) (Agrawal et al., 2009, Papatsoris et al., 2007). As these studies were included as part of a cost-effectiveness review, this checklist was not judged to be appropriate. The EAC agrees that it was appropriate not to critically appraise the 3rd study given that it is a PowerPoint with insufficient information on the methodology and sources used (AUH).

The EAC critically appraised Gonzalez *et al* (2011) using the Drummond checklist (see Appendix G). The study was considered to be poorly conducted and reported. Further, because the cost information is specific to a Spanish hospital with no resource units provided, its external validity to the decision problem and the NHS is poor (Gonzalez et al., 2011).

The AUH analysis was judged unsuitable for full critical appraisal. As a cost-consequence analysis is reported, the estimated cost-savings assume the Memokath-051 and double-J stents are clinically equivalent in terms of complications. Further, the analysis assumes that Memokath-051 will remain in situ for 24 months (AUH).

Zaman *et al*. (2012) was also unsuitable for full critical appraisal given that it was published as an abstract only. The analysis included the costs associated with the insertion and follow-up of both types of stent and also considered the costs of replacing blocked and migrated stents (Zaman et al., 2012).

4.1.6 Does the company's review of economic evidence draw conclusions from the data available?

The company drew no conclusion from its included cost-effectiveness studies. The EAC concludes that based upon its included studies, Memokath-051 may be cost saving compared to double-J stents. However, these analyses are poorly reported meaning it is not possible to judge whether all consequences for patients with either stent are fully costed. There is insufficient information provided regarding unit costs to assess whether these are generalisable to the decision problem. Follow-up is poorly reported meaning that is it difficult to judge whether Memokath-051 will be in situ for long enough for cost savings to be realised. Should the device be removed, or the patient die, such cost savings may not be realised. Furthermore, the complications associated with Memokath-051 have not been fully or accurately captured within the cost analyses. Therefore, the EAC deems the company's decision to produce a *de novo* cost analysis appropriate.

4.2 Company de novo cost analysis

A *de novo* cost model was created by the company which was appropriate given the limited UK based economic evidence available on Memokath-051. The model was largely based on 1 of the cost consequence analyses included within the cost-effectiveness review (AUH). The structure of the model is described below.

4.2.1 PICO analysis

Patients

The company described the patients within the model as “all patients of chronic ureteric strictures (obstruction) due to both benign and malignant causes” (Section 9.1.2, Submission). This is largely consistent with the scope, with the exception that the scope does not specify that the ureteric strictures are chronic.

Within the scope, 3 subgroups (patients unfit for surgery, with malignant or benign stricture and antegrade or retrograde insertion) were listed for consideration. The company deviated from the scope as no subgroups were considered in their analysis (Section 9.6.1, Submission). This is not a major issue given there were no robust clinical data for any of the subgroups.

Technology

The technology considered in the model was the Memokath-051, consistent with the scope.

Comparator(s)

The comparator included in the model was double-J stents. Details were not provided on whether the data included in the model for double-J stents were reflective of a specific brand of double-J stent or if this was aggregated data. The company stated that the comparator is the same as in the scope (Section 9.1.3, Submission). However, the scope also lists metallic and alloy stents, nephrostomy and reconstructive surgery as comparators. The company provides a justification for only including double-J stents as a comparator in the model by stating that the other “procedures are more related to medical intervention decision and not the price or time factors” (Section 9.1.1, Submission).

The EAC disagrees with this justification. The clinical evidence review conducted by the EAC (reported in Section 3) identified comparative data for other comparators listed in the scope. Specifically, data are available comparing Memokath-051 to double-J stents, metallic and alloy stents and reconstructive surgery. The EAC identified no evidence to inform a comparison between Memokath-051 and nephrostomy. The EAC included all comparators listed in the scope except nephrostomy in its updates to the company’s model.

Outcome(s)

The primary outcome modelled is total cost per patient at 2.5 years. No consequences were considered outside of the cost analysis. Such

consequences with evidence to support their inclusion include pain and quality of life (Maan et al., 2010).

The perspective used for the analysis is not reported, but given that all costs included in the model were sourced from a single English hospital (AUH), a NHS hospital perspective was taken whereby staff costs comprised salary costs only. This is not in line with the final scope which specifies that an NHS and Personal Social Services (PSS) perspective should be used whereby broader costs including other overheads are included. No PSS costs are considered relevant to the analysis, hence these have not been incorrectly omitted.

4.2.2 Model structure

The *de novo* economic model produced by the company was a simple costing model. Whilst the form of the economic analysis was not stated by the company, the analysis used a cost-benefit approach given that measurement of costs for both alternatives and the valuation of the consequence (replacement stent resulting from a risk factor of an unplanned exchange) was expressed in monetary units (criteria given in (Drummond et al., 2015)).

The model has a time horizon of 2.5 years. The company noted follow-up studies for Memokath-051 are up to 11 years adding we "wanted to show benefit over a much shorter period and it goes without saying that the longer the stent in situ will be even more cost effective" (Section 9.1.8, Submission).

A model structure and model diagram, both created in Microsoft Excel® were provided by the company as attachments to their submission. The diagram did not accurately display the structure of the model. The following points were noted by the EAC:

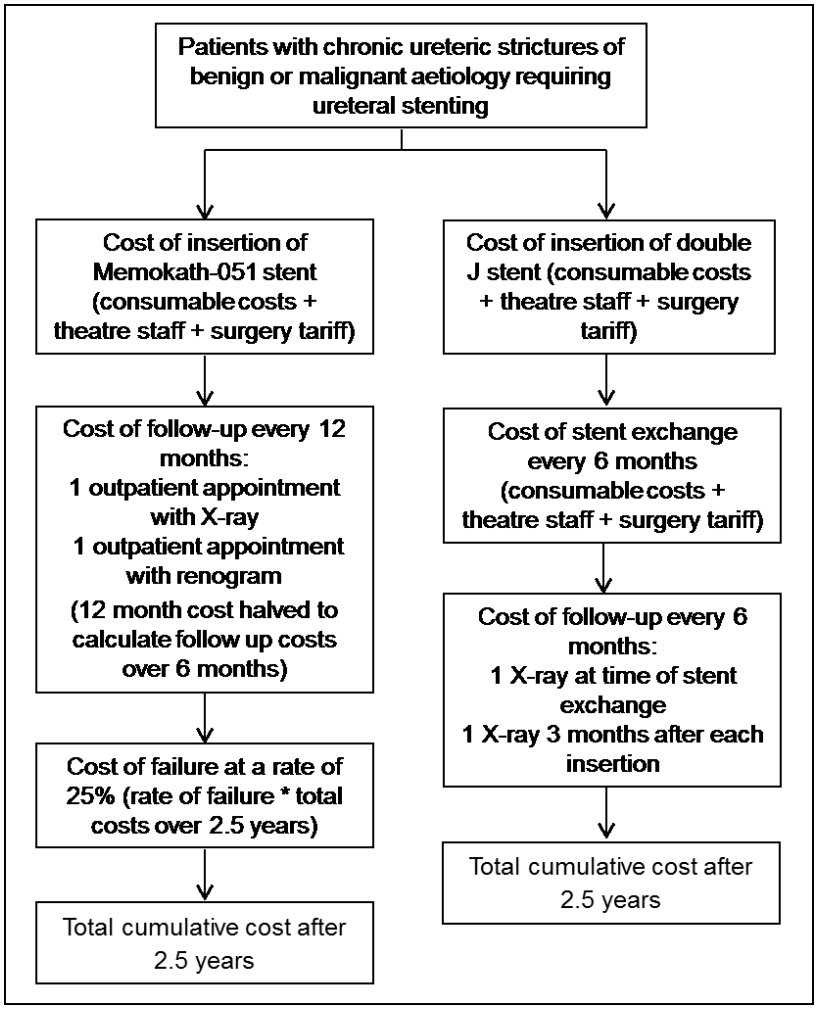
- Patients who were treated with either Memokath-051 or double-J stents are shown to be discharged after 1 night following stent insertion (company's model structure diagram). The cost of an overnight stay in hospital was not included in the model;

- Patients who were treated with double-J stents are shown in the model diagram to have a follow-up X-ray at 3 months then every 6 months. In the model, 2 X-rays were costed for every 6 month period;

- Patients who were treated with Memokath-051 are shown in the model diagram to only have a follow-up X-ray every 4 months. In the model, the cost of 2 outpatient appointments and a renogram, as well as an X-ray were included per 12 month period.

Figure 4.1 was created by the EAC to provide a diagram which correctly reflects the model structure developed by the company to aid understanding.

Figure 4.1: Company's *de novo* model diagram (EAC created)



The company produced a simple cost model in Microsoft Excel®. The model consisted of 1 worksheet and the formulae used in the calculations were provided. For both technologies the following parameters were included in the model:

- The cost of insertion (including the cost of theatre staff, consumables and the theatre tariff, given separately in the model);
- The cost of follow-up visits.

Complications associated with the device were only included in the Memokath-051 arm of the model and were encapsulated within a risk factor for an unplanned stent exchange.

All patients entering the model undergo stent insertion. A total cost for the first 6 months was calculated by summing the cost of insertion and patient follow-up. In the Memokath-051 arm, for the remaining 2 years of the model time horizon the cost of patient follow-up was applied as an annual cost. A risk factor

for complications (unplanned stent exchange for Memokath-051) was applied by multiplying the sum of these pathway-related costs per patient over the 2.5 year time horizon by 25%. This cost premium was added to generate a total cost per patient for Memokath-051.

In the double-J arm, stent exchange occurs every 6 months within the model, hence the cost of insertion and follow-up appointments in the first 6 months are applied every 6 months. Thus, the cost of the initial double-J stent insertion and 4 stent exchanges, as well as the patient follow-up appointments, are summed to generate the total per patient cost over 2.5 years for double-J stents. The company calculates its costs every 6 months over a total of 2.5 years.

The company justified its choice of model structure by reporting that it aligns with the clinical pathway given in the clinical context section of the submission (Section 9.1.5, Submission). Further, in the validation section of the submission (Section 9.7), the company state that, “the model structure was designed to emulate the clinical pathways derived from a published study and an audit report for NHS”. This statement was not developed further and the published study and audit report were not referenced. The EAC did not deem the model structure to be a fully appropriate representation of the clinical pathway of care. A full critique of the company’s model is given in Section 4.2.3.

4.2.2.1 Assumptions

The company lists the following assumptions included in the model (Section 9.1.6, Submission). Each is discussed in detail by the EAC.

All patients with double-J insertions have no early removal or early complication. This assumption was applied in the model by setting the risk factor for an unplanned exchange of double-J stents to zero. The company justifies this assumption by stating that it makes it easier for any evaluator “to see the value of Memokath-051 even when putting the comparator in the ideal situation” (Section 9.1.6, Submission). In Section 9.1.1 of the company’s submission, they acknowledge that the period between stent exchanges included in the model is longer than the ‘known’ period between stent exchanges for double-J stents. The company state this as 3 to 4 months.

No complications require any surgical interference or long term side effects. The company justified this assumption by stating that, “99% of complications for both Memokath-051 and double-J stents are only treated by exchange” (Section 9.1.6, Submission). The EAC has been unable to verify this statement as no reference was provided. Evidence from the clinical review conducted by the EAC suggests that there are differences in the risk of complications occurring between arms. This evidence is presented in Table 3.10 in Section 3.6.2. Of the complications reported, the EAC has identified UTIs as a complication that is unlikely to require the need for stent exchange. This

variable has therefore been included in the analysis conducted by the EAC and is explained in Section 4.2.5.

Risk factor of early exchange of Memokath-051 is 25%. This assumption was justified by reference to a clinical study (Papatsoris and Buchholz, 2010) which the company has used to determine that the overall success rate of Memokath-051 was, "about 75% in 4 years and more" (Section 9.1.6, Submission) and this rate was applied to the shorter modelled timeframe. The EAC asked the company to clarify exactly where the figure of 25% was derived from; however, this remains unclear. The 25% risk of an unplanned stent exchange was applied in the Memokath-051 arm of the model only.

The EAC has identified the following additional assumptions made by the company relating to the model structure:

- By applying the 25% risk factor for complications to the total cost of Memokath-051 over the 2.5 year time horizon of their model, the company have included an inflated cost for Memokath-051 exchange as they include the cost of all follow-up appointments and hence include costs that extend beyond the 2.5 year time horizon. This is discussed in further detail in Section 4.2.3;

- The resource use required for stent exchange is the same as for stent insertion (e.g. duration of the procedure, follow-up);

- Outcomes excluded from the model include device related adverse events (e.g. infection, encrustation, migration). These may or may not be captured by the risk factor applied for Memokath-051. The company states that "all adverse effects for both techniques are the same and treated by exchange" (Section 9.3.9, Submission). Therefore, any adverse events not requiring exchange are assumed to be equal between treatment arms.

4.2.3 EAC critique of model structure and assumptions

The EAC critically appraised the model using the methodology of Drummond and Jefferson (Drummond and Jefferson, 1996). The completed appraisal checklist is reported in Appendix H.

The EAC independently replicated the company's calculations employed in the model in order to check their accuracy. No errors were identified with the company's base case results as calculated in its model.

A time horizon of 2.5 years was used. It is not clear from the submission why this time horizon was used. The EAC asked the company for clarification on this point who reported that the cost savings were generated at around 1 year,

hence beyond this time point cost savings increased (correspondence log). Limited data were reported in the comparative trials in relation to the length of time the stent remained in situ and these data were driven by the follow-up of the studies (Table 3.7). Further, the company's model assumes that all patients remain alive at 2.5 years following insertion. This may not be the case for those patients with malignant stricture who have a short life expectancy (see Section 2.1.2).

The company state that all adverse events are included within a replacement risk of 25% over 2.5 years (Section 9.2.4, Submission). This is reported as the average of the failure rate of the clinical papers mentioned in the clinical submission. This statement is not explained further and so it is unclear how this value was calculated. The EAC asked the company to provide clarity around this but the company's response did not address the EAC's query (correspondence log). The EAC identified stent replacement rates of between 8% and 23% over a variety of follow-up periods (Table 3.7). The company do not conclude on the rate of replacement stents, but do state that the range of reported migration frequencies varied from 8% to 20% (Section 7.9.1, Submission). The omission of other associated adverse events that may not require the removal of the stent, such as infection, was not explained. The clinical review identified that some patients experienced a UTI as an adverse event associated with stenting with Memokath-051 that would not require replacement or removal of the stent (Table 3.10). This has been inappropriately omitted from the company's analysis, but does not have a large influence on the results of the analysis.

The EAC identified an issue with the way in which the company had applied the risk factor for an unplanned stent exchange for Memokath-051. The company had applied the risk factor to the total per patient cost over 2.5 years rather than the cost of insertion only. Hence, the cost of follow-up visits will be double counted. This error impacts on the model in that the costs in the Memokath-051 arm are overestimated and the thus the cost savings underestimated, assuming that the risk of replacement of 25% over 2.5 years is valid.

The cost of training clinicians was not included in the model and justification for its omission was not given by the company. Clinical experts have stated that PNN Medical provide free training. In principle staff time to attend training should still be considered even if training is free to reflect the opportunity cost of staff attending the training. However the EAC judges the cost per patient is too small to warrant its inclusion in its model (see Section 4.2.6). Two clinical experts provided advice on how many stents would need to be inserted for a clinician to become competent with the procedure. One expert reported 20 stents and the other reported 5.

In addition, the cost of pain medication following stent insertion was omitted from both arms of the model. It is understood that all patients would receive pain medication (Table 2.1). Although this won't impact upon the initial insertion cost there will be an impact relating to different replacement rates. However, the cost of this is low hence the impact of this on the results of the model will be small.

The company's model did not capture benefits relating to reduced pain and improved quality of life with Memokath-051 (Maan et al., 2010). As part of a cost-consequence analysis the company might have reported these alongside its cost savings.

Discounting was not applied within the model for those costs incurred beyond year 1. The company stated that "no discount was calculated" (Section 9.1.8). This approach is valid for a budget impact model but not a cost-benefit analysis (CBA). The EAC has applied discounting in its revised model.

Sensitivity analyses were omitted from the company's submission. The company state that no sensitivity analysis was needed for the product (Section 9.4.1, Submission). Conducting sensitivity analyses around model input parameters would have allowed the company to determine the key drivers of the economic model. Further, the impact of the uncertainty around input parameters such as the 25% risk factor should have been explored.

Overall, whilst the company's *de novo* cost model captured the key aspects of treatment, it is simplistic in respect of certain structural issues. As a result, the EAC has developed a *de novo* model to explore the assumptions and criticisms above and assess their impact on the total costs. This additional work is described in Sections 4.2.5, 4.2.6 and 4.2.8.

4.2.3.1 EAC model structure

The EAC adapted the company's model to address the decision problem stated in the scope. The patients and interventions included in the EAC's model are aligned with the scope except the omission of nephrostomy as a comparator as no evidence was identified from the clinical review. The EAC's model compares Memokath-051 to the following: double-J stents, metallic stents (specifically UVENTA, Allium and Resonance) and reconstructive surgery. Costs were modelled over a 5 year time frame, reflecting the indwelling duration for Memokath-051 after which planned replacement is required according to the topic briefing (NICE, 2017b).

The EAC updated the model such that time was explicitly modelled by month meaning the break-even point between Memokath-051 and its comparators

could be determined. For Memokath-051, double-J stents and other metallic stents the following costs were considered:

- Initial insertion and replacement cost comprising device cost, consumable costs, staff costs, theatre costs and immediate follow-up costs for all patients;

- Ongoing follow-up for all patients;

- Unplanned replacement costs where necessitated by an adverse event. Costs included consumable costs, staff costs, theatre costs and immediate follow-up costs. The monthly risk of unplanned replacements was derived from the clinical studies; however, the follow-up of these studies was shorter than the time horizon of the model. Therefore, 3 extrapolation methods were considered: (1) the monthly risk of unplanned replacement was applied for the full time horizon of the model; (2) the monthly risk of unplanned replacement was applied for 2 years followed by no risk of unplanned replacement; (3) the monthly risk of unplanned replacement was applied for 2 years followed by a reduced risk of unplanned replacement. The latter 2 scenarios attempt to capture scenarios in which unplanned replacements occur early in the stents lifespan, rather than spontaneously occurring after the stent has been in situ with no complications for 2 years;

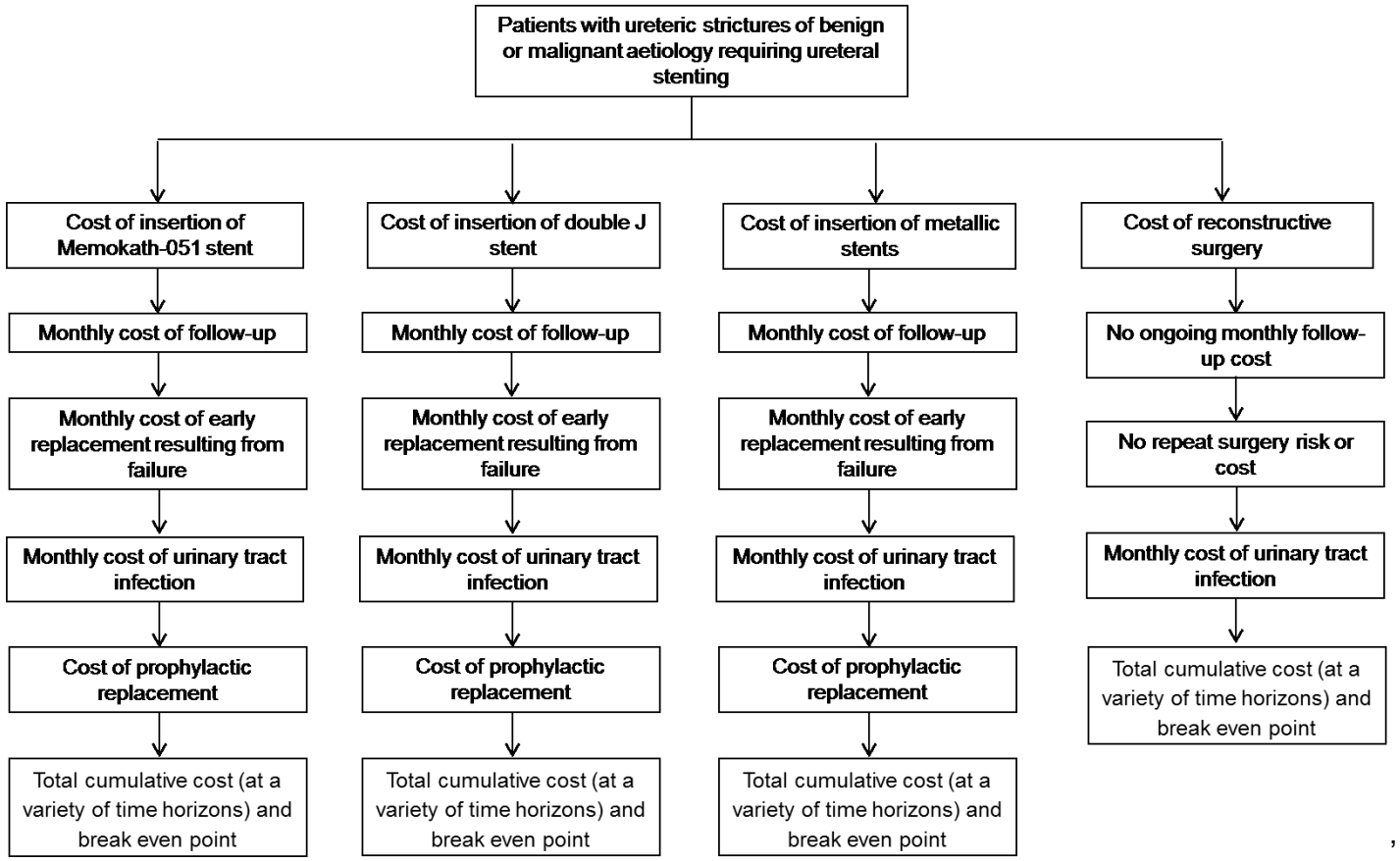
- UTI costs for those patients experiencing UTI. A monthly probability of UTI was estimated based upon the data reported in the clinical studies and converted assuming a uniform distribution (Drummond et al., 2015). Costs included a GP visit and antibiotics;

- Planned replacement for all patients as per an estimation of the number of patients requiring replacement based upon the instructions for use (IFU) for each comparator device.

As the patient pathway for surgery differs to the other comparators a different approach was followed. Patients underwent reconstructive surgery, the cost of which was applied. Further, all patients required post-surgery follow-up, the cost of which was assumed to be incurred in the first month following surgery as a simplifying assumption. According to expert advice, some follow-up visits will occur after 3 and potentially 12 months. The impact of applying these costs up front is very limited and relates to the discounting of the costs, only. No ongoing monthly follow-up costs were included as expert advice indicated that most patients will not have continued follow-up over time. All reconstructive surgery is assumed to be successful (i.e. no further procedures are required). In reality, some patients may require additional surgery; however the magnitude

of this could not be identified from either the literature or the experts. As such, a conservative assumption was made.

Figure 4.2: EAC model structure



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4.2.4 Summary of the base case

Results from the company's economic model were provided in Section 9.5 of the submission and were verified by the EAC. Results from the company's model are reported in Table 4.5. The company did not present the cost saving per patient; this was calculated by the EAC.

Table 4.5: Company's base case results as presented in the model

	Memokath-051	Double-J stent	Incremental cost per patient
Total cost of insertion and follow-up over 2.5 years	£3,781	£8,882	-£5,101
Risk factor	£945	N/A	£945
Total cost per patient over 2.5 years with calculation of risk	**£4,726**	**£8,882**	**-£4,156**

Whilst the EAC's replication of the company's calculations gave the same results as the company's model, these did not align with the results that the company reported in its submission (Section 9.5, Submission). Specifically, Appendix I gives the costs that differed between the company's model and the submission for the Memokath-051 arm of the model (Section 9.5.3, Submission). There were no discrepancies between the results reported in the model and submission of the double-J stent arm. The company overstated the overall cost for Memokath-051 over a 2.5 year time horizon by £144. This resulted in an understatement of the cost savings by the same value. The company reported savings of £4,012 (Section 9.5.2, Submission) as opposed to the correct value generated from their model, £4,156.

4.2.5 Clinical parameters and variables

A description and critique of the clinical parameters included in the company's model is now provided. Appendix O reports those adopted in the EAC's model, with differences between the company and the EAC highlighted.

A key clinical parameter modelled by the company in the Memokath-051 arm was to assume 25% of patients require a stent replacement over 2.5 years (see Section 4.2.3.1). Hence the pathway related cost of Memokath-051 over 2.5 years were increased by 25% to derive total cost. The company make no reference to any input from expert advisors in their submission. The EAC determined that a probability of replacement of 25% over 2.5 years is equivalent to a monthly probability of replacement of 0.89% using the method outlined by Drummond *et al*. (Drummond et al., 2015).

The review of clinical evidence (reported in Section 3) did not justify using this value. Nine studies reported on the probability of stent replacement (Agrawal et al., 2009, Arya et al., 2001, Bourdoumis et al., 2014, Kulkarni and Bellamy, 1999, Maan et al., 2010, Papadopoulos et al., 2010, Papatsoris and Buchholz, 2010, Zaman et al., 2011 {Kim, 2014 #225, Kim et al., 2014). In Table 4.7 the monthly unplanned replacement of Memokath-051 is reported by study and an overall value of 1.4% per month determined for use in the model's base case. This was derived by dividing the total number of stent replacements by the total number of patient months. Data from 2 studies were excluded from this analysis because the values required are not reported (Klarskov et al., 2005, Maan et al., 2010).

Table 4.7: Monthly unplanned stent replacement

Study	Mean follow-up (months)	Number of patients	Estimated total number of patient months	Total stent replacements
Kim (Kim et al., 2014)	13.6	10	136	**6**
Agarawel (Agrawal et al., 2009)	16	55	880	**14**
Arya (Arya et al., 2001)	18	11	198	**3**
Bourdoumis (Bourdoumis et al., 2014)	22.5	14	315	**2**
Kulkarmi (Kulkarni and Bellamy, 2001)	19.3	28	540.4	**6**
Papadopoulos (Papadopoulos et al., 2010)	14.3	13	185.9	**3**
Papatsoris (Papatsoris and Buchholz, 2010)	17.1	73	1,248.3	**15**
Total			**3,503.6**	**49**

Data from individual studies were adopted in sensitivity analyses reported in Section 4.4 using a range of 0.63% to 4.41% monthly probabilities of unplanned replacements with Memokath-051.

In the double-J arm of the company's model all double-J stents have a planned replacement every 6 months and there was no risk of an unplanned stent exchange. This is in line with clinical practice as reported by the clinical experts and a UK-based comparative study of Memokath-051 versus double-J stents. This study reported zero stent replacement and migration in the double-J arm (Maan et al., 2010). However, the duration of follow-up was not reported, hence the EAC were unable to use this head-to-head data to inform the parameter value for both arms of the study as the follow-up period is required to calculate the monthly probability used within the EAC model.

For the head-to-head comparison of Memokath-051 versus UVENTA, the EAC used data from a Korean comparative study to inform the rate of stent removal and replacement (Kim et al., 2014). This study was identified through the EAC clinical review (Section 3). Over a 13.6 month follow-up, the study reported a

probability of stent replacement of 43% (6 of 14 stents) for Memokath-051. This involved assuming that all migrated stents were replaced; an assumption verified by a clinical expert. This was converted to a monthly probability of 4.41% by the EAC. For UVENTA, patients were followed up for 12 months and the rate of stent replacement was 6%. This was converted to a monthly probability of 0.49% by the EAC.

For the separate head-to-head comparisons of Memokath-051 versus Allium and Resonance, no data were identified by the EAC for the rate of stent replacement for Allium and Resonance. The EAC used advice from 1 clinical expert to inform their assumption that the rate of stent replacement for Allium is equal to UVENTA, 0.49%. The clinical expert advised that the performance of Allium stents is superior to that of Memokath-051. For the Resonance stent, the EAC assumed that the rate of stent replacement was equal to Memokath-051 given the lack of evidence available. These assumptions were tested during sensitivity analyses. Reconstructive surgery had no risk of revision surgery as described in Section 4.2.8.

The stent replacement discussed above refers to replacement due to complications associated with the stent. However, planned replacement of the stent occurs as part of clinical practice as correctly implied by the company as they included the replacement of double-J stents every 6 months in its analysis. This is in line with the indwelling time reported in the NICE topic briefing and advice sought by the EAC from 2 clinical experts.

The company did not include planned stent replacement for Memokath-051, which was appropriate given the time horizon of its model. The indwelling time reported in the NICE topic briefing is 4 to 6 years for Memokath-051 and the company's IFU report an indwelling time of several years (NICE, 2017b, PNN Medical, 2016). The EAC has applied an indwelling time of 5 years (60 months) for Memokath-051 in its model.

For the UVENTA stent, the EAC used the indwelling time reported in the NICE topic briefing, 18 months (NICE, 2017b). The EAC were unable to verify this value as it was not reported in the manufacturer's IFU (TaeWoong Medical, 2016). A study identified through the EAC clinical review reported an indwelling time of 16 months for the UVENTA stent (Kim et al., 2014). However, the EAC recognises that this reported indwelling time would be driven by the duration of the study's follow-up and not the life span of the stent in situ.

The indwelling time for the Allium and Resonance stents was taken from the manufacturer's IFU to inform the EAC's model. These values were 36 and 12 months respectively (Allium Medical, 2016, Cook Medical, 2012). Given that reconstructive surgery corrects the ureteric stricture, no further planned reconstructive surgery is included in the EAC's model.

The EAC assumed a monthly probability of 0.4% for UTI for Memokath-051 and each stent comparator (double-J stents, UVENTA, Allium and Resonance). This was informed by the single-arm, UK-based study reported by Papatsoris on Memokath-051 (Papatsoris and Buchholz, 2010). No comparator data were available for other stents hence the EAC assumed that the probability would be equal between arms in the base case (this assumption was varied during sensitivity analysis). However, for the EAC's comparison of Memokath-051 versus reconstructive surgery, comparative data were available from a published abstract. The abstract reported that over a 42 month follow-up period the probability of UTI with Memokath-051 was 41% and for reconstructive surgery was 7% over the same follow-up period (Akbarov et al., 2017). The EAC converted these probabilities into monthly probabilities for inclusion in the EAC's model and these were 1.25% and 0.2% for Memokath-051 and reconstructive surgery, respectively.

4.2.6 Resource identification, measurement and valuation

This section provides a critique of the resource identification, measurement and valuation conducted by the company for use in its *de novo* economic model. This is summarised in Appendix J. All unreported parameters are assumed to be equal in the Memokath-051 and double-J arms of the company's model. Where discrepancies existed between the company's model and submission document, the input used within the model has been reported.

In Section 9.2.1 of the submission the company report that all of the cost data were derived from the clinical papers included in the clinical submission and an analysis produced by AUH (AUH). However, the costs included in the company's model were sourced solely from the AUH analysis. The company shared the business case document (a Microsoft PowerPoint® slide set) with the EAC. This document included a breakdown of the costs included in the company's model but did not identify the resource use and unit costs used to calculate the costs. Rather, the combined values were reported.

The company reported that the cost and clinical outcomes were not extrapolated beyond the study follow-up period because they state that, "it is all coming within the normal follow-up periods in the clinical submission".

Theatre staff and recovery costs with Memokath-051, double-J stents and other metallic stents

The cost of theatre staff was included in the company's model as a single cost. The source for this input was data provided by AUH. These costs are salary only and hence omit other staff related costs such as national insurance and superannuation and all overhead costs. The hospital data breakdown theatre staff costs by staff grade but did not report the staff time used to calculate the

cost of the staff for the procedure explicitly. The EAC has calculated the staff time required. Appendix K gives the breakdown of the theatre staff costs and duration provided by AUH. The same staff costs were used for both Memokath-051 and double-J stents. Expert advice verified that the composition of theatre staff included in the company's analysis was appropriate.

For all theatre staff apart from the surgeon, a procedure time of 4.5 hours was used in the company's model. Two single-arm studies conducted in a UK setting reported on the procedure time for the insertion of Memokath-051 (Section 3). Papatsoris *et al.* reported a procedure time of 23 minutes and Zaman reported 26 minutes (Papatsoris and Buchholz, 2010, Zaman et al., 2011). Two clinical experts advised a procedure time of 45 minutes with Memokath-051. The experts also provided comparative information for the other stent types. Therefore, the EAC adopted a procedure time of 45 minutes for the insertion of Memokath-051 based upon the experts (enabling a like-for-like comparison with other stents).

No included clinical studies reported on the procedure time for insertion of double-J stents and metallic stents within the UK setting. Advice from 2 clinical experts was that the insertion of double-J stents takes 15 minutes and 30 minutes (average of 22.5 minutes) and the insertion of metallic stents takes 30 minutes and 45 minutes (average of 37.5 minutes). Within its model, the EAC updated the staff costs used in the analysis to reflect the revised procedure time as reported in Appendix L.

The company assumed all cases were day cases which is consistent with EAC's expert advice and the EAC's base case. In the EAC's sensitivity analysis all patients were assumed to have the procedure during an elective admission.

The company included the cost of recovery staff (bands 5 and 6) in their cost of theatre staff. The EAC also included such a cost for all patients undergoing any procedure, as well as addition time spent in hospital, with detailed costings reported in Appendix M.

Theatre consumables with Memokath-051

The cost of theatre consumables was calculated from data provided by AUH (see Appendix N). The cost modelled was £1,874 which included a cost of the device of £1,630 giving other costs of £244. The device cost is discussed in detail below (under the heading Memokath-051). A slight discrepancy of £1 was identified between the AUH cost breakdown and the modelled value.

Given the lack of evidence to validate the cost of £244 the EAC judged this value is appropriate and the cost year, although not stated, was assumed to be 2016. The EAC used a value of £243 due to the £1 discrepancy between the

bottom-up costing from the data and the value used in the company's model. This value was also applied to the other metallic stents based upon input from clinical experts and a comparator device company (correspondence log).

Theatre consumables with double-J stents

The cost included in the model was £109 which comprises a £60 cost for a double-J stent and theatre consumables of £49. Neither the company, nor the information provided from AUH described the consumables included in this cost. The EAC estimates that the resources costed are a cystoscopy pack, instilagel, 20ml syringe and sensor guidewire given that the summation of these unit costs is £49. The individual costs for these items are given in Appendix N. The EAC agrees with adopting £49 for this element and assumed that the cost year is 2016. It applied this value to the double-J stents only.

The cost of the double-J stent is described separately under the 'technology cost' heading below.

Procedure code/surgery tariff

The company included a cost for the procedure code/surgery tariff of £34 in the Memokath-051 arm and £407 in the double-J stent arm in their model but did not explain why this was included. This cost is not appropriate as the hospital provider does not incur this cost.

Follow-up costs with Memokath-051

The follow-up cost applied in the company's model for Memokath-051 was £285 for 1 year. This cost includes 2 outpatient appointments, 1 X-ray and 1 renogram appointment (company's bottom-up costing is given in Appendix N). These cost were sourced from the AUH data. Based upon expert advice, the EAC included a follow-up visit within the same month as insertion for a renogram (£255) and further follow-ups applied as a monthly cost (£42.50), reported in Appendix O.

Follow-up costs with double-J stents

The company applied a follow-up cost of £100 for 2 X-rays with double-J stents every 6 months. This cost was not included in the AUH data and the EAC judges this is unnecessary given that all double-J stents are replaced every 6 months. The company did not clarify this follow-up cost in either their submission or during follow-up questions (correspondence log). The EAC included 1 follow-up visit as advised by the clinical experts (£105), detailed in Appendix O.

Cost of complication risk with Memokath-051

The cost of an unplanned stent exchange in the Memokath-051 arm was calculated based upon 25% of the pathway related cost over 2.5 years. As discussed in Section 4.2.3, the EAC suggests that this cost has been calculated incorrectly given the time horizon of 2.5 years adopted by the company. The revised EAC cost is reported in Appendix O.

Cost of complication risk with double-J stents

The company assumed the cost of complications in the double-J arm was zero given that no unplanned replacement occurs. This was judged appropriate given that double-J stents have a planned replacement every 6 months. The company's cost of planned replacement was judged high by the EAC, due to a long procedure time, as reported in Appendix O.

4.2.6.1 Technology and comparators' costs

The cost of the Memokath-051 and double-J stent devices are shown in Table 4.8.

Table 4.8: Device costs used in the company's model

Variable	Value	Source	EAC comment
Cost of Memokath-051	£1,630	AUH (AUH)	This cost is £60 lower than the list price of £1,690 provided by the company
Cost of double-J stent	£60	AUH (AUH)	This cost is deemed appropriate based upon the range of costs available from NHS supply chain

Cost of Memokath-051

The company modelled a value of £1,630 (AUH), but provided a list price of £1,690 (Section 9.3.5, Submission). The company was asked to justify this difference (Section 9.3.6, Submission), but incorrectly replied that the same price was used. The EAC sought further clarification, whereby the company confirmed the list price of £1,690 (correspondence log). This price was used by the EAC in its analysis.

The EAC has not included the cost of training in its analysis as it is negligible (estimated cost of under £160 given duration of 1.5 hours as reported by a clinical expert and cost of £105 per hour (Personal Social Services Research Unit (PSSRU), 2016)). This cost would be divided by the number of insertions over the surgeon's lifetime. Moreover, Memokath-051 and double-J stents have been available for a number of years and so surgeons using the device may already be trained.

A training cost has not been applied to the other metallic stents given that the cost per patient is also likely to be negligible.

Cost of double-J stents

The cost of the double-J stent was not stated in the company's model or the submission. From the data from the AUH, the EAC has identified that the cost of the double-J stent used was £60 (included within the cost of theatre consumables within the company's model) (AUH). This value is judged reasonable given the range of costs available for double-J stents on NHS supply chain. An expert reported that the brand used depends upon the company that the hospital currently has an agreement with.

4.2.7 Sensitivity analysis

The company did not include any sensitivity analyses in their submission. In Section 9.5.10 (Submission) the company noted that the key drivers of the model are the cost of stents versus the in situ time of the stent. However, this statement was not backed by any evidence in the model or its submission. The EAC judged that sensitivity analysis should have been conducted to assess the impact of parameter uncertainty on the results of the model.

The EAC conducted sensitivity analysis. The ranges used by the EAC are reported in Appendix S.

4.2.8 Table of full EAC revisions to the company's model

As described in Sections 4.2.4 and 4.2.5, the EAC disagreed with some of the input parameters and assumptions used by the company within its *de novo* cost analysis. The EAC updated a number of the input parameters and added additional inputs. Appendix O provides the company and EAC values and assumptions for all of parameters and highlights differences between the values. The grey-shaded rows at the bottom of the table give the total cost of insertion, follow-up, replacement and UTI. The breakdown of these costs are given earlier in the appendix. Table 4.9 provides a summary of the inputs used by both the company and the EAC for each comparator.

Table 4.9: EAC revisions to the company's model (full details and references in Appendix O)

Parameter	Memokath-051	Double-J stent	UVENTA	Allium	Resonance	Reconstructive surgery
Length of time in situ (no complications)	Company = 30 months	Company = 6 months	Company = N/A	Company = N/A	Company = N/A	Company = N/A
	EAC = 60 months	EAC = 6 months	EAC = 18 months	EAC = 36 months	EAC = 12 months	EAC = N/A
Monthly risk for unplanned stent removal and replacement	Company = 0.95% (reported as 25% over 30 months)	0%	N/A	N/A	N/A	N/A
	EAC = 1.4% (4.41% versus UVENTA)	0%	0.49%	0.49%	1.4%	N/A
Monthly risk of UTI	Company = N/A	N/A	N/A	N/A	N/A	N/A
	EAC = 0.42% (1.25% versus surgery)	0.42%	0.42%	0.42%	0.42%	0.17%
Total cost of insertion	Company = £3,068	£1,676	N/A	N/A	N/A	N/A
	EAC = £3,010	£786	£2,736	£2,936	£2,148	£7,414 (includes all follow-up costs)
Monthly follow-up cost	Company = £23.75	£16.67	N/A	N/A	N/A	N/A
	EAC = £42.50	£0	£42.50	£42.50	£21.25	N/A
Total cost of replacement	Company = £3,781	£1,676	N/A	N/A	N/A	N/A
	EAC = £3,347	£1,052	£3,157	£3,357	£2,569	N/A
Cost of UTI	Company = N/A					
	EAC = £37.32					

4.3 Interpretation of economic evidence

The company reported that there is no difference between the results of their cost analysis and the published economic literature apart from an update to the current market price of Memokath-051 (Section 9.8.1, Submission). It is unclear which study the company refers to; however, the EAC assumes that this is the AUH analysis (AUH). If so, the company's statement is incorrect in that the current market price of Memokath-051 was not used by the company. Rather, the only difference between the company's model and the AUH analysis is the inclusion by the company of a 25% replacement risk.

The company raised no issues of generalisability of the results of their cost analysis and reported that their cost analysis is relevant to all groups of patients and NHS settings in England that could potentially use the technology as identified in the scope (Section 9.8.2, Submission). However, the company's model assumes that all patients will be alive and requiring a stent after 2.5 years and can thus benefit from Memokath-051 for the full time horizon of the model. Some patients with malignant strictures may have a life expectancy of less than 2.5 years, as discussed in Section 2.1.2.

Further, the company deviated from the scope in the comparators and subgroups considered. Only double-J stents were considered as a comparator within the model. Hence, the cost-consequences versus other metallic stents, nephrostomy and reconstructive surgery are unknown. No subgroups were analysed by the company. This may result from a paucity of evidence; however, this was not discussed by the company.

The company was given the opportunity to describe the main strengths and weaknesses of its cost analysis (Section 9.8.3, Submission). In its response it noted that "the product is very simple so there is no deep analysis for the cost related issues", adding this is the reason why it "tried to use the max safety for calculations to show the maximum cost effectiveness over time comparted with the comparator". The company did not explain how this may affect the interpretation of the results. The EAC calculated the 25% risk of replacement over 2.5 years is equal to a monthly risk of 0.95%. This is lower than the values used by the EAC based upon the clinical evidence reported in Section 3 and hence the company's assumption is not judged to be conservative.

The company suggested that updating the parameters to the most recent values available would enhance the robustness/completeness of the results. As reported in Sections 4.2.2 and 4.2.8, the EAC judges that other amendments are required to improve robustness and completeness. Namely, additional comparators could have considered, more accurate values for replacement of stents and costs used and additional adverse events considered. The amendments have been made by the EAC and are reported in Section 4.3.

4.4 Results of EAC analysis

Base-case analysis results

As stated in Section 4.1.2, various scenarios have been considered within the EAC's analysis relating to unplanned stent replacement (for all stents). These are:

- Constant unplanned replacements over a 5 year time horizon, i.e. the monthly risk of replacement from the clinical studies is applied over the full time horizon of the model;
- Constant unplanned replacements for the first 2 years, followed by no unplanned replacements thereafter;
- Constant unplanned replacements for the first 2 years, followed by a halved risk of unplanned replacements thereafter;
- Constant unplanned replacements over a 2 year time horizon.

Memokath-051 versus double-J stents

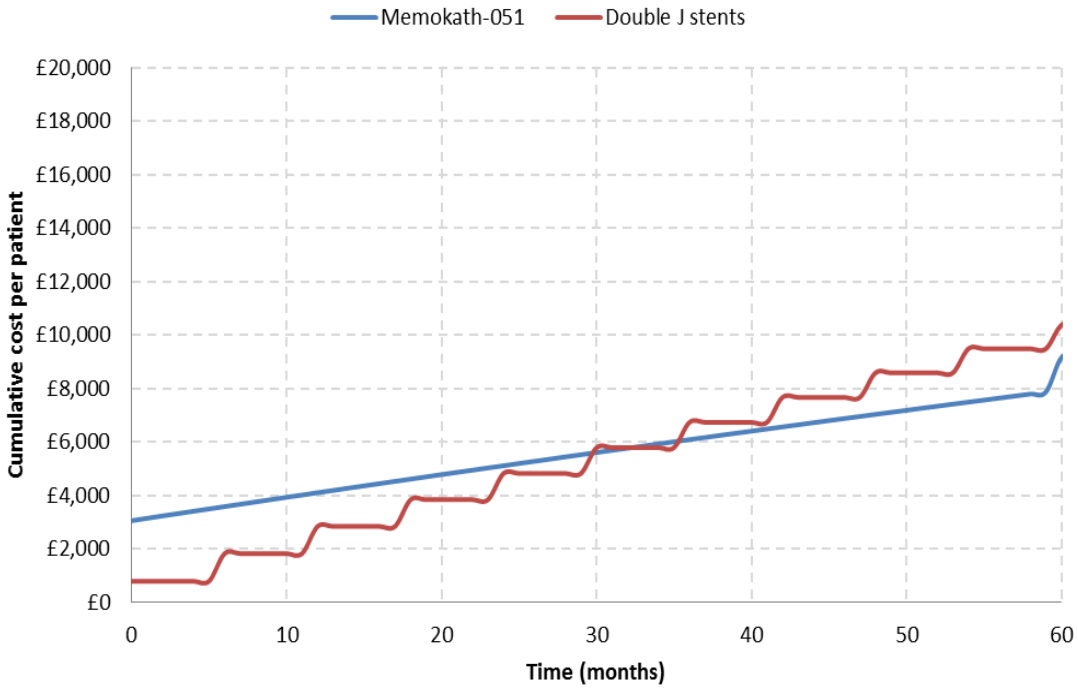
The full results for all 4 scenarios are presented in Appendix P. In all scenarios with a 5-year time horizon Memokath-051 is cost saving compared with double-J stents. A breakdown of the costs associated with Memokath-051 and double-J Stents is provided in Table 4.10, and a breakdown of the costs over time presented in

Figure 4.3 based upon the most conservative results (i.e. constant risk of replacement over full 5 year time horizon). The breakeven point between Memokath-051 and double-J stents is 30 months in all scenarios.

Table 4.10: EAC's base case results by component (per patient over 5 years)

	Memokath-051	Double-J Stents	Incremental cost
Total insertion cost	£3,010	£786	£2,224
Follow-up cost	£2,346	£0	£2,346
Unplanned replacement cost	£2,503	£0	£2,503
Planned replacement cost	£0	£8,692	-£8,692
Adverse event cost	£9	£9	£0
Total	**£7,868**	**£9,487**	**-£1,619**
Breakeven point = 30 months			

Figure 4.3: Costs over time Memokath-051 vs Double-J Stents



Memokath-051 versus reconstructive surgery

When comparing Memokath-051 to reconstructive surgery, the incremental cost per patient after 5 years ranged from £467 to -£1,009 depending upon the assumptions made around the extrapolation of unplanned replacement of Memokath-051 stents. Compared with surgery, Memokath-051 is cost saving up to 53 months, suggesting that if costs are the only criterion the Memokath-051 is the optimal choice for patients with a lower life expectancy. Reconstructive surgery would be the preferred option for patients able to tolerate it and anticipated to live longer than 4.5 years. Full results are presented in Appendix Q.

Memokath-051 versus other metallic stents

The key factor in comparisons between Memokath-051 and other metallic stents is the planned stent replacement for each comparator. Appendix R presents the costs over time of Memokath-051 versus the alternative metallic stents (with constant replacement over time and no replacement after 2 years). Over time, the lines on these graphs consistently cross. Therefore, Memokath-051 is judged to be cost neutral compared to UVENTA and Allium in the worst case, but may generate cost savings with more positive assumptions (i.e. no unplanned replacements after 2 years). Compared with Resonance, Memokath-05 was cost saving after 12 months. However, for both Allium and

Resonance the EAC stresses that these results should be interpreted with caution as they are based on assumptions not comparative clinical data.

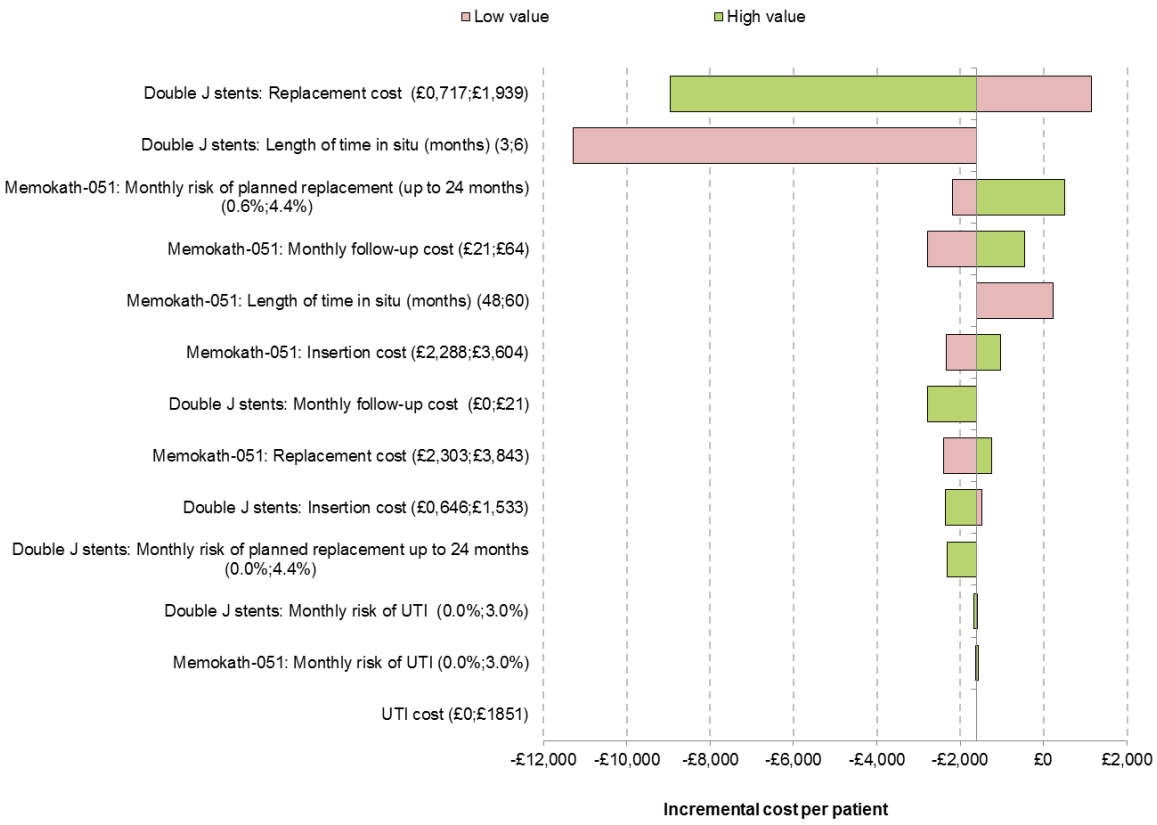
Sensitivity analysis results

The EAC identified a plausible range for each input parameter and varied the input parameter within this range. The parameters and ranges of values used for the EAC's sensitivity analyses are given in Appendix S.

Univariate sensitivity analyses were conducted with Memokath-051 versus double-J stents. The results are presented in Figure 4.4 for the scenario with a constant risk of unplanned replacement over 5 years given that these results are the most conservative. These results are sensitive to the procedure costs to replace double-J stents and the risk of unplanned replacements with Memokath-051. Where the replacement procedure cost for double-J stents is below £860 or the monthly risk of unplanned replacements with Memokath-051 above 3.6% per month Memokath-51 is cost incurring. A replacement cost of less than £856 is consistent with a procedure time of 38 minutes of less. This may be plausible for uncomplicated procedures, but is likely to be less than the average procedure time. A monthly risk of replacement of above 4% was only reported in 1 non-UK study (Kim et al., 2014). All of the remaining studies reported monthly risk of replacements of 1.6% or below, hence a risk of 3.6% or above is considered unlikely.

The break-even month ranged from month 9 to never cost saving (where the replacement procedure cost for double-J stents takes its lowest value) during the time horizon of the model. In all univariate analysis except those varying the procedure costs to replace double-J stents and the risk of unplanned replacements with Memokath-051, break even occurs by month 42 (see Figure 4.4).

Figure 4.4: Tornado diagram based on EAC sensitivity analysis



Sensitivity analysis against the remaining comparators are summarised and are reported in full in Appendix S. Compared with reconstructive surgery in the worst case scenario (i.e. constant risk of unplanned Memokath-051 replacement over 5 years) the model is highly sensitive to many input values. In the best case scenario (i.e. no risk of unplanned replacement after 2 years) the model is most sensitive to the cost of surgery, the risk of unplanned replacement up to 24 months and the planned time in situ. Compared with the other metallic stents, results were most sensitive to the risk of unplanned replacement with Memokath-051 stents. In the best case scenario, results were typically favourable to Memokath-051, whilst in the worst case there was far more uncertainty.

Subgroup analysis

The EAC did not identify appropriate data during the clinical review (Section 3) to conduct subgroup analysis. In Table 3.12 the EAC has extracted relevant information from studies reporting on malignant and benign patients independently. The data, particularly comparative data, are very limited and as such the EAC agrees with the company's judgement that there is a paucity of information to inform any subgroup analyses.

Model validation

The company reported that its model was validated in that it was designed to emulate the clinical pathway presented in the AUH analysis. The EAC judges that as the company's model was based on this analysis the company's model is externally validated against it.

The EAC's model was internally and externally validated. All input parameters were cross checked and verified by a second health economist, and all model calculations were hand checked by a colleague independent from the project. Its results were compared against published sources where they existed, i.e. comparing Memokath-051 with double-J stents. In line with these sources, the EAC found the Memokath-051 generated cost savings provided that it is in situ for a long enough period. For the remaining comparisons the EAC was unable to identify any external sources against which to validate its results. Rather, the EAC considered the clinical consequences, e.g. number of unplanned replacement stents, to confirm that were reasonable based upon clinical studies.

4.5 EAC Interpretation of economic evidence

The results of the EACs analysis comparing Memokath-051 to double-J stents is reported in Table 4.11. Memokath-051 was always cost-saving but the magnitude changed. The EAC's savings with Memokath-051 were seldom as high as the company's (£4,156).

The impact of individual changes made by the EAC on the results reported by the company are also reported in Table 4.11. Given the change in model structure by the EAC, the impact of some changes could not be assessed.

Table 4.11: Impact on the cost difference between the technology and comparator of additional clinical and economic analyses undertaken by the EAC

Action	Incremental cost per patient	Change from company's base case	Percentage of base case cost saving	Impact of action (compared with the company's base case incremental cost of -£4,156 per patient)
Company's base case result (Memokath-051 versus double-J stents at 2.5 years)	**-£4,156**	**N/A**	**N/A**	**N/A**
Risk factor for stent replacement (using EAC's monthly risk of unplanned replacement converted to a risk over 2.5 years = 34.5%)	-£3,797	£359	91%	The incremental cost per patient decreased as the risk factor for Memokath-051 stent replacement increased to the higher EAC value meaning there are more unplanned replacements
EAC insertion cost for Memokath-051 = £3,010	-£4,229	-£73	102%	The incremental cost per patient increased as the cost of insertion of Memokath-051 reduced to the lower EAC value making Memokath-051 cheaper
EAC insertion cost for double-J = £680	£826	£4,982	-20%	The incremental cost per patient changed substantially and Memokath-051 became cost-incurring as the cost of insertion of the double-J stent reduced to the lower EAC value
EAC unplanned replacement cost for Memokath-051 = £3,347	-£4,265	-£109	103%	The incremental cost per patient increased as the cost of unplanned replacement of Memokath-051 reduced to the lower EAC value hence unplanned replacement has less impact on the overall costs
EAC planned replacement cost for double-J (with no follow-up cost) = £1,052	-£1,259	-£2,897	30%	The incremental cost per patient reduced substantially as the cost of planned replacement of double-J stents reduced to the lower EAC value reducing overall cost for double-J stents
All changes made simultaneously including those not reported above (EAC base case)	**-£1,619**	**-£2,537**	**39%**	The change in the incremental cost per patient is driven heavily by the reduction in the cost of insertion of the double-J stent within the EAC's base case analysis. This is largely driven by the updated procedure time used by the EAC

5 Conclusions

5.1 Conclusions on the clinical evidence

The EAC conducted a full critique of the company's clinical review and identified significant limitations across the methodology and results. In its submission, the company identified and included 6 publications, which reported on 5 studies. The EAC conducted new searches for relevant evidence. Following study selection, 16 studies reported in 22 records were included by the EAC, including the 5 studies that were included by the company.

The clinical evidence comprises:

- 6 comparative studies (2 reported as full-text publications, 3 reported as an abstract and 1 presented in a clinical trial record), which compared Memokath-051 to 1 of 5 comparators; namely, IUR, double-J stents, UVENTA stents, Allium stents and Resonance stents;
- 10 single-arm, observational studies (each reported as a full-text publication).

Recognising the lack of quality RCT evidence, all of the comparative and 8 single-arm studies were considered to be of sufficient quality and substance to provide relevant results. Two of the single-arm studies were deemed to not provide acceptable levels of external validity and had low internal validity, hence their results were discounted.

Reporting was generally poor across all of the included studies. Limited details were provided by authors about patient characteristics, stent insertion procedures, follow-up, statistical analysis and uncertainty around the results. As a result, there was insufficient information available for the EAC to accurately assess the heterogeneity across studies. The most common outcomes reported by studies were clinical success and rates of migration. Clinical success, however, was not consistently defined across the studies, which meant statistical pooling could not be conducted.

In the comparative studies, Memokath-051 had a lower clinical success rate than Allium stents (81% vs 100%) (Bolton et al., 2015), UVENTA (43% vs 82%, p= 0.31) (Kim et al., 2014) and IUR (35% vs 89%) (Akbarov et al., 2017) but was comparable to double-J stents (100% success rate in both arms) (Granberg et al., 2010) and Resonance stents (82% and 86% for Memokath-051 and Resonance stents respectively) (Nam et al., 2015). Only 1 study reported details of statistical significance. The difference observed between UVENTA and Memokath-051 was not statistically significant (Kim et al., 2014).

In a pooled analysis of the Memokath-051 treatment arms, 16.3% of stents were removed, 16% were removed and replaced, 17.7% migrated and 6.9% became encrusted. No data were available for any of the comparator stents in relation to stent removal and replacement. No migration data were reported for double-J stents or Allium stents. One stent (5.9%) in the UVENTA group migrated compared to 6 in the memokath-051 arm of that trial (p=0.004).

Memokath-051 is judged acceptable to patients and evidence from a well conducted study with acceptable external validity supports improved quality of life (Maan et al., 2010).

Insufficient evidence was identified to inform any subgroup analysis of patients unfit for surgery or antegrade or retrograde insertion. There were no data reported on number and rate of repeat procedures requiring anaesthesia and surgery. There was limited comparative evidence for Memokath-051 compared to double-J stents, reconstructive surgery (IUR) and other metallic and alloy stents (UVENTA, Allium and Resonance) and no evidence was identified for nephrostomy.

Overall, the entirety of the low quality evidence suggests Memokath-051 has similar success rates compared to double-J stents and Resonance stents but had worse outcomes than the other devices. The most commonly reported adverse event associated with Memokath-051 was stent migration which occurred more frequently in Memokath-051 than in any of the comparators assessed.

This review has been informed by mainly small, poorly reported, observational studies and for that reason there is material uncertainty around these data, with only 2 comparative studies judged to have acceptable internal and external validity. Hence the results and conclusions could change in the light of further studies. Although the observational nature of the studies may be more reflective of real life, due to the heterogeneity across them it is difficult to draw reliable conclusions. A large, well conducted RCT or prospective comparative study would improve the evidence base and provide more reliable estimates of the efficacy and safety of these devices.

5.2 Conclusions on the economic evidence

The company included 3 economic studies, only 1 of which (AUH) the EAC judged suitable for inclusion and it identified 2 other relevant studies from its own literature search (AUH, Gonzalez et al., 2011, Zaman et al., 2012)). The studies were poorly reported, but indicated that Memokath-051 is likely to be cost saving versus double-J stents provided that it remains in situ for sufficient time. No evidence on the cost-effectiveness of Memokath-051 versus any other comparator was identified.

The *de novo* model submitted by the company was not executable and reported results based on an unpublished analysis comparing Memokath-051 to double-J stents (AUH). The model had a 2.5 year time horizon, captured the key differences between the 2 stent types (namely the cost of insertion, planned replacements with double-J stents and unplanned replacements with Memokath-051) and reported savings of £4,156 per patient with Memokath-051. No sensitivity analyses were conducted. It did not fully address the scope, excluding comparisons to nephrostomy, reconstructive surgery and other metallic stents.

The EAC replicated the company's model making it fully executable and modified it to improve its usefulness. Changes included:

- Extending the time horizon to 5 years;
- Facilitating the model to report a break-even time point between Memokath-051 and it's comparators;
- Including reconstructive surgery and other metallic stents as comparators. A paucity of data precluded the inclusion of nephrostomy;
- Including the risk of UTIs;
- Revising some inputs used by the company as reported in Appendix O;
- Introducing scenario analysis to model the risk of unplanned replacement of Memokath-051 stents in 4 scenarios. In the worst case, the monthly risk of unplanned replacement for Memokath-051 was assumed constant across the 5 year time horizon, whilst in the best case there was no risk of unplanned replacement after 2 years;
- Introducing deterministic sensitivity analyses.

In the revised comparison against double-J stents, in the worst case scenario, the estimated savings per patient were £1,619 over 5 years, increasing to £3,095 with the best-case scenario. Across all scenarios, break even occurred at month 30 indicating that should the patient require a stent for 30 months or greater then, using cost as the decision factor, Memokath-051 should be preferred over double-J stents. The results were robust to the univariate sensitivity analysis conducted whereby the values taken to generate cost incurring results appeared improbable based on the information available.

Results from the EAC's model suggest Memokah-051 is likely to be cost neutral compared with other metallic stents (namely UVENTA, Resonance and Allium). There were very limited clinical data to inform results for the comparisons with Resonance and Allium and hence the results are uncertain and could change with new clinical evidence. Compared with reconstructive surgery, Memokath-051 was reported to be cost saving at 5 years, with results being most sensitive to the planned time in situ for Memokath-051. Hence Memokath-051 is a cost-

effective alternative for patients requiring stent duration below the planned replacement time for Memokath-051.

There are limitations associated with the economic analyses conducted by both the company and the EAC. Firstly, the low quality of the clinical evidence in terms of the paucity of comparative data for some alternatives and the low quality of studies impacts the quality of the economic analysis. Secondly, no data were available to support any comparison with nephrostomy. Thirdly, no benefit was attributed to the improved quality of life and reduced pain associated with Memokath-051 compared to double-J stents. These were reported in a comparative clinical study (Maan et al., 2010) and supported by an expert. Fourthly, there are uncertainties around the clinical management and hence costs arising, in part because of variation in practice. Moreover, it was not possible to capture any organisational issues that may arise if 1 stent is required for only a few patients per year in a specific hospital, noting the company judged Memokath-051 may benefit only 2,900 patients annually.

Finally, no subgroup analysis was possible, hence the relative cost-effectiveness of Memokath-051 across its various indications is unknown. The EAC has attempted to mitigate against this by reporting the break-even point, allowing decision makers to determine whether or not Memokath-051 is a cost-effective alternative based upon life expectancy. The EAC understands from the experts that the population within this scope are heterogeneous particularly in terms of their life expectancy. Therefore, all comparators are unlikely to be feasible treatment options for all patients. As such, patient selection is likely to be key. Based on the EAC's cost analysis, only, it appears that double-J stents are likely to be cost saving for patients with a life expectancy of less than 30 months and surgery for patients with a life expectancy beyond 4.5 years. Hence, there is a 2 year window (30–53 months following insertion) in which Memokath-051 is cost saving. Other metallic stents may also be plausible treatment options based on overall costs for these patients.

6 Summary of the Combined Clinical and Economic Sections

The current evidence base informing the EAC's assessment is mainly small, poorly reported, observational studies meaning that all conclusions are uncertain and could alter with new evidence. Compared with double-J stents, Memokath-051 appears to be have similar success rates and improved patient related quality of life. The cost analysis estimates Memokath-051 to generate cost savings with a break-even point at month 30. Therefore, on the basis of cost Memokath-051 would be the preferred choice for patients with a life expectancy of 30 months or greater. The additional patient benefits around quality of life may warrant its use in patients with a shorter life expectancy.

The modelled results suggests Memokath-051 and UVENTA have similar costs over 5 years. Results comparing Memokath-051 to Allium and Resonance suggest that Memokath-051 may be cost saving but there is greater uncertainty around these because of the poor clinical evidence. No comparative evidence reporting on quality of life were available.

Compared with reconstructive surgery, Memokath-051 is estimated to be cost saving if no planned replacement is necessary. However, if after 5 years, replacement is required then surgery (where possible) is the more cost-effective option. Given that reconstructive surgery aims to be curative then for patients with a longer life expectancy who are able to tolerate major surgery the experts advise that surgery should always be considered.

No data were available comparing Memokath-051 to nephrostomy, hence a comparison of clinical or cost effectiveness is not possible.

To conclude, Memokath-051 appears to be a plausible treatment option in patients who are not indicated for reconstructive surgery and who are expected to require a ureteral stent for at least 30 months. The careful selection of patients is consistent with expert opinion as reported at Section 2.1.2 in the clinical overview.

7 Implications for Research

There were a number of gaps within the evidence base for Memokath-051 leading to uncertainty within this assessment. There was limited comparative evidence for Memokath-051 compared to double-J stents, reconstructive surgery and other metallic and alloy stents (UVENTA, Allium and Resonance) and no evidence was identified for nephrostomy.

In order to overcome the remaining uncertainties within the EAC's conclusions further evidence would need to be collected. Such a study should ideally have the following design:

- RCT or prospective comparative studies;
- Clearly defined eligibility criteria to ensure that the patients in each of the treatment groups are comparable;
- Comparing Memokath-051 to:
    - Other metallic stents (specifically Resonance, Allium and UVENTA);
    - Nephrostomy.
- Adequately powered with predefined outcomes and estimates of clinical effect and resource utilisation;
- Outcomes including clinical success, procedure duration, length of stay, number of stent replacements and removals, length of time stent

is in situ, quality of life outcomes and rates of adverse events (including migration and encrustation);

- Pre-defined subgroup analysis comparing patients with benign and malignant strictures and antegrade vs retrograde insertion.

Auditing decisions to use double-J and Memokath-051 stents could be used to understand reasons for non-adoption more clearly.

References

Abdallah, M.M., Selim, M. & Abdelbakey, T. 2013. Thermo-expandable metallic urethral stents for managing recurrent bulbar urethral strictures: To use or not? *Arab Journal of Urology*, 11 (1), 85-90.Available: http://www.sciencedirect.com/science/article/pii/S2090598X12001672

Agrawal, S., Brown, C.T., Bellamy, E.A. & Kulkarni, R. 2009. The thermo-expandable metallic ureteric stent: an 11-year follow-up. *BJU International*, 103 (3), 372-6.Available: https://dx.doi.org/10.1111/j.1464-410X.2008.08018.x

Akbarov, I., Al-Mahmid, M., Pfister, D. & Heidenreich, A. 2017. Upper Urinary Tract Decompression Using Ileal Ureter Replacement in Comparison to Endoureteral Thermoexpandable Stent [Memokath 051]. *Journal of Urology*, 197 (4), E303-E304

Al Aown, A., Iason, K., Panagiotis, K. & Liatsikos, E.N. 2010. Clinical experience with ureteral metal stents. *Indian J Urol*, 26 (4), 474-9.Available: https://www.ncbi.nlm.nih.gov/pubmed/21369375

Allen, D.J., Longhorn, S.E., Philp, T., Smith, R.D. & Choong, S. 2010. Percutaneous urinary drainage and ureteric stenting in malignant disease. *Clinical Oncology*, 22 (9), 733-739.Available: http://dx.doi.org/10.1016/j.clon.2010.07.004

Allium Medical. 2012. *The URS-Ureteral Stent* [Online]. Available: http://www.allium-medical.com/uploads/images/bto/URS.PDF [Accessed 18th May 2017].

Allium Medical 2016. *Allium Ureteral Stent (URS): Instructions for use*. Available: http://www.allium-medical.com/uploads/images/IFU%20for%20URS-243-0217-Brochure.pdf

Armatys, S.A., Mellon, M.J., Beck, S.D.W., Koch, M.O., Foster, R.S. & Bihrle, R. 2009. Use of Ileum as Ureteral Replacement in Urological Reconstruction. *The Journal of Urology*, 181 (1), 177-181.Available: http://www.sciencedirect.com/science/article/pii/S0022534708024373

Arya, M., Mostafid, H., Patel, H.R., Kellett, M.J. & Philp, T. 2001. The self-expanding metallic ureteric stent in the long-term management of

benign ureteric strictures. *BJU International*, 88 (4), 339-42.Available: https://www.ncbi.nlm.nih.gov/pubmed/11564017

AUH Cost-effectiveness of using permanent Memokath Stent (MMK) compared to JJ stent. Aintree University Hospital.

Azizi, A., Pasticier, G., Bénard, A., Lapouge, O., Ferrière, J.M., Ballanger, P. & Robert, G. 2012. Tolerance and effectiveness of Memokath® 051 ureteral stents : a prospective 3 year follow-up study. *Prog Urol.*, 22 (5), 266-72

Bach, C., Kabir, M.N., Goyal, A., Malliwal, R., Kachrilas, S., El Howairis, M.E., Masood, J., Buchholz, N. & Junaid, I. 2013. A self-expanding thermolabile nitinol stent as a minimally invasive treatment alternative for ureteral strictures in renal transplant patients. *Journal of Endourology*, 27 (12), 1543-5.Available: https://dx.doi.org/10.1089/end.2013.0180

Bach, C., Moraitis, K., Pullis, C., Massod, J., Junaid, I. & Buchholz, N. 2011. Management of ureteric strictures with nickeltitanium ureteric stents with thermal-shape memory: A comparison of the outcome between benign and malignant strictures. *European Urology, Supplements*, 10 (2), 223.Available: http://dx.doi.org/10.1016/S1569-9056%2811%2960686-6

Barts Health NHS Trust. 2012a. *Preparing for your endopyelotomy* [Online]. Available: https://bartshealth.nhs.uk/media/163525/Urology-Surgery%20-%20Preparing%20for%20your%20endopyelotomy.pdf [Accessed 22nd May 2017].

Barts Health NHS Trust. 2012b. *Preparing for your retrograde ureteric stent* [Online]. Available: https://bartshealth.nhs.uk/media/163545/Urology-Surgery%20Preparing%20for%20your%20retrograde%20ureteric%20stent.pdf [Accessed 11th May 2017].

Bolton, E.M., Considine, S., Moran, D., Siddiqui, R., Cham, A., Nusrat, N., Durkan, G., Rogers, E., Walsh, K. & Jaffry, S. 2015. Tailored length permanent stents for the treatment of ureteric obstruction. *BJU International*, 116, 25.Available: http://dx.doi.org/10.1111/bju.13221

Boston Scientific. 2014. *Percuflex Ureteral Stent Set: Prescriptive Information* [Online]. Available: http://www.bostonscientific.com/content/dam/bostonscientific/uro-wh/portfolio-group/prescriptive-information/URO-238208-AA_Percuflex_Stent_Prescriptive_Information-FINAL.pdf [Accessed 15th June 2017].

Bourdoumis, A., Kachrilas, S., Kapoor, S., Zaman, F., Papadopoulos, G., Buchholz, N. & Masood, J. 2014. The use of a thermoexpandable metal alloy stent in the minimally invasive management of retroperitoneal fibrosis: a single center experience from the United kingdom. *Journal of Endourology*, 28 (1), 96-9.Available: https://dx.doi.org/10.1089/end.2013.0332

Bourdoumis, A., Kachrilas, S., Kapoor, S., Zaman, F., Wardak, S., Papatsoris, A., Buchholz, N. & Masood, J. 2013. The use of a thermoexpandable metal alloy stent in the minimally invasive treatment of retro peritoneal fibrosis-A single centre experience. *Journal of Endourology*, 27, A211.Available: http://dx.doi.org/10.1089/end.2013.2001

Boyvat, F., Aytekin, C., Colak, T., Firat, A., Karakayali, H. & Haberal, M. 2005. Memokath metallic stent in the treatment of transplant kidney ureter stenosis or occlusion. *Cardiovascular & Interventional Radiology*, 28 (3), 326-30.Available: https://dx.doi.org/10.1007/s00270-004-0028-2

Centre for Reviews and Dissemination 2009. *Systematic reviews: CRD's guidance for undertaking reviews in health care,* York, University of York.

Chow, P.-M., Chiang, I.N., Chen, C.-Y., Huang, K.-H., Hsu, J.-S., Wang, S.-M., Lee, Y.-J., Yu, H.-J., Pu, Y.-S. & Huang, C.-Y. 2015. Malignant Ureteral Obstruction: Functional Duration of Metallic versus Polymeric Ureteral Stents. *PLOS ONE*, 10 (8), e0135566.Available: https://doi.org/10.1371/journal.pone.0135566

Claudon, M., Joffre, F., Escourrou, G., Mazerolles, M. & Sarramon, J.P. 2003. The Normal Ureter. *In:* JOFFRE, F., OTAL, P. & SOULIE, M. (eds.) *Radiological Imaging of the Ureter.* Springer - Berlin Heidelberg.

Cook Medical. 2012. *Resonance Metallic Ureteral Stent Set: Instructions for use* [Online]. Available: https://www.cookmedical.com/data/IFU_PDF/IFU0020-14.PDF [Accessed 11th May 2017].

Dartford and Gravesham NHS Trust. 2014. *Having a ureteric stent: frequently asked questions* [Online]. Available: http://www.windsorurology.co.uk/Clinical_Information/Kidney/JJ_Stent.aspx [Accessed 2nd June 2017].

Department of Health. 2016. *NHS Reference Costs 2015-16* [Online]. London. Available: https://www.gov.uk/government/publications/nhs-reference-costs-collection-guidance-for-2015-to-2016.

Drummond, M., Sculpher, M., Calxton, K., Stoddart, G. & Torrance, G. 2015. *Methods for the Economic Evaluation of Health Care Programmes (Forth Edition),* Oxford.

Drummond, M.F. & Jefferson, T.O. 1996. Guidelines for authors and peer reviewers of economic submissions to the BMJ. The BMJ Economic Evaluation Working Party. *BMJ : British Medical Journal*, 313 (7052), 275-283.Available: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2351717/

Ellsworth, P., Patel, C. & Maddox, M. 2016. *Ureteroneocystostomy* [Online]. Medscape. Available: http://emedicine.medscape.com/article/1893904-overview [Accessed 22nd May 2017].

Franke, M., Ryhammer, A., Holm-nielsen, A., Graversen, P., Nohr, M., Faber, J.E. & Osther, P.J.S. 2010. Long-term outcome of the thermoexpandable ureteral metal stent (MemokathTM051) for the treatment of chronic ureteral stictures: Results of the Danish Memokath

study. *Journal of Endourology*, 24, A174.Available: http://dx.doi.org/10.1089/end.2010.2003.supp

Gonzalez, L.L., Borda, A.P., Gonzalez, E.R., Medina, J.S., Martinez, L.C. & Parra, R.O.A. 2011. Decision analysis for economic evaluation of the management of chronic obstructive uropathy. *Archivos Espanoles de Urologia*, 64 (9), 875-81.Available: https://www.ncbi.nlm.nih.gov/pubmed/22155875

Granberg, C., Russell, S., Siddiqui, S., Nehra, A., Frie, K., Leroy, A. & Mynderse, L. 2010. Long term drainage of malignant extrinsic ureteral obstruction secondary to inoperable pelvic or abdominal malignancies using the Memokath 051 ureteral stent. *Journal of Urology*, 1), e495.Available: http://dx.doi.org/10.1016/j.juro.2010.02.850

Guy's and St Thomas' NHS Foundation Trust. 2013. *Having a nephrostomy catheter inserted (in the Interventional Radiology Department)* [Online]. Available: http://www.guysandstthomas.nhs.uk/resources/patient-information/radiology/having-a-nephrostomy-catheter-inserted.pdf [Accessed 11th May 2017].

Hausegger, K.A. & Portugaller, H.R. 2006. Percutaneous nephrostomy and antegrade ureteral stenting: technique—indications—complications. *European Radiology*, 16 (9), 2016.Available: http://dx.doi.org/10.1007/s00330-005-0136-7

Health and Social Care Information Centre. 2015. *Hospital Episode Statistics, Admitted Patient Care - England, 2014-15: Procedures and interventions: 4 character* [Online]. Available: http://content.digital.nhs.uk/catalogue/PUB19124 [Accessed 11th May 2017].

Higgins, J., Lasserson, T., Chandler, J., Tovey, D. & Churchill, R. 2012. Standards for the conduct of new Cochrane Intervention Reviews 2012 V2.3. London: Cochrane.

ISD Scotland. 2016. *Scottish Health Service Costs* [Online]. Available: http://www.isdscotland.org/Health-Topics/Finance/Costs/ [Accessed 7th June 2017].

Joint Formulary Committee. 2016. *British National Formulary (online)* [Online]. London: BMJ Group and Pharmaceutical Press. Available: http://www.medicinescomplete.com.

Kachrilas, S., Bourdoumis, A., Karaolides, T., Nikitopoulou, S., Papadopoulos, G., Buchholz, N. & Masood, J. 2013. Current status of minimally invasive endoscopic management of ureteric strictures. *Ther Adv Urol*, 5 (6), 354-65.Available: https://www.ncbi.nlm.nih.gov/pubmed/24294293

Kim, K.S., Choi, S., Choi, Y.S., Bae, W.J., Hong, S.-H., Lee, J.Y., Kim, S.W., Hwang, T.-K. & Cho, H.J. 2014. Comparison of efficacy and safety between a segmental thermo-expandable metal alloy spiral stent (Memokath 051) and a self-expandable covered metallic stent (UVENTA) in the management of ureteral obstructions. *Journal of*

Laparoendoscopic & Advanced Surgical Techniques. Part A, 24 (8), 550-5.Available: https://dx.doi.org/10.1089/lap.2014.0056

Kim, K.S., Choi, Y.S., Hong, S.H., Cho, H.J. & Hwang, T.K. 2013. Effectiveness of a segmental thermo-expandable metal alloy spiral stent (memokath 051TM) and self-expandable covered metallic stent (UVENTATM) in the management of ureteral obstruction. *Journal of Endourology*, 27, A205-A206.Available: http://dx.doi.org/10.1089/end.2013.2001

Klarskov, P., Nordling, J. & Nielsen, J.B. 2005. Experience with Memokath 051 ureteral stent. *Scandinavian Journal of Urology & Nephrology*, 39 (2), 169-72.Available: https://dx.doi.org/10.1080/00365590510007720

Kulkarni, R. 2014. Metallic stents in the management of ureteric strictures. *Indian J Urol*, 30 (1), 65-72.Available: https://www.ncbi.nlm.nih.gov/pubmed/24497686

Kulkarni, R. & Bellamy, E. 2001. Nickel-titanium shape memory alloy Memokath 051 ureteral stent for managing long-term ureteral obstruction: 4-year experience. *Journal of Urology*, 166 (5), 1750-4.Available: https://www.ncbi.nlm.nih.gov/pubmed/11586216

Kulkarni, R.P. & Bellamy, E.A. 1999. A new thermo-expandable shape-memory nickel-titanium alloy stent for the management of ureteric strictures. *BJU Int*, 83 (7), 755-9.Available: https://www.ncbi.nlm.nih.gov/pubmed/10368191

Lee, G., Longhorn, S., Ayra, M., Foley, C., Choong, S. & Philp, T. 2005. Thermo-expandable ureteric stent in the treatment of refractory benign ureteric strictures: 7 year experience. *Journal of Endourology*, 19, A22-A22

Lehmann, S. 2002. *Double-J stents: They're not trouble free* [Online]. Modern Medicine. Available: http://www.modernmedicine.com/modern-medicine/content/double-j-stents-theyre-not-trouble-free [Accessed 11th May 2017].

Liatsikos, E.N., Kagadis, G.C., Barbalias, G.A. & Siablis, D. 2005. Ureteral metal stents: a tale or a tool? *Journal of Endourology*, 19 (8), 934-9.Available: https://dx.doi.org/10.1089/end.2005.19.934

Maan, Z., Patel, D., Moraitis, K., El-Husseiny, T., Papatsoris, A.G., Buchholz, N.-P. & Masood, J. 2010. Comparison of stent-related symptoms between conventional Double-J stents and a new-generation thermoexpandable segmental metallic stent: a validated-questionnaire-based study. *Journal of Endourology*, 24 (4), 589-93.Available: https://dx.doi.org/10.1089/end.2009.0318

Macmillan. 2014. *Nephrostomy* [Online]. Available: http://www.macmillan.org.uk/information-and-

support/treating/supportive-and-other-treatments/supportive-therapies/nephrostomy.html [Accessed 11th May 2017].
McFarlane, J.P., Cowan, C., Holt, S.J. & Cowan, M.J. 2001. Outpatient ureteric procedures: a new method for retrograde ureteropyelography and ureteric stent placement. *BJU Int*, 87 (3), 172-6.Available: https://www.ncbi.nlm.nih.gov/pubmed/11167637

McGowan, J., Sampson, M. & Lefebvre, C. 2010. An Evidence Based Checklist for the Peer Review of Electronic Search Strategies (PRESS EBC). *Evidence Based Library and Information Practice; Vol 5, No 1 (2010)DO - 10.18438/B8SG8R*.Available: https://journals.library.ualberta.ca/eblip/index.php/EBLIP/article/view/7402/6436

Moraitis, K., El-husseiny, T., Wazait, H., Junaid, I., Masood, J. & Buchholz, N. 2010. Segmental nickel-titanium ureteric stents with thermal-shape memory in the management of ureteric strictures. *Journal of Endourology*, 24, A173.Available: http://dx.doi.org/10.1089/end.2010.2003.supp

Moskovitz, B., Halachmi, S. & Nativ, O. 2012. A new self-expanding, large-caliber ureteral stent: results of a multicenter experience. *J Endourol*, 26 (11), 1523-7
Nam, J., Han, J., Lee, D., Park, S. & Chung, M. 2015. Comparison of initial experiences between full-length metallic stent and segmental metallic stent in malignant ureteral obstruction. *World Congress of Endourology & SWL Annual Meeting*
NCT00166361 2014. Drainage of Malignant Extrinsic Ureteral Obstruction Using the Memokath Ureteral Stent.
NHS North Bristol Trust. 2014. *Having a ureteric stent: what to expect and how to manage* [Online]. Available: https://www.nbt.nhs.uk/sites/default/files/attachments/Having%20a%20Ureteric%20Stent_NBT002639.pdf [Accessed 10th May 2017].
NICE. 2004. *Laparoscopic pyeloplasty* [Online]. Available: https://www.nice.org.uk/guidance/ipg46/chapter/2-The-procedure [Accessed 11th May 2017].
NICE. 2009. *Endopyelotomy for pelviureteric junction obstruction* [Online]. Available: https://www.nice.org.uk/guidance/ipg325/chapter/2-the-procedure [Accessed 5th June 2017].
NICE. 2013. *Acute kidney injury: prevention, detection and management* [Online]. Available: https://www.nice.org.uk/guidance/cg169 [Accessed 11th May 2017].
NICE. 2014. *Prostate cancer: diagnosis and management* [Online]. Available: https://www.nice.org.uk/guidance/cg175 [Accessed 11th May 2017].
NICE. 2015. *Bladder cancer: diagnosis and management* [Online]. Available: https://www.nice.org.uk/guidance/ng2 [Accessed 11th May 2017].
NICE 2017a. Adoption Scoping Report MTG311 Memokath-051 stent for ureteral obstruction.
NICE 2017b. Briefing note for the selection and routing of: The Memokath-051 stent for ureteral obstruction

Papadopoulos, G.I., Middela, S., Srirangam, S.J., Szczesniak, C.A. & Rao, P.N. 2010. Use of Memokath 051 metallic stent in the management of ureteral strictures: a single-center experience. *Urologia Internationalis*, 84 (3), 286-91.Available: https://dx.doi.org/10.1159/000288230

Papatsoris, A., Masood, J., El-Husseiny, T., Ndirika, S. & Buchholz, N. 2007. A novel long-term thermo-expandable ureteric metal stent: Memokath 051. *BJU Int*, 1-10

Papatsoris, A.G. & Buchholz, N. 2010. A novel thermo-expandable ureteral metal stent for the minimally invasive management of ureteral strictures. *Journal of Endourology*, 24 (3), 487-91.Available: https://dx.doi.org/10.1089/end.2009.0138

Patel, C., Loughran, D., Jones, R., Abdulmajed, M. & Shergill, I. 2017. The resonance® metallic ureteric stent in the treatment of chronic ureteric obstruction: a safety and efficacy analysis from a contemporary clinical series. *BMC Urology*, 17 (1)

Patel, D., Maan, Z., El-Husseiny, T., Moraitis, K., Junaid, I., Buchholz, N. & Masood, J. 2011. Characterising stent symptoms associated with a segmental thermo-expandable metallic stent using a validated stent symptoms questionnaire. *Current Urology*, 5 (2), 72-78.Available: http://dx.doi.org/10.1159/000327454

Pavlovic, K., Lange, D. & Chew, B. 2016. Stents for malignant ureteral obstruction. *Asian Journal of Urology*, 3 (3), 142-9.Available: http://www.sciencedirect.com/science/article/pii/S2214388216300182

Personal Social Services Research Unit (PSSRU) 2016. *Unit Costs of Health & Social Care 2016,* Canterbury, University of Kent. Available: http://www.pssru.ac.uk/project-pages/unit-costs/2016/

PNN Medical. Available: http://www.pnnmedical.com/memokath/solutions/memokath-051-ureter/ [Accessed 10th May 2017].

PNN Medical 2016. *Memokath 051CW: Instructions for Use [Not publicly available]*.

Rao, M.V., Polcari, A.J. & Turk, T.M. 2011. Updates on the use of ureteral stents: focus on the Resonance((R)) stent. *Med Devices (Auckl)*, 4, 11-5.Available: https://www.ncbi.nlm.nih.gov/pubmed/22915925

Sampson, M., McGowan, J., Lefebvre, C., Moher, D. & Grimshaw, J. 2008. PRESS: Peer Review of Electronic Search Strategies. Ottawa: Canadian Agency for Drugs and Technologies in Health.

Schenck, M., Treckmann, J., Ruebben, H. & Paul, A. 2010. Metallstent (Memokath051) Versorgung von Transplantatharnleiterengen. *Kongress der Nordrhein-Westfälischen Gesellschaft für Urologie e.V.Dortmund.* , 56

Schenck, M., Weise, S., Jaeger, T., Hess, J. & Ruebben, H. 2008. Perioperative Anwendungsbeobachtung von thermolabilen

Ureterstents (Memokath 051) und anderen handelsüblichen Ureterschienen. *Urologische Universitätsklinik Essen*,
Sountoulides, P., Kaplan, A., Kaufmann, O.G. & Sofikitis, N. 2010. Current status of metal stents for managing malignant ureteric obstruction. *BJU International*, 105 (8), 1066-72.Available: https://dx.doi.org/10.1111/j.1464-410X.2009.09140.x

TaeWoong Medical. 2016. *UVENTA Urethral stent* [Online]. Available: http://www.stent.net/products/urology/uventa-urology-stent/uventa-urethral-stent-2/ [Accessed 18th May 2017].
Tai, F., Willson, M. & Ghersi, D. Implications of searching multiple trial registries: how should we search ClinicalTrials.gov and WHO ICTRP? . Cochrane Colloquium, 30 Sep-3 Oct 2012 2012 Auckland NZ.
Talyor, W., El-Husseiny, T. & Buchholz, N. 2013. The Current Role of Memokath 051 Thermo-Expandable Metal Stent in Management of Benign and Malignant Ureteric Strictures. *Med Surg Urol*, S4:003. doi:10.4172/2168-9857.S4-003

University Hospital Southampton NHS Foundation Trust. 2000. *Antegrade ureteric stenting* [Online]. Available: http://www.uhs.nhs.uk/OurServices/Radiology-scansandimaging/PatientInformation/AntegradeUretericStenting.aspx [Accessed 11th May 2017].
University Hospital Southampton NHS Foundation Trust. 2016. *Percutaneous Nephrostomy* [Online]. Available: http://www.uhs.nhs.uk/OurServices/Radiology-scansandimaging/PatientInformation/PercutaneousNephrostomy.aspx [Accessed 11th May 2017].
Wein, A.J., Kavoussi, L.R., Novik, M.D., Partin, A.W. & Peters, C.A. 2011. Campbell-Walsh Urology: Expert Consult Premium Edition.
Yu, S.C., Wu, H.Y., Wang, W., Xu, L.W., Ding, G.Q., Zhang, Z.G. & Li, G.H. 2016. High-pressure balloon dilation for male anterior urethral stricture: single-center experience. *J Zhejiang Univ Sci B*, 17 (9), 722-7.Available: https://www.ncbi.nlm.nih.gov/pubmed/27604864

Zaman, F., Poullis, C., Bach, C., Moraitis, K., Junaid, I., Buchholz, N. & Masood, J. 2011. Use of a segmental thermoexpandable metal alloy stent in the management of malignant ureteric obstruction: a single centre experience in the UK. *Urologia Internationalis*, 87 (4), 405-10.Available: https://dx.doi.org/10.1159/000326081

Zaman, M.F., Goyal, A., Bach, C., Kachrilas, S., Mukherjee, K., Junaid, I., Buchholz, N. & Masood, J. 2012. A cost-effectiveness model for the memokath 051TM in malignant ureteric obstruction. *Journal of Endourology*, 26, A434-A435

Appendices

Appendix A: Full critique of company search strategy, detailed EAC search strategy and PRISMA diagram

Appendix B: PRISMA flow diagram showing studies assessed from the EAC's literature search – Clinical review

Appendix C: Excluded studies table

Appendix D: Detailed critical appraisal of clinical studies

Appendix E: Full Critique of Company Search Strategy, Detailed EAC Search Strategy and PRISMA Diagram – Economic Evidence

Appendix F: PRISMA flow diagram showing studies assessed from the EAC's literature search – Cost-effectiveness review

Appendix G: Quality assessment of Gonzelez et al. (Gonzalez et al., 2011)

Appendix H: Quality assessment of company's *de novo* economic model

Appendix I Discrepancy in costs between company's model and submission for Memokath-051

Appendix J: Resource use in company's model

Appendix K: Company's bottom-up costing of theatre staff costs with Memokath-051

Appendix L: EAC's bottom-up costing of theatre staff costs (stent insertion)

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Appendix N: Company's bottom-up costing of theatre consumable costs and follow-up with Memokath-051

Appendix O: Detailed table of full EAC revisions to the company's model

Appendix P: EAC's full results – Memokath-051 versus double-J stents

Appendix Q: EAC's full results – Memokath-051 versus reconstructive surgery

Appendix R: EAC full results – Memokath-051 versus other metallic stents

Appendix S: EAC's sensitivity analysis

Appendix A: Full critique of company search strategy, detailed EAC search strategy and PRISMA diagram

Company search strategy to identify clinical evidence

The Peer Review of Electronic Search Strategies (PRESS) Checklist was used to inform the critique of the company's search strategies (McGowan et al., 2010). The PRESS checklist is an evidence-based tool used to critically appraise literature search strategies. The PRESS project was funded by the Canadian Agency for Drugs and Technologies in Health (CADTH) and this approach to peer reviewing search strategies is supported by the Cochrane Collaboration's Information Retrieval Methods Group (Sampson et al., 2008).

Search reporting

The Medical Technologies Evaluation Programme (MTEP) Submission Template states that the strategies used to retrieve relevant clinical data from the published literature and unpublished sources should be clearly described in sufficient detail to enable the methods to be reproduced. Whilst Section 7.1 does contain some information about search methodology, this is very limited and is not sufficient to accurately replicate the company's search. The full search strategies, exactly as run in each resource, are not provided. Section 10, Appendix 1 of the submission, where it is expected that they are recorded, is blank.

Relevant keywords used to identify published evidence are listed, and it is stated that these terms were:

> "…*combined into search "blocks", each consisting of the search term Memokath, and one or more of the other search terms. The terms were combined using the Boolean operator AND. A wildcard was used with the terms when appropriate*." (Section 7.1.1, Submission)

However, no information was provided as to which fields were searched. Although it is stated that MeSH was used, for example, it is not made clear which of the listed terms were searched for in the subject indexing field and which were keyword searches. Moreover, keyword searches could involve searches of several fields including title, abstract, and key terms supplied by the author. Which specific keyword fields were included in the search strategy is not made explicit. Neither is it indicated which specific terms had truncation or wildcard commands applied, or whether the syntax was applied at the end of the search term or used internally.

The resources searched to identify published evidence are also ambiguous. The only reference to databases and other search resources in the submission states that:

> *"MeSH was used to find preferred and related terms in the PubMed-database, medline, Campbell Urology tenth edition and the Cochrane library"* (Section 7.1.1, Submission).

This statement is unclear and could refer to either the use of these resources to simply identify search terms, or for the execution of the final search strategies. The company also does not report which interface was used to search each resource, which is a requirement of the submission template (Appendix 10.1, Submission). MEDLINE may be searched via many interfaces including Ovid, ProQuest, EBSCO, and Web of Science. The Cochrane Library may be searched via Wiley or Centre for Reviews and Dissemination (CRD) interfaces. Although each interface contains the same records, the platforms may require different syntax and provide varying functionality. This may impact on both the construction of the search and the performance of the strategy, making the database interface significant when attempting to replicate or evaluate a search. Finally, the company does not report which segments of MEDLINE and the Cochrane Library were searched. The Cochrane Library is made up of 6 individual databases and MEDLINE has a number of different segments including those containing records that are not fully processed and indexed. The segments searched can have a significant impact on the number and type of records retrieved.

During a post-submission telephone conference (27 April 2017) the company was asked whether they were able to provide full strategies for each database searched, including the number of records retrieved per resource. As a result, additional information related to the searches for clinical evidence was received by email on 01 May 2017. Whilst some information that was omitted from the original submission (specifically the number of records retrieved per resource) was provided in this document, exact search strategies for each resource were still missing. Moreover, rather than providing clarification, the additional information contradicted the original submission in several places. The original submission (Section 7.1.1) describes a strategy by which the search term Memokath was combined with other search terms (ureter stents, metal stent, ureteric stricture, ureteral stricture, stenting ureteral obstructions, urinary stenting, stenting complications, adverse events, and urinary stenting) using Boolean AND. The additional information, however, states that the resources were searched using Memokath alone. The additional information also reported the use of different resources to the original submission; Cochrane Library and Campbell Urology tenth edition no longer appear and seem to have been replaced with searches of Embase, ClinicalTrials.gov and Google. These

contradictions make it difficult to understand and evaluate the search methodology employed by the company.

Search sources

The company submission states that searches were undertaken of PubMed, MEDLINE, Cochrane Library and Campbell Urology tenth edition. The latter appears to be a urology textbook which is an unusual choice of resource for a systematic search to identify clinical effectiveness data. As noted above, additional information retrieved after the initial submission reported a different set of resources; MEDLINE/PubMed, EMBASE, ClinicalTrials.com (we assume this is an error and should be ClinicalTrials.gov) and Google. This lack of clarity makes it difficult to evaluate the choice of search sources; it is unclear whether the company has searched the sources specified in Appendix 10.1 of the submission template. By not searching the resources recommended by the submission template as a minimum for searches of published clinical evidence and adverse effects, the company may have increased the risk of missed relevant studies.

The NICE submission template indicates that the company should describe the strategies used to retrieve relevant clinical data from unpublished sources. The MTEP Methods guide indicates that search sources should include registers or databases of ongoing clinical trials, and conference proceedings. Although a search of ClinicalTrials.gov was reported in the additional information provided by the company, the section of the submission where searches for unpublished data should be reported simply states that:

> *"Up to best of our knowledge, we do not know any studies or papers which have been finished or unfinished and were not published yet"* (Section 7.1.2, Submission).

Whilst the company may be expected to have knowledge of all the studies they have undertaken on Memokath-051 themselves, it is possible that they are unaware of unpublished trials of the device that may have been carried out externally by a competitor or independent researcher. We also note that 1 of the included studies (Drainage of Malignant Extrinsic Ureteral Obstruction Using the Memokath Ureteral Stent, Table B3, Submission) relates to a ClinicalTrials.gov entry. Whilst the company may have defined this data as published, because it is publically available, it is likely to be identifiable only by the use of search resources traditionally used to identify unpublished evidence such as of trial registries. This would seem to raise questions regarding the rationale for not conducting a search for unpublished studies.

The submission methodology would have been enhanced by including a wider search for conference abstracts and by searching additional trial registers suggested by methods guidance (Higgins et al., 2012) and research (Tai et al., 2012). By not searching for unpublished or ongoing studies, the company increased the risk of missed relevant data.

Search strategy structure, search terms and syntax, search restrictions

We have not been supplied the exact search strategies used by the company and the contradictory information provided makes it impossible to ascertain the structure and content of the strategies run. The approach reported in the additional information supplied by the company by email states that single terms Memokath, then Memokath-051, then Memokath 51 were searched on. Whilst Memokath alone would be sufficient, this single concept approach is reasonably sensitive as the results are not restricted by additional concepts. However, the original submission reports a more focused, less sensitive 2 concept search with a somewhat restrictive set of search terms.

Retrieval could have been enhanced by additionally searching for records which may not have explicitly referred to Memokath-051 by name in the database record, but instead may have described notable features of the device such as “thermoexpandable” or “shape memory”.

The documented searches were restricted to studies published in English from 1991 to current. No rationale for these limits was provided although Memokath-051 seems to have been developed in the early 1990s and this being the case the date restriction is appropriate. The search strategy does not appear to be limited by study design or publication type which is also appropriate as the most sensitive approach.

Rerun of the company’s searches

As exact search strategies were not provided by the company, the EAC were unable to replicate and re-run the searches. However, it can be noted that 1 of the search result numbers provided in the additional information received by email (01 May 2017) appears to be unlikely. It is reported that the search of Embase using the terms Memokath, Memokath-051, and Memokath 51 retrieved 0 results. Although it is not clear what fields were searched using these terms, nor whether any limits were applied, as of 10 May 2017 there were 162 records in Embase (1974 to 9 May 2017) containing the term Memokath in any field. This suggests that a total of 0 results from company’s search of Embase is potentially inaccurate.

Additional EAC searches

A *de novo* literature search was undertaken by the EAC. This search aimed to identify evidence on the Memokath-051-051 stent for patients with ureteric obstruction as a result of benign or malignant strictures.

A strategy was developed for MEDLINE (Ovid interface). The strategy was devised using a combination of subject indexing terms and free text search terms in the title, abstract and keyword heading word fields. The search terms were identified through assessment of the company strategy, discussion within the research team, scanning background literature, browsing database thesauri and use of the PubMed PubReminer tool (http://hgserver2.amc.nl/cgi-bin/miner/miner2.cgi). The approach taken to the search strategy development aimed to balance sensitivity and precision, reflecting the project resource and timelines.

The MEDLINE strategy (Figure A1) searches for both records which name Memokath-051 or the company explicitly, or describe the unique features of the device in order to identify studies which do not name Memokath-051 in the title, abstract or indexing of the database record.

Terms specifically related to the device brand name, manufacturer name, or thermoexpandable or shape memory stents were precision enough to be searched as a single concept (search lines 1 to 6, Figure A1). Terms related to nickel-titanium, self-expanding, or long-lasting stents were overly sensitive and returned an unacceptably large volume of irrelevant records (search lines 7-11, Figure A1). In order to increase precision these terms were combined with an additional concept for the population: ureteric obstruction (search lines 12-17, Figure A1).

Figure A1: EAC search strategy for Ovid MEDLINE and MEDLINE In-Process

Database: Ovid MEDLINE(R) Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) <1946 to Present>	
Search Strategy:	
---	---
1	(memokath$ or mk051 or mk-051 or memo-kath$ or memocath$ or memo-cath$ or pnn medical$ or (engineers adj2 doctors$)).ti,ab,kf,in. (100)
2	(stents/ or self expandable metallic stents/) and (temperature/ or hot temperature/) (94)
3	((thermal memory or shape memory or smart metal$ or memory metal$ or memory alloy$ or muscle wire$ or smart alloy$) and stent$).ti,ab,kf. (151)
4	((thermoexpan$ or thermo-expan$ or thermoactiv$ or thermo-activ$ or thermoformable or thermo-formable or thermosensitiv$ or thermo-sensitiv$ or thermoresponsiv$ or thermo-responsiv$ or thermoreactiv$ or thermo-reactiv$) and stent$).ti,ab,kf. (65)
5	(((thermal$ or temperature$ or heat) adj5 (expand$ or expansion$ or activat$ or reactiv$ or sensitiv$ or responsiv$ or formable)) and stent$).ti,ab,kf. (42)
6	or/2-5 (299)
7	(stents/ or self expandable metallic stents/) and ((nickel/ and titanium/) or alloys/) (1282)
8	((niti or nitinol or (nickel and titanium)) and stent$).ti,ab,kf. (1827)
9	((long-term or longterm or long-lasting or longlasting or permanent$ or semipermanent$) adj5 stent$).ti,ab,kf. (2855)
10	((self-expand$ or selfexpand$) and stent$).ti,ab,kf. (5351)
11	or/7-10 (9294)
12	Ureter/ or exp Ureteral Diseases/ or Hydronephrosis/ (48583)
13	(ureter$ or pelviuret$).ti,ab,kf. (53395)
14	((upj or uvj or puj or urinary or urine$ or urogenital$ or urologic$) adj5 (block$ or obstruct$ or narrow$ or constrict$ or compress$ or occlu$ or retention$ or strictur$ or stenos$ or abnormal$ or malform$ or insufficien$ or dysfunction$ or impair$ or duplicat$ or stone$ or calculi$)).ti,ab,kf. (39065)
15	(hydronephros$ or hydroureter$ or megaureter$ or ((kidney$ or renal) adj5 (disten$ or dilat$))).ti,ab,kf. (14036)
16	or/12-15 (104631)
17	11 and 16 (306)
18	1 or 6 or 17 (638)
19	exp animals/ not humans/ (4388801)
20	(news or comment or editorial or letter or case reports).pt. or case report.ti. (3471915)
21	18 not (19 or 20) (470)
22	limit 21 to english language (403)

The strategy excluded animal studies using a standard algorithm. Publication types that are unlikely to yield relevant information; comments, editorial, news, letters and case reports were also excluded. The search was limited to studies published in English as project timelines and resource precluded the translation of foreign language papers. The strategy was not restricted by date or study design.

The final MEDLINE strategy was translated appropriately for the other information resources containing both published and unpublished research (Table A1). The PubMed search was restricted to just those records not fully indexed in MEDLINE.

Table A1: Databases and information sources searched

Resource	Interface / url
MEDLINE In-Process & Other Non-Indexed Citations and MEDLINE	OvidSP
Embase	OvidSP
Cochrane Central Register of Controlled Trials	Cochrane Library / Wiley
Database of Abstracts of Reviews of Effect	Cochrane Library / Wiley
Health Technology Assessment Database	Cochrane Library / Wiley
Cochrane Database of Systematic Reviews	Cochrane Library / Wiley
PubMed	http://www.ncbi.nlm.nih.gov/pubmed
Science Citation Index Expanded (SCI-EXPANDED)	Web of Science
Conference Proceedings Citation Index-Science (CPCI-S)	Web of Science
Clinicaltrials.gov	https://clinicaltrials.gov/
WHO International Clinical Trials Registry Platform	http://apps.who.int/trialsearch/
ISRCTN registry	http://www.isrctn.com/
Euroscan	https://www.euroscan.org/

The EAC additionally searched the webpages of relevant organisations:

- Action on Bladder Cancer http://actionbladdercanceruk.org/
- Bladder and Bowel Foundation https://www.bladderandbowelfoundation.org/
- British Kidney Patient Association http://www.britishkidney-pa.co.uk/
- Fight Bladder Cancer http://fightbladdercancer.co.uk/
- Jo's Trust https://www.jostrust.org.uk/
- Kidney Cancer UK (KCUK) https://www.kcuk.org.uk/
- Kidney Research UK http://www.kidneyresearchuk.org/
- Ovacome http://www.ovacome.org.uk/
- Ovarian Cancer Action http://ovarian.org.uk/
- Pelvic Pain Support Network http://www.pelvicpain.org.uk/

- Prostate Cancer UK (formerly prostate cancer charity) https://prostatecanceruk.org/
- Target Ovarian Cancer http://www.targetovariancancer.org.uk/
- British Uro-oncology Group (BUG) http://www.bug.uk.com/
- British Association of Urological Surgeons (BAUS) http://www.baus.org.uk/
- British Association of Urological Nurses (BAUN) http://www.baun.co.uk/
- British Association of Pediatric Urologists http://www.bapu.org.uk/
- PNN Medical http://www.pnnmedical.com/

Relevant conferences were searched for recent proceedings from 2014 to current, which are not included in Embase (as per the conference coverage information provided by Elsevier) and would therefore be unlikely to be identified by database searches. The clinical experts were asked to suggest any conference titles they felt were particularly important to hand-search.

- British Uro-oncology Group (BUG) Annual Meeting 2014, 2015, 2016. 2017 Annual Meeting had not been held at the time of the search;
- British Association of Urological Surgeons (BAUS) Annual Scientific Meeting 2014, 2015, 2016. 2017 Annual Meeting had not been held at the time of the search;
- Société Internationale d'Urologie (SIU) Annual Congress 2015, 2016, 2015. 2014 proceedings are indexed in Embase and so are covered by the database searches;
- European Association of Urology (EAU) Congress 2017. 2014, 2015, 2016 proceedings are indexed in Embase and so are covered by the database searches;
- American Urological Association Annual Meeting (AUA) 2017. 2014, 2015, 2016 proceedings are indexed in Embase and so are covered by the database searches;
- World Congress of Endourology & SWL Annual Meeting 2015 and 2016. 2014 proceedings are indexed in Embase and so are covered by the database searches, 2017 Annual Meeting had not been held at the time of the search.

The EAC also checked reference lists in relevant studies and reviews which were identified, and formally contacted the clinical experts to ask if they knew of any studies which were ongoing, unpublished, or likely to be published soon.

Searching a number of databases produces a degree of duplication in the results. To manage this issue, the titles and abstracts of bibliographic records were downloaded and imported into EndNote bibliographic management software and duplicate records were removed using several algorithms. Where result format did not facilitate loading into EndNote, Word documents or Excel spreadsheets were used as appropriate.

EAC Literature Search Results

The EAC identified 2,061 records: the database and webpage searches retrieved 2,046 records, an additional 14 records were identified by hand-searching conference abstracts, and 1 further record was identified from the company submission (Table A2). Following deduplication, 1,274 records were assessed for relevance.

Table A2: Literature search results

Resource	Records identified
MEDLINE In-Process & Other Non-Indexed Citations and MEDLINE	403
Embase	790
Cochrane Central Register of Controlled Trials (CENTRAL)	25
Database of Abstracts of Reviews of Effect (DARE)	1
Health Technology Assessment Database (HTA Database)	0
Cochrane Database of Systematic Reviews (CDSR)	2
PubMed	116
Science Citation Index Expanded (SCI-EXPANDED)	522
Conference Proceedings Citation Index- Science (CPCI-S)	120
Euroscan	0
Clinicaltrials.gov	36
WHO International Clinical Trials Registry Platform (ICTRP)	16
ISRCTN registry	10
Website searches	5
Conference hand-searches	14
Records identified from other sources (reference checking, supplied by experts etc.)	1
Total	**2,061**
Total after deduplication	**1,274**

EAC search – full search strategies

A.1: Source: :Ovid MEDLINE(R) Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) <1946 to Present>

Interface / URL: Ovid SP

Database coverage dates: 1946 to current. Updated daily.

Search date: 26/04/17

Retrieved records: 403

Search strategy:

Database: Ovid MEDLINE(R) Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) <1946 to Present>

Search Strategy:

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1 (memokath$ or MK051 or MK-051 or memo-kath$ or memocath$ or memo-cath$ or pnn medical$ or (engineers adj2 doctors$)).ti,ab,kf,in. (100)

2 (stents/ or self expandable metallic stents/) and (temperature/ or hot temperature/) (94)

3 ((thermal memory or shape memory or smart metal$ or memory metal$ or memory alloy$ or muscle wire$ or smart alloy$) and stent$).ti,ab,kf. (151)

4 ((thermoexpan$ or thermo-expan$ or thermoactiv$ or thermo-activ$ or thermoformable or thermo-formable or thermosensitiv$ or thermo-sensitiv$ or thermoresponsiv$ or thermo-responsiv$ or thermoreactiv$ or thermo-reactiv$) and stent$).ti,ab,kf. (65)

5 (((thermal$ or temperature$ or heat) adj5 (expand$ or expansion$ or activat$ or reactiv$ or sensitiv$ or responsiv$ or formable)) and stent$).ti,ab,kf. (42)

6 or/2-5 (299)

7 (stents/ or self expandable metallic stents/) and ((nickel/ and titanium/) or alloys/) (1282)

8 ((niti or nitinol or (nickel and titanium)) and stent$).ti,ab,kf. (1827)

9 ((long-term or longterm or long-lasting or longlasting or permanent$ or semipermanent$) adj5 stent$).ti,ab,kf. (2855)

10 ((self-expand$ or selfexpand$) and stent$).ti,ab,kf. (5351)

11 or/7-10 (9294)

12 Ureter/ or exp Ureteral Diseases/ or Hydronephrosis/ (48583)

13 (ureter$ or pelviuret$).ti,ab,kf. (53395)

14 ((upj or uvj or puj or urinary or urine$ or urogenital$ or urologic$) adj5 (block$ or obstruct$ or narrow$ or constrict$ or compress$ or occlu$ or retention$ or strictur$ or stenos$ or abnormal$ or malform$ or insufficien$ or dysfunction$ or impair$ or duplicat$ or stone$ or calculi$)).ti,ab,kf. (39065)

15 (hydronephros$ or hydroureter$ or megaureter$ or ((kidney$ or renal) adj5 (disten$ or dilat$))).ti,ab,kf. (14036)

16 or/12-15 (104631)

17 11 and 16 (306)

18 1 or 6 or 17 (638)

19 exp animals/ not humans/ (4388801)

20 (news or comment or editorial or letter or case reports).pt. or case report.ti. (3471915)

21 18 not (19 or 20) (470)

22 limit 21 to english language (403)

A.2: Source: Embase <1974 to 2017 April 25>

Interface / URL: Ovid SP

Database coverage dates: 1974 to 2017 April 25

Search date: 26/04/17

Retrieved records: 790

Search strategy:

Database: Embase <1974 to 2017 April 25>

Search Strategy:

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1 (memokath$ or MK051 or MK-051 or memo-kath$ or memocath$ or memo-cath$).ti,ab,kw,dv. (184)

2 (pnn medical$ or (engineers adj2 doctors$)).ti,ab,kw,dm. (138)

3 1 or 2 (251)

4 (stent/ or exp self expanding stent/ or ureter stent/) and (temperature/ or high temperature/ or heat sensitivity/) (176)

5 ((thermal memory or shape memory or smart metal$ or memory metal$ or memory alloy$ or muscle wire$ or smart alloy$) and stent$).ti,ab,kw. (222)

6 ((thermoexpan$ or thermo-expan$ or thermoactiv$ or thermo-activ$ or thermoformable or thermo-formable or thermosensitiv$ or thermo-sensitiv$ or thermoresponsiv$ or thermo-responsiv$ or thermoreactiv$ or thermo-reactiv$) and stent$).ti,ab,kw. (114)

7 (((thermal$ or temperature$ or heat) adj5 (expand$ or expansion$ or activat$ or reactiv$ or sensitiv$ or responsiv$ or formable)) and stent$).ti,ab,kw. (50)

8 or/4-7 (515)

9 exp nitinol stent/ (1247)

10 (stent/ or exp self expanding stent/ or ureter stent/) and ((nickel/ and titanium/) or alloy/ or nitinol/) (2208)

11 ((niti or nitinol or (nickel and titanium)) and stent$).ti,ab,kw. (2919)

12 ((long-term or longterm or long-lasting or longlasting or permanent$ or semipermanent$) adj5 stent$).ti,ab,kw. (4510)

13 ((self-expand$ or selfexpand$) and stent$).ti,ab,kw. (8380)

14 or/9-13 (15121)

15 Ureter/ or exp Ureter disease/ (49055)

16 hydronephrosis/ (19553)

17 (ureter$ or pelviuret$).ti,ab,kw. (66270)

18 ((upj or uvj or puj or urinary or urine$ or urogenital$ or urologic$) adj5 (block$ or obstruct$ or narrow$ or constrict$ or compress$ or occlu$ or retention$ or strictur$ or stenos$ or abnormal$ or malform$ or insufficien$ or dysfunction$ or impair$ or duplicat$ or stone$ or calculi$)).ti,ab,kw. (52580)

19 (hydronephros$ or hydroureter$ or megaureter$ or ((kidney$ or renal) adj5 (disten$ or dilat$))).ti,ab,kw. (18084)

20 or/15-19 (136022)

21 14 and 20 (522)

22 3 or 8 or 21 (1114)

23 (animal/ or animal experiment/ or animal model/ or animal tissue/ or nonhuman/) not exp human/ (5549666)

24 (editorial or letter or note).pt. or case report/ (4081299)

25 22 not (23 or 24) (886)

26 limit 25 to english language (790)

A.3: Source: Cochrane Central Register of Controlled Trials (CENTRAL)

Interface / URL: Cochrane Library, Wiley

Database coverage dates: Issue 3 of 12, March 2017

Search date: 28/04/17

Retrieved records: 25

Search strategy:

ID	Search	Hits
#1	memokath* or mk051 or mk-051 or memo next kath* or memocath* or memo next cath* or pnn next medical* or (engineers near/2 doctors*)	8
#2	[mh ^stents] or [mh ^"self expandable metallic stents"]	3410
#3	[mh ^temperature] or [mh ^"hot temperature"]	2857

#4 #2 and #3 0

#5 ("thermal memory" or "shape memory" or smart next metal* or memory next metal* or memory next alloy* or muscle next wire* or smart next alloy*) and stent* 4

#6 (thermoexpan* or thermo next expan* or thermoactiv* or thermo next activ* or thermoformable or thermo next formable or thermosensitiv* or thermo next sensitiv* or thermoresponsiv* or thermo next responsiv* or thermoreactiv* or thermo next reactiv*) and stent* 3

#7 ((thermal* or temperature* or heat) near/5 (expand* or expansion* or activat* or reactiv* or sensitiv* or responsiv* or formable)) and stent* 4

#8 #4 or #5 or #6 or #7 11

#9 [mh ^stents] or [mh ^"self expandable metallic stents"] 3410

#10 [mh ^nickel] and [mh ^titanium] 180

#11 [mh ^alloys] 124

#12 #9 and (#10 or #11) 54

#13 (niti or nitinol or (nickel and titanium)) and stent* 212

#14 ("long-term" or longterm or "long-lasting" or longlasting or permanent* or semipermanent*) near/5 stent* 420

#15 (self next expand* or selfexpand*) and stent* 465

#16 #12 or #13 or #14 or #15 964

#17 [mh ^ureter] or [mh "ureteral diseases"] or [mh ^hydronephrosis] 640

#18 ureter* or pelviuret* 2010

#19 (upj or uvj or puj or urinary or urine* or urogenital* or urologic*) near/5 (block* or obstruct* or narrow* or constrict* or compress* or occlu* or retention* or strictur* or stenos* or abnormal* or malform* or insufficien* or dysfunction* or impair* or duplicat* or stone* or calculi*) 5091

#20 hydronephros* or hydroureter* or megaureter* or ((kidney* or renal) near/5 (disten* or dilat*)) 347

#21 #17 or #18 or #19 or #20 6768

#22 #16 and #21 22

#23 #1 or #8 or #22 35

#24 #23 in Trials25

A.4: Source: Database of Abstracts of Reviews of Effect (DARE)

Interface / URL: Cochrane Library, Wiley

Database coverage dates: Issue 2 of 4, April 2015

Search date: 26/04/17

Retrieved records: 1

Search strategy:

ID	Search	Hits
#1	memokath* or mk051 or mk-051 or memo next kath* or memocath* or memo next cath* or pnn next medical* or (engineers near/2 doctors*)	8
#2	[mh ^stents] or [mh ^"self expandable metallic stents"]	3410
#3	[mh ^temperature] or [mh ^"hot temperature"]	2857
#4	#2 and #3	0
#5	("thermal memory" or "shape memory" or smart next metal* or memory next metal* or memory next alloy* or muscle next wire* or smart next alloy*) and stent*	4
#6	(thermoexpan* or thermo next expan* or thermoactiv* or thermo next activ* or thermoformable or thermo next formable or thermosensitiv* or thermo next sensitiv* or thermoresponsiv* or thermo next responsiv* or thermoreactiv* or thermo next reactiv*) and stent*	3
#7	((thermal* or temperature* or heat) near/5 (expand* or expansion* or activat* or reactiv* or sensitiv* or responsiv* or formable)) and stent*	4
#8	#4 or #5 or #6 or #7	11
#9	[mh ^stents] or [mh ^"self expandable metallic stents"]	3410
#10	[mh ^nickel] and [mh ^titanium]	180

#11 [mh ^alloys] 124

#12 #9 and (#10 or #11) 54

#13 (niti or nitinol or (nickel and titanium)) and stent* 212

#14 ("long-term" or longterm or "long-lasting" or longlasting or permanent* or semipermanent*) near/5 stent* 420

#15 (self next expand* or selfexpand*) and stent* 465

#16 #12 or #13 or #14 or #15 964

#17 [mh ^ureter] or [mh "ureteral diseases"] or [mh ^hydronephrosis] 640

#18 ureter* or pelviuret* 2010

#19 (upj or uvj or puj or urinary or urine* or urogenital* or urologic*) near/5 (block* or obstruct* or narrow* or constrict* or compress* or occlu* or retention* or strictur* or stenos* or abnormal* or malform* or insufficien* or dysfunction* or impair* or duplicat* or stone* or calculi*) 5091

#20 hydronephros* or hydroureter* or megaureter* or ((kidney* or renal) near/5 (disten* or dilat*)) 347

#21 #17 or #18 or #19 or #20 6768

#22 #16 and #21 22

#23 #1 or #8 or #22 35

#24 #23 in Other Reviews 1

A.5: Source: Health Technology Assessment Database (HTA Database)

Interface / URL: Cochrane Library, Wiley

Database coverage dates: Issue 4 of 4, October 2016

Search date: 26/04/17

Retrieved records: 0

Search strategy:

ID Search Hits

#1 memokath* or mk051 or mk-051 or memo next kath* or memocath* or memo next cath* or pnn next medical* or (engineers near/2 doctors*) 8

#2 [mh ^stents] or [mh ^"self expandable metallic stents"] 3410

#3 [mh ^temperature] or [mh ^"hot temperature"] 2857

#4 #2 and #3 0

#5 ("thermal memory" or "shape memory" or smart next metal* or memory next metal* or memory next alloy* or muscle next wire* or smart next alloy*) and stent* 4

#6 (thermoexpan* or thermo next expan* or thermoactiv* or thermo next activ* or thermoformable or thermo next formable or thermosensitiv* or thermo next sensitiv* or thermoresponsiv* or thermo next responsiv* or thermoreactiv* or thermo next reactiv*) and stent* 3

#7 ((thermal* or temperature* or heat) near/5 (expand* or expansion* or activat* or reactiv* or sensitiv* or responsiv* or formable)) and stent* 4

#8 #4 or #5 or #6 or #7 11

#9 [mh ^stents] or [mh ^"self expandable metallic stents"] 3410

#10 [mh ^nickel] and [mh ^titanium] 180

#11 [mh ^alloys] 124

#12 #9 and (#10 or #11) 54

#13 (niti or nitinol or (nickel and titanium)) and stent* 212

#14 ("long-term" or longterm or "long-lasting" or longlasting or permanent* or semipermanent*) near/5 stent* 420

#15 (self next expand* or selfexpand*) and stent* 465

#16 #12 or #13 or #14 or #15 964

#17 [mh ^ureter] or [mh "ureteral diseases"] or [mh ^hydronephrosis] 640

#18 ureter* or pelviuret* 2010

#19 (upj or uvj or puj or urinary or urine* or urogenital* or urologic*) near/5 (block* or obstruct* or narrow* or constrict* or compress* or occlu* or retention* or strictur* or stenos* or abnormal* or malform* or insufficien* or dysfunction* or impair* or duplicat* or stone* or calculi*) 5091

#20 hydronephros* or hydroureter* or megaureter* or ((kidney* or renal) near/5 (disten* or dilat*)) 347

#21 #17 or #18 or #19 or #20 6768

#22 #16 and #21 22

#23 #1 or #8 or #22 35

#24 #23 in Technology Assessments 0

A.6: Source: Cochrane Database of Systematic Reviews (CDSR)

Interface / URL: Cochrane, Wiley

Database coverage dates: Issue 4 of 12, April 2017

Search date: 26/04/17

Retrieved records: 2

Search strategy:

ID Search Hits

#1 (memokath* or mk051 or mk-051 or memo next kath* or memocath* or memo next cath* or pnn next medical* or (engineers near/2 doctors*)):ti,ab,kw 6

#2 [mh ^stents] or [mh ^"self expandable metallic stents"] 3410

#3 [mh ^temperature] or [mh ^"hot temperature"] 2857

#4 #2 and #3 0

#5 (("thermal memory" or "shape memory" or smart next metal* or memory next metal* or memory next alloy* or muscle next wire* or smart next alloy*) and stent*):ti,ab,kw 3

#6 ((thermoexpan* or thermo next expan* or thermoactiv* or thermo next activ* or thermoformable or thermo next formable or thermosensitiv* or thermo next sensitiv* or thermoresponsiv* or thermo next responsiv* or thermoreactiv* or thermo next reactiv*) and stent*):ti,ab,kw 2

#7 (((thermal* or temperature* or heat) near/5 (expand* or expansion* or activat* or reactiv* or sensitiv* or responsiv* or formable)) and stent*):ti,ab,kw 4

#8 #4 or #5 or #6 or #7 9

#9 [mh ^stents] or [mh ^"self expandable metallic stents"] 3410

#10 [mh ^nickel] and [mh ^titanium] 180

#11 [mh ^alloys] 124

#12 #9 and (#10 or #11) 54

#13 ((niti or nitinol or (nickel and titanium)) and stent*):ti,ab,kw 167

#14 (("long-term" or longterm or "long-lasting" or longlasting or permanent* or semipermanent*) near/5 stent*) ;ti,ab,kw 3

#15 ((self next expand* or selfexpand*) and stent*):ti,ab,kw 411

#16 #12 or #13 or #14 or #15 490

#17 [mh ^ureter] or [mh "ureteral diseases"] or [mh ^hydronephrosis] 640

#18 (ureter* or pelviuret*):ti,ab,kw 1845

#19 ((upj or uvj or puj or urinary or urine* or urogenital* or urologic*) near/5 (block* or obstruct* or narrow* or constrict* or compress* or occlu* or retention* or strictur* or stenos* or abnormal* or malform* or insufficien* or dysfunction* or impair* or duplicat* or stone* or calculi*)):ti,ab,kw 4329

#20 (hydronephros* or hydroureter* or megaureter* or ((kidney* or renal) near/5 (disten* or dilat*))):ti,ab,kw 282

#21 #17 or #18 or #19 or #20 5925

#22 #16 and #21 9

#23 #1 or #8 or #22 23

#24 #23 in Cochrane Reviews (Reviews and Protocols) 2

A.7: Source: PubMed

Interface / URL: https://www.ncbi.nlm.nih.gov/pubmed/

Database coverage dates: 1940s to current. Updated daily.

Search date: 27/04/17

Retrieved records: 116

Search strategy:

#29 Search #26 NOT #27 Filters: English 116

#28 Search #26 NOT #27 123

#27 Search medline[sb] 23973104

#26 Search #23 NOT (#24 OR #25) 969

#25 Search (news[pt] OR comment[pt] OR editorial[pt] OR letter[pt] OR case reports[pt]) OR case report[ti] 3393095

#24 Search animals[mh] NOT humans[mh:noexp] 4320340

#23 Search #4 OR #9 OR #221233

#22 Search #15 AND #21 839

#21 Search #16 OR #17 OR #18 OR #19 OR #20 175867

#20 Search (kidney*[tiab] OR renal[tiab]) AND (disten*[tiab] OR dilat*[tiab]) 10874

#19 Search hydronephros*[tiab] OR hydroureter*[tiab] OR megaureter*[tiab] 11702

#18 Search (upj[tiab] OR uvj[tiab] OR puj[tiab] OR urinary[tiab] OR urine*[tiab] OR urogenital*[tiab] OR urologic*[tiab]) AND (block*[tiab] OR obstruct*[tiab] OR narrow*[tiab] OR constrict*[tiab] OR compress*[tiab] OR occlu*[tiab] OR retention*[tiab] OR strictur*[tiab] OR stenos*[tiab] OR abnormal*[tiab] OR malform*[tiab] OR insufficien*[tiab] OR dysfunction*[tiab] OR impair*[tiab] OR duplicat*[tiab] OR stone*[tiab] OR calculi*[tiab]) 112495

#17 Search ureter*[tiab] OR pelviuret*[tiab] 52750

#16 Search "Ureter"[Mesh:NoExp] OR "Ureteral Diseases"[Mesh] OR "Hydronephrosis"[Mesh:NoExp] 48071

#15 Search #10 OR #11 OR #12 OR #13 OR #14 17694

#14 Search (self-expand*[tiab] OR selfexpand*[tiab]) AND stent*[tiab] 5136

#13 Search (long-term[tiab] OR longterm[tiab] OR long-lasting[tiab] OR longlasting[tiab] OR permanent*[tiab] OR semipermanent*[tiab]) AND stent*[tiab] 12214

#12 Search (niti[tiab] OR nitinol[tiab] OR (nickel[tiab] AND titanium[tiab])) AND stent*[tiab] 1757

#11 Search ("Stents"[Mesh:NoExp] OR "Self Expandable Metallic Stents"[Mesh:NoExp]) AND "Alloys"[Mesh:NoExp] 1195

#10 Search ("Stents"[Mesh:NoExp] OR "Self Expandable Metallic Stents"[Mesh:NoExp]) AND "Nickel"[Mesh:NoExp] AND "Titanium"[Mesh:NoExp] 88

#9 Search #5 OR #6 OR #7 OR #8 388

#8 Search (thermal*[tiab] OR temperature*[tiab] OR heat[tiab]) AND (expand*[tiab] OR expansion*[tiab] OR activat*[tiab] OR reactiv*[tiab] OR sensitiv*[tiab] OR responsiv*[tiab] OR formable[tiab]) AND stent* 150

#7 Search (thermoexpan*[tiab] OR thermo-expan*[tiab] OR thermoactiv*[tiab] OR thermo-activ*[tiab] OR thermoformable[tiab] OR thermo-formable[tiab] OR thermosensitiv*[tiab] OR thermo-sensitiv*[tiab] OR thermoresponsiv*[tiab] OR thermo-responsiv*[tiab] OR thermoreactiv*[tiab] OR thermo-reactiv*[tiab]) AND stent*[tiab] 62

#6 Search (thermal memory[tiab] OR shape memory[tiab] OR smart metal*[tiab] OR memory metal*[tiab] OR memory alloy*[tiab] OR smart alloy*[tiab]) AND stent*[tiab] 153

#5 Search ("Stents"[Mesh:NoExp] OR "Self Expandable Metallic Stents"[Mesh:NoExp]) AND ("Temperature"[Mesh:NoExp] OR "Hot Temperature"[Mesh:NoExp]) 91

#4 Search #1 OR #2 OR #3 82

#3 Search engineers[ad] AND doctors[ad] 1

#2 Search memokath*[ad] OR MK051[ad] OR MK-051[ad] OR memo-kath*[ad] OR memocath*[ad] OR memo-cath*[ad] OR (pnn[ad] AND medical*[ad]) 1

#1 Search memokath*[tiab] OR MK051[tiab] OR MK-051[tiab] OR memo-kath*[tiab] OR memocath*[tiab] OR memo-cath*[tiab] OR (pnn[tiab] AND medical*[tiab]) 80

A.8: Source: Science Citation Index Expanded (SCI-EXPANDED)

Interface / URL: Web of Science

Database coverage dates: 1900 to current. Last update 25/04/17

Search date: 27/04/17

Retrieved records: 522

Search strategy:

20 (#19) AND LANGUAGE: (English) 522

Indexes=SCI-EXPANDED Timespan=All years

19 #17 OR #8 OR #4 560

Refined by: [excluding] DOCUMENT TYPES: (NOTE OR EDITORIAL MATERIAL OR LETTER OR NEWS ITEM)

18 #17 OR #8 OR #4 583

Indexes=SCI-EXPANDED Timespan=All years

17 #16 AND #12 312

Indexes=SCI-EXPANDED Timespan=All years

16 #13 OR #14 OR #15 74,214

Indexes=SCI-EXPANDED Timespan=All years

15 TS=(hydronephros* OR hydroureter* OR megaureter* OR ((kidney* OR “renal”) NEAR/5 (disten* OR dilat*))) 10,132

Indexes=SCI-EXPANDED Timespan=All years

14 TS=((“upj” OR “uvj” OR “puj” OR “urinary” OR urine* OR urogenital* OR urologic*) NEAR/5 (block* OR obstruct* OR narrow* OR constrict* OR compress* OR occlu* OR retention* OR strictur* OR stenos* OR abnormal* OR malform* OR insufficien* OR dysfunction* OR impair* OR duplicat* OR stone* OR calculi*)) 30,547

Indexes=SCI-EXPANDED Timespan=All years

13 TS=(ureter* OR pelviuret*) 42,846

Indexes=SCI-EXPANDED Timespan=All years

12 #9 OR #10 OR #11 10,473

Indexes=SCI-EXPANDED Timespan=All years

11 TS=((self-expand* OR selfexpand*) AND stent*) 5,346

Indexes=SCI-EXPANDED Timespan=All years

10 TS=((“long-term” OR “longterm” OR “long-lasting” OR “longlasting” OR permanent* OR semipermanent*) NEAR/5 stent*) 3,554

Indexes=SCI-EXPANDED Timespan=All years

9 TS=((“niti” OR “nitinol” OR “thermal memory” OR “shape memory” OR “smart metal*” OR “memory metal*” OR “memory alloy*” OR “muscle wire*” OR “smart alloy*” OR (“nickel” AND “titanium”)) AND stent*) 2,855

Indexes=SCI-EXPANDED Timespan=All years

8 #5 OR #6 OR #7 204

Indexes=SCI-EXPANDED Timespan=All years

7 TS=(((thermal* OR temperature* OR “heat”) NEAR/5 (expand* OR expansion* OR activat* OR reactiv* OR sensitiv* OR responsiv* OR “formable”)) AND stent*) 56

Indexes=SCI-EXPANDED Timespan=All years

6 TS=((thermoexpan* OR thermo-expan* OR thermoactiv* OR thermo-activ* OR “thermoformable” OR “thermo-formable” OR thermosensitiv* OR thermo-sensitiv* OR thermoresponsiv* OR thermo-responsiv* OR thermoreactiv* OR thermo-reactiv*) AND stent*) 89

Indexes=SCI-EXPANDED Timespan=All years

5 TS=((“thermal memory” OR “shape memory” OR “smart metal*” OR “memory metal*” OR “memory alloy*” OR “muscle wire*” OR “smart alloy*”) NEAR/5 stent*) 82

Indexes=SCI-EXPANDED Timespan=All years

4 #1 OR #2 OR #3 130

Indexes=SCI-EXPANDED Timespan=All years

3 OO=(memokath* OR MK051 OR MK-051 OR memo-kath* OR memocath* OR memo-cath* OR pnn medical* OR ("engineers" NEAR/2 doctors*)) 0

Indexes=SCI-EXPANDED Timespan=All years

2 AD=(memokath* OR “MK051” OR “MK-051” OR memo-kath* OR memocath* OR memo-cath* OR “pnn medical*” OR ("engineers" NEAR/2 doctors*)) 0

Indexes=SCI-EXPANDED Timespan=All years

1 TS=(memokath* OR “MK051” OR “MK-051” OR memo-kath* OR memocath* OR memo-cath* OR “pnn medical*” OR ("engineers" NEAR/2 doctors*)) 130

Indexes=SCI-EXPANDED Timespan=All years

A.9: Source: Conference Proceedings Citation Index- Science (CPCI-S)

Interface / URL: Web of Science

Database coverage dates: 1990 to current. Last update 25/04/17

Search date: 27/04/17

Retrieved records: 120

Search strategy:

19 (#18) AND LANGUAGE: (English) 120

Indexes=CPCI-S Timespan=All years

18 #17 OR #8 OR #4 122

Indexes=CPCI-S Timespan=All years

17 #16 AND #12 32

Indexes=CPCI-S Timespan=All years

16 #13 OR #14 OR #15 5,863

Indexes=CPCI-S Timespan=All years

15 TS=(hydronephros* OR hydroureter* OR megaureter* OR ((kidney* OR “renal”) NEAR/5 (disten* OR dilat*))) 613

Indexes=CPCI-S Timespan=All years

14 TS=((“upj” OR “uvj” OR “puj” OR “urinary” OR urine* OR urogenital* OR urologic*) NEAR/5 (block* OR obstruct* OR narrow* OR constrict* OR compress* OR occlu* OR retention* OR strictur* OR stenos* OR abnormal* OR malform* OR insufficien* OR dysfunction* OR impair* OR duplicat* OR stone* OR calculi*)) 2,490

Indexes=CPCI-S Timespan=All years

13 TS=(ureter* OR pelviuret*) 3,346

Indexes=CPCI-S Timespan=All years

12 #9 OR #10 OR #11 1,794

Indexes=CPCI-S Timespan=All years

11 TS=((self-expand* OR selfexpand*) AND stent*) 819

Indexes=CPCI-S Timespan=All years

10 TS=((“long-term” OR “longterm” OR “long-lasting” OR “longlasting” OR permanent* OR semipermanent*) NEAR/5 stent*) 682

Indexes=CPCI-S Timespan=All years

9 TS=((“niti” OR “nitinol” OR “thermal memory” OR “shape memory” OR “smart metal*” OR “memory metal*” OR “memory alloy*” OR “muscle wire*” OR “smart alloy*” OR (“nickel” AND “titanium”)) AND stent*) 487

Indexes=CPCI-S Timespan=All years

8 #5 OR #6 OR #7 52

Indexes=CPCI-S Timespan=All years

7 TS=(((thermal* OR temperature* OR “heat”) NEAR/5 (expand* OR expansion* OR activat* OR reactiv* OR sensitiv* OR responsiv* OR “formable”)) AND stent*) 13

Indexes=CPCI-S Timespan=All years

6 TS=((thermoexpan* OR thermo-expan* OR thermoactiv* OR thermo-activ* OR “thermoformable” OR “thermo-formable” OR thermosensitiv* OR thermo-sensitiv* OR thermoresponsiv* OR thermo-responsiv* OR thermoreactiv* OR thermo-reactiv*) AND stent*) 15

Indexes=CPCI-S Timespan=All years

5 TS=((“thermal memory” OR “shape memory” OR “smart metal*” OR “memory metal*” OR “memory alloy*” OR “muscle wire*” OR “smart alloy*”) NEAR/5 stent*) 27

Indexes=CPCI-S Timespan=All years

4 #1 OR #2 OR #3 50

Indexes=CPCI-S Timespan=All years

3 OO=(memokath* OR MK051 OR MK-051 OR memo-kath* OR memocath* OR memo-cath* OR pnn medical* OR ("engineers" NEAR/2 doctors*)) 0

Indexes=CPCI-S Timespan=All years

2 AD=(memokath* OR “MK051” OR “MK-051” OR memo-kath* OR memocath* OR memo-cath* OR “pnn medical*” OR ("engineers" NEAR/2 doctors*)) 0

Indexes=CPCI-S Timespan=All years

1 TS=(memokath* OR “MK051” OR “MK-051” OR memo-kath* OR memocath* OR memo-cath* OR “pnn medical*” OR ("engineers" NEAR/2 doctors*)) 50

Indexes=CPCI-S Timespan=All years

A.10: Source: Euroscan

Interface / URL: https://www.euroscan.org/

Database coverage dates: No information provided.

Search date: 27/04/17

Retrieved records:

Search strategy:

Site wide search option used. No sophisticated search functionality available. The following search terms were used individually and were not limited using any of the available options. Results were assessed online by the information specialist for relevance. Only search results returned under the headings 'Devices', 'Procedures' or 'Other' were assessed. Only results judged to be potentially relevant and which were not duplicates of results already found were retrieved.

Memokath – 0 results

Stent – 72 results - 0 retrieved, all clearly irrelevant

Stents – 41 results - 0 retrieved, all clearly irrelevant

Stenting – 44 results - 0 retrieved, all clearly irrelevant

A.11: Source: ClinicalTrials.gov

Interface / URL: https://clinicaltrials.gov/

Database coverage dates: Information not provided

Search date: 27/04/17

Retrieved records: 37

Search strategy:

The following 7 searches were carried out separately, using the expert interface available at: https://www.clinicaltrials.gov/ct2/results/refine?show_xprt=Y.

1) memokath OR memo-kath OR memocath OR memo-cath OR MK051 OR MK-051. 4 results

2) ("thermal memory" OR "shape memory" OR "smart metal" OR "smart metals" OR "memory metal" OR "memory metals" OR "memory alloy" OR "memory alloys" OR "muscle wire" OR "muscle wires" OR "smart alloy" OR "smart alloys") AND (stent OR stents OR stenting) 10 results

3) (thermoexpanding OR thermoexpandable OR thermoexpansion OR "thermo-expanding" OR "thermo-expandable" OR "thermo-expansion" OR thermoactive OR thermoactivated OR thermoactivation OR "thermo-active" OR "thermo-activated" OR "thermos-activation" OR thermoformable OR "thermo-formable" OR thermosensitive OR "thermo-sensitive" OR thermoresponsive OR "thermo-responsive" OR thermoreactive OR "thermo-reactive") AND (stent OR stents OR stenting) 2 results

4) (thermal OR thermally OR temperature OR temperatures OR heat) AND (expand OR expanding OR expands OR expandable OR expansion OR activated OR reactive OR reactivity OR sensitive OR sensitivity OR responsive OR responsivity OR formable) AND (stent OR stents OR stenting) 9 results

5) (niti OR nitinol) AND (stent OR stents OR stenting) AND (ureter OR ureters OR ureteric OR ureteral OR pelviureter OR pelviureteric OR pelviureteral OR ureteropelvic OR ureterovesical OR urinary OR urine OR urogenital OR urologic OR urological) 3 results

6) (nickel AND titanium) AND (stent OR stents OR stenting) AND (ureter OR ureters OR ureteric OR ureteral OR pelviureter OR pelviureteric OR pelviureteral OR ureteropelvic OR ureterovesical OR urinary OR urine OR urogenital OR urologic OR urological) 1 result

7) ("long-term" OR longterm OR "long-lasting" OR longlasting OR permanent OR semipermanent OR selfexpanding OR "self-expanding") AND (stent OR stents OR stenting) AND (ureter OR ureters OR ureteric OR ureteral OR pelviureter OR pelviureteric OR pelviureteral OR ureteropelvic OR ureterovesical OR urinary OR urine OR urogenital OR urologic OR urological) 7 results

A.12: Source: International Clinical Trials Registry Platform (ICTRP)

Interface / URL: http://apps.who.int/trialsearch/Default.aspx

Database coverage date: Information not provided

Search date: 27/04/17

Retrieved records: 16

Search strategy:

The following 15 searches were carried out separately, using the search interface at: http://apps.who.int/trialsearch/Default.aspx

1) memokath OR memo-kath OR memocath OR memo-cath OR MK051 OR MK-051 5 results

2) thermal memory AND stent* OR shape memory AND stent* OR smart metal* AND stent* OR memory metal* AND stent* OR memory alloy* AND stent* OR muscle wire* AND stent* OR smart alloy* AND stent* 0 results

3) thermoexpand* AND stent* OR thermo-expand* AND stent* OR thermoactiv* AND stent* OR thermo-activ* AND stent* OR thermoformable AND stent* OR thermo-formable AND stent* OR thermosensitiv* AND stent* OR thermo-sensitiv* AND stent* OR thermoresponsiv* AND stent* OR thermo-responsiv* AND stent OR thermoreactiv* AND stent* OR thermo-reactiv* AND stent* 1 result

4) thermal* AND stent* OR temperature* AND stent* OR heat AND stent* 4 results

5) niti AND stent* AND ureter* 0 results

6) nitinol AND stent* AND ureter* 1 result

7) nickel AND titanium AND stent* 0 results

8) long-term AND stent* AND ureter* 3 results

9) longterm AND stent* AND ureter* 1 result

10) long-lasting AND stent* AND ureter* 0 results

11) longlasting AND stent* AND ureter* 0 results

12) permanent* AND stent* AND ureter* 0 results

13) semipermanent* AND stent* AND ureter* 0 results

14) selfexpand* AND stent* AND ureter* 0 results

15) self-expand* AND stent* AND ureter* 1 result

The 3 concept searches for long lasing/nickel titanium/self expanding AND stent AND ureteric obstructions could not be performed with the relatively limited search functionality available in this interface. A 2 concept search – for example ureter* AND stent* or long-term AND stent* - was insufficiently precise and returned unacceptably high volumes of irrelevant records. Given that these are supplementary, rather than core terms to describe the device, very simple strategies using the most precise terms only were used to replicate this section of the MEDLINE strategy (searches 5-15).

A.13: Source: ISRCTN Registry

Interface / URL: https://www.isrctn.com/

Database coverage dates: Information not provided

Search date: 02/05/17

Retrieved records: 10

Search strategy:

The following searches were carried out separately, using the homepage search interface. 0 results were retrieved.

1) memokath OR memo-kath OR memocath OR memo-cath OR MK051 OR MK-051 1 result

2) (“thermal memory” OR “shape memory” OR “smart metal” OR “smart metals” OR “memory metal” OR “memory metals” OR “memory alloy” OR “memory alloys” OR “muscle wire” OR “muscle wires” OR “smart alloy” OR “smart alloys”) AND (stent OR stents OR stenting) 0 results

3) (thermoexpanding OR thermoexpandable OR thermoexpansion OR “thermo-expanding” OR “thermo-expandable” OR “thermo-expansion” OR thermoactive OR thermoactivated OR thermoactivation OR “thermo-active” OR “thermo-activated” OR “thermos-activation” OR thermoformable OR “thermo-formable” OR thermosensitive OR “thermo-sensitive” OR thermoresponsive OR “thermo-responsive” OR thermoreactive OR “thermo-reactive”) AND (stent OR stents OR stenting) 0 results

4) (thermal OR thermally OR temperature OR temperatures OR heat) AND (expand OR expanding OR expands OR expandable OR expansion OR activated OR reactive OR reactivity OR sensitive OR sensitivity OR responsive OR responsivity OR formable) AND (stent OR stents OR stenting) 1 result

5) (niti OR nitinol) AND (stent OR stents OR stenting) AND (ureter OR ureters OR ureteric OR ureteral OR pelviureter OR pelviureteric OR pelviureteral OR ureteropelvic OR ureterovesical OR urinary OR urine OR urogenital OR urologic OR urological) 0 results

6) (nickel AND titanium) AND (stent OR stents OR stenting) AND (ureter OR ureters OR ureteric OR ureteral OR pelviureter OR pelviureteric OR pelviureteral OR ureteropelvic OR ureterovesical OR urinary OR urine OR urogenital OR urologic OR urological) 0 results

7) (“long-term” OR longterm OR “long-lasting” OR longlasting OR permanent OR semipermanent OR selfexpanding OR “self-expanding”) AND (stent OR stents OR stenting) AND (ureter OR ureters OR ureteric OR ureteral OR pelviureter OR pelviureteric OR pelviureteral OR ureteropelvic OR ureterovesical OR urinary OR urine OR urogenital OR urologic OR urological) 8 results

A.14: Source: Action on Bladder Cancer

Interface / URL: http://actionbladdercanceruk.org/
Search date: 02/05/17
Retrieved records: 0
Search strategy:
Site wide search: Memokath
Search Google using site limit: site:http://actionbladdercanceruk.org/ memokath

A.15: Source: Bladder and Bowel Foundation

Interface / URL: https://www.bladderandbowelfoundation.org/
Search date: 02/05/17
Retrieved records: 0
Search strategy:
Site wide search: Memokath
Search Google using site limit: site:https://www.bladderandbowelfoundation.org/ Memokath

A.16: Source: British Kidney Patient Association

Interface / URL: http://www.britishkidney-pa.co.uk/
Search date: 02/05/17
Retrieved records: 0
Search strategy:
Site wide search: Memokath
Search Google using site limit: site:http://www.britishkidney-pa.co.uk/ Memokath

A.17: Source: Fight Bladder Cancer

Interface / URL: http://fightbladdercancer.co.uk/
Search date: 02/05/17
Retrieved records: 0
Search strategy:
Site wide search: Memokath
Search Google using site limit: site:http://fightbladdercancer.co.uk/ Memokath

A.18: Source: Jo's Trust

Interface / URL: https://www.jostrust.org.uk/
Search date: 02/05/17
Retrieved records: 0
Search strategy:
Site wide search: Memokath – only result found on patient discussion form, rather than reference to trial. Not selected
Search Google using site limit: site:https://www.jostrust.org.uk/ memokath - as above, result from patient discussion forum not selected.

A.19: Source: Kidney Cancer UK (KCUK)
Interface / URL: https://www.kcuk.org.uk/
Search date: 02/05/17
Retrieved records: 0
Search strategy:
Site wide search: Memokath
Search Google using site limit: site:https://www.kcuk.org.uk/ Memokath

A.20: Source: Kidney Research UK
Interface / URL: http://www.kidneyresearchuk.org/
Search date: 02/05/17
Retrieved records: 0
Search strategy:
Site wide search: Memokath
Search Google using site limit: site:http://www.kidneyresearchuk.org/ Memokath

A.21: Source: Ovacome
Interface / URL: http://www.ovacome.org.uk/
Search date: 02/05/17
Retrieved records: 0
Search strategy:
Site wide search: Memokath
Search Google using site limit: site:http://www.ovacome.org.uk/ Memokath

A.22: Source: Ovarian Cancer Action
Interface / URL: http://ovarian.org.uk/
Search date: 02/05/17
Retrieved records: 0
Search strategy:
No site wide search option
Search Google using site limit: site:http://ovarian.org.uk/ memokath

A.23: Source: Pelvic Pain Support Network
Interface / URL: http://www.pelvicpain.org.uk/
Search date: 02/05/17
Retrieved records: 0
Search strategy:
Site wide search: Memokath
Search Google using site limit: site:http://www.pelvicpain.org.uk/ Memokath

A.24: Source: Prostate Cancer UK
Interface / URL: https://prostatecanceruk.org/
Search date: 02/05/17
Retrieved records: 0
Search strategy:
Site wide search: Memokath
Search Google using site limit: site:https://prostatecanceruk.org/ Memokath

A.25: Source: Target Ovarian Cancer
Interface / URL: http://www.targetovariancancer.org.uk/
Search date: 02/05/17
Retrieved records: 0
Search strategy:
Site wide search: Memokath
Search Google using site limit: site:http://www.targetovariancancer.org.uk/ Memokath

A.26: Source: British Uro-oncology Group (BUG)
Interface / URL: http://www.bug.uk.com/
Search date: 02/05/17
Retrieved records: 0
Search strategy:
No site wide search option
Search Google using site limit: site:http://www.bug.uk.com/ Memokath

A.27: Source: British Association of Urological Surgeons (BAUS)
Interface / URL: http://www.baus.org.uk/
Search date: 02/05/17
Retrieved records: 4
Search strategy:
Site wide search: Memokath
Search Google using site limit: site:http://www.baus.org.uk/ Memokath

A.28: Source: British Association of Urological Nurses (BAUN)
Interface / URL: http://www.baun.co.uk/
Search date: 02/05/17
Retrieved records: 0
Search strategy:
No site wide search option
Search Google using site limit: site:http://www.baun.co.uk/ Memokath

A.29: Source: British Association of Pediatric Urologists
Interface / URL: http://www.bapu.org.uk/
Search date: 02/05/17
Retrieved records: 0
Search strategy:
Site wide search: Memokath
Search Google using site limit: site:http://www.bapu.org.uk/ Memokath

A.30: Source: British Association of Pediatric Urologists
Interface / URL: http://www.bapu.org.uk/
Search date: 02/05/17
Retrieved records: 0
Search strategy:
Site wide search: Memokath
Search Google using site limit: site:http://www.bapu.org.uk/ Memokath

A.31: Source: PNN Medical
Interface / URL: http://www.pnnmedical.com/
Search date: 02/05/17
Retrieved records: 1
Search strategy:
Browsed "Memokath" section of the webpage – specifically the cost savings and clinical evidence sections. Results were only selected and downloaded for assessment if they were not identified by the previous database searches AND were specific to Memokath-051.

A.32: Source: American Urological Association Annual Meeting (AUA)
Search date: 02/05/17
Retrieved records: 2
Search strategy:
2016, 2015, 2014 indexed in Embase – covered by database searches – handsearches not required.
Proceedings from 2017 Annual Meeting (May 12-16 Boston) searchable via the conference webpages: https://www.eventscribe.com/2017/AUA2017/search.asp
Boolean search not supported – single terms or phrases only. Can search only on device name: Memokath – searching for stent alone returns over 300 records.

A.33: Source: European Association of Urology (EAU) Congress

Search date: 02/05/17
Retrieved records: 2
Search strategy: 2
2016, 2015, 2014 indexed in Embase – covered by database searches – handsearches not required.
2017 (March 24-28 London) published in European Urology Supplements Vol 16 Issue 3 March 2017 http://www.sciencedirect.com/science/journal/15699056/16/3
Search across whole issue for Memokath as a single term
Search across whole issue for stent as a single term
Records rapidly assessed for eligibility by information specialist – only relevant records selected and downloaded

A.34: Source: Société Internationale d'Urologie (SIU) Annual Congress

Search date: 03/05/17
Retrieved records: 1
Search strategy:
2014 indexed in Embase – covered by database searches – handsearches not required.
SIU Congress 2017 not to be held until September
2016 (20-23 October, Buenos Aires) searchable here as a supplement to World Journal of Urology https://link.springer.com/article/10.1007/s00345-016-1931-2
2015 (15-18 October, Melbourne) searchable here as a supplement to World Journal of Urology https://link.springer.com/journal/345/33/1/suppl/page/1
Control + F used to find the terms Memokath, and stent
Records rapidly assessed for eligibility by information specialist – only relevant records selected and downloaded

A.35: Source: British Association of Urological Surgeons (BAUS) Annual Scientific Meeting

Search date: 03/05/17
Retrieved records: 0
Search strategy:
Not indexed in Embase since 2013
BAUS ASM 2017 not due to take place until June 2017
2016 (27-30 June, Liverpool) Searchable here via BAUS e-Portal http://baus.multilearning.com/baus/#!*menu=6*browseby=3*sortby=2*ce_id=949
Memokath and stent used as single search terms
2015 (15-18 July, Manchester) Searchable here via BAUS e-Portal http://baus.multilearning.com/baus/#!*menu=6*browseby=3*sortby=2*ce_id=822

2014 Searchable here (supplement to BJU Vol 113 Suppl S5) http://onlinelibrary.wiley.com/doi/10.1111/bju.2014.113.issue-s5/issuetoc
Search this issue for memokath and stent as single terms

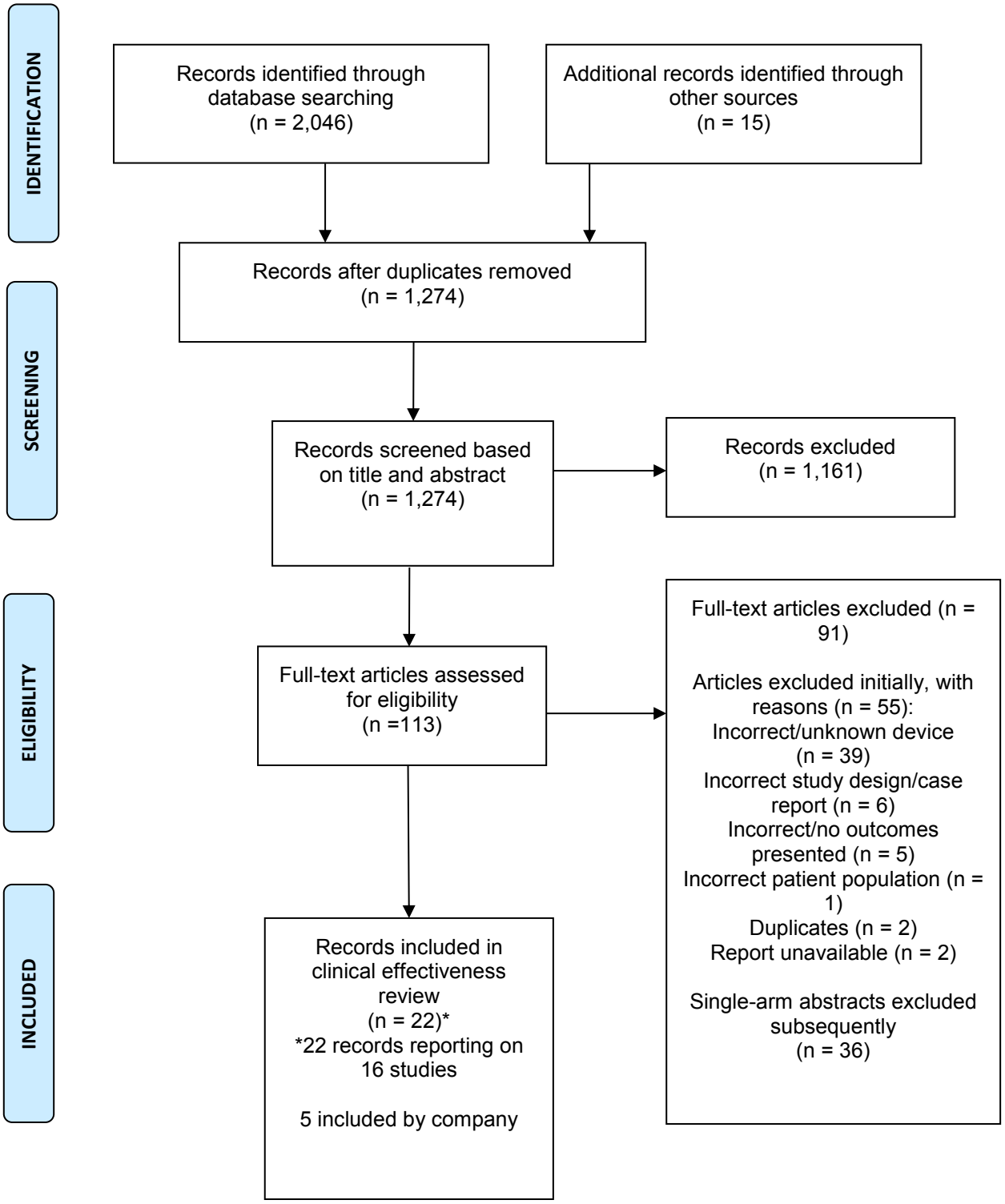
A.36: Source: British Uro-oncology Group (BUG) Annual Meeting

Search date: 03/05/17
Retrieved records: 1
Search strategy:
Not indexed by Embase. BUG Annual Meeting 2017 will not take place until September 2017.
2016, 2015 and 2014 published in Clinical Oncology (confirmed by email to BUG). Unclear which issue/supplement the abstracts are found in – therefore the term “memokath” was searched for across all journal content. 1 result.

A.37: Source: World Congress of Endourology & SWL Annual Meeting

Search date: 24/08/17
Retrieved records: 8
Search strategy:
2014 indexed by Embase. Annual Meeting 2017 will not take place until September 2017.
Proceedings from 2015 Annual Meeting available as conference supplement Journal of Endourology. September 2015, 29(S1): P1-A457 https://doi.org/10.1089/end.2016.29020.abstracts
Proceedings from 2016 Annual Meeting available as conference supplement Journal of Endourology. November 2016, 30(S2): P1-A464. https://doi.org/10.1089/end.2016.29020.abstracts
Control and F for “Memokath” as single search term – 8 records.

Appendix B: PRISMA flow diagram showing studies assessed from the EAC's literature search – Clinical review



Appendix C: Excluded studies table

Studies initially excluded at full paper review	Primary reason for exclusion
Al Aown, A., Iason, K., Panagiotis, K. & Liatsikos, E. N. 2010. Clinical experience with ureteral metal stents. *Indian Journal of Urology*, 26 (4), 474-479	Incorrect study design
Al Otaibi, K. & Al Damanhori, R. 2013. Minimally invasive treatment of ureterovaginal fistula: A review and report of a new technique. *Journal of Endourology*, 27, A266	Incorrect study design
Al Otaibi, K., Barakat, A.-E., El Darawany, H., Sheikh, A., Fadaak, K., Al Sowayan, O., Alsuhaibani, S., Al Damanhouri, R., Madi, M. & Elsadr, A. 2012. Minimally invasive treatment of ureterovaginal fistula: A review and report of a new technique. *Arab Journal of Urology Print*, 10 (4), 414-7	Case report
Bach, C., Kabir, M., Zaman, F., Kachrilas, S., Masood, J., Junaid, I. & Buchholz, N. 2011. Endourological management of ureteric strictures after kidney transplantation: Stenting the stent. *Arab Journal of Urology Print*, 9 (3), 165-9	Case report
Beiko, D. T., Knudsen, B. E. & Denstedt, J. D. 2003. Advances in ureteral stent design. *Journal of Endourology*, 17 (4), 195-199	Incorrect study design
Buchholz, N. P. N., Bafaloukas, N., Staios, D., Salahuddin, S. & Junaid, I. 2006. Memokath051((R)) stent for benign ureteral strictures in transplanted and non-transplanted kidneys. An attractive alternative. *Journal of Endourology*, 20, A318-A318	No outcomes
Burgos, F. J., Bueno, G., Gonzalez, R., Diaz, N. V. & Pascual, J. 2008. Long-term follow-up of self-expanding metallic stents for treatment of ureteral obstruction. *European Urology Supplements*, 7 (3), 107-107	Incorrect device
Chan, T. Y., Yu, C., Lam, K. M., Chu, S. K. & Man, C. W. 2010. Thermo-expandable titanium-nickel spiral ureteric stent for ureteric stricture early experience in a local hospital in hong kong. *International Journal of Urology*, 17, A173	Incorrect device
Cox, A. C. & Thomas, J. A. 2016. Insertion of thermoexpandable metallic ureteric stents can be aided by ureteric predilation. *Annals of the Royal College of Surgeons of England*, 98 (2), 158-9	Incorrect study design
Daskalopoulos, G., Hatzidakis, A., Triantafyllou, T., Delakas, D., Anezinis, P., Metaxari, M. & Cranidis, A. 2001. Intraureteral metallic endoprosthesis in the treatment of ureteral strictures. *European Journal of Radiology*, 39 (3), 194-200	Incorrect device
Diaz Romero, J. M., Torrecilla Garcia-Ripoll, J. R., Martin Martin, S., Trueba Arguinarena, F. J., Pascual Fernandez, M. A., Bedate Nunez, M., Pesquera Ortega, L. & Cortinas Gonzalez, J. R. 2013. Our experience with metallic ureteric stents for treating ureteral strictures and fistulae. *European Urology, Supplements*, 12 (3), 56-57	Incorrect device
Fernando, A., Hutchinson, S. & Anson, K. 2013. Experience with a novel technique for removal of metallic ureteric stents. *European Urology, Supplements*, 12 (3), 57	Incorrect outcomes
Flueckiger, F., Lammer, J., Klein, G. E., Hausegger, K., Lederer, A., Szolar, D. & Tamussino, K. 1993. Malignant ureteral obstruction: preliminary results of treatment with metallic self-expandable stents. *Radiology*, 186 (1), 169-73	Incorrect device
Flueckiger, F., Lugmayer, H., Klein, G. E. & Hausegger, K. 1992. Treatment of Malignant Ureteral Obstructions with Placement of Self-Expandable Metal Stents. *Radiology*, 185, 230-230	Incorrect device
Frederick, L., Ellimoottil, C., Kadlec, A., Shah, A., Turk, T. & Schwartz, B. F. 2017. Cost Analysis of Metallic Stents for Chronic Ureteral Obstruction: A Multicenter Study. *Urology Practice*, 4 (1), 21-24	Incorrect device
Gabriel, C. E. L., Nedilko, T., Paulose, P. A., Bach, C., Buchholz, N. & Knight, M. M. 2011. Can shockwave lithotripsy remove encrustation from ureteric nitinol stents? *European Urology, Supplements*, 10 (7), 482	Incorrect outcomes

Studies initially excluded at full paper review	Primary reason for exclusion
Geavlete, P., Georgescu, D., Multescu, R., Mirciulescu, V. & Geavlete, B. 2016. Bipolar approach in ureteral stenosis. *Journal of Endourology*, 30, A328-A329	Unknown device
Gomez, V., Laso, I., Nicolas, V. D., Patron, R. R. & Burgos, F. 2011. Are self-expanding metallic stents effective to resolve ureteral obstruction in the long-term follow-up? *Journal of Urology*, 1), e558-e559	Unknown device
Guliev, B., Komyakov, B., Novikov, A. & Shibliev, R. 2010. Long-term results of ureteral endoprostetics with nitinol metal stents. *Journal of Endourology*, 24, A316	Unknown device
Guliev, B., Komyakov, B. & Zagazezhev, A. 2016. Use of metallic ureteral stents in the treatment of benign and malignant ureteral stenosis. *Journal of Endourology*, 30, A136	Unknown device
Han, J. Y., Lee, S. S., Jeong, S. C., Park, S. W. & Chung, M. K. 2016. Comparison of initial experiences between full-length metallic stent and segmental metallic stent in malignant ureteral obstruction. *European Urology, Supplements*, 15 (3), e132+e132a	Incorrect device
Kallidonis, P., Katsanos, K., Karnabatidis, D., Kyriazis, I., Al Aown, A. & Liatsikos, E. 2009. Ureteral metal stents: Ten years experience for the treatment of malignant ureteral obstruction. *Journal of Endourology*, 23, A169	Unknown device
Kamata, S., Usui, N., Kamiyama, M., Yoneda, A., Tazuke, Y. & Ooue, T. 2005. Application of memory metallic stents to urinary tract disorders in pediatric patients. *Journal of Pediatric Surgery*, 40 (3), E43-5	Incorrect device
Kao, M. H. & Wang, C. C. 2014. The benefit of ureteral dilatation and multiple ureteral stents for patient with ureteral obstruction. *Journal of Endourology*, 28, A188	Incorrect device
Kao, M. H. & Wang, C. C. 2015. The efficacy and safety of ureteral dilation and long-term type ureteral stent for patients with ureteral obstruction. *Urological Science*, 26 (1), 65-68	Incorrect device
Khorsandi, M. J., Eigler, N. L., Lambert, T., Weinstock, B. S., Whiting, J. S. & Litvack, F. 1992. Temporary Stenting with the Heat Activated Recoverable Temporary Stent - Implantations up to 6 Weeks. *Circulation*, 86 (4), 800-800	Incorrect device
Komyakov, B. K., Guliev, B. G. & Zagazeshev, A. V. 2012. Efficacy of nitinol metallic stents for treatment of ureteral obstruction. *European Urology, Supplements*, 11 (1), e1103-e1103a	Unknown device
Kulkarni, R. & Bellamy, E. 2007. Duel expansion memokath 051 ureteric stent: Early experience with a novel design. *Journal of Endourology*, 21, A252-A252	Document unavailable
Liatsikos, E., Kagadis, G., Karnabatidis, D., Katsanos, K., Kallidonis, P., Perimenis, P., Nikiforidis, G. & Siablis, D. 2007. Application of self-expandable metal stents in ureteroileal anastomotic strictures: long-term results. *Journal of Endourology*, 21, A256-A256	Unknown device
Liatsikos, E. N., Karnabatidis, D., Katsanos, K., Kallidonis, P., Katsakiori, P., Kagadis, G. C., Christeas, N., Papathanassiou, Z., Perimenis, P. & Siablis, D. 2009. Ureteral metal stents: 10-year experience with malignant ureteral obstruction treatment. *Journal of Urology*, 182 (6), 2613-7	Incorrect device
Moraitis, K., Patel, D., El-Husseiny, T., Maan, Z., Papatsoris, A., Masood, J. & Buchholz, N. 2009. The Bart's modified Valdivia position: Our experience with simultaneous anterograde and retrograde urinary tract access for complex endourological procedures. *Archivio Italiano di Urologia e Andrologia*, 81 (3), 160	Incorrect device
Naryshkin, S. A., Teodorovich, O. V., Borisenko, G. G. & Kochiev, D. G. 2011. Uretero-pelvic junction memokath stenting with following laser mucous membrane hyperplasia coagulation. *Journal of Endourology*, 25, A256	Incorrect outcomes
NCT00166361 2004. Drainage of Malignant Extrinsic Ureteral Obstruction Using the Memokath Ureteral Stent	Duplicate
NCT00790686 2008. Tolerance and Effectiveness of Ureteral Stents MEMOKATH ® 051 in Chronic Strictures of the Ureter	No outcomes

Studies initially excluded at full paper review	Primary reason for exclusion
Ngoo, K. S. & Malek, R. 2015. The use of prostatic urethral stent in elderly and unfit men with benign prostatic enlargement: A nine-year analysis. *BJU International*, 116, 6-7	Incorrect device
Osther, P. J. S., Hansen, F., Al-Gameel, G. S. G., Nielsen, A. H., Hansen, M. B., Holm, M. & Andreassen, K. H. 2016. A new dual cone thermo-expandable metal stent for management of malignant ureteral obstruction in prostate cancer. *Journal of Urology*, 1), e448-e449	Duplicate

Studies subsequently excluded at full paper review	Primary reason for exclusion
2012. Abstracts for the BAUS Section of Endourology Annual Meeting 2012. *British Journal of Medical and Surgical Urology. Conference: BAUS Section of Endourology Annual Meeting*, 5 (3)	Abstract of a single-arm study
Agrawal, S., Brown, C. T., Bellamy, E. & Kulkarni, R. P. 2008. The Memokath (TM) 051 thermo-expandable metallic stent for ureteric obstruction: long-term experience. *BJU International*, 101, 40-40	Abstract of a single-arm study
Bach, C., Kabir, M. N., Zaman, F., Kachrilas, S., Masood, J., Islam, J. & Buchhloz, N. 2012. Ureteric strictures following renal transplantation: A minimal invasive treatment approach with a thermo-expandable nitinol ureteric stent. *Journal of Urology*, 1), e861	Abstract of a single-arm study
Bach, C., Karolides, T., Kabir, M., Kachrilas, S., Buchholz, N., Masood, J. & Junaid, I. 2012. Ureteric strictures after renal transplantation - A minimal invasive treatment approach using novel long-term nitinol stents. *British Journal of Medical and Surgical Urology*, 5 (3), 148-149	Abstract of a single-arm study
Bach, C., Moraitis, K., Pullis, C., Massod, J., Junaid, I. & Buchholz, N. 2011. Management of ureteric strictures with nickeltitanium ureteric stents with thermal-shape memory: A comparison of the outcome between benign and malignant strictures. *European Urology, Supplements*, 10 (2), 223	Abstract of a single-arm study
Bier, S., Rausch, S., Aufderklamm, S., Todenhofer, T., Amend, B., Neumann, E., Bedke, J., Schwentner, C., Stenzl, A. & Kruck, S. 2016. Memokath 051-a save alternative for treatment of ureteric strictures. *Journal of Urology*, 1), e474	Abstract of a single-arm study
Bourdoumis, A., Kachrilas, S., Kapoor, S., Zaman, F., Wardak, S., Papatsoris, A., Buchholz, N. & Masood, J. 2013. The use of a thermoexpandable metal alloy stent in the minimally invasive treatment of retro peritoneal fibrosis-A single centre experience. *Journal of Endourology*, 27, A211	Abstract of a single-arm study
Chetwood, A., Ni Raghallaigh, H., Agrawal, S. & Kulkarni, R. 2016. Memokath 051 stent in benign ureteric strictures: Long-term follow-up. *Journal of Endourology*, 30, A141-A142	Abstract of a single-arm study
Elbaroni, W., Dooher, M., Hennessey, D., Connolly, D. & Thompson, T. 2016. Management of ureteric strictures with Memokath 051 metallic stent: updated experience from a single centre. *BJU International*, 118, 47-47	Abstract of a single-arm study
Forster, L., Watson, L., Breeze, C., Di Benedetto, A., Graham, S., Patki, P. & Patel, A. 2017. Analysing 5-Year Memokath Outcomes for Malignant and Benign Ureteric Obstruction: A Proposed Update to Clinical Guidelines. *Journal of Urology*, 197 (4), E1186-E1186	Abstract of a single-arm study
Franke, M., Allan, R., Holm-Nielsen, A., Walter, S., Andreassen, K. H. & Osther, P. J. S. 2011. Use of the thermo-expandable ureteralmetal stent (MemokathTM051) for thetreatment of chronic ureteral strictures dueto retroperitoneal/periaortal fibrosis. *Journal of Endourology*, 25, A91-A92	Abstract of a single-arm study
Franke, M., Ryhammer, A., Holm-Nielsen, A., Graversen, P., Nohr, M., Faber, J. E. & Osther, P. J. S. 2010. Long-term outcome of the thermoexpandable ureteral metal stent (MemokathTM051) for the treatment of chronic ureteral stictures: Results of the Danish Memokath study. *Journal of Endourology*, 24, A174	Abstract of a single-arm study

Studies subsequently excluded at full paper review	Primary reason for exclusion
Franke, M., Ryhammer, A., Holm-Nielsen, A., Nohr, M. & Osther, P. J. S. 2011. Use of the thermo-expandable ureteral metal stent (MemokathTM051) for the treatment of chronic ureteral strictures in patients with prior stone disease. *European Urology, Supplements*, 10 (7), 481-482	Abstract of a single-arm study
Franke, M., Ryhammer, A., Holm-Nielsen, A. H., Walter, S., Faber, J. E., Graversen, P., M, N. O. & Osther, P. J. S. 2011. Thermo-expandable ureteral metal stent (MemokathTM051) for the treatment of chronic ureteral strictures: Long-term data of the Danish Memokath study. *European Urology, Supplements*, 10 (2), 223-224	Abstract of a single-arm study
Geavlete, P., Nita, G. & Geavlete, B. 2008. Memokath stenting in neoplastic extrinsic ureteral stenosis. *European Urology Supplements*, 7 (3), 335-335	Abstract of a single-arm study
Ghani, K. R., Patel, U. & Manson, K. 2004. Close encounters with the Memokath 051 ureteric stent - Lessons learnt from unusual complications. *Journal of Endourology*, 18, A89-A89	Abstract of a single-arm study
Kabir, M. N., Goyal, A., Bach, C., Masood, J., Buchholz, N. & Islam, J. 2012. Ureteric memokath in the management of ureteric strictures following renal transplantation. *Journal of Endourology*, 26, A140-A141	Abstract of a single-arm study
Kulkarni, R. & Bellamy, E. 2007. Memokath 051 ureteric stent: Has it found its place after 11 years? *Journal of Endourology*, 21, A253-A253	Abstract of a single-arm study
Kulkarni, R. & Bellamy, E. 2011. Duel expansion memokath 051 stent in the management of ureteric strictures: An outcome analysis. *Journal of Endourology*, 25, A92	Abstract of a single-arm study
Kulkarni, R., Bellamy, E. & Thomas, K. 2005. Management of benign ureteric strictures with memokath 051 ureteric stent - 8 year experience. *Journal of Endourology*, 19, A21-A21	Abstract of a single-arm study
Kulkarni, R. P. & Bellamy, E. A. 1999. A new thermo-expandable shape-memory nickel-titanium alloy stent for the management of ureteric strictures. *BJU International*, 83 (7), 755-9	Abstract of a single-arm study
Lee, G., Longhorn, S., Ayra, M., Foley, C., Choong, S. & Philp, T. 2005. Thermo-expandable ureteric stent in the treatment of refractory benign ureteric strictures: 7 year experience. *Journal of Endourology*, 19, A22-A22	Abstract of a single-arm study
Lee, G., Longhorn, S., Kellett, M., Allen, C., Rickards, D., Choong, S. & Philp, T. 2006. Thermo-expandable ureteric stent in the management of complex refractory benign ureteric strictures: Long term efficacy and risk factors associated with complications. *Journal of Urology*, 175 (4), 349-350	Abstract of a single-arm study
Lee, G., Longhorn, S., Kellett, M., Allen, C., Rickards, D., Choong, S. & Philp, T. 2006. Thermo-expandable ureteric stent in the management of complex refractory benign ureteric strictures: Long-term efficacy and risk factors associated with complications. *European Urology Supplements*, 5 (2), 70-70	Abstract of a single-arm study
Masood, J., Hajdinjak, T., Papatsoris, A. G., Sheikh, T., Junaid, I. & Buchholz, N. 2008. A long-term indwelling thermo-expandable metal stent (Memokath (R) 051CW) in the treatment of chronic ureteric strictures. *BJU International*, 101, 52-52	Abstract of a single-arm study
Moraitis, K., El-Husseiny, T., Wazait, H., Islam, J., Masood, J. & Buchholz, N. 2010. Thermo expandable segmental metal ureteric stents in the management of ureteric strictures: A single centre experience from the UK. *Journal of Urology*, 1), e422-e423	Abstract of a single-arm study
Moraitis, K., El-Husseiny, T., Wazait, H., Junaid, I., Masood, J. & Buchholz, N. 2010. Segmental nickel-titanium ureteric stents with thermal-shape memory in the management of ureteric strictures. *Journal of Endourology*, 24, A173	Abstract of a single-arm study
Nita, G. D., Moldoveanu, C., Mirciulescu, V., Arabagiu, I., Persu, C., Geavlete, B., Multescu, R. & Geavlete, P. 2010. Long-term complications of the memokath stent. *European Urology, Supplements*, 9 (6), 638	Abstract of a single-arm study
Osther, P. J. S., Al-Gameel, G. S. G., Hansen, F., Nielsen, A. H., Hansen, M. B., Holm, M. & Andreassen, K. H. 2016. A New Dual Cone Thermo-	Abstract of a single-arm study

Studies subsequently excluded at full paper review	Primary reason for exclusion
Expandable Metal Stent for Management of Malignant Ureteral Obstruction in Prostate Cancer. *Journal of Urology*, 195 (4), E448-E449	
Papatsoris, A., Staios, D., Shaikh, T., Masood, J., Junaid, I. & Buchholz, N. 2007. Treating chronic ureteric strictures with a permanent indwelling thermo-expandable metal stent (Memokath((R)) 051CW). *Journal of Endourology*, 21, A253-A253	Abstract of a single-arm study
Reyes, H. V., Canals, L. R., Elias, J. D., Galarza, L. P. & Miranda, E. F. 2015. Follow-up after 4 years of ureteral stenosis in transplant kidney managed with long-term thermoexpandable metallic stent. *Journal of Urology*, 1), e1017	Abstract of a single-arm study
Torrecilla Garcia-Ripoll, J. R., Diaz Romero, J. M., Martin Martin, S., Trueba Arguiñarena, F. J., Udaondo Cascante, M. A., Bedate Nuñez, M., Rivero Martinez, M. D. & Cortiñas Gonzalez, J. R. U4-13 Treatment Of Urinary Fistula In Ureteropyelostomy Through Metallic Stents (Memokath051®). Proceedings from 2015 Annual Meeting available as conference supplement Journal of Endourology, 2015. P1-A457.	Abstract of a single-arm study
Umranikar, S., Besarani, D., Khan, S. a. A. & Kulkarni, R. P. 2010. Long term results of the Memokath ureteric stent: A 15 year retrospective analysis. *Journal of Endourology*, 24, A273	Abstract of a single-arm study
Vila Reyes, H., Riera Canals, L., Dominguez Elias, J., Pujol Galarza, L. & Franco Miranda, E. 2015. Follow-up after 4 years of ureteral stenosis in transplant kidney managed with long-term thermo-expandable metallic stent (Memokath 051). *European Urology, Supplements*, 14 (2), e849	Abstract of a single-arm study
Zaman, F., Wazait, H., El-Husseiny, T., Junaid, I., Masood, J. & Buchholz, N. 2010. A thermoexpandable segmental metallic ureteric stent in the management of malignant ureteric obstruction - A single centre experience in the UK. *Journal of Endourology*, 24, A318	Abstract of a single-arm study
Zhao, J., Bishara, S. & Dasgupta, R. U4-12 The management of severe ureteric stricture disease with Memokath stents. Proceedings from 2015 Annual Meeting available as conference supplement Journal of Endourology, 2015. P1-A457	Abstract of a single-arm study
Pandey, P. K., Gupta, A. & Sood, R. 2014. The use of a thermoexpandable metal alloy stent in the minimally invasive urology: Our initial experience. *Indian Journal of Urology*, 30, S125	Unknown device
Patel, D., El-Husseiny, T., Moraitis, K., Maan, Z., Masood, J. & Buchholz, N. 2010. A validated questionnaire study comparing stent-related symptoms between conventional JJ stents and a novel thermo-expandable segmental ureteric metal stent. *Journal of Urology*, 1), e822	Unknown device
Patel, D., Maan, Z., El-Husseiny, T., Papatsoris, A., Masood, J. & Buchholz, N. 2009. A validated questionnaire study comparing stent-related symptoms between conventional JJ stents and a novel thermo-expandable segmental ureteric metal stent. *Journal of Endourology*, 23, A168	Unknown device
Patel, P., Maan, Z., Moraitis, K., El-Husseiny, T., Masood, J., Junaid, I. & Buchholz, N. 2010. A retrospective comparative validated questionnaire study comparing stent-related symptoms between conventional JJ stents and a novel thermo-expandable segmental ureteric metal stent. *European Urology, Supplements*, 9 (2), 101-102	Unknown device
Ranasinghe, A., Wong, J., Tse, V. & Wong, E. 2016. Long-term results of the urethral MemokathTM stent trial for stabilisation of recurrent bulbar urethral strictures. *BJU International*, 117, 67	Incorrect device
Ricciotti, G., Bozzo, W., Perachino, M., Pezzica, C. & Puppo, P. 1994. Heat-expandable intraurethral stents: Indications, technique, results and complications. *Acta Urologica Italica*, 8 (4), 195-201	Incorrect device
Ricciotti, G., Bozzo, W., Perachino, M., Pezzica, C. & Puppo, P. 1995. Heat-expansible permanent intraurethral stents for benign prostatic hyperplasia and urethral strictures. *Journal of Endourology*, 9 (5), 417-22	Incorrect device

Studies subsequently excluded at full paper review	Primary reason for exclusion
Shakir, F., Burmagin, A. & Sorokin, K. 2012. Ureteral thermo-expandable stent placement in modified supine-lateral position. *Journal of Endourology*, 26, A234	Unknown device
Soni, B. M., Vaidyanatham, S. & Krishnan, K. R. 1994. Use of Memokath, a second generation urethral stent for relief of urinary retention in male spinal cord injured patients. *Paraplegia*, 32 (7), 480-8	Incorrect patient population
Spernat, D. & King, Q. M. 2009. Safety and Efficacy of the Urethral Thermo-Expandable Metallic Stent. *BJU International*, 103, 2-2	Incorrect device
Takahashi, R., Kimata, R., Hamasaki, T., Kawarasaki, Y. & Kondo, Y. 2013. Memokath(TM) urethral stents induce incontinence in patients with urethral balloon catheters. *Journal of Nippon Medical School = Nihon Ika Daigaku Zasshi*, 80 (6), 433-7	Incorrect device
Wakui, M., Takeuchi, S., Isioka, J., Iwabuchi, K. & Morimoto, S. 2000. Metallic stents for malignant and benign ureteric obstruction. *BJU International*, 85 (3), 227-32	Incorrect device
Watson, L. E., Forster, L., Di Benedetto, A., Tanabalan, C., Mosli-Lynch, C., Chari, N., Almushatat, A., Graham, S., Patel, A. & Patki, P. 2016. A 3rd party independent retrospective review of the use of Memokath stents to manage ureteric strictures in a high-volume tertiary referral centre. *Journal of Endourology*, 30, A137-A138	Unknown device
Wedderburn, A. & Harrison, M. 1999. Long-term stenting for benign ureteric disease. *Journal of the Royal Society of Medicine*, 92 (7), 368-9	Unknown device
2010. Thermo-expandable metallic ureteric stents provide an alternative to standard JJ stenting. *BJU International*, 106, 1-1	Incorrect device
2012. Abstracts of the Hong Kong Urological Association Annual Scientific Meeting 2012. *BJU International. Conference: Hong Kong Urological Association Annual Scientific Meeting*, 111 (no pagination)	Incorrect device
2012. SNIS 9th Annual Meeting. *Journal of NeuroInterventional Surgery. Conference: 9th Annual Meeting of the Society of NeuroInterventional Surgery, SNIS*, 4 (no pagination)	Incorrect device
2013. 33rd Congress of the Societe Internationale d'Urologie. *Urology. Conference: 33rd Congress of the Societe Internationale d'Urologie. Vancouver, BC Canada. Conference Publication:*, 82 (3 SUPPL. 1)	Incorrect device
2014. 30th Iranian Congress of Radiology. *Iranian Journal of Radiology*, 11, S16	Document unavailable

Appendix D: Detailed critical appraisal of clinical studies

Study name (acronym)	Was the cohort recruited in an acceptable way[1]?	Was the exposure accurately measured to minimise bias[2]?	Was the outcome accurately measured to minimise bias[3]?	Have the authors identified all important confounding factors?	Have the authors taken account of the confounding factors in the design and/or analysis?	Was the follow-up of patients complete?	How precise (for example, in terms of confidence interval and p values) are the results?
Comparative studies							
Maan 2010 (Maan et al., 2010)	**Yes** – Questionnaire was mailed to 70 consecutive patients who underwent insertion of double-J stent or Memokath-051. Patients were statistically similar in both groups for age and sex	**Unclear** – A description of the stent procedure is provided, but there is insufficient information reported to assess whether there was any variation in the procedure	**Yes** – Responses to the USSQ were analysed. The USSQ is a validated questionnaire	**Unclear** – Patient groups were well matched for age and sex. Other factors have not been clearly identified/reported by the authors	**Unclear** – Confounding factors are not clearly identified/reported by the authors	**Not applicable**	**Unclear** – Domain scores were compared for the double-J and Memokath-051 groups. Median values and p-values are reported but no standard deviations or confidence intervals
Kim 2014 (Kim et al., 2014)	**Yes** – All patients that received 1 of 2 metallic stents (Memokath-051 or UVENTA) from	**Yes** – A description of the insertion procedure carried out for all	**Unclear** – Outcomes and outcome measures defined. Measurement methods were the	**Unclear** – Confounding factors are not clearly identified/report	**Unclear** – Confounding factors are not clearly identified/report	**Yes** – All patients were followed up completely and the 2 patients	**Unclear** – P-values and standard deviations reported but no

1 Cohort recruitment was considered acceptable providing sufficient detail on the selection and similarity of patients had been reported by the authors.
2 The exposure was considered accurately measured if a description of the stent insertion procedure was provided, the authors reported that the same procedure was carried out for all patients, and all procedures were performed by surgeons with a similar level of experience.
3 The outcomes were considered accurately measured providing they (and their measurements) were clearly defined by the authors, and appropriate consideration / action had been taken to minimise detection bias.

Study name (acronym)	Was the cohort recruited in an acceptable way[1]?	Was the exposure accurately measured to minimise bias[2]?	Was the outcome accurately measured to minimise bias[3]?	Have the authors identified all important confounding factors?	Have the authors taken account of the confounding factors in the design and/or analysis?	Was the follow-up of patients complete?	How precise (for example, in terms of confidence interval and p values) are the results?
	Nov 2011 to May 2013 were included. Differences between patients across both groups were not statistically significant	patients is reported. Stents were inserted by 1 of 2 experienced surgeons	same in both groups. No evidence that assessors were blinded	ed by the authors	ed by the authors	lost to follow-up (death) are reported	confidence intervals. Insufficient information to permit judgement
NCT00166361 2014 (NCT00166361, 2014)	**Yes -** Patients were recruited from a single practice to either Memokath-051 or double-J groups from Feb 2004 to May 2011. Eligibility criteria for patients is reported	**Unclear –** No details of the stent insertion procedure are provided	**Unclear –** Outcome measure defined (mean stent dwell time). Assessors were not blinded. Insufficient information in clinical trial record to permit judgement	**Unclear –** Confounding factors are not clearly identified/reported in the clinical trial record	**Unclear –** Confounding factors are not clearly identified/reported in the clinical trial record	**Yes –** All patients were followed up	**Unclear -** No statistical analysis provided. Insufficient information to permit judgement
Single-arm studies							
Agrawal 2009 (Agrawal et al., 2009)	**Unclear** – Between Nov 1996 and Nov 2007, data were collected for all patients who had Memokath-051	**Unclear** – A standard protocol was used for all insertions. Stents were inserted by 1 surgeon, their level of	**Unclear** – Outcome measures were not clearly defined. Follow-up procedure was not described. No evidence that	**Unclear** – Confounding factors are not clearly identified/reported by the authors	**Unclear** – Confounding factors are not clearly identified/reported by the authors	**Unclear** – Patients were followed up for between 1.5 and 33 months. The reasons for the difference in	**Unclear –** No statistical analysis provided. Insufficient information to permit judgement

Study name (acronym)	Was the cohort recruited in an acceptable way[1]?	Was the exposure accurately measured to minimise bias[2]?	Was the outcome accurately measured to minimise bias[3]?	Have the authors identified all important confounding factors?	Have the authors taken account of the confounding factors in the design and/or analysis?	Was the follow-up of patients complete?	How precise (for example, in terms of confidence interval and p values) are the results?
	inserted. Authors do not comment on the similarity of patients	experience is not reported	assessors were blinded			follow-up is unclear	
Arya 2001 (Arya et al., 2001)	**Unclear** – Authors report that from Nov 1997 to July 2000, 13 Memokath-051 stents were placed in 11 patients (collected retrospectively). Unclear whether these patients were specifically selected or whether this was the total number receiving the stent. Authors do not comment on the similarity of patients	**Unclear** – All patients were assessed for baseline urea, electrolytes, creatinine, urine microscopy and culture, but specific data and detail of the measurement methods used are not reported. A description of the insertion procedure carried out for all patients is reported. Authors do not report who inserted the stents	**Unclear** – Outcome measures not clearly defined. Patient follow-up intervals not reported. No evidence that assessors were blinded	**Unclear** – Confounding factors have not been clearly identified by the authors	**Unclear** – Confounding factors are not clearly identified/reported by the authors	**Unclear** – Patients were followed up for between 1.5 and 33 months. The reasons for the difference in follow-up is unclear	**Unclear** – No statistical analysis provided. Insufficient information to permit judgement

Study name (acronym)	Was the cohort recruited in an acceptable way[1]?	Was the exposure accurately measured to minimise bias[2]?	Was the outcome accurately measured to minimise bias[3]?	Have the authors identified all important confounding factors?	Have the authors taken account of the confounding factors in the design and/or analysis?	Was the follow-up of patients complete?	How precise (for example, in terms of confidence interval and p values) are the results?
Bach 2013 (Bach et al., 2013)	**Unclear** – 8 patients who had received a renal transplant were referred to the author's clinic with ureteral stenosis over a 7 year period (2003 - 2010). Authors do not comment on the similarity of patients	**No** – Stent insertion was carried out differently in some of the patients	**Unclear** – Outcome measures not clearly defined. Patients were followed-up 6 weeks, 3 months and every 6 months thereafter. No evidence that assessors were blinded	**Unclear** – Confounding factors have not been clearly identified by the authors	**Unclear** – Confounding factors were not clearly identified/reported, so it is unclear if they were taken into account	**Yes** – All patients were followed up	**Unclear** – Descriptive statistics (n and % of patients) provided only. No statistical analysis
Bourdoumis 2014 (Bourdoumis et al., 2014)	**Unclear** – Authors reviewed (retrospectively) records of 14 patients between Apr 2008 and Feb 2013. Unclear whether these patients were specifically selected or whether they were total number that received the	**Unclear** – No details of the stent insertion procedure are provided	**Unclear** – Outcome measures defined and measurements reported. Patient were followed-up at 6 weeks, 3 months, 6 months and annually thereafter. No evidence that assessors were blinded	**Unclear** – Confounding factors have not been clearly identified by the authors	**Unclear** – Confounding factors were not clearly identified/reported, so it is unclear if they were taken into account	**Yes** – All patients were followed up	**Unclear** – p-values and standard deviations are reported but no confidence intervals

Study name (acronym)	Was the cohort recruited in an acceptable way[1]?	Was the exposure accurately measured to minimise bias[2]?	Was the outcome accurately measured to minimise bias[3]?	Have the authors identified all important confounding factors?	Have the authors taken account of the confounding factors in the design and/or analysis?	Was the follow-up of patients complete?	How precise (for example, in terms of confidence interval and p values) are the results?
	stent. Authors do not comment on the similarity of patients						
Boyvat 2005 (Boyvat et al., 2005)	**Unclear** – From Oct 1985 to Jan 2004, data were collected for patients who developed recurrent renal transplant ureter obstruction. Authors do not comment on the similarity of patients	**Unclear** – A description of the insertion procedure carried out for all patients is reported. Authors do not report who inserted the stents	**Unclear** – Outcome measures not clearly defined. Patients were followed up on the first and tenth days, then monthly intervals for the first 3 months, then 3 months thereafter. No evidence that assessors were blinded	**Unclear** – Confounding factors have not been clearly identified by the authors	**Unclear** – Confounding factors are not clearly identified/reported by the authors	**Yes** – All patients followed up	**Unclear** – Low number of patients. No statistical analysis provided. Insufficient information to permit judgement
Klarskov 2005 (Klarskov et al., 2005)	**Unclear** – 33 consecutive patients at 7 Danish centres were included. Authors do not comment on the similarity of patients	**Unclear** – A description of the insertion procedure carried out for all patients is reported. Authors do not report who inserted the stents	**Unclear** – Outcome measures were not clearly defined. Patients were followed up after 1 month and then every 3 months for at least 1 year. Patients were assessed clinically and by lab tests and by x-ray and	**Unclear** – Confounding factors are not clearly identified/reported by the authors	**Unclear** – Confounding factors are not clearly identified/reported by the authors	**Unclear** – Patients were followed up for between 3 and 30 months. The reasons for the difference in follow-up is unclear	**Unclear** – Kaplan Meier curve is presented for time to migration. Descriptive statistics are presented for complications

Study name (acronym)	Was the cohort recruited in an acceptable way[1]?	Was the exposure accurately measured to minimise bias[2]?	Was the outcome accurately measured to minimise bias[3]?	Have the authors identified all important confounding factors?	Have the authors taken account of the confounding factors in the design and/or analysis?	Was the follow-up of patients complete?	How precise (for example, in terms of confidence interval and p values) are the results?
			renography at months 3 and 12. No evidence that assessors were blinded				
Kulkarni 2001 (Kulkarni and Bellamy, 1999)	**Unclear** – Between Nov 1996 and Nov 2000, data were collected for all patients who had Memokath-051. Authors do not comment on the similarity of patients	**Unclear** – No non-exposure group. All insertion procedures carried out the same way. Indications reported but limited baseline patient information to inform assessment. A description of the insertion procedure carried out for all patients is reported. Authors do not report who inserted the stents	**Unclear** – Outcome measures not clearly defined. Patients were followed up on the first and tenth days, then monthly intervals for the first 3 months, then 3 months thereafter. No evidence that assessors were blinded	**Unclear** – Confounding factors have not been clearly identified by the authors.	**Unclear** – Confounding factors are not clearly identified/reported by the authors.	**Yes** – All patients were followed up and the 8 patients lost to follow-up (death) are reported	**Unclear** – No statistical analysis provided. Insufficient information to permit judgement.

Study name (acronym)	Was the cohort recruited in an acceptable way[1]?	Was the exposure accurately measured to minimise bias[2]?	Was the outcome accurately measured to minimise bias[3]?	Have the authors identified all important confounding factors?	Have the authors taken account of the confounding factors in the design and/or analysis?	Was the follow-up of patients complete?	How precise (for example, in terms of confidence interval and p values) are the results?
Papadopoulos 2010 (Papadopoulos et al., 2010)	**Unclear** – Authors report that over a 5 year period metal stents were placed in 13 patients who were monitored prospectively but it is unclear whether these patients were specifically chosen or whether this is the total number receiving the stent. Authors do not comment on the similarity of patients	**Unclear** – Limited information about the procedure reported and whether there was any variation amongst patients	**Unclear** – Outcome measures were not clearly defined. Patients underwent postoperative X-ray to ensure stent position was correct. Patients were followed up at 3 months and then every 6 months after No evidence that assessors were blinded	**Unclear** – Confounding factors are not clearly identified/reported by the authors	**Unclear** – Confounding factors are not clearly identified/reported by the authors	**Yes** – All patients were followed up completely and the 3 patients lost to follow-up (death) are reported	**No** – Results are presented for each individual patient. There is no further statistical analysis
Papatsoris 2010 (Papatsoris and Buchholz, 2010)	**Unclear** - All patients who underwent Memokath-051 insertion from April 2004 to March 2009 were	**Unclear** – A description of the procedure carried out for all patients is reported	**Unclear** – Outcome measures were not clearly defined. Patients underwent follow-up protocol at 2 weeks, 3 months and every 6 months	**Unclear** – Confounding factors are not clearly identified/reported by the authors	**Unclear** – Confounding factors are not clearly identified/reported by the authors	**Yes** – All patients were followed up completely	**Unclear** – Authors provide descriptive statistics (n and % of patients) only

Study name (acronym)	Was the cohort recruited in an acceptable way[1]?	Was the exposure accurately measured to minimise bias[2]?	Was the outcome accurately measured to minimise bias[3]?	Have the authors identified all important confounding factors?	Have the authors taken account of the confounding factors in the design and/or analysis?	Was the follow-up of patients complete?	How precise (for example, in terms of confidence interval and p values) are the results?
	included. Authors do not comment on the similarity of patients		after. No evidence that assessors were blinded				
Zaman 2011 (Zaman et al., 2011)	**Unclear** – All patients referred to the centre over a 4-year period with malignant ureteric strictures were considered for insertion of Memokath-051. Authors do not comment on the similarity of patients	**Yes** – All of the stents were inserted by 1 of 3 experienced surgeons in the same hospital using a standard protocol	**Unclear** – Outcome measures were quite vague and subjective, defined in the paper as efficacy, tolerability and safety associated with Memokath-051. Patients were followed up with renal biochemistry and ultrasonography at 3,6,12 months and annually thereafter. No evidence that assessors were blinded	**Unclear** – Confounding factors are not clearly identified/reported by the authors	**Unclear** – Confounding factors are not clearly identified/reported by the authors	**Yes** – All patients were followed up completely and the 3 patients lost to follow-up (death) are reported	**Unclear** – Authors provide descriptive statistics (n and % of patients) only

Appendix E: Full Critique of Company Search Strategy, Detailed EAC Search Strategy and PRISMA Diagram – Economic Evidence

Company search strategy to identify economic evidence

The Peer Review of Electronic Search Strategies (PRESS) Checklist was used to inform the critique of the company's search strategies (McGowan et al., 2010). The PRESS checklist is an evidence-based tool used to critically appraise literature search strategies. The PRESS project was funded by the Canadian Agency for Drugs and Technologies in Health (CADTH) and this approach to peer reviewing search strategies is supported by the Cochrane Collaboration's Information Retrieval Methods Group (Sampson et al., 2008).

Search reporting

The MTEP Submission Template requires that the search strategies used to retrieve economic evidence are described. Whilst Section 8.1.1 does contain some information about search methodology, this is very limited and is not sufficient to accurately replicate the company's search. The full search strategies, exactly as run in each resource, are not provided. Section 10, Appendix 3 of the submission, where it is expected that they are recorded, is blank.

As with the clinical evidence searches, search terms are listed but no information is provided on the fields these terms were searched for in, making it impossible to assess or accurately reproduce the strategy. The company state that after searching for the device name, "*then the search was for the cost related studies" (*Section 8.1.1, Submission). It is not clear whether this refers to combining the intervention terms with an additional concept, economic evidence, as part of the search strategy or whether this comment describes the screening of records by reviewers to identify economic evidence rather than the search itself. This ambiguity makes it difficult to comment on the appropriateness of the strategy.

The resources searched by the company are listed. However, information about search interfaces, date of searches, and the number of records retrieved per database is not provided.

Search sources

The company submission states that searches were undertaken using MEDLINE, PubMed, Embase, ClinicalTrials.com, Google and in-house sources. We assume ClinicalTrials.com is an error and refers to ClinicalTrials.gov. Whilst these resources are appropriate, the company omitted

to search any resources that specifically cover economic evidence such as EconLit, NHS EED, CEA Registry, or HTA Database. All of these resources, with the exception of EconLit, are freely available and can be searched without a subscription. EconLit and NHS EED are specified in Appendix 10.1 of the submission template as resources that should be searched as a minimum to identify economic evidence, not searching them may have increased the risk of missed relevant studies.

The company do not specifically describe a strategy to identify unpublished economic evidence, although this may have been identified by searches of Google, ClinicalTrials.gov and their own internal records. The submission methodology may have been enhanced by including a wider search for conference abstracts and by searching additional trial registers suggested by methods guidance and research.

Search strategy structure, search terms and syntax, search restrictions

We have not been supplied the exact search strategies used by the company which makes it impossible to ascertain the structure and content of the strategies run. The approach reported states that single terms Memokath, then Memokath-051, then Memokath 51 were searched on. Whilst Memokath alone would be sufficient, this single concept approach is reasonably sensitive as the results are not restricted by additional concepts. However, the following statement "*then the search was for the cost related studies" (Section 8.1.1, Submission)* raises the possibility that an additional concept for economic outcomes was included. If an additional concept was used, the search terms that formed this are not supplied, and therefore the appropriateness of this approach cannot be assessed.

Retrieval could have been enhanced by additionally searching for records which may not have explicitly referred to Memokath-051 by name in the database record, but instead may have described notable features of the device such as "thermoexpandable" or "shape memory".

No information was provided on whether any date, language or other limits were applied.

Rerun of the company's searches

As exact search strategies were not provided by the company, the EAC were unable to replicate and re-run the searches.

Additional EAC searches

A *de novo* literature search was undertaken by the EAC.

The searches carried out by the EAC to identify clinical effectiveness evidence (reported in Section 3.1 and Appendix A) were not restricted by study design and were prospectively designed to retrieve both clinical effectiveness and economic evidence. The sources searched were extensive and included those required as a minimum by NICE for the search of economic evidence, as specified in the submission template (MEDLINE, MEDLINE In-Process and Embase). The additional search for economic evidence carried out by the EAC consisted of searches of the economic-specific resources required as a minimum by NICE (EconLit and NHS EED), in addition to the CEA Registry. The clinical evidence search strategy (Figure A1, Appendix A) was adapted appropriately for use in these resources.

Table E1: Databases and information sources searched

Resource	Interface / url
NHS Economic Evaluation Database (NHS EED)	Cochrane Library
EconLit	OvidSP
CEA Registry	http://healtheconomics.tuftsmedicalcenter.org/cear4/Home.aspx

Results of the searches were downloaded in EndNote reference management software and deduplicated using several algorithms, both against each other and the results of the clinical evidence search.

EAC Literature Search Results

The EAC economic evidence searches identified 9 records, an additional record was supplied via NICE expert advisers. After deduplication, 9 records remained. When added to the results of the clinical evidence searches, this gave a total of 2,071 records, of which 1,286 remained after deduplication for assessment.

Table E2: Literature search results – economic evidence

Resource	Records identified
NHS Economic Evaluation Database (NHS EED)	1
EconLit	8
CEA Registry	0
Records identified from other sources (reference checking, supplied by experts etc.)	1
Total	**10**
Total after deduplication	**9**

EAC search – full search strategies – economic evidence

E.1: Source: EconLit

Interface / URL: Ovid SP
Database coverage dates: 1886 to March 2017
Search date: 27/04/17
Retrieved records: 8
Search strategy:
Database: Econlit <1886 to March 2017>
Search Strategy:
---

1 (memokath$ or MK051 or MK-051 or memo-kath$ or memocath$ or memo-cath$ or pnn medical$ or (engineers adj2 doctors$)).ti,ab,kw. (9)

2 ((thermal memory or shape memory or smart metal$ or memory metal$ or memory alloy$ or muscle wire$ or smart alloy$) and stent$).ti,ab,kw. (0)

3 ((thermoexpan$ or thermo-expan$ or thermoactiv$ or thermo-activ$ or thermoformable or thermo-formable or thermosensitiv$ or thermo-sensitiv$ or thermoresponsiv$ or thermo-responsiv$ or thermoreactiv$ or thermo-reactiv$) and stent$).ti,ab,kw. (0)

4 (((thermal$ or temperature$ or heat) adj5 (expand$ or expansion$ or activat$ or reactiv$ or sensitiv$ or responsiv$ or formable)) and stent$).ti,ab,kw. (0)

5 ((niti or nitinol or (nickel and titanium)) and stent$).ti,ab,kw. (0)

6 ((long-term or longterm or long-lasting or longlasting or permanent$ or semipermanent$) adj5 stent$).ti,ab,kw. (1)

7 ((self-expand$ or selfexpand$) and stent$).ti,ab,kw. (0)

8 or/1-7 (10)

9 limit 8 to english (8)

E.2: Source: NHS Economic Evaluation Database (NHS EED)

Interface / URL: Cochrane Library, Wiley
Database coverage dates: Issue 2 of 4, April 2015
Search date: 26/04/17
Retrieved records: 1
Search strategy:

ID	Search	Hits
#1	memokath* or mk051 or mk-051 or memo next kath* or memocath* or memo next cath* or pnn next medical* or (engineers near/2 doctors*)	8
#2	[mh ^stents] or [mh ^"self expandable metallic stents"]	3410
#3	[mh ^temperature] or [mh ^"hot temperature"]	2857
#4	#2 and #3	0
#5	("thermal memory" or "shape memory" or smart next metal* or memory next metal* or memory next alloy* or muscle next wire* or smart next alloy*) and stent*	4
#6	(thermoexpan* or thermo next expan* or thermoactiv* or thermo next activ* or thermoformable or thermo next formable or thermosensitiv* or thermo next sensitiv* or thermoresponsiv* or thermo next responsiv* or thermoreactiv* or thermo next reactiv*) and stent*	3
#7	((thermal* or temperature* or heat) near/5 (expand* or expansion* or activat* or reactiv* or sensitiv* or responsiv* or formable)) and stent*	4
#8	#4 or #5 or #6 or #7	11
#9	[mh ^stents] or [mh ^"self expandable metallic stents"]	3410
#10	[mh ^nickel] and [mh ^titanium]	180
#11	[mh ^alloys]	124
#12	#9 and (#10 or #11)	54
#13	(niti or nitinol or (nickel and titanium)) and stent*	212
#14	("long-term" or longterm or "long-lasting" or longlasting or permanent* or semipermanent*) near/5 stent*	420
#15	(self next expand* or selfexpand*) and stent*	465

#16 #12 or #13 or #14 or #15 964

#17 [mh ^ureter] or [mh "ureteral diseases"] or [mh ^hydronephrosis] 640

#18 ureter* or pelviuret* 2010

#19 (upj or uvj or puj or urinary or urine* or urogenital* or urologic*) near/5 (block* or obstruct* or narrow* or constrict* or compress* or occlu* or retention* or strictur* or stenos* or abnormal* or malform* or insufficien* or dysfunction* or impair* or duplicat* or stone* or calculi*) 5091

#20 hydronephros* or hydroureter* or megaureter* or ((kidney* or renal) near/5 (disten* or dilat*)) 347

#21 #17 or #18 or #19 or #20 6768

#22 #16 and #21 22

#23 #1 or #8 or #22 35

#24 #23 in Economic Evaluations 1

E.3: Source: CEA Registry

Interface / URL:
http://healtheconomics.tuftsmedicalcenter.org/cear4/SearchingtheCEARegistry/SearchtheCEARegistry.aspx
Database coverage dates: Information not provided
Search date: 26/04/17
Retrieved records: 0
Search strategy:
Freely available search functionality is very basic – only single term search supported. Boolean operators required to search for necessary concepts are not available. As a result this resource was searched on the device name only.

Memokath - 0 results

Memo-kath - 0 results

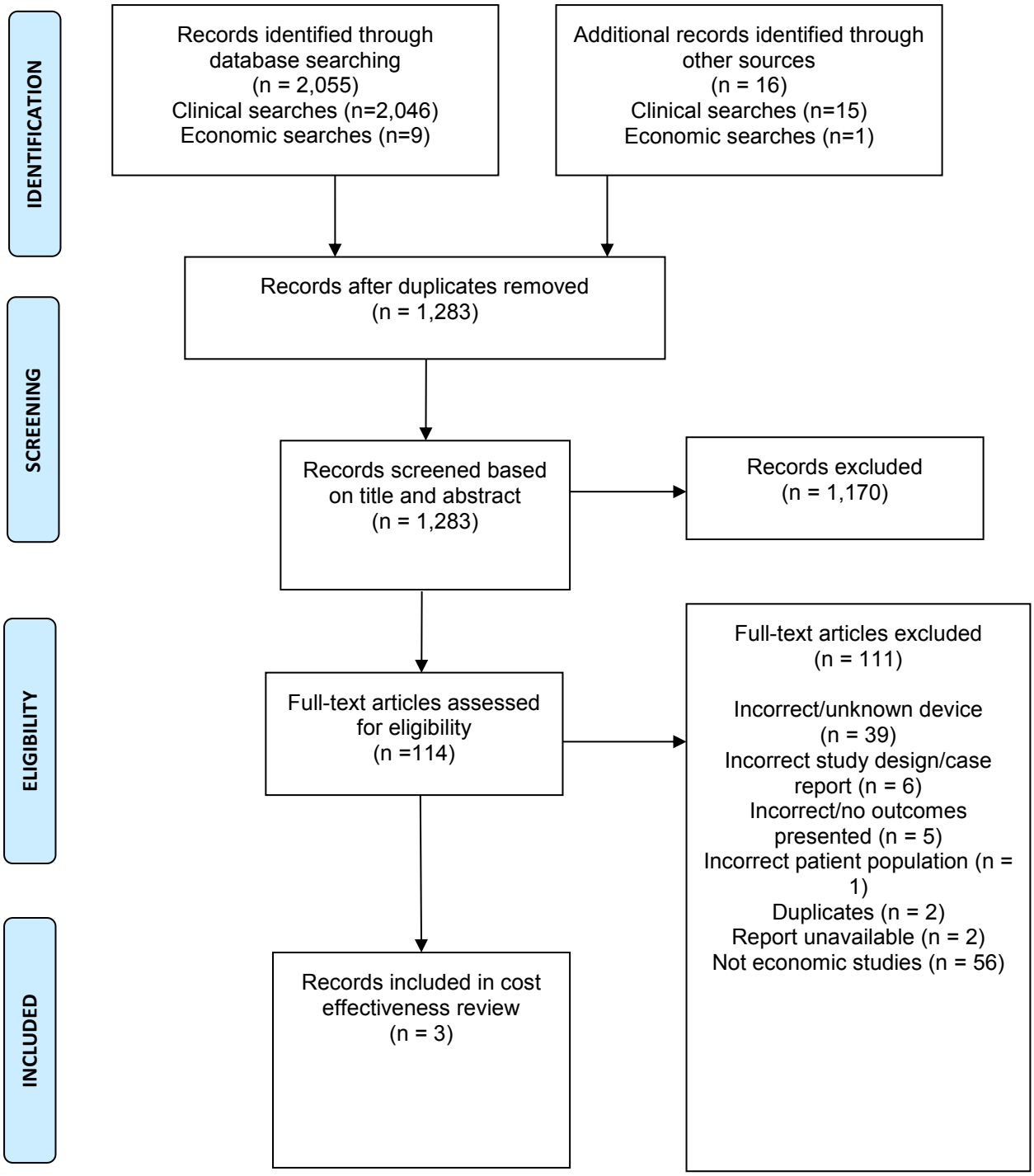
Memocath- 0 results

Memo-cath - 0 results

MK051 – 0 results

MK 051 – 0 results

Appendix F: PRISMA flow diagram showing studies assessed from the EAC's literature search – Cost-effectiveness review



Appendix G: Quality assessment of Gonzelez *et al*. (Gonzalez et al., 2011)

Study question	Response	EAC comments
1. Was the research question stated?	Yes	
2. Was the economic importance of the research question stated?	Yes	
3. Was/were the viewpoint(s) of the analysis clearly stated and justified?	Not clear	The perspective appears to be that of a hospital in Madrid; however, this is not clearly state
4. Was a rationale reported for the choice of the alternative programmes or interventions compared?	Yes	
5. Were the alternatives being compared clearly described?	Not clear	No rationale is provided as to why Memokath-051 is the metal stent considered
6. Was the form of economic evaluation stated?	Not clear	The analysis was described broadly as a cost-effectiveness analysis. However, the analysis appeared just to report the costs by treatment option. No cost effective ratio reported
7. Was the choice of form of economic evaluation justified in relation to the questions addressed?	No	
8. Was/were the source(s) of effectiveness estimates used stated?	Yes	However, the values modelled did not correspond with the complication rates reported from the literature (i.e. 20% migration and 10% incrustation reported, but 0% modelled)
9. Were details of the design and results of the effectiveness study given (if based on a single study)?	No	
10. Were details of the methods of synthesis or meta-analysis of estimates given (if based on an overview of a number of effectiveness studies)?	N/A	
11. Were the primary outcome measure(s) for the economic evaluation clearly stated?	No	
12. Were the methods used to value health states and other benefits stated?	N/A	
13. Were the details of the subjects from whom valuations were obtained given?	No	
14. Were productivity changes (if included) reported separately?	N/A	
15. Was the relevance of productivity changes to the study question discussed?	N/A	
16. Were quantities of resources reported separately from their unit cost?	No	

Study question	Response	EAC comments
17. Were the methods for the estimation of quantities and unit costs described?	No	
18. Were currency and price data recorded?	Not clear	Currency was reported, but cost year was not
19. Were details of price adjustments for inflation or currency conversion given?	No	
20. Were details of any model used given?	Yes	
21. Was there a justification for the choice of model used and the key parameters on which it was based?	No	
22. Was the time horizon of cost and benefits stated?	No	
23. Was the discount rate stated?	N/A	
24. Was the choice of rate justified?	N/A	
25. Was an explanation given if cost or benefits were not discounted?	No	However, the time horizon of the model appeared to be short
26. Were the details of statistical test(s) and confidence intervals given for stochastic data?	N/A	
27. Was the approach to sensitivity analysis described?	No	None was undertaken
28. Was the choice of variables for sensitivity analysis justified?	N/A	
29. Were the ranges over which the parameters were varied stated?	N/A	
30. Were relevant alternatives compared?	Not clear	Other potentially relevant alternatives such as other metal stents may be available
31. Was an incremental analysis reported?	No	
32. Were major outcomes presented in a disaggregated as well as aggregated form?	No	
33. Was the answer to the study question given?	Yes	
34. Did conclusions follow from the data reported?	Yes	
35. Were conclusions accompanied by the appropriate caveats?	Yes	
36. Were generalisability issues addressed?	No	There was no discussion around generalisability. Costs were specific to 1 hospital; whilst effectiveness data were not
Adapted from Drummond MF, Jefferson TO (1996) Guidelines for authors and peer reviewers of economic submissions to the BMJ (59). Cited in Centre for Reviews and Dissemination (2008) Systematic reviews. CRD's guidance for undertaking reviews in healthcare. York: Centre for Reviews and Dissemination		

Appendix H: Quality assessment of company's *de novo* economic model

Study question	Response	EAC comments
1. Was the research question stated?	No	
2. Was the economic importance of the research question stated?	No	
3. Was/were the viewpoint(s) of the analysis clearly stated and justified?	No	Data provided by a single UK hospital were used to inform the costs in the model. This implies a hospital perspective was used but this was not explicitly stated by the company.
4. Was a rationale reported for the choice of the alternative programmes or interventions compared?	Yes	Although a rationale was not explicitly stated in the appropriate section of the company's submission (Section 9.1.3, Submission), in Section 9.1.1 justification was given for excluding the other comparators from the economic analysis that are listed in the scope.
5. Were the alternatives being compared clearly described?	Not clear	A clear description of Memokath-051 is given in Section 2.2 of the report. Whilst reference is made to double-J stents, a clear description is not provided.
6. Was the form of economic evaluation stated?	No	A CBA was conducted given that the measurement of costs for both alternatives were given in monetary units and the valuation of the consequence (risk factor of early exchange) was given in monetary units (criteria given in Drummond *et al.* (2015)). This was not stated by the company.
7. Was the choice of form of economic evaluation justified in relation to the questions addressed?	No	
8. Was/were the source(s) of effectiveness estimates used stated?	Not clear	The company state a risk factor of early stent exchange for Memokath-051. It is not clear is this is a measure of effectiveness.
9. Were details of the design and results of the effectiveness study given (if based on a single study)?	No	
10. Were details of the methods of synthesis or meta-analysis of estimates given (if based on an overview of a number of effectiveness studies)?	N/A	

Study question	Response	EAC comments
11. Were the primary outcome measure(s) for the economic evaluation clearly stated?	Not clear	The company included a risk factor for early (unplanned) exchange of Memokath-051. This was not clearly stated or explained as an outcome measure.
12. Were the methods used to value health states and other benefits stated?	No	Whilst not strictly health states, the methods used to determine the frequency of stent exchange for double-J stents was not explicitly stated.
13. Were the details of the subjects from whom valuations were obtained given?	N/A	
14. Were productivity changes (if included) reported separately?	N/A	
15. Was the relevance of productivity changes to the study question discussed?	N/A	
16. Were quantities of resources reported separately from their unit cost?	No	The company did not present upfront the disaggregated quantities and unit costs of the aggregated costs that were included in the analysis. The AUH data were supplied by the company as an attachment and this gave a breakdown of costs and the quantities of resources used could be calculated. This was not presented separately for each of the comparators and lacked clarity.
17. Were the methods for the estimation of quantities and unit costs described?	No	The quantities and unit costs were estimated from the experience of a single hospital. No detail further detail was provided by the company.
18. Were currency and price data recorded?	Not clear	The currency was recorded but the price year was not clear.
19. Were details of price adjustments for inflation or currency conversion given?	No	No costs were reported to be inflated. All costs included in the model were in the same currency as in the source.
20. Were details of any model used given?	Not clear	
21. Was there a justification for the choice of model used and the key parameters on which it was based?	Yes	Whilst the company justify the model structure as being in line with the clinical pathway of care this justification is very limited. Justification of inclusion of the risk factor is also very limited.
22. Was the time horizon of cost and benefits stated?	Yes	
23. Was the discount rate stated?	Not clear	The company state that “no discount was calculated” which implies that the discount rate was zero.

Study question	Response	EAC comments
24. Was the choice of rate justified?	No	
25. Was an explanation given if cost or benefits were not discounted?	No	The company only state that “no discount was calculated”.
26. Were the details of statistical test(s) and confidence intervals given for stochastic data?	N/A	
27. Was the approach to sensitivity analysis described?	No	No sensitivity analyses were included. This was justified by the company by noting that no sensitivity analysis is needed for the product.
28. Was the choice of variables for sensitivity analysis justified?	N/A	
29. Were the ranges over which the parameters were varied stated?	N/A	
30. Were relevant alternatives compared?	No	Only double-J stents were included as a comparator. The company did not include nephrostomy, reconstructive surgery or metallic and alloy stents as comparators, as listed in the scope.
31. Was an incremental analysis reported?	Yes	In the model the company include an incremental analysis. In the report an incremental cost is given (Section, 9.5.2, Submission) but this differs from the incremental total cost calculated from the values in the model.
32. Were major outcomes presented in a disaggregated as well as aggregated form?	Yes	Although, some of the costs given in the report differed from those in the model.
33. Was the answer to the study question given?	No	The study question being the decision problem as outlined in the scope. The analysis was conducted from a hospital perspective for a time horizon of 2.5 years. Costs were not discounted appropriately. No sensitivity analysis was conducted. No subgroups were considered despite subgroups being listed in the scope.
34. Did conclusions follow from the data reported?	No	The company did not make any clear conclusions about the economic analysis.
35. Were conclusions accompanied by the appropriate caveats?	No	
36. Were generalisability issues addressed?	No	The company stated that the cost analysis is relevant to all groups of patients and NHS setting that could

Study question	Response	EAC comments
		potentially use the device. However, the costs included in the model were sourced from a single UK hospital. How these cost generalise to other hospitals in the UK was not discussed. No comment was made about the generalisability of the 25% risk of an unplanned stent exchange for Memokath-051.
Adapted from Drummond MF, Jefferson TO (1996) Guidelines for authors and peer reviewers of economic submissions to the BMJ (59). Cited in Centre for Reviews and Dissemination (2008) Systematic reviews. CRD's guidance for undertaking reviews in healthcare. York: Centre for Reviews and Dissemination		

Appendix I: Discrepancy in costs between company's model and submission for Memokath-051

Cost parameter	Value in submission	Value in model (verified by the EAC)	Difference between model and submission
Total for year 1	£3,326	£3,353	£27
Total for months 24 to 30	£285	£143	£143
Total cost per treatment/patient over 2.5 years	£3,896	£3,781	-£116
Total cost per treatment/patient over 2.5 years with calculation of risk	£4,870	£4,726	-£144

Appendix J: Resource use in company's model

Variable	Value per patient	Source	EAC critique
Theatre staff costs: Memokath-051	£1,160	AUH data provided by the company. Comprises the following, details of which are provided in the write up below: Anaesthetist, surgeon, Band 6 and Band 5 scrub, Band 5 anaesthetist, Band 2 circulating, Band 2 porter, Band 6 and Band 5 recovery	• **Duration of procedure:** The company used a procedure time of 4 hours and a theatre time (all staff present apart from the surgeon) of 4.5 hours. This duration is judged by the EAC to be too long based upon information provided by the company and experts (correspondence log) and the clinical studies (Section 3). • **Recovery staff:** The company included the cost of a band 5 and band 6 recovery staff appropriately given that no additional hospital stay was included following insertion. • **Staff costs:** The company sourced their staff costs per hour from the AUH which did not include national insurance and superannuation costs. These are directly related to earnings and should be included
Theatre staff costs: Double-J stent	£1,160	AUH data reported: Anaesthetist, surgeon, Band 6 and Band 5 scrub, Band 5 anaesthetist, Band 2 circulating, Band 2 porter, Band 6 and Band 5 recovery	• **Duration of procedure:** The company used a procedure time of 4 hours and a theatre time (all staff present apart from the surgeon) of 4.5 hours. This duration is judged by the EAC to be too long based upon information provided by the experts and from evidence from studies. • **Recovery staff:** as above. • **Staff costs:** as above
Theatre consumable costs: Memokath-051	£1,874	AUH data and comprises: Device, cystoscopy pack, instilagel, 20ml syringe, sensor guidewire, passport, jug, pink needle, green needle	• The company's consumable cost includes a cost of £1,630. This is lower than the current list price of £1,690 reported in Section 9.3.5, submission
Theatre consumable costs: Double-J stent	£109	AUH data. comprising: Device, cystoscopy pack, instilagel, 20ml syringe, sensor guidewire	• The EAC deems this value appropriate based upon the AUH data
Procedure code/surgery tariff: Memokath-051	£34	AUH data	• The EAC judges the inclusion of a tariff cost is inappropriate for analysis from the NHS and PSS perspective and excluded this parameter from its analysis

Variable	Value per patient	Source	EAC critique
Procedure code/surgery tariff: Double-J stent	£407	AUH data	As above
6 month follow-up costs: Memokath-051	£143	AUH data. comprising: X-ray abdomen, NM renogram and 2 outpatient appointments over 1 year. 1 year cost divided by 2 to estimate the 6 month cost	• The EAC deems this value appropriate based upon the AUH data. However, using national sources for unit costs would increase the cost (Department of Health, 2016)
6 month follow-up costs: Double-J stent	£100	No source provided	• It is unclear how this cost was derived and is not included within the AUH data, thus is deemed inappropriate
Risk of unplanned exchange: Memokath-051	£945	Calculated as 25% of the undiscounted pathway related cost for 2.5 years	• The EAC judges that this cost has been applied incorrectly as reported in Section 4.2.4
Risk of unplanned exchange: Double J stent	£0	Zero as no risk factor for complications	• Given that double-J stents undergo planned replacement this is considered appropriate and is in line with clinical evidence (Maan et al., 2010)

Appendix K: Company's bottom-up costing of theatre staff costs with Memokath-051

Parameter	Company base-case (cost per full theatre hour, staff time*)
Anaesthetist (Band not stated)	£361.61 (£80.36, 4.5 hours)
Surgeon	£321.43 (£80.36, 4 hours)
Band 6 scrub	£104.89 (£23.31, 4.5 hours)
Band 5 scrub	£86.95 (£19.32, 4.5 hours)
Band 5 anaesthetist	£86.95 (£19.32, 4.5 hours)
Band 2 circulating	£54.58 (£12.13, 4.5 hours)
Band 2 porter	£54.58 (£12.13, 4.5 hours)
Band 6 recovery	£11.65 (£23.31, 0.5 hours)
Band 5 recovery	£77.29 (£19.32, 4 hours)
Total (as used in the company's model)	**£1,159.93**

* Please note that the duration of the procedure was not stated in the data provided by AUH but was calculated by the EAC using data provided on the cost per full theatre hour and the cost per theatre operating session.

Appendix L: EAC's bottom-up costing of theatre staff costs (stent insertion)

Parameter	Memokath-051 total cost (Unit cost, time required in minutes)	Double-J stent total cost (Unit cost, time required in minutes)	Metallic stent total cost (Unit cost, time required in minutes)	Source and explanation
Anaesthetist (Band not stated)	£79 (£105, 45 minutes)	£39 (£105, 22.5 minutes)	£66 (£105, 37.5 minutes)	PSSRU 2016, Section 15. Consultant: surgical, cost per working hour
Surgeon	£79 (£105, 45 minutes)	£39 (£105, 22.5 minutes)	£66 (£105, 37.5 minutes)	PSSRU 2016, Section 15. Consultant: surgical, cost per working hour
Band 6 scrub	£33 (£44, 45 minutes)	£17 (£44, 22.5 minutes)	£28 (£44, 37.5 minutes)	PSSRU 2016, Section 14. Band 6 hospital-based nurse, cost per hour of patient contact
Band 5 scrub	£26 (£35, 45 minutes)	£13 (£35, 22.5 minutes)	£22 (£35, 37.5 minutes)	PSSRU 2016, Section 14. Band 5 hospital-based nurse, cost per hour of patient contact
Band 5 anaesthetist	£26 (£35, 45 minutes)	£13 (£35, 22.5 minutes)	£22 (£35, 37.5 minutes)	PSSRU 2016, Section 14. Band 5 hospital-based nurse, cost per hour of patient contact
Band 2 circulating	£17 (£23, 45 minutes)	£9 (£23, 22.5 minutes)	£14 (£23, 37.5 minutes)	PSSRU 2016, Section 14. Band 2 hospital-based nurse, cost per working hour
Band 2 porter	£17 (£23,45 minutes)	£9 (£23, 22.5 minutes)	£14 (£23, 37.5 minutes)	PSSRU 2016, Section 14. Band 2 hospital-based nurse, cost per working hour
Recovery (band 5 and 6)	Not included in the theatre staff cost in the EAC model	Not included in the theatre staff cost in the EAC model	Not included in the theatre staff cost in the EAC model	Not included as included within the hospital stay within the EAC model
Total (as used in the EAC's model)	**£278**	**£139**	**£231**	

Appendix M: EAC's bottom-up costing of recovery time for patients following insertion/replacement

Initial insertion

In the base case, all patients (receiving all stent types) were assumed to have a day case procedure based upon expert advice. Day case patients incurred the following costs:

- £57 for nurse care during their stay in the recovery room comprising 30 minutes of 1-to1 time with a band 6 nurse and 240 minutes of band 5 nurse time shared with 3 other patients. Nurse costs were taken from PSSRU and staff time from AUH (AUH, Personal Social Services Research Unit (PSSRU), 2016);
- £51 for their time in hospital based upon a weighted average of the non-elective excess bed day for LB19C (Ureteric or Bladder Disorders, with Interventions, with CC Score 4+) and LB19D (Ureteric or Bladder Disorders, with Interventions, with CC Score 0-3) and an assumed 4 hour hospital stay (Department of Health, 2016).

Therefore, patients had a total recovery cost of £108.

During sensitivity analysis inpatients were considered. These patients incurred the £57 recovery room cost and also the excess bed day for their time spent in hospital. The time spent in hospital was set to 1.47 days, an average from the 2 studies reporting on hospital stay following Memokath-051 insertion (Agrawal et al., 2009, Papatsoris and Buchholz, 2010). As these 2 studies may include day case procedures the value may be an underestimate. The total recovery cost for inpatients was £505.

There is also the option within the model to consider inpatients who a stent inserted whilst in hospital, but stent insertion isn't the reason for their admission. The cost for these patients is equivalent to a day case patient in that an additional 4 hour recovery time is assumed.

Replacement

In the base case, patients having double-J stents replaced were assumed to have these as a day case as per expert advice. Patients having other metallic stents replaced comprised 50% day case, 25% inpatient and 25% current inpatient (i.e. already admitted to hospital for other reasons). The recovery costs for each patient cohort are in line with the recovery costs following insertion, i.e. £108 for day case and current in patients and £505 for inpatients admitted for stent replacement. These costs are consistent across different stent types.

Appendix N: Company's bottom-up costing of theatre consumable costs and follow-up with Memokath-051

Table N.1: Company's theatre consumable costs

Parameter	Company base-case	Source and explanation
Device	£1,630	Taken directly from AUH data (AUH)
Cystoscopy pack	£24.13	Taken directly from AUH data (AUH)
Instilagel	£1.22	Taken directly from AUH data (AUH)
20ml syringe	£0.09	Taken directly from AUH data (AUH)
Sensor guidewire	£24.00	Taken directly from AUH data (AUH)
Passport	£193.00	Taken directly from AUH data (AUH)
Jug	£0.47	Taken directly from AUH data (AUH)
Pink needle	£0.07	Taken directly from AUH data (AUH)
Green needle	£0.14	Taken directly from AUH data (AUH)
'Other'	£1.04	Value required to reconcile the consumable cost reported in Taken directly from (AUH)
Total (as used in the company's model)	**£1,874.16**	

Table N.2: Company's follow-up costs

Parameter	Company base-case (1 year)	Source and explanation
X-ray abdomen	£22	Taken directly from (AUH)
NM renogram	£103	Taken directly from (AUH)
Outpatient appointment (2 appointments in 12 months)	£80	Taken directly from (AUH)
Total (as used in the company's model)	**£285**	Taken directly from (AUH)

Appendix O: Detailed table of full EAC revisions to the company's model

Parameter	Company's value	EAC's value	Agreement?	Reason for difference
Clinical parameters				
Length of time in situ (no complications)				
Memokath-051	**2.5 years** Justification was that this was conservative and adopting a longer follow-up would increase potential savings	**5 years** NICE topic briefing reports 4-6 years. Company IFU reports an indwelling time of 'several years'	✗	The EAC extended the time horizon to capture costs over the full potential lifespan of Memokath-051
Double-J stent	**6 months** AUH data provided by the company (AUH)	**6 months** AUH data provided by the company (AUH), supported by clinical experts, advising a 6 months maximum	✓	N/A
UVENTA	Not included in the company's model	**18 months** NICE topic briefing (NICE, 2017b). This cannot be verified by the EAC. Maximum reported in Kim *et al.* is 16 months but this was driven by duration of follow-up (Kim et al., 2014)	✗	The company did not include metallic stents as a comparator in their model. The EAC identified relevant evidence to support the inclusion of metallic stents in the EAC model
Allium	Not included in the company's model	**36 months** NICE topic briefing and manufacturer's IFU (Allium Medical, 2016, NICE, 2017b)	✗	As above
Resonance	Not included in the company's model	**12 months** NICE topic briefing and manufacturer's IFU (Cook Medical, 2012, NICE, 2017b)	✗	As above
Reconstructive surgery	Not included in the company's model	**None** Driven by the maximum time horizon of the EAC's model. Surgery is reconstructive with no further procedures required (hence no additional planned surgery occurs)	✗	The company did not model reconstructive surgery as a comparator. The EAC identified relevant evidence to support the inclusion of reconstructive surgery in their model
Risk factor for unplanned stent removal and replacement				

Parameter	Company's value	EAC's value	Agreement?	Reason for difference
Memokath-051 vs Double-J stent	**Memokath-051** **25% per 2.5 years (30 months)** **0.95% per month** No source was explicitly provided by the company. The EAC converted the company's value to a monthly probability for comparison (Drummond et al., 2015). **Double-J stent** Not included in the company's model	**Memokath-051** **1.4% per month** **Double-J stent** **0.0% per month** Scenarios were explored for years 2 to 5 described in section 4.2.5	✘	The EAC was unable to verify the company's value for Memokath-051 as it did not provide the EAC with information on the source of evidence used to inform the input. From their clinical review, the EAC identified appropriate studies reporting stent replacement and the average probability per patient month was calculated
Memokath-051 vs UVENTA	Not included in the company's model	**Memokath-051** **4.41% per month** Comparative, non-UK- based study (Korea). Calculated as a monthly probability based on 13.6 month follow-up and 43% probability (Kim et al., 2014). The EAC assumed that all migrated stents were replaced **UVENTA** **0.49% per month** Comparative, non-UK study (Korea).Calculated as a monthly probability based on 12 month follow-up and 6% probability (Kim et al., 2014). The EAC assumed that all migrated stents were replaced as verified by 1 clinical expert. Scenarios were explored after 2 year time horizon, see section 4.2.5	✘	The company did not include UVENTA as a comparator in their model. The EAC identified relevant evidence to support the inclusion of UVENTA in their model. To inform the probability of early stent replacement in the head-to-head comparison of Memokath-051 versus UVENTA, comparative data were available from a Korean study. The clinical review deemed the internal and external validity of this paper to be acceptable in relation to the decision problem
Memokath-051 vs Allium	Not included in the company's model.	**Memokath-051** **1.4% per month** From their clinical review, the EAC identified appropriate studies reporting stent	✘	The company did not include Allium within its model. No comparative data were available providing information on the risk of stent replacement between

Parameter	Company's value	EAC's value	Agreement?	Reason for difference
		replacement and the average probability per patient month was calculated. **Allium** **0.49% per month** The EAC assumed that the probability for Allium is equal to UVENTA based on advice from 1 expert of superior performance of Allium stents compared with Memokath-051. Scenarios were explored after 2 year time horizon, see section 4.2.5		Memokath-051 and Allium. Hence, for Memokath-051 the best available UK data and the average probability per patient month was calculated. For Allium an assumption was made based upon the advice from an expert. This comparison is therefore subject to severe limitations
Memokath-051 vs Resonance	Not included in the company's model	**Memokath-051** **1.4% per month** See Memokath-051 versus Allium **Resonance** **1.4% per month** The EAC assumed that the probability for Resonance is equal to Memokath-051 as no evidence was available. Scenarios were explored after 2 year time horizon, see section 4.2.5	✘	The company did not include Resonance within its model. No comparative data were available providing information on the risk of stent replacement between Memokath-051 and Resonance. Hence, for Memokath-051 the best available UK data and the average probability per patient month was calculated. For Resonance assumed to be consistent with Memokath-051. This comparison is therefore subject to severe limitations
Memokath-051 vs reconstructive surgery	Not included in the company's model	**Memokath-051** **1.4% per month** See Memokath-051 versus double-J **Reconstructive surgery** **0.0% per month** Conservative assumption that no further procedures are required following reconstructive surgery as no evidence available to inform the number of patients or what it would involve	✘	The company did not include surgery within its model. No comparative data were available providing information on the risk of stent replacement between Memokath-051 and surgery. From their clinical review, the EAC identified appropriate studies reporting stent replacement for Memokath-051 and the average

Parameter	Company's value	EAC's value	Agreement?	Reason for difference
				probability per patient month was calculated
Urinary tract infection				
Memokath-051 vs double-J stent	Not included in the company's model	**Memokath-051** **0.42% per month** Single-arm study, UK-based study. Calculated as a monthly probability based on 17.1 month follow-up and 7% probability (Papatsoris and Buchholz, 2010) **Double-J: 0.42%** The EAC assumed that the probability for double-J stents is equal to Memokath-051 as no evidence was available	✗	The company stated that all side effects are mainly treated by stent exchange. The EAC identified that UTIs are associated with the treatment of ureteric strictures and so deemed it relevant for inclusion in the analysis
Memokath-051 vs Metallic stent (UVENTA, Allium or Resonance)	Not included in the company's model	**Memokath-051** **0.42% per month** See Memokath-051 versus double-J **Metallic stent: 0.42%** The EAC assumed that the probability for metallic stents is equal to Memokath-051 as no evidence was available	✗	As above
Memokath-051 vs reconstructive surgery	Not included in the company's model	**Memokath-051: 1.25%** Abstract reporting on a comparative observational study of Memokath-051 versus ileal ureteral replacement (IUR). Calculated as a monthly probability based on 42 month follow-up and 41% probability (Akbarov et al., 2017). **Reconstructive surgery: 0.17%** Calculated as a monthly probability based on 42 month follow-up and 7% probability (Akbarov et al., 2017)	✗	As above
Resource use and unit costs				
Device cost/Reconstructive surgery cost				

Parameter	Company's value	EAC's value	Agreement?	Reason for difference
Memokath-051	**£1,630 per device** AUH Data provided by the company	**£1,690 per device** Company's submission and confirmed via email	✗	The company used an incorrect price of Memokath-051, which was rectified by the EAC
Double-J stent	**£60 per device** AUH Data provided by the company. Appears to be for a 6x24 stent as reported in the AUH data	**£60 per device** Company's submission	✗	The EAC did not have sufficient evidence to update this cost. Range on NHS supply chain for variety of brands is £29.82 to £241.24.
UVENTA	Not included in the company's model	**£1,500 per device** The EAC contacted the manufacturer to determine the list price of the device. List price per unit provided by Gareth Longden, Sales Director for Macromed (UK) Ltd, the local sales representative of UVENTA in the UK	✗	The company did not include UVENTA as a comparator in their model. The EAC identified relevant evidence to support the inclusion of UVENTA in their model
Allium	Not included in the company's model	**£1,700 per device** The EAC contacted the manufacturer to determine the list price of the device. List price per unit provided by Martin Hill, National Sales Manager for Sigmacon, the distributor of Allium in the UK	✗	As above for Allium
Resonance	Not included in the company's model	**£911.75 per device** NHS supply chain. Resonance metallic ureteral stent	✗	As above for Resonance
Reconstructive surgery	Not included in the company's model	**Total cost £6,290** NHS reference costs 2015/16 (Department of Health, 2016). Complex/major kidney or ureter procedures. Weighted average of LB60C - LB62D for all elective and non-elective inpatients	✗	The EAC identified the total cost of reconstructive surgery from the NHS reference costs. This cost incorporates all care provided to the average patient during their episode of care including hospital stay
Theatre consumable costs for insertion and replacement				
Memokath-051	**Total cost excl. device: £244.16**	**Total cost excl. device: £243.12** AUH data provided by the company.	✗	The EAC used lower price due to £1 unexplained discrepancy.

Parameter	Company's value	EAC's value	Agreement?	Reason for difference
	AUH data provided by the company. Includes: Cystoscopy pack, £24.13 Instilagel, £1.22 20ml syringe, £0.09 Sensor guidewire, £24.00 Passport, £193.00 Jug, £0.47 Pink needle, £0.07 Green needle, £0.14 £1 discrepancy between value in company's model and bottom-up costing from the AUH data	The EAC assumed that the cost year of the AUH data provided by the company was 2016. Therefore this cost was not inflated by the EAC to keep it consistent with the cost year used for the analysis		A clinical expert verified the use of a passport balloon catheter for the insertion of Memokath-051
Double-J stent	**Total cost incl. device: £109.44** **Total cost excl. device: £49.44** AUH data provided by the company. EAC believes this includes: Cystoscopy pack, £24.13 Instilagel, £1.22 20ml syringe, £0.09 Sensor guidewire, £24.00	**Total cost excl. device: £49.44** AUH data provided by the company. The EAC assumed that the cost year of the AUH data provided by the company was 2016. Therefore this cost was not inflated by the EAC to keep it consistent with the cost year used for the analysis	✓	The base case value used by the company is consistent with the data specified. A clinical expert verified that a passport balloon catheter is not required for the insertion of a double-J stent
Metallic stent (UVENTA, Allium and Resonance)	Not included in the company's model	**Total cost excl. device: £243.12** The EAC assumed that the cost of theatre consumables for metallic stents is equal to Memokath-051. Simon Angove, Area Manager for Sigmacon, the UK distributor of Allium, advised that insertion of Allium requires a dilator. EAC has assumed a passport balloon dilator (£193) is also required to insert UVENTA and Resonance stents	✗	The company did not include metallic stents as a comparator in their model
Theatre staff costs for insertion				

Parameter	Company's value	EAC's value	Agreement?	Reason for difference
Memokath-051	**Procedure time: 4 hours** Calculated by the EAC using AUH data submitted by the company (AUH). **Total cost: £1,159.93** AUH data provided by the company. Includes: Anaesthetist (4.5 hours at £80.36 p/h) Surgeon (4 hours at £80.36 p/h) Band 6 scrub (4.5 hours at £23.31 p/h) Band 5 scrub (4.5 hours at £19.32 p/h) Band 5 anaesthetist (4.5 hours at £19.32 p/h) Band 2 circulating (4.5 hours at £12.13 p/h) Band 2 porter (4.5 hours at £12.13 p/h) Band 6 recovery (0.5 hours at £23.31 p/h) Band 5 recovery (4 hours at £19.32 p/h)	**Procedure time: 45 minutes** Published evidence identified for Memokath-051 but not for other comparators (Papatsoris and Buchholz, 2010) (Zaman et al., 2011). For consistency and comparability, input informed by 2 clinical experts. **Total cost: £278** PSSRU 2016, cost per working hour. Anaesthetist (45 minutes at £105 p/h) Surgeon (45 minutes at £105 p/h) Band 6 scrub (45 minutes at £44 p/h) Band 5 scrub (45 minutes at £35 p/h) Band 5 anaesthetist (45 minutes at £35 p/h) Band 2 circulating (45 minutes at £23 p/h) Band 2 porter (45 minutes at £23 p/h)	✘	**Procedure time** The company used a procedure time of 4 hours for the surgeon and 4.5 hours for all other theatre staff. The EAC used a procedure time of 45 minutes. The EAC did not include the cost of recovery staff as theatre staff. **Costing** The staff cost per hour used by the EAC is higher than that used by the company. However, the total cost used by the EAC is much lower than that given differences in procedure times. Composition of theatre staff (excluding recovery staff) was verified by a clinical expert
Double-J	**Procedure time: 4 hours** Calculated by the EAC using AUH data submitted by the company. **Total cost £1,159.93** AUH data provided by the company. Includes: Anaesthetist (4.5 hours at £80.36 p/h) Surgeon (4 hours at £80.36 p/h)	**Procedure time: 22.5 minutes** No published evidence identified. Informed by 2 clinical experts. **Total cost: £139** PSSRU 2016, cost per working hour. Anaesthetist (22.5 minutes at £105 p/h) Surgeon (22.5 minutes at £105 p/h) Band 6 scrub (22.5 minutes at £44 p/h) Band 5 scrub (22.5 minutes at £35 p/h)	✘	As above but with a procedure time of 22.5 minutes. The total cost used by the EAC is much lower than that reported by the company due to differences in procedure time

Parameter	Company's value	EAC's value	Agreement?	Reason for difference
	Band 6 scrub (4.5 hours at £23.31 p/h) Band 5 scrub (4.5 hours at £19.32 p/h) Band 5 anaesthetist (4.5 hours at £19.32 p/h) Band 2 circulating (4.5 hours at £12.13 p/h) Band 2 porter (4.5 hours at £12.13 p/h) Band 6 recovery (0.5 hours at £23.31 p/h) Band 5 recovery (4 hours at £19.32 p/h)	Band 5 anaesthetist (22.5 minutes at £35 p/h) Band 2 circulating (22.5 minutes at £23 p/h) Band 2 porter (22.5 minutes at £23 p/h)		
Metallic stent (UVENTA, Allium and Resonance)	Not included in the company's model	**Procedure time: 37.5 minutes** No published evidence identified. Informed by 2 clinical experts. **Total cost: £231** PSSRU 2016, cost per working hour. Anaesthetist (37.5 minutes at £105 p/h) Surgeon (37.5 minutes at £105 p/h) Band 6 scrub (37.5 minutes at £44 p/h) Band 5 scrub (37.5 minutes at £35 p/h) Band 5 anaesthetist (37.5 minutes at £35 p/h) Band 2 circulating (37.5 minutes at £23 p/h) Band 2 porter (37.5 minutes at £23 p/h)	✗	The company did not include metallic stents as a comparator in their model
Theatre staff costs for replacement				
Memokath-051	The cost of insertion was used by the company. **Total cost: £1,159.93**	**Procedure time: 75 minutes** Assumption based on the Company and experts (additional 30 minutes to exchange than insert). **Total cost: £463**	✗	The total cost used by the EAC is much lower than that reported by the company due to the discrepancy in procedure time

Parameter	Company's value	EAC's value	Agreement?	Reason for difference
		PSSRU 2016, cost per working hour. Anaesthetist (60 minutes at £105 p/h) Surgeon (60 minutes at £105 p/h) Band 6 scrub (60 minutes at £44 p/h) Band 5 scrub (60 minutes at £35 p/h) Band 5 anaesthetist (60 minutes at £35 p/h) Band 2 circulating (60 minutes at £23 p/h) Band 2 porter (60 minutes at £23 p/h)		
Double-J stents	The cost of insertion was used by the company. **Total cost: £1,159.93**	**Procedure time: 55 minutes** Assumption based on clinical expert advice (22.5 minutes for insertion and 10-30 minutes for an easy replacement, longer where there is encrustation). **Total cost: £339** PSSRU 2016, cost per working hour. Anaesthetist (55 minutes at £105 p/h) Surgeon (55 minutes at £105 p/h) Band 6 scrub (55 minutes at £44 p/h) Band 5 scrub (55 minutes at £35 p/h) Band 5 anaesthetist (55 minutes at £35 p/h) Band 2 circulating (55 minutes at £23 p/h) Band 2 porter (55 minutes at £23 p/h)	✗	The total cost used by the EAC is much lower than that reported by the company due to the discrepancy in procedure time
Metallic stent (UVENTA, Allium and Resonance)	Not included in the company's model	**Procedure time: 75 minutes** Assumed equal to Memokath-051. **Total cost: £463** PSSRU 2016, cost per working hour. See Memokath-051 above	✗	The company did not include metallic stents as a comparator in their model
Theatre cost for insertion				
Memokath-051	Not included in the company's model	**Procedure time: 45 minutes** Informed by 2 clinical experts. **Total cost: £224** ISD Scottish Tariff 2015-16. Allocated costs per hour of theatre time (ISD Scotland, 2016) (£299 per hour)	✗	The cost of the theatre was not included within the company's model, but has been included by the EAC

Parameter	Company's value	EAC's value	Agreement?	Reason for difference
Double-J stent	Not included in the company's model	**Procedure time: 22.5 minutes** No published evidence identified. Informed by 2 clinical experts. **Total cost: £112** ISD Scottish Tariff 2015-16. Allocated costs per hour of theatre time (ISD Scotland, 2016) (£299 per hour)	✗	The cost of the theatre was not included within the company's model, but has been included by the EAC
Metallic stents (UVENTA, Allium and Resonance)	Not included in the company's model	**Procedure time: 37.5 minutes** No published evidence identified. Informed by 2 clinical experts. **Total cost: £187** ISD Scottish Tariff 2015-16. Allocated costs per hour of theatre time (ISD Scotland, 2016) (£299 per hour)	✗	Metallic stents were not included as a comparator by the company. Further, the cost of the theatre was not included within the company's model, but has been included by the EAC
Theatre cost for replacement				
Memokath-051 and metallic stents (UVENTA, Allium and Resonance)	Not included in the company's model	**Procedure time: 75 minutes** Memokath-051: Assumption based on the Company and experts (additional 30 minutes to exchange than insert). Metallic stents: assumed equal to Memokath-051. **Total cost: £373** ISD Scottish Tariff 2015-16. Allocated costs per hour of theatre time (ISD Scotland, 2016) (£299 per hour)	✗	The cost of the theatre was not included within the company's model, but has been included by the EAC
Double-J stent	Not included in the company's model	**Procedure time: 55 minutes** Assumption based on clinical expert advice. **Total cost: £274** ISD Scottish Tariff 2015-16. Allocated costs per hour of theatre time (ISD Scotland, 2016) (£299 per hour)	✗	The cost of the theatre was not included within the company's model, but has been included by the EAC
Diagnostic test before insertion procedure				

Parameter	Company's value	EAC's value	Agreement?	Reason for difference
Memokath-051 and all stent comparators	Not included in the company's model	**Resource use: CT scan** Informed by the clinical experts that CT scan would be performed prior to insertion. **Total cost: £96** Weighted average of: IMAGOP, CT Scan of 1 area, without contrast, 19 years and over, outpatient IMAGOP, CT Scan of 1 area, with post contrast only, 19 years and over, outpatient (Department of Health, 2016)	✗	The cost of diagnostic tests were not included within the company's model, but have been included by the EAC
Diagnostic test before replacement procedure				
Memokath-051 and all stent comparators	Not included in the company's model	**Resource use: No test** **Total cost: £0** One clinical expert reported that no CT scan would be needed prior to replacement but an ureteroscopy is likely to be necessary. Second expert reports no diagnostic test. The EAC has assumed zero cost given inconsistency between experts	✓	N/A
Diagnostic test during the insertion and replacement procedure				
All stents	Not included in the company's model	**Total cost: £92** Clinical expert stated the use of fluorscopy to confirm the placement of the stent. The 2nd clinical expert stated image intensifier. IMAGOP, Contrast Fluoroscopy, Mobile or Intraoperative Procedures, with duration of less than 20 minutes, £92, outpatient (Department of Health, 2016)	✗	No cost was included by the company. The EAC notes that there may be some variation in practice as published evidence report the use of other types of imaging to confirm the placement of the stent. UK based study report confirmation of stent placement - nephrostogram/IVU - contrast medium studies (Arya et al., 2001).A 2nd UK study reports retrograde urogram to confirm position (Papatsoris and Buchholz, 2010)

Parameter	Company's value	EAC's value	Agreement?	Reason for difference
Medication during the insertion and replacement procedure				
All stents	Not included in the company's model	**Element: Gentamicin** 3 UK-based studies report that gentamicin is given during the insertion of Memokath-051 (Agrawal et al., 2009, Kulkarni and Bellamy, 2001, Zaman et al., 2011). **Total cost: £15.54** British National Formulary (BNF) Online (Joint Formulary Committee, 2016). Intrathecal injection assuming 70kg adult	✗	No cost was included by the company. However, the omitted cost is minor
Hospital stay following insertion and replacement				
Memokath-051 and all stent comparators	Not included in the company's model	**Day case and current inpatient** **Total cost: £108** Includes cost of hospital stay for 4 hours and recovery cost. Hospital stay: NHS reference costs 2015/16. Weighted average of the non-elective excess bed day for LB19C and LB19D (Department of Health, 2016). Recovery cost: Staff time for recovery band 5 and recovery band 6. **Inpatient** **Total cost: £505** As above with hospital stay cost applied to duration of stay: 1.47 days. Average from 2 UK single-arm studies. Agrawal reported 1.43 days (Agrawal et al., 2009) and Papatsoris reported 1.5 days (Papatsoris and Buchholz, 2010)	✗	No cost was explicitly included by the company given that the procedure was considered to be conducted during a day case. The cost of staff during recovery, was included. All insertions are day case procedures in EAC base case as verified by 1 clinical expert. All double-J replacements are day case procedures as verified by 1 clinical expert. Replacements of Memokath-051 and metallic stent replacements assumed by the EAC to be 50% day case, 25% inpatients and 25% current inpatients as no evidence available
Post-operative medication following insertion and replacement				
Memokath-051	Not included in the company's model	**Element: Norfloxacin** 2 UK-based studies report that norfloxacin is given following the insertion of Memokath-	✗	No cost was included by the company. There is likely to be variation in practice given that the EAC noted that an additional UK-

Parameter	Company's value	EAC's value	Agreement?	Reason for difference
		051 (Agrawal et al., 2009, Kulkarni and Bellamy, 2001). **Total cost: £8.57** BNF 2016 (Joint Formulary Committee, 2016) , Norfloxacin. 14-tab pack = £12.00 Per tablet price = £0.857 £8.57 per patient given that pack sharing may occur.(Twice daily for 5 days. 10 tabs required)		based study reported that 3 days of oral broad-spectrum antibiotics are given (Zaman et al., 2011)
Double-J stent and metallic stents (UVENTA, Allium and Resonance)	Not included in the company's model	**Element: Norfloxacin** **Total cost: £8.57** The EAC assumed that the medication is the same as for Memokath-051 as no evidence was available	✘	No cost was included by the company. The EAC rationale is as above
Follow-up visit after insertion or replacement				
Memokath-051	Not included in the company's model	**Resource use: Renogram** 1 visit approximately 4 weeks following insertion as stated in the Memokath-051 IFU (PNN Medical, 2016). 1 clinical expert said that an x-ray and renogram would be conducted at follow-up. The 2nd expert said that follow-up would be a clinical assessment. Lack of consistency so EAC included cost of renogram only. **Total cost per month: £255** The cost of a renogram from NHS reference costs 2015/16 used. NMOP, outpatient, Renogram, 19 years and over (Department of Health, 2016). This cost will include the cost of the clinical assessment	✘	The company did not include an immediate follow-up visit, but did include subsequent follow-ups as detailed below. The additional visit was included by the EAC as per the Memokath-051 IFU (PNN Medical, 2016)

Parameter	Company's value	EAC's value	Agreement?	Reason for difference
Double-J stent	Not included in the company's model	**Resource use: Urology outpatient appointment** Advised by clinical experts. **Total cost: £105** NHS reference costs 2015/16 (Department of Health, 2016)	✓	The company did not include an immediate follow-up visit, but did include subsequent follow-ups as detailed below
Metallic stents	Not included in the company's model	**Resource use: Renogram** **Total cost: £255** The EAC assumed that the follow-up is the same as for Memokath-051 as no evidence was available	✗	Metallic stents were not included within the company's model, but were considered by the EAC
Reconstructive surgery	Not included in the company's model	**Resource use: Removal of double-J stent and 2 follow-up renograms** Advised by a clinical expert that follow-up imaging is the same for all comparators and double-J stent (inserted during surgery) is removed as a day case procedure. **Total cost: £1,124** Removal double-J stent: NHS reference costs 2015/16 (Department of Health, 2016). Day case. Percutaneous, Attention to or Removal of, Ureteric Stent or Nephrostomy, YL12Z. Renogram: Based on 2 visits per year with a cost of £255 per visit. NMOP, outpatient, Renogram, 19 years and over (Department of Health, 2016). This cost will include the cost of the clinical assessment	✗	Reconstructive surgery was not included within the company's model, but were considered by the EAC. Applied within the cost of insertion and not as a monthly cost. Clinical expert advised that follow-up only required for a maximum of 1 year (unless undergoing radiotherapy)
Follow-up beyond post-insertion and replacement				
Memokath-051	**Total cost per year: £285** **Total cost per month: £23.75** AUH data.	**Resource use: 2 renogram visits per year** Memokath-051 IFU states that follow-up visits would occur at 3, 6 and 12 months post-procedure (PNN Medical, 2016). No	✗	The cost used by the EAC was higher than that used by the company given that 2 renograms per year were included based on clinical advice and

Parameter	Company's value	EAC's value	Agreement?	Reason for difference
	X-ray of abdomen: £22, 1 per year NM renogram: £103, 1 per year Outpatient department follow-up: £80, 2 visits per year (AUH).Total cost per month was calculated by the EAC	consistency between experts on follow-up procedure. EAC included renogram but not x-ray. **Total cost per month: £42.50** Based on 2 visits per year with a cost of £255 per visit. NMOP, outpatient, Renogram, 19 years and over (Department of Health, 2016). This cost will include the cost of the clinical assessment. The cost of an x-ray is relatively small, approx. £30 (Department of Health, 2016) and was only reported to be used by 1 of 2 experts		the manufacturer's IFU (PNN Medical, 2016)
Double-J stent	**Total cost per year: £200** **Total cost per month: £16.67** The company included 2 x-rays every 6 months in their model at a cost of £100. The company informed the EAC that this was included in a study but failed to state which study so the EAC could not verify this (correspondence log). The AUH data did not include follow-up visits for double-J stents. Total cost per month was calculated by the EAC	**Total cost per month: £0** Deemed not applicable as double-J stents have a planned replacement every 6 months	✗	The EAC has not included follow-up for the double-J stent given that they have a planned replacement every 6 months
UVENTA and Allium	Not included in the company's model	**Element: 2 renogram visits per year** **Total cost per month: £42.50**	✗	Metallic stents were not included by the company. The EAC assumed the

Parameter	Company's value	EAC's value	Agreement?	Reason for difference
		The EAC assumed that the follow-up is the same as for Memokath-051 as no evidence was available		same follow-up as with Memokath-051
Resonance	Not included in the company's model	**Element: 1 renogram visit per year** **Total cost per month: £21.25** Given that Resonance has a planned replacement every 12 months, 1 follow-up visit is included	✘	Metallic stents were not included by the company. The EAC has included 1 follow-up visit for Resonance
Urinary tract infection				
Memokath-051 and all comparators	Not included in the company's model	**Resource use: GP appointment and antibiotics** Treatment for 7 days with trimethoprim, nitrofurantoin or amoxicillin; medicine costs from BNF (Joint Formulary Committee, 2016). GP appointment included to obtain the prescription. **Total cost: £37.32** Cost of antibiotics from the BNF: Trimethoprim - Dose = 200mg every 12 hours. 14 tab pack, 200mg per tab = £4.37. Nitrofurantoin - Dose = 500mg every 6 hours. 28 tabs, 50mg = £13.02. Amoxicillin - Dose 500mg every 8 hours. 21 tabs, 500mg = £1.57. Gross average = £6.32 Cost of GP appointment £31 (Personal Social Services Research Unit (PSSRU), 2016)	✘	The company did not include UTI within its model. Given that there are some clinical data pertaining to UTI, the EAC has included this cost
Total cost of insertion (breakdown as provided above)				

Parameter	Company's value	EAC's value	Agreement?	Reason for difference
Memokath-051	Total cost: £3,068	Total cost: £3,010	×	• The company used an incorrect price of Memokath-051, this has been rectified by the EAC. • The company used a procedure time of 4 hours for the surgeon and 4.5 hours for all other staff. The EAC used a shorter procedure time, 45 minutes. The company included a higher cost for recovery staff (£89 vs £57). • The company used staff costs provided by AUH. The EAC used staff costs from PSSRU. The company included surgery tariff. The EAC included the cost of surgery, theatre time, hospital stay, follow-up, and medication. It excluded tariff
Double-J	Total cost: £1,676	Total cost: £786	×	As above but with procedure time of 22.5
UVENTA	Not included in the company's model.	Total cost: £2,736	×	The company did not include UVENTA within its model. The EAC included the cost of insertion, theatre time, hospital stay, follow-up and medication
Allium	Not included in the company's model.	Total cost: £2,936	×	The company did not include Allium within its model. The EAC included the cost of insertion, theatre time, hospital stay, follow-up and medication

Parameter	Company's value	EAC's value	Agreement?	Reason for difference
Resonance	Not included in the company's model.	Total cost: £2,148	×	The company did not include Resonance within its model. The EAC included the cost of insertion, theatre time, hospital stay, follow-up and medication
Surgery	Not included in the company's model.	Total cost: £7,414 (includes all follow-up costs)	×	The company did not include surgery within its model. The EAC identified the total cost of reconstructive surgery from the NHS reference costs and added the cost of follow-up This cost incorporates all care provided to the average patient during their episode of care including hospital stay and follow-up costs over 3 months post-surgery
Cost of follow-up per month (breakdown as provided above)				
Memokath-051	Monthly cost: £23.75 Calculated by the EAC to be a monthly cost.	Monthly cost: £42.50	×	The cost used by the EAC was higher than that used by the company given that 2 renograms per year were included based on clinical advice and the manufacturer's IFU (PNN Medical, 2016)
Double-J	Monthly cost: £16.67 Calculated by the EAC to be a monthly cost.	Monthly cost: £0	×	The EAC have not included follow-up for the double-J stent given that they have a planned replacement every 6 months
UVENTA and Allium	Not included in the company's model.	Monthly cost: £42.50	×	Metallic stents were not included by the company. The EAC assumed the same follow-up as with Memokath-051
Resonance	Not included in the company's model.	Monthly cost: £21.25	×	The EAC have not included 1 follow-up for Resonance given that they

Parameter	Company's value	EAC's value	Agreement?	Reason for difference
				have a planned replacement every 12 months
Total replacement costs (breakdown as provided above)				
Memokath-051	Total cost: £3,781 Total cost for 2.5 years as calculated within the company's model.	Total cost: £3,347	×	• The company used an incorrect price of Memokath-051, this has been rectified by the EAC. • The company used a procedure time of 4 hours for the surgeon and 4.5 hours for all other staff. The EAC used a shorter procedure time, 60 minutes. • The company included a higher cost of recovery staff than the EAC. • The company used staff costs provided by AUH. The EAC used staff costs from PSSRU. The company included surgery tariff. The EAC included the cost of surgery, theatre time, hospital stay, follow-up, and medication
Double-J	Not explicitly included in the company's model. Calculated by the EAC to be £1,676 based on theatre staff costs, theatre consumable costs and surgery tariff for insertion.	Total cost: £1,052	×	As above with procedure time of 55 minutes
UVENTA	Not included in the company's model.	Total cost: £3,157	×	The company did not include UVENTA within its model. The EAC included the cost of replacement,

Parameter	Company's value	EAC's value	Agreement?	Reason for difference
				theatre time, hospital stay, follow-up and medication
Allium	Not included in the company's model.	Total cost: £3,357	×	The company did not include Allium within its model. The EAC included the cost of replacement, theatre time, hospital stay, follow-up and medication
Resonance	Not included in the company's model.	Total cost: £2,569	×	The company did not include Resonance within its model. The EAC included the cost of replacement, theatre time, hospital stay, follow-up and medication
Surgery	Not included in the company's model.	Total cost: £0	×	The company did not include surgery within its model. The EAC made a conservative assumption that no further procedures are required following reconstructive surgery, No evidence available to inform the number of patients who may require further surgery or what this would involve
UTI total cost				
All comparators	Not included in the company's model.	Total cost: £37.32	×	The company did not include UTI within its model. Given that there are some clinical data pertaining to UTI, the EAC has included this cost

Appendix P: EAC's full results – Memokath-051 versus double-J stents

Table P.1: EAC's base case results (per patient) – constant risk of unplanned replacement over 5 year time horizon

	Memokath-051	Double-J Stents	Incremental cost
Total insertion cost	£3,010	£786	£2,224
Follow-up cost	£2,346	£0	£2,346
Unplanned replacement cost	£2,503	£0	£2,503
Planned replacement cost	£0	£8,692	-£8,692
Adverse event cost	£9	£9	£0
Total	**£7,868**	**£9,487**	**-£1,619**
Breakeven point = 30 months			

Table P.2: EAC's results (per patient) – constant risk of unplanned replacement to 2 years and no risk thereafter

	Memokath-051	Double-J Stents	Incremental cost
Total insertion cost	£3,010	£786	£2,224
Follow-up cost	£2,346	£0	£2,346
Unplanned replacement cost	£1,027	£0	£1,027
Planned replacement cost	£0	£8,692	-£8,692
Adverse event cost	£9	£9	£0
Total	**£6,391**	**£9,487**	**-£3,095**
Breakeven point = 30 months			

Table P.3: EAC's results (per patient) – constant risk of unplanned replacement to 2 years and halved risk thereafter

	Memokath-051	Double-J Stents	Incremental cost
Total insertion cost	£3,010	£786	£2,224
Follow-up cost	£2,346	£0	£2,346
Unplanned replacement cost	£1,770	£0	£1,770
Planned replacement cost	£0	£8,692	-£8,692
Adverse event cost	£9	£9	£0
Total	**£7,134**	**£9,487**	**-£2,352**
Breakeven point = 30 months			

Table P.4: EAC's results (per patient) – with 2 year time horizon

	Memokath-051	Double-J Stents	Incremental cost
Total insertion cost	£3,010	£786	£2,224
Follow-up cost	£987	£0	£987
Unplanned replacement cost	£1,027	£0	£1,027
Planned replacement cost	£0	£3,048	-£3,048
Adverse event cost	£4	£4	£0
Total	**£5,027**	**£3,837**	**£1,190**
Breakeven point = None within 2 years			

Appendix Q: EAC's full results – Memokath-051 versus reconstructive surgery

Table Q.1: EAC's base case results (per patient) – constant risk of unplanned replacement over 5 year time horizon

	Memokath-051	Reconstructive surgery	Incremental cost
Total insertion cost	£3,010	£7,414	-£4,404
Follow-up cost	£2,346	£0	£2,346
Unplanned replacement cost	£2,503	£0	£2,503
Planned replacement cost	£0	£0	£0
Adverse event cost	£26	£4	£22
Total	**£7,885**	**£7,417**	**£467**
Breakeven point = 53 months			

Table Q.2: EAC's results (per patient) – constant risk of unplanned replacement to 2 years and no risk thereafter

	Memokath-051	**Reconstructive surgery**	**Incremental cost**
Total insertion cost	£3,010	£7,414	-£4,404
Follow-up cost	£2,346	£0	£2,346
Unplanned replacement cost	£1,027	£0	£1,027
Planned replacement cost	£0	£0	£0
Adverse event cost	£26	£4	£22
Total	**£6,408**	**£7,417**	**-£1,009**
Breakeven point = beyond model time horizon			

Table Q.3: EAC's results (per patient) – constant risk of unplanned replacement to 2 years and halved risk thereafter

	Memokath-051	**Reconstructive surgery**	**Incremental cost**
Total insertion cost	£3,010	£7,414	-£4,404
Follow-up cost	£2,346	£0	£2,346
Unplanned replacement cost	£1,770	£0	£1,770
Planned replacement cost	£0	£0	£0
Adverse event cost	£26	£4	£22
Total	**£7,151**	**£7,417**	**-£266**
Breakeven point = 59 months			

Table Q.4: EAC's results (per patient) – with 2 year time horizon

	Memokath-051	**Reconstructive surgery**	**Incremental cost**
Total insertion cost	£3,010	£7,414	-£4,404
Follow-up cost	£987	£0	£987
Unplanned replacement cost	£1,027	£0	£1,027
Planned replacement cost	£0	£0	£0
Adverse event cost	£11	£1	£9
Total	**£5,034**	**£7,415**	**-£2,381**
Breakeven point = beyond model time horizon			

Appendix R: EAC's full results – Memokath-051 versus other metallic stents

Figure R.1: Costs over time Memokath-051 vs UVENTA (constant unplanned replacement over 5 years)

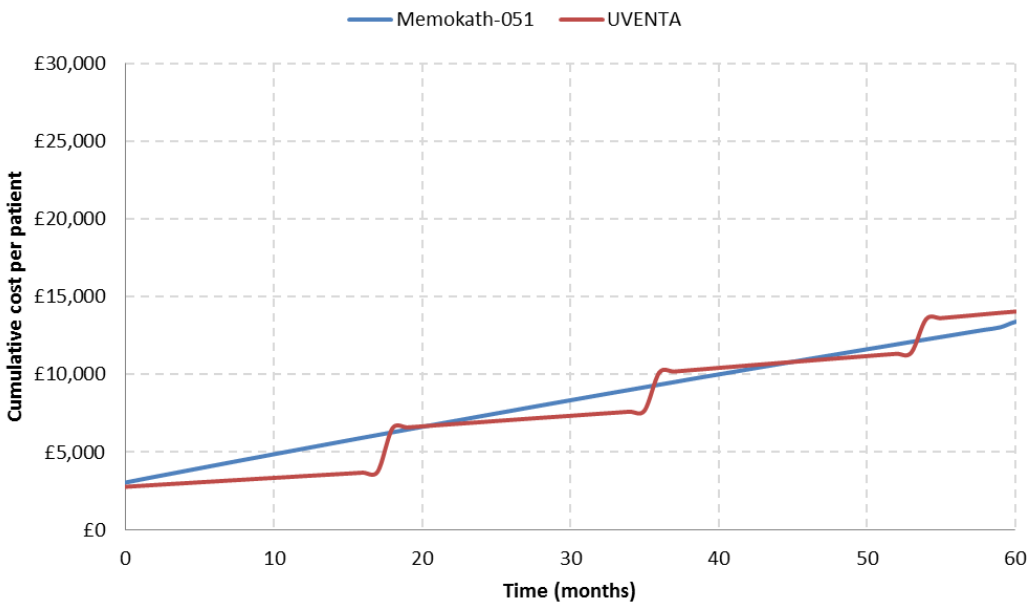


Figure R.2: Costs over time Memokath-051 vs UVENTA (no unplanned replacement after 2 years)

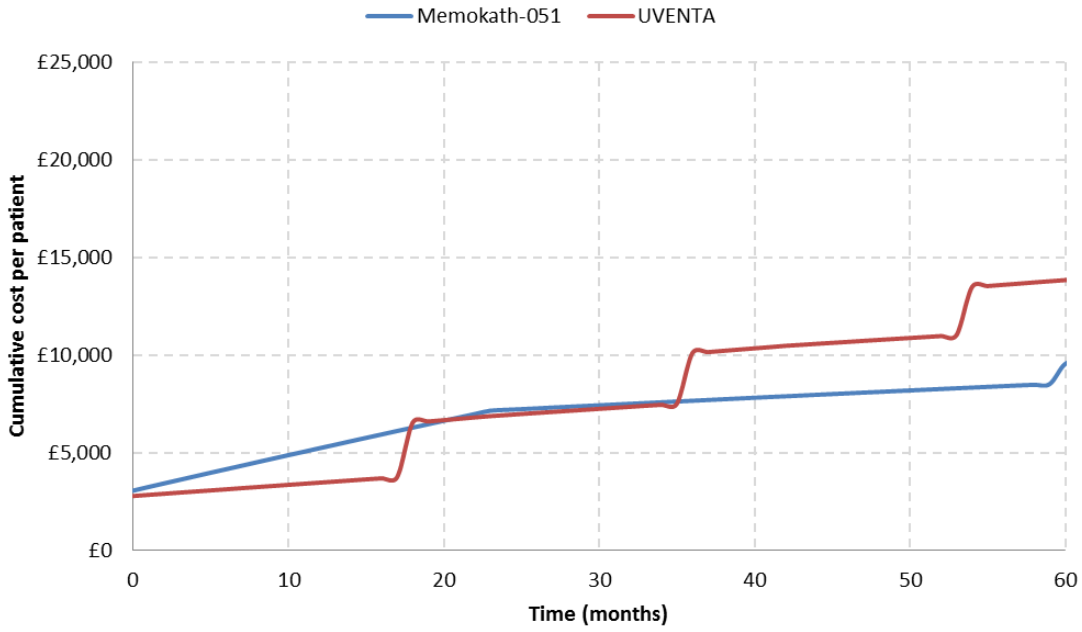


Figure R.3: Costs over time Memokath-051 vs Allium (constant unplanned replacement over 5 years)

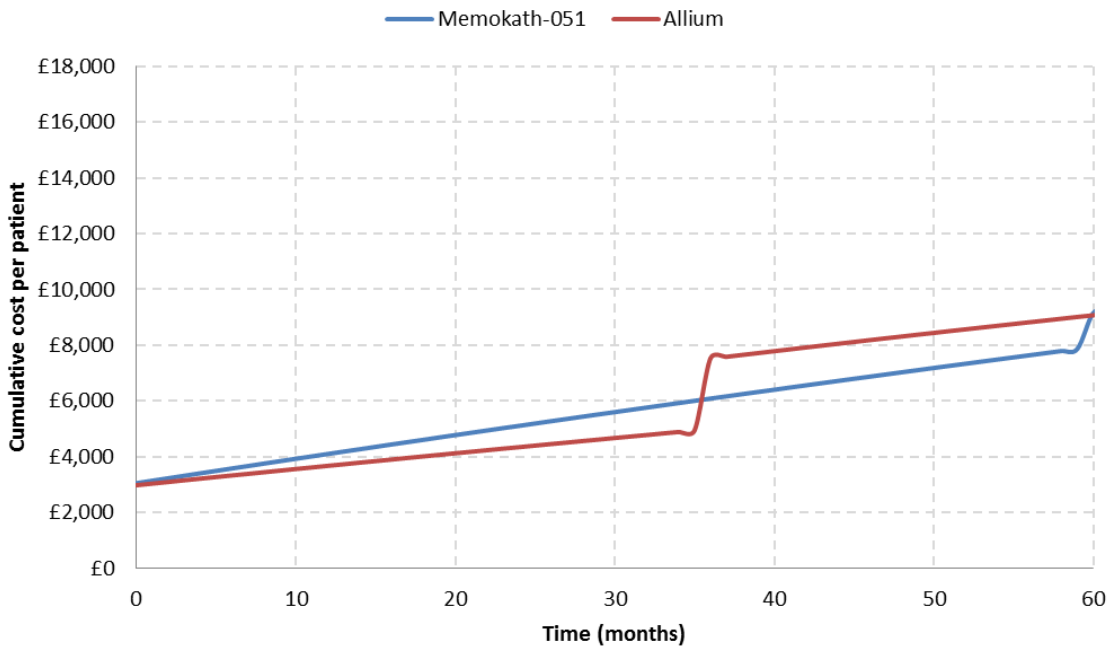


Figure R.4: Costs over time Memokath-051 vs Allium (no unplanned replacement after 2 years)

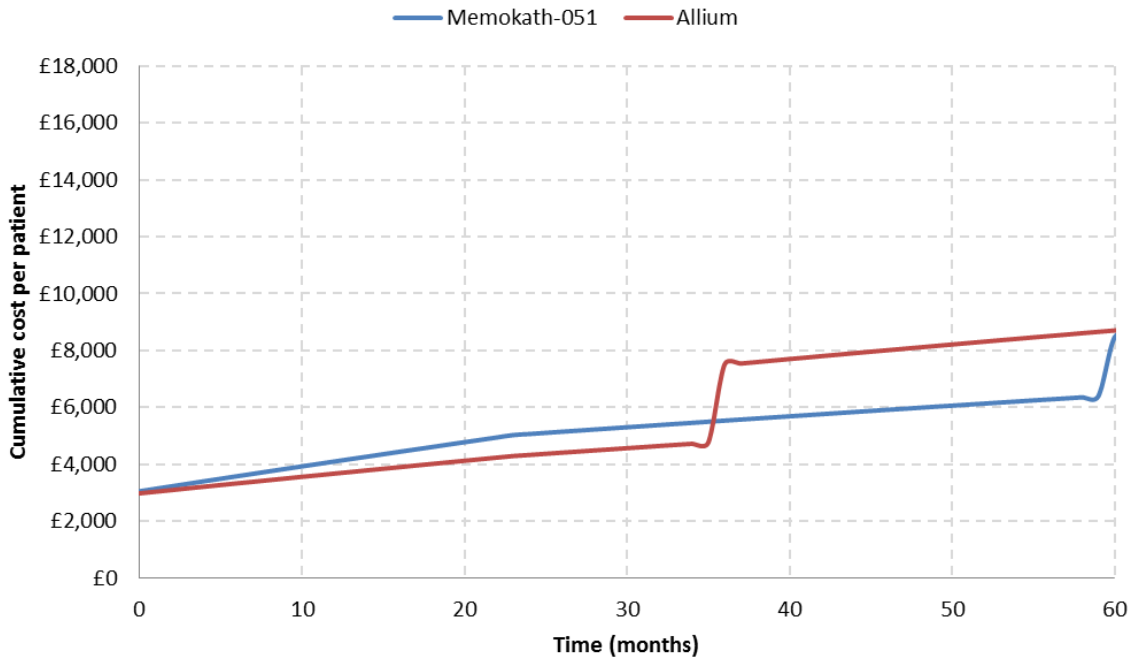


Figure R.5: Costs over time Memokath-051 vs Resonance (constant unplanned replacement over 5 years)

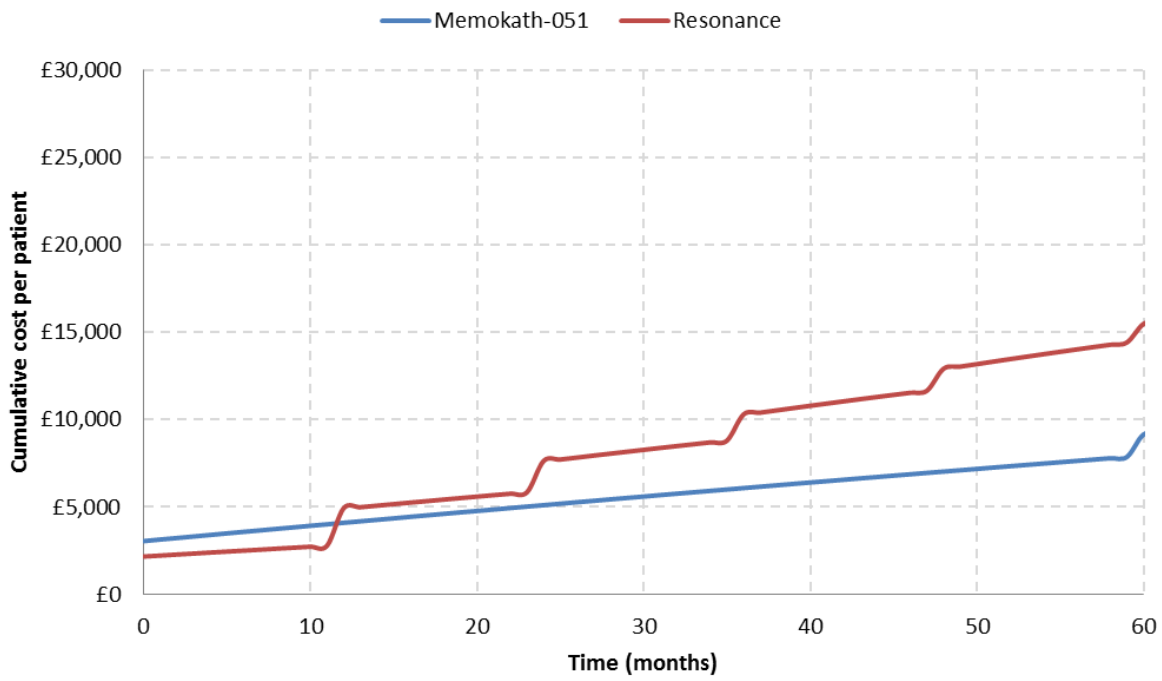
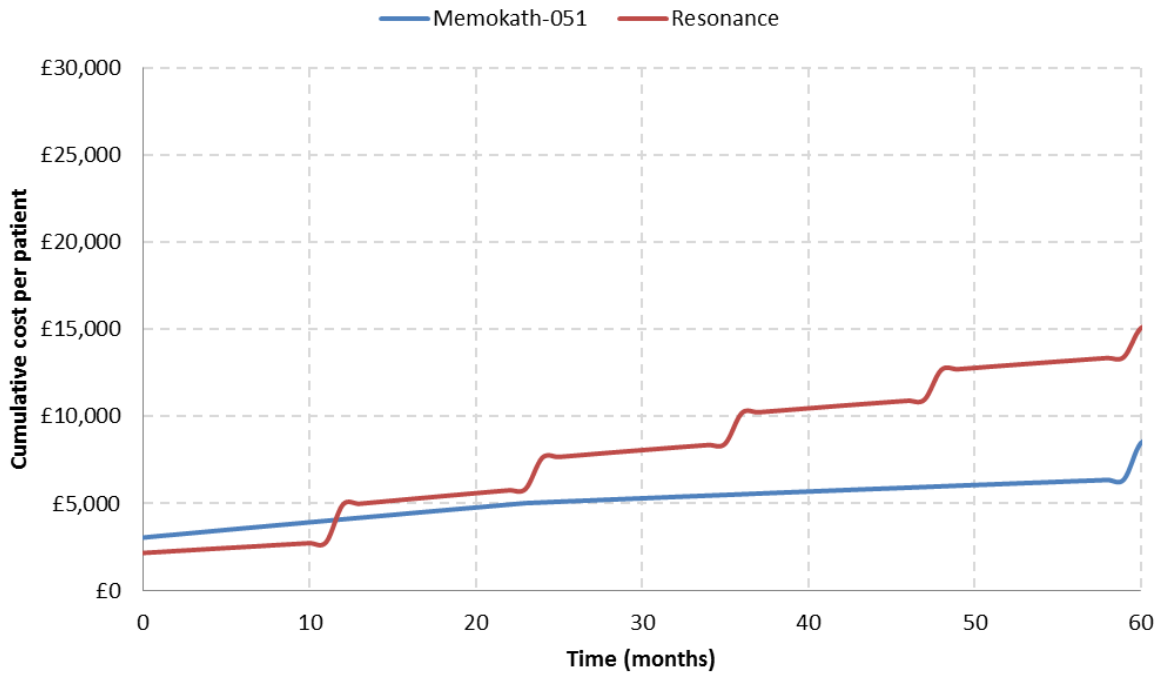


Figure R.6: Costs over time Memokath-051 vs Resonance (no unplanned replacement after 2 years)



Appendix S: EAC's sensitivity analysis

Table S.1: Values used in EAC sensitivity analysis

Model parameter and base case value	Low value and rationale	High value and rationale
Memokath-051		
Length of time in situ = 60 months	**48 months** Lower limit provided during topic scoping (NICE, 2017b).	**60 months** Although Memokath-051 may be in situ for longer than 60 months, the model time horizon does not extend beyond this.
Monthly risk of early replacement (up to 24 months) = 1.4%	**0.6%** Lowest value reported in clinical study (Bourdoumis et al., 2014)	**4.4%** Highest value reported in clinical study (Kim et al., 2014)
Monthly risk of UTI = 1.2%	**0.0% -** Assumption	**3.0% -** Assumption
Insertion cost = £3,010	**£2,288** Based on: 1. 20 minute insertion time 2. 2 hour hospital stay and all day cases 3. X-ray rather than renogram at follow-up 4. No passport catheter required	**£3,604** Based on: 1. 60 minute insertion time 2. All inpatients 3. X-ray and renogram at follow-up
Monthly follow-up cost = £42.50	**£21.25** Based on 1 visit per year	**£63.75** Based on 3 visits per year
Replacement cost = £3,347	**£2,303** Based on: 1. 30 minute replacement time 2. 2 hour hospital stay and all day cases 3. X-ray rather than renogram at follow-up 4. No passport catheter required	**£3,843** Based on: 1. 90 minute replacement time 2. All inpatients 3. X-ray and renogram at follow-up
Double-J stents		
Length of time in situ = 6 months	**3 months** Lower limit provided by experts	**6 months** Upper limit provided by experts
Monthly risk of early replacement (up to 24 months) = 0%	**0%** Lowest possible value.	**4.4%** Assumed equal to the highest value reported for Memokath-051

Model parameter and base case value	Low value and rationale	High value and rationale
Monthly risk of UTI = 0.4%	**0.0% -** Assumption	**3.0% -** Assumption
Insertion cost = £786	**£646** Based on: 1. 15 minute insertion time 2. 2 hour hospital stay and all day cases 3. £29.82 cost of stent	**£1,533** Based on: 1. 35 minute insertion time 2. All inpatients 3. X-ray and clinical assessment at follow-up 4. £241.24 cost of stent
Monthly follow-up cost = £0	**£0** Lowest plausible value as per base case	**£21.25** 1 follow-up visit per year
Replacement cost = £1,052	**£717** Based on: 1. 30 minute replacement time 2. 2 hour hospital stay and all day cases 3. £29.82 cost of stent	**£1,939** Based on: 1. 80 minute replacement time 2. All inpatients 3. X-ray and clinical assessment at follow-up 4. £241.24 cost of stent
UVENTA		
Length of time in situ = 18 months	**12 months** Assumption	**24 months** Assumption
Monthly risk of early replacement (up to 24 months) = 0.49%	**0%** Lowest possible value.	**4.4%** Assumed equal to the highest value reported for Memokath-051
Monthly risk of UTI = 0.42%	**0.0% -** Assumption	**3.0% -** Assumption
Insertion cost = £2,736	**£2,153** Based on: 1. 25 minute insertion time 2. 2 hour hospital stay and all day cases 3. X-ray rather than renogram at follow-up 4. No passport catheter required	**£3,359** Based on: 1. 55 minute insertion time 2. All inpatients 3. X-ray and renogram at follow-up
Monthly follow-up cost = £42.50	**£21.25** Based on 1 visit per year	**£63.75** Based on 3 visits per year
Replacement cost = £3,157	**£2,113** Based on: 1. 30 minute replacement time 2. 2 hour hospital stay and all day cases	**£3,653** Based on: 1. 90 minute replacement time 2. All inpatients

Model parameter and base case value	Low value and rationale	High value and rationale
	3. X-ray rather than renogram at follow-up 4. No passport catheter required	3. X-ray and renogram at follow-up
Allium		
Length of time in situ = 36 months	**12 months** Assumption	**36 months** IFU states up to 3 years (Allium Medical, 2016)
Monthly risk of early replacement (up to 24 months) = 0.49%	**0%** Lowest possible value.	**4.4%** Assumed equal to the highest value reported for Memokath-051
Monthly risk of UTI = 0.42%	**0.0% -** Assumption	**3.0% -** Assumption
Insertion cost = £2,936	**£2,353** Based on: 1. 25 minute insertion time 2. 2 hour hospital stay and all day cases 3. X-ray rather than renogram at follow-up 4. No passport catheter required	**£3,559** Based on: 1. 55 minute insertion time 2. All inpatients 3. X-ray and renogram at follow-up
Monthly follow-up cost = £42.50	**£21.25** Based on 1 visit per year	**£63.75** Based on 3 visits per year
Replacement cost = £3,357	**£2,313** Based on: 1. 30 minute replacement time 2. 2 hour hospital stay and all day cases 3. X-ray rather than renogram at follow-up 4. No passport catheter required	**£3,853** Based on: 1. 90 minute replacement time 2. All inpatients 3. X-ray and renogram at follow-up
Resonance		
Length of time in situ = 12 months	**6 months** Assumption	**12 months** IFU states up to 12 months (Cook Medical, 2012)
Monthly risk of early replacement (up to 24 months) = 1.4%	**0%** Lowest possible value.	**4.4%** Assumed equal to the highest value reported for Memokath-051
Monthly risk of UTI = 0.42%	**0.0% -** Assumption	**3.0% -** Assumption
Insertion cost = £2,148	**£1,565** Based on: 1. 25 minute insertion time 2. 2 hour hospital stay and all day case	**£2,770** Based on: 1. 55 minute insertion time 2. All inpatients

Model parameter and base case value	Low value and rationale	High value and rationale
	3. X-ray rather than renogram at follow-up 4. No passport catheter required	3. X-ray and renogram at follow-up
Monthly follow-up cost = £21.25	**£21.25** Based on 1 visit per year	**£63.75** Based on 3 visits per year
Replacement cost = £2,569	**£1,525** Based on: 1. 30 minute replacement time 2. 2 hour hospital stay and all day cases 3. X-ray rather than renogram at follow-up 4. No passport catheter required	**£3,064** Based on: 1. 90 minute replacement time 2. All inpatients 3. X-ray and renogram at follow-up
Reconstructive surgery		
Length of time in situ = equal to time horizon of the model	Not varied, equal to the time horizon of the model.	Not varied, equal to the time horizon of the model.
Monthly risk of early replacement (up to 24 months) = 0%	Not varied, reconstructive surgery is assumed to be successful.	Not varied, reconstructive surgery is assumed to be successful.
Monthly risk of UTI = 0.17%	**0.0% -** Assumption	**3.0% -** Assumption
Surgery cost = £7,414	**£5,966** Based on: 1. Lowest applicable elective inpatient NHS reference cost (LB62D) = £5,352 2. Removal of double-J stent with no further imaging (£614)	**£12,656** Based on: 1. Highest applicable elective inpatient NHS reference cost (LB60C) = £11,277 2. Removal of double-J stent with 3 renograms (£1,379)
Monthly follow-up cost = £0	Not varied, captured in surgery cost	Not varied, captured in surgery cost
Replacement cost = £0	Not varied, no further surgery	Not varied, no further surgery
All comparators: UTI cost = £37	**£0** Assumption – UTI so mild that no treatment or visit required.	**£1,851** NHS reference costs, total HRGs weighted average of Kidney or UTIs (LA04H to LA04S) (Department of Health, 2016)

Results versus reconstructive surgery

Figure S.1 shows the tornado diagram for the worst case scenario for Memokath-051 versus reconstructive surgery. The key drivers of the result are the cost of surgery, monthly risk of unplanned Memokath-051 replacement, the costs of insertion, replacement and monthly follow-up for Memokath-051.

Figure S.1: Tornado diagram for Memokath-051 versus reconstructive surgery with constant unplanned replacement over 5 year time horizon

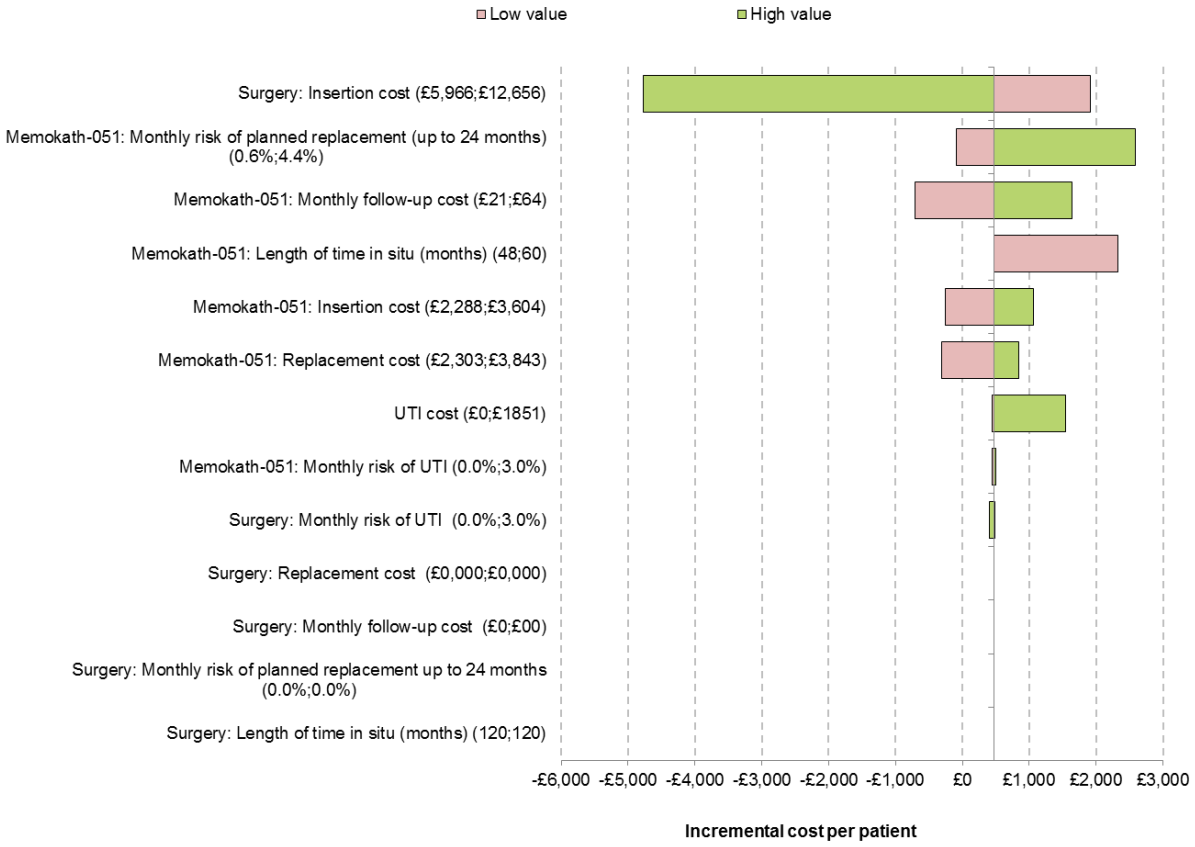
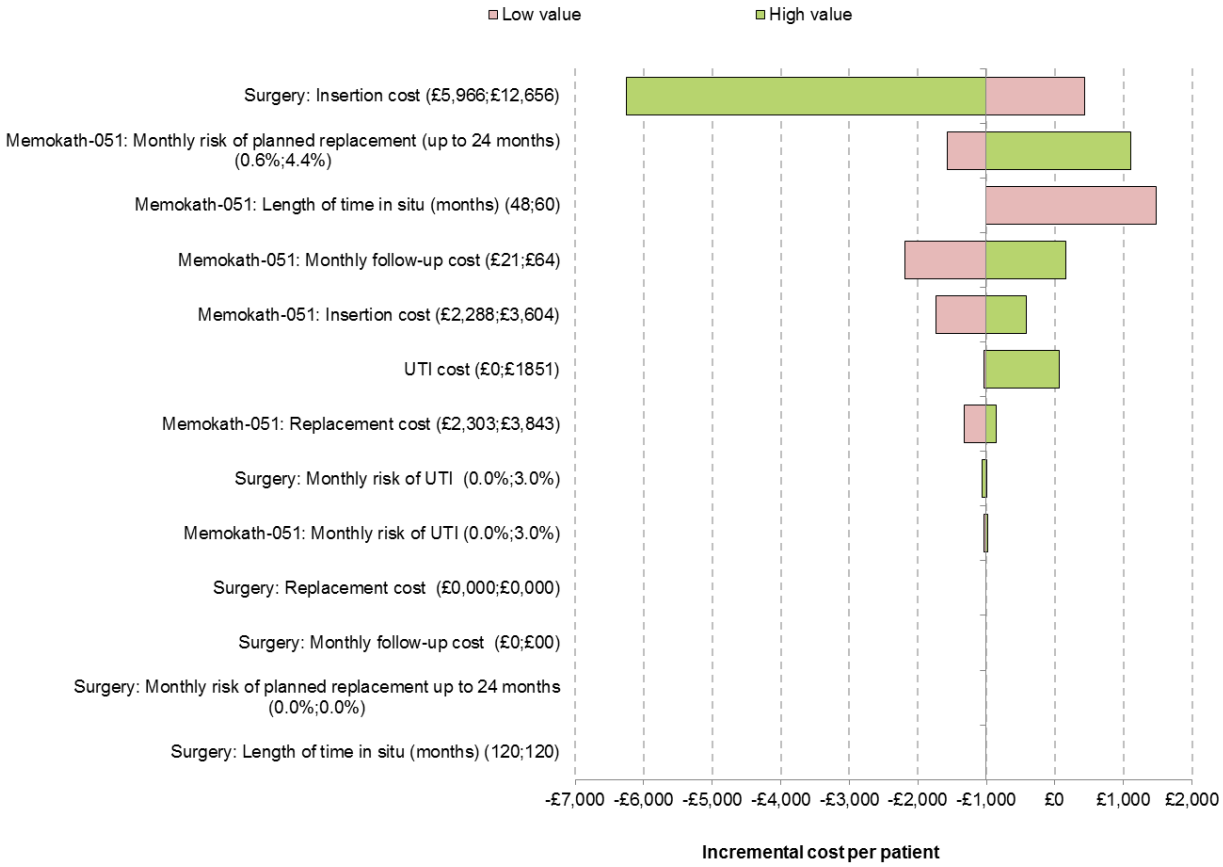


Figure S.2 shows the tornado diagram for the best case scenario for Memokath-051 versus reconstructive surgery.

Figure S.2: Tornado diagram for Memokath-051 versus reconstructive surgery with unplanned replacement over 2 years only, and 0% thereafter



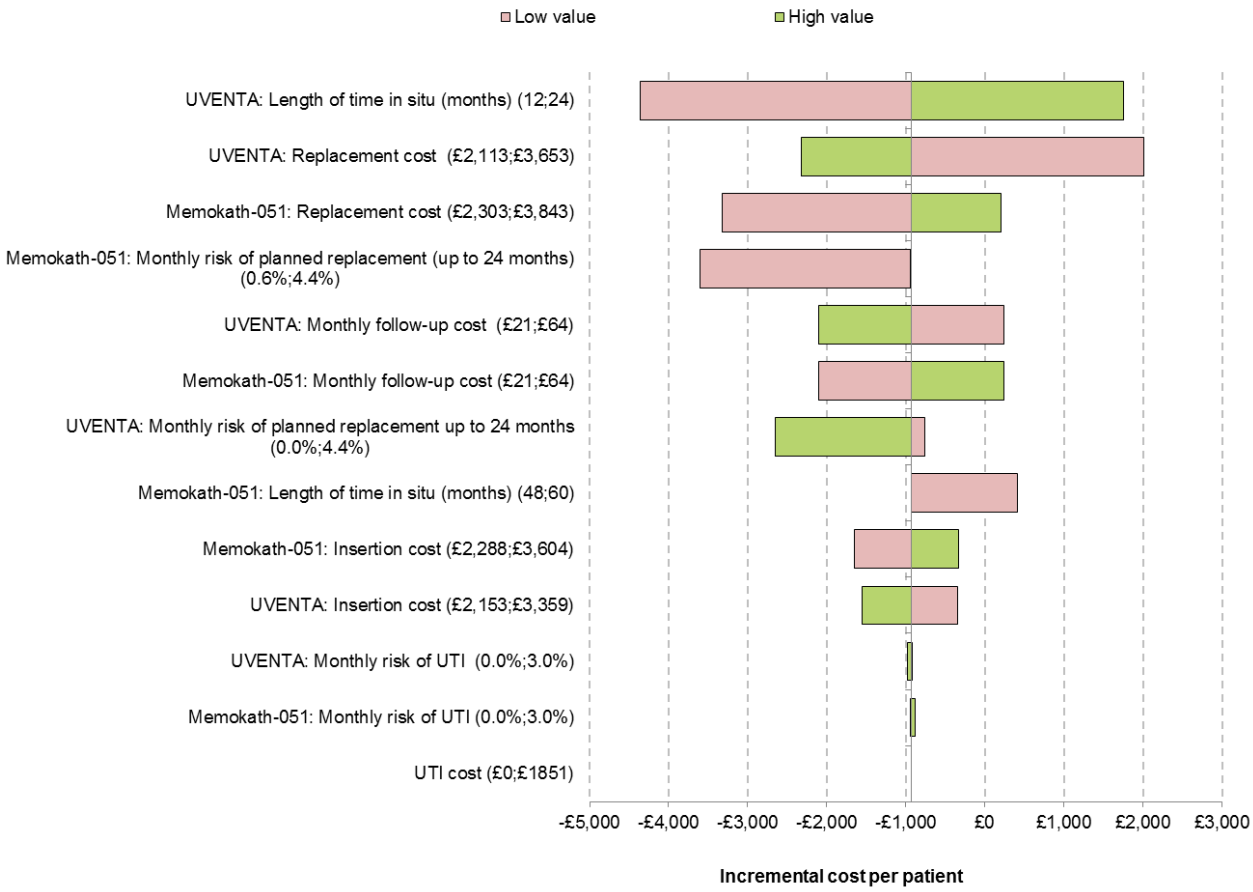
The 3 key drivers of the result are detailed below:

- Surgery cost: This value is £7,414 in the base case. When the cost of surgery is £6,400 or less, Memokath-051 is no longer cost saving over a 5 year time horizon;
- Monthly risk of unplanned Memokath-051 replacement (up to 24 months): This value is 1.4% in the base case. When it is 2.8% or above, Memokath-051 is no longer cost saving over a 5 year time horizon;
- Length of time in situ for Memokath-051: This value is 60 months in the base case. Memokath-051 is cost saving until planned replacement. Hence, if this happens any earlier than 60 months then the breakeven point is at that time point too.

Results versus UVENTA

Figure S.3 shows the tornado diagram for the worst case scenario for Memokath-051 versus UVENTA. This shows that the results are sensitive to change in most parameter, due to the costs being very similar between the treatment and comparator arms in the base case. The results for the best case scenario show that the results are robust.

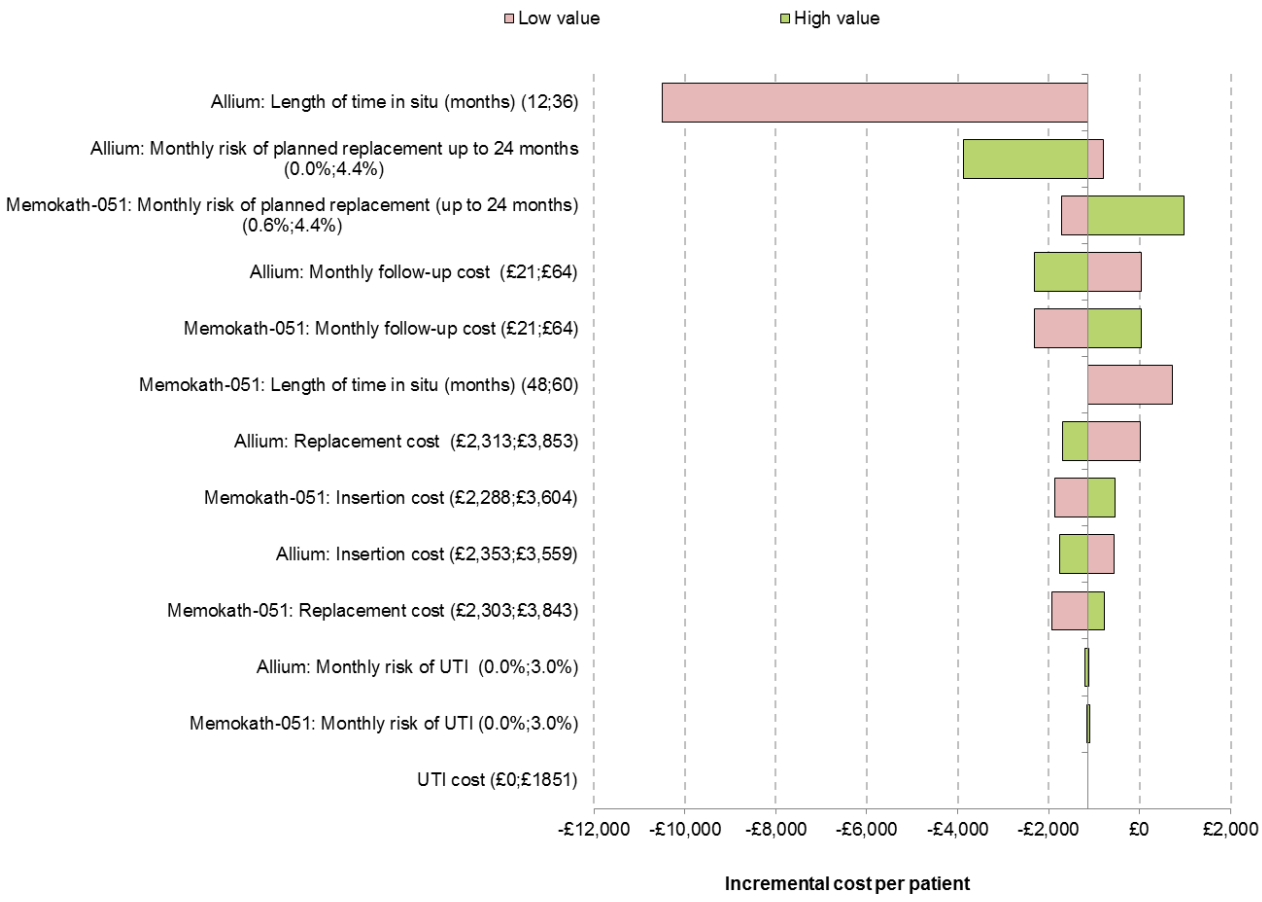
Figure S.3: Tornado diagram for Memokath-051 versus UVENTA with constant unplanned replacement over 5 years



Results versus Allium

Figure S.4 shows the tornado diagram for the worst case scenario for Memokath-051 versus Allium. This shows that the results are sensitive to change in most parameters, due to the costs being very similar between the treatment and comparator arms in the base case. The results for the best case scenario show that the results are robust. Memokath-051 becomes cost-incurring only when the length of time in situ for Memokath-051 is 53 months or less in the best case scenario.

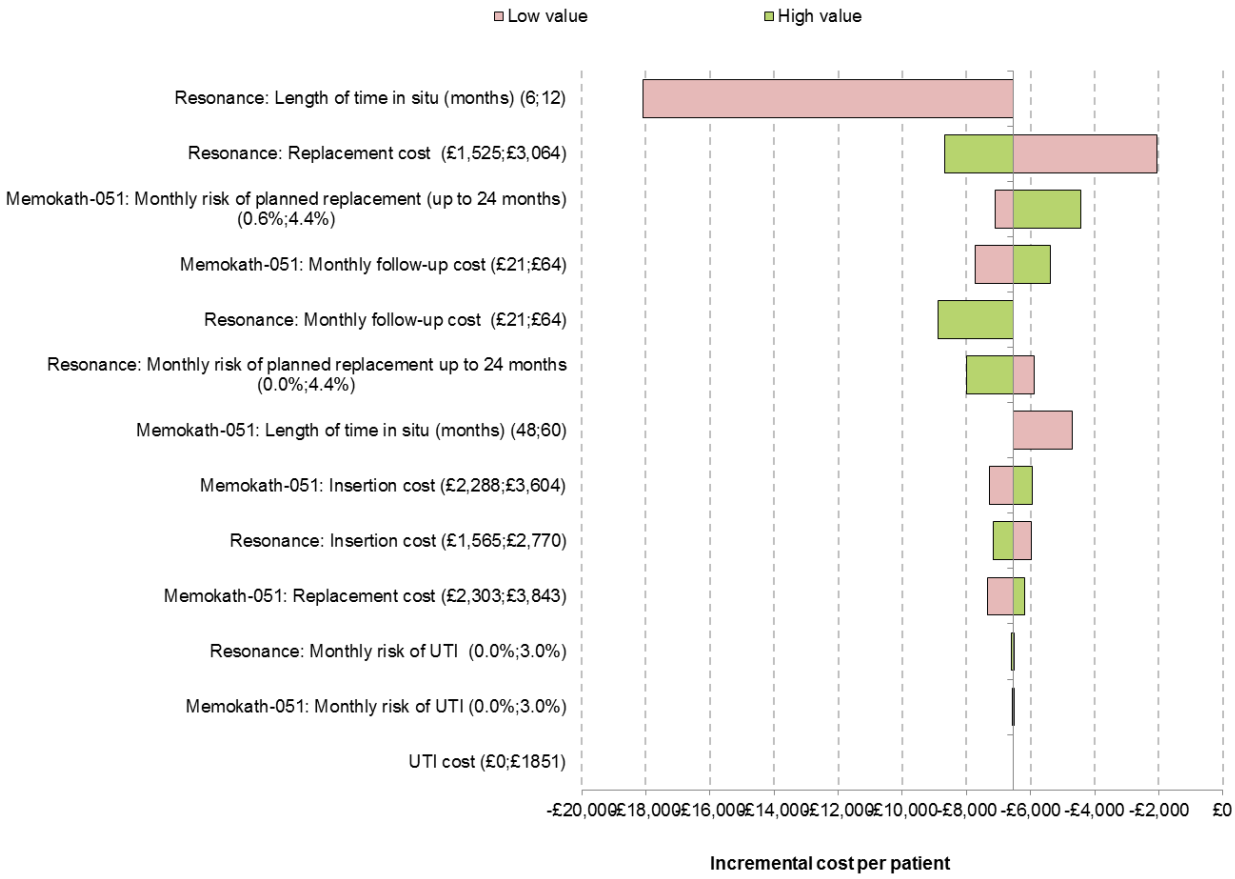
Figure S.4: Tornado diagram for Memokath-051 versus Allium with constant unplanned replacement over 5 year



Results versus Resonance

Figure S.5 shows the tornado diagram for the worst case scenario for Memokath-051 versus Resonance. The results appear to be robust. However, the efficacy values for Resonance were assumed based on expert opinion and so the results should be interpreted with caution.

Figure S.5: Tornado diagram for Memokath-051 versus Resonance with constant unplanned replacement over 5 years



NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Medical technology guidance

Assessment report overview

The Memokath-051 stent for the treatment of ureteric obstruction

This assessment report overview has been prepared by the Medical Technologies Evaluation Programme team to highlight the significant findings of the External Assessment Centre (EAC) report. It includes **brief** descriptions of the key features of the evidence base and the cost analysis, any additional analysis carried out, and additional information, uncertainties and key issues the Committee may wish to discuss. It should be read along with the company submission of evidence and with the EAC assessment report. The overview forms part of the information received by the Medical Technologies Advisory Committee when it develops its recommendations on the technology.

Key issues for consideration by the Committee are described in section 6, following the brief summaries of the clinical and cost evidence.

This report contains no confidential information. This overview also contains:

- Appendix A: Sources of evidence
- Appendix B: Comments from professional bodies
- Appendix C: Comments from patient organisations
- Appendix D: Claimed benefits and decision problem from scope

1 The technology

The Memokath-051 is a thermo-expandable, nickel-titanium shape memory alloy ureteric stent. The indication for this technology is as an alternative to conventional ureteric stents for people with ureteric obstruction as a result of benign or malignant strictures. The thermo-expandable alloy allows the stent to be more easily inserted and anchored in position. A spiral coil design aims to prevent endothelial ingrowth of the tumour or stricture into the stent so that it can be easily removed. Four different versions of Memokath-051 are available: either single or double cone design; for each design there are 2 versions for either antegrade or retrograde insertion, and each version is available in a variety of lengths. The use of other Memokath stents used for treating obstruction elsewhere in the urinary tract, are not considered in this evaluation.

2 Proposed use of the technology

2.1 Disease or condition

Ureteric stricture is characterised by a narrowing of the ureter and can have malignant or benign causes. When the ureter is obstructed, the normal flow of urine from the kidney to the bladder is disrupted which can lead to pressure build-up in the kidneys and acute kidney injury, which may lead to chronic kidney disease. People with ureteric obstruction are also more prone to kidney and urinary tract infections.

2.2 Patient group

There are no definitive estimates of the number of people who require a long-term ureteric stent as a result of malignant or benign ureteric strictures. In the NHS in England in 2014-15, there were 7,674 retrograde insertions and 2,733 retrograde removals of ureteric stents, but the type of stent (plastic or metallic), or the reason for insertion was not specified. The numbers of people having antegrade insertions are lower with few firm estimates currently

available. There were 80 cases of percutaneous insertions and 22 replacements of ureteric metallic stents in 2014-15.

2.3 Current management

People with complete ureteric obstruction require urgent referral and treatment to relieve the blockage and avoid the development of obstructive renal failure. The relief of ureteric obstruction can be achieved either by stenting the ureter, by creating a nephrostomy or by undertaking reconstructive surgery. The NICE guideline for acute kidney injury (AKI) states that all people with upper urinary tract obstruction should be referred to a urologist, and that when nephrostomy or stenting is undertaken, it should be done as soon as possible and certainly within 12 hours of diagnosis.

For people with malignant ureteric strictures, there are specific recommendations for those with prostate or bladder cancer. In the NICE guideline for prostate cancer, decompression of the upper urinary tract is recommended by nephrostomy or by insertion of a double J stent for men with obstructive uropathy secondary to hormone-relapsed prostate cancer. In the NICE guideline for bladder cancer, nephrostomy or retrograde stenting is recommended (if technically feasible) for people with locally advanced or metastatic bladder cancer with ureteric obstruction who need treatment to relieve pain, treat AKI or improve renal function before undergoing further therapy.

2.4 Proposed management with new technology

The Memokath 051 stent is intended for the first line treatment for adults with chronic ureteric strictures associated with benign or malignant diseases. Introducing Memokath 051 would mean limited changes to the pathway, because it would be a replacement for a double J stent or for a nephrostomy.

The adoption team has produced a scoping report for this technology.

3 Company claimed benefits and the decision problem

Details of the company's claimed benefits and the decision problem are described in Appendix D.

Table 1 Details of variation from the scope

Decision problem	Variation proposed by company	EAC view of the variation
Comparator	Comparison with double J stents only.	The EAC considered all comparators in their review of the clinical evidence

The company proposed a variation from the scope to include only 1 comparator however the EAC considered all the comparators specified. The EAC also thought other aspects of the company's submission did not address some of the decision problem, further details can be found in table 2.2 of the assessment report. The EAC noted that the technology is contraindicated for use in children and so the population considered was restricted to adults.

4 The evidence

4.1 Summary of evidence of clinical benefit

The company carried out 2 separate literature searches for identifying single arm and comparative studies. The EAC considered the eligibility criteria reported by the company were not in alignment with the scope, details of which can be found in section 3.2 of the assessment report. The company submission did not contain a clear description of the search methodology to enable the EAC to replicate or evaluate the search strategy. Therefore the EAC undertook a de novo literature search. Details of all the included and excluded studies are in the table below, a full description of the rationale can be found in section 3.3 of the assessment report.

Table 2 Included studies

Study	Type of publication	Type of study	Comment
Studies included by both EAC and company			
5 studies included by both	*1 abstract and 4 full papers.*	*5 observational studies* *<u>Comparative:</u>* *Maan et al. (2010)*** *NCT00166361 (2014)**** *<u>Single arm:</u>* *Agrawal et al. (2009)* *Kulkarni et al (2001)** *Papatsoris et al. (2010)*****	
Studies in submission excluded by EAC			
NA	*NA*	*NA*	*NA*
Studies not in submission included by EAC			
Akbarov et al. (2017)	*Abstract*	*Comparative observational study*	*Not identified by the company*
Arya et al. (2001)	*Full text*	*Observational study*	*Less than 20 patients therefore did not the company's eligibility criteria.*
Bach et al. (2013)	*Full text*	*Observational study*	*Excluded by the company because they could not obtain the full paper*
Bolton et al. (2015)	*Abstract*	*Comparative observational study*	*Not identified by the company*
Bourdoumis et al. (2014)	*Full text*	*Observational study*	*Excluded by the company because it includes retroperitoneal fibrosis patients.*
Boyvat et al. (2005)	*Full text*	*Observational study*	*Not identified by the company*
Kim et al. (2014)	*Full text*	*Comparative observational study*	*Excluded by the company because they could not obtain the full paper*
Klarskov et al. (2005)	*Full text*	*Observational study*	*Excluded by the company because they could not obtain the full paper*

Nam et al. (2015)	*Abstract*	*Comparative observational study*	*Not identified by the company*
Papadopoulos et al. (2010)	*Full text*	*Observational study*	*Excluded by the company because they could not obtain the full paper*
Zaman et al. (2011)	*Full text*	*Observational study*	*Malignant patients only, therefore did not meet the company's eligibility criteria*

*Kulkarni et al. (2001) – update of Kulkarni et al. (1999)

**Maan et al. (2010) – company submitted Patel et al. (2011) which is the same comparative study but reports on a subgroup only. See page section 3.2 of the Assessment Report for further details.

***NCT00166361 (2014) – Granberg et al. (2010) is an associated comparative study published as an abstract identified by the EAC.

****Papatsoris et al. (2010) - company submitted Papatsoris et al. (2007), which could not be located by the EAC. EAC found Papatsoris et al. (2010) which is an updated version of the 2007 study. See section 3.3 of the assessment report for further details.

EAC critical appraisal of the clinical evidence

The EAC reviewed the clinical evidence and noted the lack of quality RCT evidence. Two studies compared Memokath-051 with double J stents (Maan et al., 2010, NCT00166361, 2014), 3 studies compared it with other metal or alloy stents Allium stents (Bolton et al., 2015), UVENTA stents (Kim et al., 2014), Resonance stents (Nam et al., 2015) and 1 study compared it with ileal ureteral replacement (IUR) (Akbarov et al., 2017). There are 10 single-arm studies all of which were published as full texts. Table 3.3 in the assessment report summarises the characteristics of each study.

The EAC conducted a critical appraisal of the evidence and concluded that all of the comparative studies and 8 of the single-arm studies were of sufficient quality and substance to provide relevant results. The EAC considered that 2 of the single-arm studies (Bach et al. 2013, Boyvat et al., 2005) did not provide acceptable levels of external validity and so discounted their results. Overall the EAC considered, the quality of evidence reported was low, mainly due to inadequate reporting of the study design, patient characteristics and

outcomes. Table 3.4 in the assessment report provides details of the EAC critique of the full text publications.

The EAC reported results for a number of outcomes in section 3.6.2 of the assessment report. Clinical success was the most widely reported outcome presented in 13 of the 14 studies reviewed. However the EAC noted the lack of a consistent definition of clinical success across the trials and therefore could not pool the results. In the comparative trials Memokath-051 had a lower clinical success rate compared with Allium stents and IUR but it had comparable rates to double J and Resonance stents. The EAC noted that 4 of the 5 comparative studies were abstracts, some with unequal group sizes. Of the single arm studies clinical success ranged from 47-100%. Table 3.6 in the assessment report provides the details of these results.

Two studies (Kim et al. 2014, Zaman et al. 2011) which the EAC deemed were well conducted and with acceptable generalisability reported stent insertion was successful in all cases.

Three comparative studies reported results of the USSQ. Memokath-051 had favourable results compared to double-J stents in relation to pain, urinary frequency, symptom bother and living with current symptoms (Maan et al., 2010). Actual outcome data were not reported in the other 2 studies but authors did report that similar results were found between Memokath-051 and Resonance stents.

Three of the 14 studies reported on length of time in situ. Of the comparative studies Kim et al. (2014) reported Memokath-051 remained in place longer than UVENTA (14 months vs 12 months). The NCT00166361 study reported Memokath-051 was in situ for 17 months compared to 4 for double-J stents. Papatsoris and Buchholz (2010) a single arm study reported Memokath-051 stayed in situ for a mean of 11 months.

Stent migration or encrustation were the most common reasons for stent removal and/or replacement. In the comparative studies, rates of stent

migration were higher in the Memokath-051 arms compared to UVENTA (43% vs 6%) (Kim et al., 2014) and double-J (11% vs 0%, Maan et al., 2010 and 7% vs 0%, NCT00166361, 2014). In the single-arm trials, rates of stent migration ranged from 8% to 46% (Arya et al., 2001 and Papadopoulos et al., 2010). In a pooled analysis (see table 3.15 of the assessment report) of migration rates Memokath-051 had the highest incidence (17.4%) compared to Allium (0%), double J (0%) and UVENTA (5.9%). Memokath-051 had higher rates of encrustation compared to Allium, 19% vs 0% (Bolton et al., 2015) and double-J stents in 1 study, 29% vs 0 (NCT00166361, 2014). In the single-arm trials, rates of encrustation ranged from 0% to 23% (Zaman et al., 2011 and Arya et al., 2001).). The EAC carried out a pooled analysis (see table 3.14 of the assessment report) on encrustation rates for Memokath-051 (6.3%), however no data was available for comparator stents.

One comparative study reported on the rate of stent removal and replacement, 2 (11%) Memokath-051 stents were removed due to resolution of stricture (Maan et al., 2010). 17% of Memokath-051 stents were replaced due to a longer stent required and migration. In the single-arm studies, the majority of stents were removed, but not replaced due to encrustation (Arya et al., 2001, Bourdoumis et al., 2014, Papatsoris and Buchholz, 2010),or progressive disease (Papatsoris and Buchholz, 2010) and it is unclear whether or not they were replaced by another stent. Stent replacement was usually due to migration (Agrawal et al., 2009, Arya et al., 2001, Bourdoumis et al., 2014, Kulkarni and Bellamy, 2001, , Papadopoulos et al., 2010, Zaman et al., 2011), suboptimal positioning (Kulkarni and Bellamy, 2001) and in a few cases encrustation (Agrawal et al., 2009) or progressive disease (Agrawal et al., 2009, Kulkarni and Bellamy, 2001). The EAC carried out a pooled analysis (see table 3.14 of the assessment report) on Memokath-051 stents removed (16.3%) and replaced (16%), however no data was available for comparator stents.

The EAC's conclusions are that the evidence base is mainly small, poorly reported, observational studies meaning that all conclusions are uncertain and

could alter with new evidence. No data were available for any of the comparator stents in relation to stent removal and replacement. Clinical success and stent migration were the most commonly reported outcomes. The EAC reported clinical success was not consistently defined across the studies, which meant statistical pooling could not be conducted. Overall the current evidence suggests that Memokath-051 has similar success compared with double J and Resonance stents but worse clinical success outcomes than other comparators. Memokath-051 had improved patient-related quality of life compared with double J stents. The EAC had no significant concerns regarding adverse events for Memokath-051. The EAC considered that a large well-conducted RCT or prospective comparative study would provide more reliable estimates of the clinical effectiveness of this technology.

4.2 Summary of economic evidence

The company identified 5 studies which met their inclusion criteria, but only included 3 (Agrawal et al. 2009, Papastsoris et al. 2007 and Aintree University Hospital [AUH]) in the remainder of their submission. The EAC could not replicate the company's search because of a lack of information and noted the company's search did not include economic resources. The EAC undertook a de novo search and identified 2 (Gonzalez et al. 2011 and Zaman et al. 2012) additional relevant studies.

The EAC considered 2 studies (Agrawal et al. 2009, Papastsoris et al. 2007) identified by the company to be out of scope and excluded them. The data provided by Aintree University Hospital (AUH), Liverpool is an unpublished cost-consequence analysis comparing Memokath-051 with double-J stents. The company shared the business case document (a Microsoft PowerPoint® slide set) with the EAC. Gonzalez et al. (2011) and Zaman et al. (2012) were also cost-consequence analyses comparing Memokath-051 with double-J stents.

The EAC stated that the AUH data was unsuitable for a full critical appraisal. The estimated cost-savings assume the Memokath-051 and double-J stents

are clinically equivalent in terms of complications and that Memokath-051 will remain insitu for 24 months. The EAC critically appraised Gonzalez et al. (2011) and found the study was poorly conducted and reported. Zaman et al. (2012) was published as an abstract only, and the EAC deemed it unsuitable for full critical appraisal. The EAC concluded that the published economic evidence was of low quality but indicated that Memokath-051 was cost saving versus double-J stents provided it remained in situ for sufficient time.

De novo analysis

The company presented a de novo economic model comparing Memokath-051 with double-J stents. No other comparators outlined in the scope were included. The population was all patients with chronic ureteric strictures due to both benign and malignant structures. The EAC produced a model diagram which can be found in section 4.2.2 of the assessment report. The de novo model submitted by the company was not executable and had a 2.5 year time horizon, capturing the key differences between the 2 stent types. The EAC replicated the company's model making it fully executable and modified it to improve its usefulness. Changes included; extending the time horizon to 5 years, facilitating the model to report a break-even time point between Memokath-051 and its comparators, inclusion of reconstructive surgery and other metallic stents as comparators, assessing the risk of UTIs, revision of some inputs used by the company (see Appendix O of the assessment report), scenario analysis to model the risk of unplanned replacement of Memokath-051 stents in 4 scenarios and deterministic sensitivity analyses.

Model parameters

The parameters that were considered in the company's model and the EACs adjustments are summarised in table 3.

Table 3 Clinical parameters and costs and resources used in the company's model (taken from Assessment Report)

Parameter	Memokath-051	Double-J stent	UVENTA	Allium	Resonance	Reconstructive surgery
Length of time in situ (no complications)	Company = 30 months	Company = 6 months	Company = N/A	Company = N/A	Company = N/A	Company = N/A
	EAC = 60 months	EAC = 6 months	EAC = 18 months	EAC = 36 months	EAC = 12 months	EAC = N/A
Monthly risk for unplanned stent removal and replacement	Company = 0.95% (reported as 25% over 30 months)	0%	N/A	N/A	N/A	N/A
	EAC = 1.4% (4.41% versus UVENTA)	0%	0.49%	0.49%	1.4%	N/A
Monthly risk of UTI	Company = N/A	N/A	N/A	N/A	N/A	N/A
	EAC = 0.42% (1.25% versus surgery)	0.42%	0.42%	0.42%	0.42%	0.17%
Total cost of insertion	Company = £3,068	£1,676	N/A	N/A	N/A	N/A
	EAC = £3,010	£786	£2,736	£2,936	£2,148	£7,414 (includes all follow-up costs)
Monthly follow-up cost	Company = £23.75	£16.67	N/A	N/A	N/A	N/A
	EAC = £42.50	£0	£42.50	£42.50	£21.25	N/A
Total cost of replacement	Company = £3,781	£1,676	N/A	N/A	N/A	N/A
	EAC = £3,347	£1,052	£3,157	£3,357	£2,569	N/A
Cost of UTI	Company = N/A					
	EAC = £37.32					

Results

The EAC's revisions to the cost model show that Memokath-051 has a cost saving of £1,619 compared with double-J stents over a 5 year time horizon. Memokath-051 is estimated to be cost neutral compared with other metallic stents. When comparing Memokath-051 with reconstructive surgery, the incremental cost per patient after 5 years ranged from £467 to -£1,009 depending upon the assumptions made around the extrapolation of unplanned replacement of Memokath-051 stents. Compared with surgery, Memokath-051 is cost saving up to 53 months.

Base case results

Table 4 Company base case

Cost category	Company's base-case		
	Memokath	**Double-J**	**Difference***
Theatre staff costs	£1,159.93	£1,159.93	£0.00
Theatre consumable costs	£1,874.16	£109.44	-£1,764.72
Procedure code/surgery tariff	34	407	
2x Patient F/U OPD X-ray 1st 6/12 NM Renogram 2nd 6/12	£142.5	£100.00	-£42.50
First six months	£3,210.59	£1,776.37	-£1,434.22
Cost of second six month	£142.5	£1,776.37	£1,633.87
Total for first year	£3,353.09	£3,552.74	£199.65
Cost for second year	£285	£3,552.74	£3,267.74
total for two years	£3,638.09	£7,105.48	£3,467.39
Cost of last six months	£142.5	£1,776.37	£1,633.87
total cost for 2.5 years	£3,780.59	£8,881.85	£5,101.26
Risk factor 25%	945.15	0	-945.15
Total cost per treatment/patient over 2.5 years with calculation of risk	**4,725.74**	**£8,881.85**	**£4,156.11**
* A minus sign indicates device is more expensive than the comparator in this cost category.			

EAC base case results

Memokath-051 versus double-J stents

Table 5 EAC base case results by component (per patient over 5 years)

	Memokath-051	Double-J Stents	Incremental cost
Total insertion cost	£3,010	£786	£2,224
Follow-up cost	£2,346	£0	£2,346
Unplanned replacement cost	£2,503	£0	£2,503
Planned replacement cost	£0	£8,692	-£8,692
Adverse event cost	£9	£9	£0
Total	£7,868	£9,487	-£1,619
Breakeven point = 30 months			

The EAC's model showed savings of at least £1,619 over 5 years with Memokath-051 compared to double-J stents. Across all scenarios, in patients who require a stent for at least 30 months, Memokath-051 is cost saving versus double-J stents.

Memokath-051 versus reconstructive surgery

The incremental cost per patient after 5 years ranged from £467 to -£1,009 depending upon the assumptions made around the extrapolation of unplanned replacement of Memokath-051 stents.

Memokath-051 versus other metallic stents

Planned stent replacement is the key factor in comparisons between Memokath-051 and other metallic stents. The EAC carried out a costs over time (see Appendix R of the assessment report) analysis. Over time, the lines on these graphs consistently cross. Therefore, Memokath-051 is judged to be cost neutral compared to UVENTA and Allium in the worst case, but may generate cost savings with more positive assumptions (i.e. no unplanned replacements after 2 years). Compared with Resonance, Memokath-05 was cost saving after 12 months. The EAC advised caution in relation to cost

comparisons for both Allium and Resonance as these results are based on assumptions not comparative clinical data.

Sensitivity analysis

The company did not include any sensitivity analyses in their submission although they stated that the key drivers of the model are the cost of stents versus the in situ time of the stent. The EAC conducted univariate sensitivity analysis to assess the impact of parameter uncertainty on the results of the model (values and ranges can be found in Appendix S of the assessment report).

The EAC considered various scenarios relating to unplanned stent replacement (for all stents). These are outlined in section 4.4 of the assessment report. Memokath-051 versus double-J stent the results are sensitive to the procedure costs to replace double-J stents and the risk of unplanned replacements with Memokath-051. For Memokath-051 compared with reconstructive surgery in the worst case scenario (i.e. constant risk of unplanned Memokath-051 replacement over 5 years) the model is highly sensitive to many input values. In the best case scenario (i.e. no risk of unplanned replacement after 2 years) the model is most sensitive to the cost of surgery, the risk of unplanned replacement up to 24 months and the planned time in situ. Compared with the other metallic stents, results were most sensitive to the risk of unplanned replacement with Memokath-051 stents. In the best case scenario, results were typically favourable to Memokath-051, whilst in the worst case there was far more uncertainty.

The EAC concluded that the economic evidence were poorly reported, but indicated that Memokath-051 is likely to be cost saving versus double-J stents provided that Memokath-051 remains in situ for sufficient time. The EAC could not find any evidence on the cost-effectiveness of Memokath-051 versus any other comparators.

5 Ongoing research

The company and the External Assessment Centre did not identify any ongoing studies on Memokath-051.

6 Issues for consideration by the Committee

Clinical evidence

- Considering the number of years Memokath-051 has been on the market, the clinical evidence for Memokath-051 is of poor quality. There is an absence of powered comparative data and uncertainties around what is deemed a clinical success. No comparative data comparing Memokath-051 with nephrostomy was identified.

- There is a disparity between the company and clinical experts regarding patient selection. Due to the quality of the evidence the subgroup analysis provides little clarity on the appropriate population.

- Some uncertainty around clinical evidence supporting the claims in terms of fewer stent-related symptoms and complications compared to some comparator devices.

Cost evidence

- Memokath-051 is cost saving or cost neutral depending on the comparator, however this is based on patient selection, length of time Memokath-051 is in situ and patient life expectancy. The EAC concluded that Memokath-051 is cost saving up to month 53 compared with reconstructive surgery and in patients not eligible for reconstructive surgery that require a stent for at least 30 months. Both these timeframes are dependent on life expectancy and the length of time the stent remains in situ.

7 Authors

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Mark Campbell, Associate Director

NICE Medical Technologies Evaluation Programme

July 2017

Appendix A: Sources of evidence considered in the preparation of the overview

Details of assessment report:

- Eaton Turner, E., Jenks, M., Marshall, C. et al. The Memokath-051 stent for the treatment of ureteric obstruction, June 2017.

Submissions from the following sponsors:

- PNN Medical

Related NICE guidance:

- Laparoscopic pyeloplasty. NICE interventional procedure guidance 46 (2004). Available from www.nice.org.uk/guidance/IPG46
- Acute kidney injury: prevention, detection and management. NICE clinical guideline 169 (2013). Available from www.nice.org.uk/guidance/CG169
- Prostate cancer: diagnosis and management. NICE clinical guideline 175 (2014). Available from www.nice.org.uk/guidance/CG175
- Bladder cancer: diagnosis and management. NICE guideline 2 (2015). Available from www.nice.org.uk/guidance/NG2

References

Agrawal, S., Brown, C.T., Bellamy, E.A. & Kulkarni, R. 2009. The thermo-expandable metallic ureteric stent: an 11-year follow-up. BJU International, 103 (3), 372-6.Available: https://dx.doi.org/10.1111/j.1464-410X.2008.08018.x

Akbarov, I., Al-Mahmid, M., Pfister, D. & Heidenreich, A. 2017. Upper Urinary Tract Decompression Using Ileal Ureter Replacement in Comparison to Endoureteral Thermoexpandable Stent [Memokath 051]. Journal of Urology, 197 (4), E303-E304

Arya, M., Mostafid, H., Patel, H.R., Kellett, M.J. & Philp, T. 2001. The self-expanding metallic ureteric stent in the long-term management of benign ureteric strictures. BJU International, 88 (4), 339-42.Available: https://www.ncbi.nlm.nih.gov/pubmed/11564017

AUH Cost-effectiveness of using permanent Memokath Stent (MMK) compared to JJ stent. Aintree University Hospital.

Bach, C., Kabir, M.N., Goyal, A., Malliwal, R., Kachrilas, S., El Howairis, M.E., Masood, J., Buchholz, N. & Junaid, I. 2013. A self-expanding thermolabile nitinol stent as a minimally invasive treatment alternative for ureteral strictures in renal transplant patients. Journal of Endourology, 27 (12), 1543-5.Available: https://dx.doi.org/10.1089/end.2013.0180

Bolton, E.M., Considine, S., Moran, D., Siddiqui, R., Cham, A., Nusrat, N., Durkan, G., Rogers, E., Walsh, K. & Jaffry, S. 2015. Tailored length permanent stents for the treatment of ureteric obstruction. BJU International, 116, 25.Available: http://dx.doi.org/10.1111/bju.13221

Bourdoumis, A., Kachrilas, S., Kapoor, S., Zaman, F., Papadopoulos, G., Buchholz, N. & Masood, J. 2014. The use of a thermoexpandable metal alloy stent in the minimally invasive management of retroperitoneal fibrosis: a single center experience from the United kingdom. Journal of Endourology, 28 (1), 96-9.Available: https://dx.doi.org/10.1089/end.2013.0332

Bourdoumis, A., Kachrilas, S., Kapoor, S., Zaman, F., Wardak, S., Papatsoris, A., Buchholz, N. & Masood, J. 2013. The use of a thermoexpandable metal alloy stent in the minimally invasive treatment of retro peritoneal fibrosis-A single centre experience. Journal of Endourology, 27, A211.Available: http://dx.doi.org/10.1089/end.2013.2001

Boyvat, F., Aytekin, C., Colak, T., Firat, A., Karakayali, H. & Haberal, M. 2005. Memokath metallic stent in the treatment of transplant kidney ureter stenosis or occlusion. Cardiovascular & Interventional Radiology, 28 (3), 326-30.Available: https://dx.doi.org/10.1007/s00270-004-0028-2

Department of Health. 2016. NHS Reference Costs 2015-16 [Online]. London. Available: https://www.gov.uk/government/publications/nhs-reference-costs-collection-guidance-for-2015-to-2016.

Gonzalez, L.L., Borda, A.P., Gonzalez, E.R., Medina, J.S., Martinez, L.C. & Parra, R.O.A. 2011. Decision analysis for economic evaluation of the management of chronic obstructive uropathy. Archivos Espanoles de Urologia, 64 (9), 875-81.Available: https://www.ncbi.nlm.nih.gov/pubmed/22155875

Granberg, C., Russell, S., Siddiqui, S., Nehra, A., Frie, K., Leroy, A. & Mynderse, L. 2010. Long term drainage of malignant extrinsic ureteral obstruction secondary to inoperable pelvic or abdominal malignancies using the Memokath 051 ureteral stent. Journal of Urology, 1), e495.Available: http://dx.doi.org/10.1016/j.juro.2010.02.850

Health and Social Care Information Centre. 2015. Hospital Episode Statistics, Admitted Patient Care - England, 2014-15: Procedures and interventions: 4 character [Online]. Available: http://content.digital.nhs.uk/catalogue/PUB19124 [Accessed 11th May 2017].

Kim, K.S., Choi, S., Choi, Y.S., Bae, W.J., Hong, S.-H., Lee, J.Y., Kim, S.W., Hwang, T.-K. & Cho, H.J. 2014. Comparison of efficacy and safety between a segmental thermo-expandable metal alloy spiral stent (Memokath 051) and a self-expandable covered metallic stent (UVENTA) in the management of ureteral obstructions. Journal of Laparoendoscopic & Advanced Surgical Techniques. Part A, 24 (8), 550-5.Available: https://dx.doi.org/10.1089/lap.2014.0056

Kim, K.S., Choi, Y.S., Hong, S.H., Cho, H.J. & Hwang, T.K. 2013. Effectiveness of a segmental thermo-expandable metal alloy spiral stent (memokath 051TM) and self-expandable covered metallic stent (UVENTATM) in the management of ureteral obstruction. Journal of Endourology, 27, A205-A206.Available: http://dx.doi.org/10.1089/end.2013.2001

Klarskov, P., Nordling, J. & Nielsen, J.B. 2005. Experience with Memokath 051 ureteral stent. Scandinavian Journal of Urology & Nephrology, 39 (2), 169-72.Available: https://dx.doi.org/10.1080/00365590510007720

Kulkarni, R. 2014. Metallic stents in the management of ureteric strictures. Indian J Urol, 30 (1), 65-72.Available: https://www.ncbi.nlm.nih.gov/pubmed/24497686

Kulkarni, R. & Bellamy, E. 2001. Nickel-titanium shape memory alloy Memokath 051 ureteral stent for managing long-term ureteral obstruction: 4-year experience. Journal of Urology, 166 (5), 1750-4.Available: https://www.ncbi.nlm.nih.gov/pubmed/11586216

Kulkarni, R.P. & Bellamy, E.A. 1999. A new thermo-expandable shape-memory nickel-titanium alloy stent for the management of ureteric strictures. BJU Int, 83 (7), 755-9.Available: https://www.ncbi.nlm.nih.gov/pubmed/10368191

Maan, Z., Patel, D., Moraitis, K., El-Husseiny, T., Papatsoris, A.G., Buchholz, N.-P. & Masood, J. 2010. Comparison of stent-related symptoms between conventional Double-J stents and a new-generation thermoexpandable segmental metallic stent: a validated-questionnaire-based study. Journal of Endourology, 24 (4), 589-93.Available: https://dx.doi.org/10.1089/end.2009.0318

Nam, J., Han, J., Lee, D., Park, S. & Chung, M. 2015. Comparison of initial experiences between full-length metallic stent and segmental metallic stent in malignant ureteral obstruction. World Congress of Endourology & SWL Annual Meeting

NCT00166361 2014. Drainage of Malignant Extrinsic Ureteral Obstruction Using the Memokath Ureteral Stent.

Papadopoulos, G.I., Middela, S., Srirangam, S.J., Szczesniak, C.A. & Rao, P.N. 2010. Use of Memokath 051 metallic stent in the management of ureteral

strictures: a single-center experience. Urologia Internationalis, 84 (3), 286-91.Available: https://dx.doi.org/10.1159/000288230

Papatsoris, A., Masood, J., El-Husseiny, T., Ndirika, S. & Buchholz, N. 2007. A novel long-term thermo-expandable ureteric metal stent: Memokath 051. BJU Int, 1-10

Papatsoris, A.G. & Buchholz, N. 2010. A novel thermo-expandable ureteral metal stent for the minimally invasive management of ureteral strictures. Journal of Endourology, 24 (3), 487-91.Available: https://dx.doi.org/10.1089/end.2009.0138

Patel, C., Loughran, D., Jones, R., Abdulmajed, M. & Shergill, I. 2017. The resonance® metallic ureteric stent in the treatment of chronic ureteric obstruction: a safety and efficacy analysis from a contemporary clinical series. BMC Urology, 17 (1)

Patel, D., Maan, Z., El-Husseiny, T., Moraitis, K., Junaid, I., Buchholz, N. & Masood, J. 2011. Characterising stent symptoms associated with a segmental thermo-expandable metallic stent using a validated stent symptoms questionnaire. Current Urology, 5 (2), 72-78.Available: http://dx.doi.org/10.1159/000327454

PNN Medical. Available: http://www.pnnmedical.com/memokath/solutions/memokath-051-ureter/ [Accessed 10th May 2017].

PNN Medical 2016. Memokath 051CW: Instructions for Use [Not publicly available].

Zaman, F., Poullis, C., Bach, C., Moraitis, K., Junaid, I., Buchholz, N. & Masood, J. 2011. Use of a segmental thermoexpandable metal alloy stent in the management of malignant ureteric obstruction: a single centre experience in the UK. Urologia Internationalis, 87 (4), 405-10.Available: https://dx.doi.org/10.1159/000326081

Zaman, M.F., Goyal, A., Bach, C., Kachrilas, S., Mukherjee, K., Junaid, I., Buchholz, N. & Masood, J. 2012. A cost-effectiveness model for the memokath 051TM in malignant ureteric obstruction. Journal of Endourology, 26, A434-A435

Appendix B: Comments from professional bodies

Expert advice was sought from experts who have been nominated or ratified by their Specialist Society, Royal College or Professional Body. The advice received is their individual opinion and does not represent the view of the society.

Mr Matthew Shaw
Consultant Urologist, British Association of Urological Surgeons

Mr Mahmoud Elfar
Consultant Urologist, British Association of Urological Surgeons

Mr Peter Guy
Consultant Urologist, British Association of Urological Surgeons

Mr Ranan Das Gupta
Consultant Urologist, British Association of Urological Surgeons

Ms Daniela Andrich
Consultant Urological Surgeon, British Association of Urological Surgeons

Professor Tony Mundy
Professor of Urology, British Association of Urological Surgeons

6 expert questionnaires were received with 4 urologists having experience of using Memokath-051.

The technology and its use

- 3 experts stated MK-051 had a unique design, but other metallic stents available
- 2 experts would only use in benign cases if unfit for surgery
- 1 expert would use if life expectancy >6months; 1 expert would only use in palliative malignancy with limited life expectancy

Patient benefits

- 5 experts stated fewer stent changes than double-J stent, with associated reduced anaesthetics
- 3 experts: improved patency with fewer stent symptoms vs. double-J
- 1 expert: more tolerated than nephrostomy

System benefits

- Reduced admissions and theatre time for stent changes
- 1 expert: shorter stay and morbidity than open surgery

Costs

- Increased cost of stent (need to stock various sizes), but cost-saving over long-term (18 months)

Other comments

- These stents can still block and migrate: follow-up needed
- Expertise needed: only in specialist centres
- 1 expert stated JJ stents are most commonly used in NHS for both malignant and benign, as not every patient is referred to specialists for reconstructive urological surgery
- Patient selection is important
- 2 experts: long term of Memokath-051 stents and repeated use in benign strictures who are fit for surgery are at a higher risk of complications

Appendix C: Comments from patient organisations

Advice and information was sought from patient and carer organisations. The following patient organisations were contacted and no response was received.

- Action on Bladder Cancer
- Bladder and Bowel Foundation
- British Kidney Patient Association
- Everyman
- Fight Bladder Cancer
- Helen Rollason Cancer Charity
- Help the Hospices
- Jo's Trust
- Kidney Cancer UK (KCUK)
- Kidney Research UK
- Macmillan Cancer Support
- Maggie's Centres
- Marie Curie
- National Council for Palliative Care
- Ovacome
- Ovarian Cancer Action
- Pelvic Pain Support Network
- Polycystic Kidney Disease Charity
- Prostate Cancer UK (formerly prostate cancer charity)
- Rarer Cancers Foundation
- Sue Ryder
- Tackle Prostate Cancer
- Target Ovarian Cancer
- The Eve Appeal
- The Robin Cancer Trust

Appendix D: Claimed benefits and decision problem

The claimed patient benefits for Memokath-051 are:

- A safe, simple and reliable ureteric stent that is better tolerated by the patient, with fewer stent-related symptoms and complications
- Avoids the need for replacement procedure surgery every 6 months requiring anaesthesia and overnight hospital stays
- Restores dignity and improves quality of life
- Reduced risk of tissue ingrowth
- Reversibility of procedure if needed with no side effects.

The claimed benefits to the healthcare system for Memokath are:

- Efficient use of theatre time as no major surgery is needed
- Significant cost savings by avoiding surgery every 6 months requiring anaesthesia and overnight hospital stays, with less social care needed
- Reversibility of procedure if needed.

	Scope issued by NICE
Population	Patients with ureteric obstruction as a result of malignant or benign strictures.
Intervention	The Memokath-051
Comparator(s)	• Double J stents • Nephrostomy • Reconstructive surgery • Metallic and alloy stents (including nitinol stents) (see also 'Cost analysis' below)
Outcomes	The outcome measures to consider include: • Number and rate of replacement stents • Number and rate of repeat procedures requiring anaesthesia and surgery • Theatre time and hospital stay • Quality of life including patient tolerability and comfort • Length of time stent remains in situ • Clinical success rate (e.g. improved renal function, no obstruction) • Frequency of stent removal/reversal

	• Device-related adverse events including procedure related complications and information pertaining to the resource use associated with these adverse events • Frequency of follow-up visits • Pain scores including from subsequent bladder irritation	
Cost analysis	Comparator(s): • Double J stents • Nephrostomy • Reconstructive surgery • Metal and alloy stents Costs will be considered from an NHS and personal social services perspective. The time horizon for the cost analysis will be sufficiently long to reflect any differences in costs and consequences between the technologies being compared. Sensitivity analysis will be undertaken to address uncertainties in the model parameter.	
Subgroups to be considered	• Patients unfit for surgery • Malignant or benign stricture • Antegrade or retrograde insertion (including the procedure performed either by an interventional radiologist or a urologist)	
Special considerations, including those related to equality	Some ureteric obstructions are a result of malignancy - all people with cancer are protected under the Equality Act from the point of diagnosis. People with ureteric strictures may benefit from Memokath-051 as an alternative to double J stents, as it may be associated with a reduced number of replacement procedures and reduced adverse events, which would improve their quality of life. Memokath-051 may also provide an alternative treatment for people with ureteric strictures who cannot tolerate or who have had failed conventional stents, who would otherwise be nephrostomy-dependent and are likely to be classed as disabled under the Equality Act.	
Special considerations, specifically related to equality issues		
	Are there any people with a protected characteristic for whom this device has a particularly disadvantageous impact or for whom this device will have a disproportionate impact on daily living, compared with people without that protected characteristics?	No
	Are there any changes that need to be considered in the scope to eliminate unlawful discrimination and to promote equality?	No
	Is there anything specific that needs to be done now to ensure MTAC will have relevant information to consider equality issues when developing guidance?	No

Medicines and Technologies Programme
Adoption Scoping Report MTG311 Memokath-051 stent for ureteral obstruction

SUMMARY – for MTAC1 meeting

Contributors thought that those with benign ureteric strictures should not be a routinely indicated patient group for this guidance (with some individual exceptions) and that these patients should be referred for corrective surgery.

Adoption Levers

- Patient tolerability was reported as being positive and much improved when compared to JJ stents.
- This stent can be left in place indefinitely unless there are problems.

Adoption Barriers

- Patient selection is key to ensuring the technology is used in a population that will benefit and to ensure cost effectiveness. Currently this technology is not being offered to the optimal population and thus a change in practice may be required.
- Training and experience: Few urologists have the skills to be able to insert Memokath-051. Conventional and established practice is to insert double J stents.
- The initial cost of Memokath is perceived to be high.
- Clinician confidence as this technology may still result in issues such as encrustation and migration.
- Lack of awareness.

1. Introduction

The Adoption team has collated information from healthcare professionals working within NHS organisations who have varying amounts of experience or awareness of Memokath-051 (Memokath). Professionals liaised with included 5 consultant urologists, and 2 consultant reconstructive urologists. As this technology has been available for over 20 years, contributors who have used Memokath have done so for between 4 and 11 years.

This adoption scoping report includes some of the benefits, considerations and difficulties that may be faced by organisations when planning to adopt the technology into routine NHS use.

2. Use of Memokath-051 in practice

The MTEP analyst requested intelligence on the following areas; patient selection, insertion procedure setting and information on patient tolerability.

Contributors said:

- Memokath may be the preferred stent of choice (with some individual exceptions) in the following patient groups:
    - Older patients with malignant terminal illness who have a life expectancy of 1 year or over. In these cases a metal stent is better as it is stronger and thus is able to withstand tissue ingrowth and larger urine outputs following the administration of fluids after chemotherapy treatment. Memokath may also reduce stent related symptoms and eradicate the need to replace stents (which can be as often as every 4-6 weeks with a conventional JJ stent in this group) in this ill population meaning they are a cost effective option when inserted for 1 year or over.
    - Those with benign or malignant strictures who have a life expectancy of less than a year and cannot tolerate a JJ stent or where the risk of repeated procedures using general anaesthetic needs reducing.
    - Those with benign strictures who are unsuitable for reconstructive surgery and/or require a stent for longer than 1 year.
- Memokath may not be used (with some individual exceptions) in the following patient groups:

- Those with benign ureteric strictures where reconstructive surgery would be curative should be referred to a tertiary centre for corrective surgery. Contributors reported that this often does not happen as it is common for consultant urologists to insert stents to manage ureter strictures. Surgery is less likely to be offered if the skills to offer this are not on site, though contributors reported that there are adequate reconstructive urologists located regionally to cover this need nationally. This patient group may be subjected to stent related symptoms and replacement procedures when they could be offered the more definitive solution of reconstructive surgery. Five contributors strongly felt that those with benign ureteric strictures should not be an indicated patient group for this guidance (with some individual exceptions).

- Those requiring a short term stent.

- Those with progressive malignant disease where the ureter may become blocked above or below the stent.

- Older people with malignant disease who are close to the end of their lives. These patients may not need a stent that will last longer though Memokath may be used if symptoms of a JJ stent cannot be tolerated.

- One contributor reported that they would not use Memokath for a stricture at the top of the ureter (close to junction with the kidney) as they have experience of these migrating.

- All contributors with experience of inserting Memokath reported that they inserted the stent within an operating theatre under general anaesthetic. Most of these procedures were carried out in day case units and some within in-patient units. This depended on the general health of the patient (e.g. those with cancer are likely to be admitted for this procedure). The reason for not inserting in an outpatient setting using local anaesthetic was the difficult nature of the procedure.

- Most contributors reported that patient tolerability and therefore quality of life was better with Memokath than for JJ stents as there is no kidney or bladder elements. Memokath was reported to be life changing when used in the correct patients. One contributor stated that their patients likened the pain related to double JJ stents to be similar to that of having kidney stones which are considered to be very painful. One contributor stated that they had found patient tolerability to be similar with both types of stent.

3. Reported benefits

The benefits of adopting Memokath, as reported to the Adoption team by the healthcare professionals using the technology are:

- Better tolerated by the patient, with fewer stent symptoms and complications and thus improved quality of life.
- Reduced replacement procedures and the associated costs of doing this. Contributors reported that Memokath has been left inserted for up to 11 years with no need to change unless there are problems.
- Reduced risk of tissue ingrowth in patients with malignant ureter strictures due to radial strength of the metallic material. This strength also means the stent can tolerate large urine outputs which may happen following the administration of fluids following chemotherapy.
- The fact that Memokath comes in different lengths to stent different size strictures.

4. Levers and barriers to adoption

The key considerations for adoption highlighted through discussions with expert contributors are:

Training and experience

JJ stents have been standard conventional practice for a long time. Contributors stated that all urologists have the skills to insert JJ stents and so many will continue to use these as a first line option as they are confident in the procedure and this practice is entrenched. Conversely, fewer urologists have the skills and experience to insert Memokath.

Contributors reported that inserting and removing Memokath is more technically challenging than for a JJ stent.

The access system required for their deployment can be difficult to insert. Inserting the access sheath along a guidewire into the ureter to the stricture site can be difficult due to its blunt tip and wider diameter and dilation of the ureter is often required to accommodate this. As Memokath is placed at the stricture site they are more difficult to place particularly if the stricture is short. Once in place there is a need to ensure that hot saline expands the cone ends properly so that the stent stays in place and is not dislodged when the sheath and guide wire are removed.

Removing Memokath is more challenging than removing a JJ stent. This is because there is no bladder element that is easy to see and pull out. The procedure involves going into the narrow ureter, locating the Memokath stent and then flushing it with cold water so that it shrinks back and can be removed.

As the technique for Memokath is specialist and requires an experienced skill set and judgement, contributors suggested that insertion and removal should be carried out, possibly within a regional centre, by skilled individuals with the level of experience required.

Contributors said that inexperienced urologists should be trained using models in the first instance and then via observation and hands on surgery with mentorship from surgeons who have experience of using Memokath. The company provides awareness raising sessions and workshops using models free of charge.

Patient Selection

All contributors commented that patient selection is key with this technology. Patients considered eligible for treatment with Memokath are a small and niche group and are usually those with more complex illnesses. Patient selection issues raised by contributors are highlighted in section 2. In summary and with some exceptions, those patients who require a stent for 1 year or longer (but not as a very long term solution in those that are otherwise well) may be suitable for having a Memokath. If these patients had a JJ stent inserted they would require this to be changed at least twice making Memokath a more cost effective option.

Resource Impact

Memokath is significantly more expensive than a JJ stent (£1630 vs £60). One contributor had to submit a business case when they started using Memokath. All contributors with experience of using Memokath stated that overall it is cost saving when inserted in the correct patients due to reduced stent changes and follow up appointments. Nevertheless, the initial outlay is likely to act as an adoption barrier for this technology.

Consultant urologists will not know which length of Memokath will be needed until they are performing the insertion procedure. A variety of sizes need to be kept in stock and most contributors kept 2 of each length. The upfront cost of this may act as an adoption challenge due to limited resources.

Clinician confidence

All contributors reported that Memokath is a good tool to use in the correct patients and that it is an important option for them to have access to.

Contributors reported that other clinicians may be reluctant to use this more expensive stent as they can encrust (though this is less likely to happen in Memokath as opposed to JJ stents) and they can migrate if the cone ends have not expanded enough to hold them in place. Patients with Memokath stents can continue to suffer from recurrent infections particularly if they have a malignant stricture. Reasons given for failed Memokath stents were: resolved stricture, progressive condition causing a stricture above or below the stent and migration.

Lack of awareness

Two contributors reported that Memokath has not been widely marketed and that many clinicians are unaware of its availability though awareness is growing particularly amongst clinicians who care for cancer patients.

5. Comparators

Contributors were aware of similar metallic stents on the market.

One contributor had experience of using Uventa and found it difficult to remove and that it had problems with encrustation.

Another contributor had experience of using a metal stent that was not thermo-expandable and commented that it was very difficult to take out because of this.

One contributor had used Allium but said this was a little more expensive (around £1750) and that it only came in one size meaning that if the stricture covered more of the ureter than the stent could cover, 2 stents were needed.

All other contributors did not have any experience of using other metallic stents (although they were aware of them) and reasons for this were: lack of evidence and experience.

National Institute for Health and Care Excellence

External Assessment Centre correspondence

Memokath-051 Stent

The purpose of this table is to show where the External Assessment Centre relied in their assessment of the topic on information or evidence not included in the sponsors' original submission. This is normally where the External Assessment Centre:

a) become aware of additional relevant evidence not submitted by the sponsor
b) need to check "real world" assumptions with NICE's expert advisers, or
c) need to ask the sponsor for additional information or data not included in the original submission, or
d) need to correspond with an organisation or individual outside of NICE

These events are recorded in the table to ensure that all information relevant to the assessment of the topic is made available to MTAC. The table is presented to MTAC in the Assessment Report Overview, and is made available at public consultation.

Submission Document Section/Sub-section number	Question / Request *Please indicate who was contacted. If an Expert Adviser, only include significant correspondence and include clinical area of expertise.*	Response *Attach additional documents provided in response as Appendices and reference in relevant cells below.*	Action / Impact / Other comments
	Twenty-nine initial clarification questions to PNN medical, Jakob Sandersen & Ossama Abuldahab, submitted by EAC on 26/04/17 for discussion at company introductory teleconference 27/04/2017, hosted by NICE. **Following the teleconference on 27/01/17, EAC emailed Jakob Sandersen & Ossama Abuldahab of PNN medical with a list of the questions which could not be answered in full detail during the initial teleconference.** **The full list of questions was as follows:**	**Verbal responses to the 29 initial questions from Jakob Sandersen & Ossama Abuldahab were recorded during the teleconference.** **Further information on questions which could not be answered in full detail during the initial teleconference was provided via email by Jakob Sandersen on 01/05/17 and 05/05/17 (Appendix 1 & 2)** **Verbal and written responses were summarised in this log by the EAC:**	
3.2	1) Where are the data on the number of procedures (in Section 3.2) taken from?	*These were from the scope*	Noted with thanks
7	2) When were your databases searches conducted?	*October 2016 for Medline and 1 month ago for Cochrane library*	Noted with thanks

7	3) Are you able provide your search strategy (e.g. the strategy inserted into PubMed and the number of results per database)?	[Answer received by email 01/05/17] *Search was done in the following sites:* • *Medline, pubmed* • *Embase* • *Clinicaltrials.com* • *General internet google search* *We have done search using word Memokath alone, then Memokath 051, Memokath 51* • *Medline revealed 51 studies. 11 of them are related to Memokath 51* • *Embase revealed no results* • *Clinical trials revealed 4 rsults* • *Google search for Memokath 051 revealed 2510 results 54 of them are studies related to Memokath 51* *Then the second step was to remove the repeated ones and count only the studies related to memokath 051* *The total number found was 24 studies* *After implementation criteria for both primary and secondary searches, the total number became 6 studies. Two of them were related as a primary*	Noted with thanks

		release of results then a new updated long term follow up, so we used them as one study. Then we reached the total of 5 studies	
7	4) Are you able to be more specific about the resources that you searched, e.g. which databases of the Cochrane library?	[Answer received by email 01/05/17] *See previous question*	Noted with thanks
7	5) We are unable to find Papatsoris (2007) in BJUI (2007). Please can provide information on where this paper was identified?	[Answer received by email 01/05/17] *Papatsoris A, Buchholz N. A novel thermo-expandable ureteric metal stent for the minimally invasive management of ureteral strictures. Journal of Endourology 2010 Mar 1;24(3):487-91.*	Noted with thanks
7	6) We are unable to find the Lance study except on ClinicalTrials.gov. Please can provide information on where this paper was identified?	[Answer received by email 01/05/17] *Mynderse L, Grandberg C. Long term drainage of malignant extrinsic ureteral obstruction secondary to inoperable pelvic or abdominal malignancies using the memokath 051 ureteral stent. 2010. AUA 2010.*	Noted with thanks. Appears that Lance is not an author on the paper

7	7) Please provide a list of the studies excluded at the full paper stage and the reason the studies exclusion as per the PRISMA diagram in Section 7.7.2	*Studies were typically excluded as they looked at only malignant or benign patients, or had fewer than 10 patients.* [Further answer received by email 01/05/17] *Table 3: Overview of publications specifically on Memokath^{TM}051* (1) *Papatsoris A, Buchholz N. A novel thermo-expandable ureteric metal stent for the minimally invasive management of ureteral strictures. Journal of Endourology 2010 Mar 1;24(3):487-91.* (2) *Klarskov P, Nordling J, Nielsen JB. Experience with Memokath 051 ureteral stent. Scand J Urol Nephrol 2005;39(2):169-72.*	Noted with thanks

Author	Accepted or excluded	Appraisal
Papatsoris et al. 2010 (1)		Abstract only. We couldnt reach the original study
Klarskov et al. 2005 (2)		Abstract only. We couldnt reach the original study
Kulkarni, R and Bellamy, E. 1999 (3)	Accepted	
Kulkarni, R and Bellamy, E. 2001 (4)	Accepted	
Arya M et al. 2001 (5)		15 patints only criteria is minimum 20
Lee, G et al. 2005 (6)		Abstract only. We couldnt reach the original study
Agrawal, S et al. 2008 (7)	Accepted	
Papatsoris, A et al. 2007 (8)	Accepted	
Liatsikos, EN et al. 2005 (9)		Abstract only. We couldnt reach the original study
Maan Z et al. 2010 (10)	Accepted	
Papadopoulos GI et al. 2010 (11)		Abstract only. We couldnt reach the original study
Franke, M et. al. 2010 (12)		Abstract only. We couldnt reach the original study
Mynderse, L et al. 2010 (13)	Accepted	
Moraitis, K et al. 2010 (14)		Abstract only. We couldnt reach the original study
Schenck, M et al 2008 (15)		Study in german
Schenck, M et al 2010 (16)		Study in german
Sountoulides P et al. 2010 (17)		Malignant cases only
Allan DJ et al. 2010 (18)		Malignant cases only
Bach C et al. 2011 (19)		Abstract only. We couldnt reach the original study
Zaman F1, Poullis C, Bach C, Moraitis K, Junaid I, Buchholz N, Masood J. (20)		Malignant cases only
Azizi A1, Pasticier G, Bénard A, Lapouge O, Ferrière JM, Ballanger P, Robert G. (21)		16 patients
Bach C1, Kabir M, Goyal A, Malliwal R, Kachrilas S, El Howairis ME, Junaid I, Masood J, Buchholz N. (22)		Abstract only. We couldnt reach the original study
Kim KS1, Choi S, Choi YS, Bae WJ, Hong SH, Lee JY, Kim SW, Hwang TK, Cho HJ. (23)		Abstract only. We couldnt reach the original study
Bourdoumis A1, Kachrilas S, Kapoor S, Zaman F, Papadopoulos G, Buchholz N, Masood J. (24)		Only retroperitoneal fibrosis cases

(3) *Kulkarni R, Bellamy EA. A new thermo-expandable shape-memory nickel-titanium alloy stent for the management of ureteric strictures. BJU Int 1999 May;83(7):755-9.*
(4) *Kulkarni R, Bellamy E. Nickel-titanium shape memory alloy Memokath 051 ureteral stent for managing long-term ureteral obstruction: 4-year experience. J Urol 2001 Nov;166(5):1750-4.*
(5) *Arya M, Mostafid H, Patel HR, Kellett MJ, Philp T. The self-expanding metallic ureteric stent in the long-term management of benign ureteric strictures. BJU Int 2001 Sep;88(4):339-42*
(6) *Lee G, Kellett MJ, Rickards D, Choong S, Philp T. Thermoexpandable ureteric stent in the treatment of refractory benign ureteric strictures: A seven year*
(7) *Agrawal S, Brown CT, Bellamy EA, Kulkarni R. The thermo-expandable metallic ureteric stent: an 11-year follow-up. BJU Int 2009 Feb 1;2009 Feb 103(3):372-6.*
(8) *Papatsoris A, Masood J, El-Husseiny T, Ndirika S, Junaid I, Buchholz NP. A novel long-term thermo-expandable ureteric metal stent: Memokath 051. BJU Int 2007;1-10.*
(9) *Liatsikos EN, Kagadis GC, Barbalias GA, Siablis D. Ureteral metal stents: a tale or a tool? J Endourol 2005 Oct;19(8):934-9.*
(10) *Maan Z, Patel D, Moraitis K, El-Husseiny T, Papatsoris AG, Buchholz NP, et al. Comparison of stent-related symptoms between conventional Double-J stents and a new-generation thermoexpandable segmental metallic stent: a validated-questionnaire-based study. J Endourol2010(4):589-93.*
(11) *Papadopoulos GI, Middela S, Srirangam SJ, Szczesniak CA, Rao PN. Use of Memokath 051 metallic stent in the management of ureteral strictures: a single-center experience. Urol Int2010;84(3):286-91.*
(12) *Franke M, Ryhammer A, Holm-nielsen P, Graversen M, Nøhr JE, Faber P, et al. Long-term outcome of the thermo-expandable ureteral metal stent (Memokath™051) for the treatment of chronic ureteral strictures: Results of the Danish Memokath study. World Congress on Endourology . 2010.*
(13) *Mynderse L, Grandberg C. Long term drainage of malignant extrinsic ureteral obstruction secondary to inoperable pelvic or abdominal malignancies using the memokath 051 ureteral stent. 2010. AUA 2010.*
(14) *Moraitis K, El-Husseiny T, Wazait H, Junaid I, Masood J, Buchholz N. Segmental Nickel-Titanium ureteric stents with thermal-shape memory in the management of ureteric strictures. World Congress on Endourology . 2010.*
(15) *Schenck M, Weise S, Jaeger T, Hess J, Ruebben H. Perioperative Anwendungsbeobachtung von thermolabilen*

		Ureterstents (Memokath 051) und anderen handelsüblichen Ureterschienen. Urologische Universitätsklinik Essen 2008. *(16) Schenck M, Treckmann J, Rübben H, Paul A. Metallstent (Memokath051) Versorgung von Transplantatharnleiterengen. 22-4-2010. 56. Kongress der Nordrhein-Westfälischen Gesellschaft für Urologie e.V.Dortmund.* *(17) Sountoulides P, Kaplan A, Kaufmann OG, Sofikitis N. Current status of metal stents for managing malignant ureteric obstruction. BJU Int 2010 Jan 8;(105):1066-72.* *(18) Allen DJ, Longhorn SE, Philp T, Smith RD, Choong S. Percutaneous urinary drainage and ureteric stenting in malignant disease. Clin Oncol (R Coll Radiol) 2010 Nov;22(9):733-9.* *(19) Bach C, Moraitis K, Pullis C, Massod J, Junaid, Buchholz N. Management of ureteric strictures with nickel-titanium ureteric stents with thermal-shape memory: A comparison of the outcome between benign and malignant strictures. Eur Urol Suppl 2011 10(2), 698. 2011.* *(20) Urol Int. 2011 Oct 18.Use of a segmental thermoexpandable metal alloy stent in the management of malignant ureteric obstruction: a single centre experience in the UK. Zaman F1, Poullis C, Bach C, Moraitis K, Junaid I, Buchholz N, Masood J* *(21) Urol. 2012 May;22.Tolerance and effectiveness of Memokath® 051 ureteral stents : a prospective 3 year follow-up study].Azizi A1, Pasticier G, Bénard A, Lapouge O, Ferrière JM, Ballanger P* *(22) J Endourol. 2013 Oct 9. A self-expanding thermo-labile nitinol stent as minimally invasive treatment alternative for ureteric strictures in renal transplant patients. Bach C1, Kabir M, Goyal A, Malliwal R, Kachrilas S, El Howairis ME, Junaid I, Masood J, Buchholz N.* *(23) Laparoendosc Adv Surg Tech 2014 Jun 11.Comparison of efficacy and safety between a segmental thermo-expandable metal alloy spiral stent (Memokath 051) and a self-expandable covered metallic stent (UVENTA) in the management of ureteral obstructions. Kim KS1, Choi S, Choi YS, Bae WJ, Hong SH, Lee JY, Kim SW, Hwang TK, Cho HJ* *(24) J Endourol. 2013 Nov 14.The use of a thermoexpandable metal alloy stent in the minimally invasive management of retroperitoneal fibrosis: a single center experience from the United kingdom.Bourdoumis A1, Kachrilas S, Kapoor S, Zaman F, Papadopoulos G, Buchholz N, Masood J*	

7.1.1	8) Section 7.1.1 states that "*Abstracts from congresses were only exceptionally included because they contain limited information".* Can you please clarify what you mean by this?	*Exception was made as there was only 1 paper with an abstract and no full paper that met the inclusion criteria.*	Noted with thanks
7.2.2	9) In Section 7.2.2 there are separate flow diagrams for the primary search (single arm studies n=5) and secondary search (comparative studies n=1). However, only 5 studies in total are reported in the submission document. Can you please confirm which studies were identified from each search?	*One study in the second PRISMA diagram was also included in the first PRISMA diagram. Hence, there are 5 included studies. All have Memokath-051 as the intervention arm and one has a comparator.*	Noted with thanks
7.8.1	10) Section 7.8.1 notes that *'exclusion of papers which contained only benign or malignant stricture was done to avoid any false impressions'*. Can you please confirm whether this was part of the eligibility criteria for the review?	*Studies were excluded where they only looked at either malignant **or** benign patients. They had to consider both groups of patients to be included.*	Noted with thanks

Overall	11) Please could you provide a full reference list of all references cited within the submission document? Specifically, please could you provide this for Papatsoris (2007) and Lance	[Answer received by email 01/05/17] *The full list of sources is already submitted at the end of the submission and an endnote. It is linked to the numbers mentioned in the submission. Here it is as follows:* *[1] Kulkarni R. Metallic ureteric stents: the current situation. BJU Int 2003 Aug;92(3):188-9.* *2 Joshi HB, Stainthorpe A, MacDonagh RP, Keeley FX, Jr., Timoney AG, Barry MJ. Indwelling ureteral stents: evaluation of symptoms, quality of life and utility. J Urol 2003 Mar;169(3):1065-9* *3 Staios D, Shergill I, Thwaini A, Junaid I, Buchholz NP. The Memokath stent. Expert Rev Med Devices 2007 Mar;4(2):99-101.* *4 Gort HB, Mali WP, van Waes PF, Kloet AG. Metallic self-expandible stenting of a ureteroileal stricture. AJR Am J Roentgenol 1990 Aug;155(2):422-3.* *5 Barbalias GA, Liatsikos EN, Kalogeropoulou C, Karnabatidis D, Siablis D. Metallic stents in gynecologic cancer: an approach to treat extrinsic ureteral obstruction. Eur Urol 2000 Jul;38(1):35-40* *6 Pauer W, Lugmayr H. Metallic Wallstents: a new therapy for extrinsic ureteral obstruction. J Urol 1992 Aug;148(2 Pt 1):281-4.* *7 Diaz-Lucas EF, Martinez-Torres JL, Fernandez MJ, Carazo MO, de la Fuente SA,Zuluaga GA. Self-expanding wallstent endoprosthesis for malignant ureteral obstruct. J Endourol 1997 Dec;11(6):441-7.* *8 http://emedicine.medscape.com/article/442469-overview#a1* *9 Campbell-Walsh Urology, Tenth Edition. Chapter 41. Page 1149. Ureteral stricture desease* *10 RJ Cetti, S Biers, and SR Keoghane\South Coast Stone Centre, Department of Urology, Queen Alexandra Hospital, Portsmouth, UK. 2011 by the Annals of The Royal College of Surgeons of England* *11 RATE OF URETERAL STRICTURE FOLLOWING URETEROSCOPY FOR NEPHROLITHIASIS USING A NATIONAL DATABASE OF INSURED PATIENTS Philip May*, Sarah Holt, Joshua Calvert, Jonathan Harper, Seattle, WA*	See questions 5 & 6 for individual references for Papatsoris and Lance

12 http://www.jurology.com/article/S0022-5347(16)00753-9/pdf

[1]3 https://urologysurgery.wordpress.com/2009/01/01/ureteral-stricture/

[1]4 https://www.nice.org.uk/guidance/cg169/chapter/1-Recommendations#managing-acute-kidney-injury

[1]5 https://www.nice.org.uk/guidance/CG175

[1]6 https://www.nice.org.uk/guidance/ng2

[1]7 https://www.nice.org.uk/guidance/CG175

[1]8 https://www.nice.org.uk/guidance/cg175/chapter/1-Recommendations#assessment-2

[1]9 Cambpell-Walsh Urology, Tenth Edition, https://books.google.com.eg/books?id=fu3BBwAAQBAJ&pg=PA1149&lpg=PA1149&dq=ureteral+stricture+campbell&source=bl&ots=Z0DAaVgjcG&sig=aZTR85U0CE_7eh9i2C-guV-rDn0&hl=en&sa=X&ved=0ahUKEwjbiceTsuLSAhWF3SYKHW64Bh4Q6AEIJzAC#v=onepage&q=ureteral%20stricture&f=false

20 Stables DP, Ginsberg NJ, Johnson ML. Percutaneous nephrostomy: a series and review of the literature. AJR Am J Roentgenol 1978 Jan;130(1):75-82

2[1] Protzel C, Dahm JB, Klebingat KJ. High frequency rotablation as a new therapeutic procedure for obstructed metallic ureter stents. J Urol 2001 Oct;166(4):1399-400.

22 Allen DJ, Longhorn SE, Philp T, Smith RD, Choong S. Percutaneous urinary drainage and ureteric stenting in malignant disease. Clin Oncol (R Coll Radiol) 2010 Nov;22(9):733-9.

23 J Endourol. 2008 Feb;22(2):295-9. doi: 10.1089/end.2007.0201.Success of ureteral stents for intrinsic ureteral obstruction.Wenzler DL1, Kim SP, Rosevear HM, Faerber GJ, Roberts WW, Wolf JS Jr.Department of Urology, University of Michigan, Ann Arbor, Michigan, USA.

24 Initial Experience with Full-Length Metal Stent to Relieve Malignant Ureteral Obstruction
James F. Borin, Ori Melamud, and Ralph V. Clayman. Journal of Endourology. May 2006

25 Ther Adv Urol. 2013 Dec; 5(6): 354–365.Current status of minimally invasive endoscopic management of ureteric strictures. Stefanos Kachrilas, Andreas Bourdoumis, Theocharis Karaolides, Stavroula Nikitopoulou, George Papadopoulos, Noor Buchholz, and Junaid Masood

26 JSLS. 2003 Apr-Jun;Percutaneous Ureteral Incision With a Small-Caliber Flexible Ureteroscope

Hatsuki Hibi, MD, Yoshiaki Yamada, MD, Hitoshi Nonomura, MD, Yukio Hatano, MD, Kenji Mitsui, MD, Tomohiro Taki, MD, Nobuaki Honda, MD, and Hidetoshi Fukatsu, MD

Hatsuki Hibi, Department of Urology, Aichi Medical University School of Medicine, Nagakute, Japan.

27 Campbell-Walsh Urology, Tenth Edition. Section IX. Upper Urinary Tract Obstruction and Trauma. Page 1154

28 Paulos Yohannes, David Gershbaum, Paul E. Rotariu, Arthur D. Smith, and Benjamin R. Lee. Journal of Endourology. July 2004, Management of Ureteral Stricture Disease during Laparoscopic Ureteroneocystostomy

29 Staios D, Shergill I, Thwaini A, Junaid I, Buchholz NP. The Memokath stent. Expert Rev Med Devices 2007 Mar;4(2):99-101.

30 Maan Z, Patel D, Moraitis K, El-Husseiny T, Papatsoris AG, Buchholz NP, et al. Comparison of stent-related symptoms between conventional Double-J stents and a new-generation thermoexpandable segmental metallic stent: a validated-questionnaire-based study. J Endourol2010(4):589-93

31 Sountoulides P, Kaplan A, Kaufmann OG, Sofikitis N. Current status of metal stents for managing malignant ureteric obstruction. BJU Int 2010 Jan 8;(105):1066-72.

32 Maan Z, Patel D, Moraitis K, El-Husseiny T, Papatsoris AG, Buchholz NP, et al. Comparison of stent-related symptoms between conventional Double-J stents and a new-generation thermoexpandable segmental metallic stent: a validated-questionnaire-based study. J Endourol2010(4):589-93.

33 Prog Urol. 2011 Jun;21(6):397-404. doi: 10.1016/j.purol.2010.11.008. Epub 2011 Jan 26.The thermoformable spiral metallic stents in the treatment of localized ureteral stenosis: an alternative to JJ stent? Prospective multicenter study. Bonniol R1, Meria P, Safsaf A, Albouy B, Sibert L.Service d'urologie, hôpital Charles-Nicolle, Rouen,

34 Urol. 2012 May;22.Tolerance and effectiveness of Memokath® 051 ureteral stents : a prospective 3 year follow-up study].Azizi A1, Pasticier G, Bénard A, Lapouge O, Ferrière JM, Ballanger P, Robert G Service d'urologie, CHU de Bordeaux, université Bordeaux-Segalen, place Amélie-Raba-Léon, 33000 Bordeaux, France

35 Papatsoris A, Buchholz N. A novel thermo-expandable ureteric metal stent for the minimally invasive management of ureteral strictures. Journal of Endourology 2010 Mar 1;24(3):487-91Efficacy in benign and malignant cases together with a prove that MK51 is more cost effective than JJ stents on the long term Usage. UK

36 Characterization of Urinary Symptoms in Patients With Ureteral Stents

HB Joshi et al. Urology 59 (4), 511-516. 4 2002

https://www.ncbi.nlm.nih.gov/labs/articles/11927301/

37 Siddique KA, Zammit P, Bafaloukas N, Albanis S, Buchholz NP. Repositioning and removal of an intra-renal migrated ureteric Memokath stent. Urol Int 2006;77(4):297-300.

38 Pearle M, Watson G. Optimal drainage of the obstructed kidney: stent versus nephrostomy. In: Yachia D, Paterson P, editors. Stenting the Urinary System. 2004. p. 139-42.

39 Pearle M, Watson G. Optimal drainage of the obstructed kidney: stent versus nephrostomy. In: Yachia D, Paterson P, editors. Stenting the Urinary System. 2004. p. 139-42.

40 Mendez-Probst CE, Fernandez A, Denstedt JD. Current status of ureteral stent technologies: comfort and antimicrobial resistance. Curr Urol Rep 2010 Mar;11(2):67-73.

41 Agarwal MM, Singh SK, Mandal AK, Bhalla V, Acharya NC, Kumar S. Endourologic management of forgotten encrusted ureteral stents: can ureteroscopic lithotripsy be avoided? Surg Laparosc Endosc Percutan Tech 2009 Feb;19(1):72-7.

42 Mendez-Probst CE, Fernandez A, Denstedt JD. Current status of ureteral stent technologies: comfort and antimicrobial resistance. Curr Urol Rep 2010 Mar;11(2):67-73.

Overall	12) When was Memokath 051 first developed?	*1992*	Noted with thanks
Overall	13) Is the Memokath listed on NHS supply chain? If so, please could you provide us with the relevant product codes?	*It is sold to many hospitals in the UK, but they were unsure if the Memokath-051 is listed on NHS supply chain. This will be checked.* [Further information received by email 05/05/17] *MK 051 is in the system of NHS hospitals like Charring Cross*	MJ noted that we had been unable to find the device listed
Overall	14) Were there any previous versions of Memokath 051? If so, when were they replaced? What are the differences between these and the current version? Do clinical studies evaluate all of these versions in combination?	*A new version was released in 2001/2002. Increased diameter by 0.5mm. An initial study which started in 1997, used old and new device. All more recent studies include the updated version as this is the only version now available.*	Noted with thanks
Overall	15) Can you recommend any review articles relating to the mechanism of action of metal stents?	[Answer received by email 05/05/17] *All the studies we have submitted have a separate paragraph about the mechanism of action of MK051*	Noted with thanks
Overall	16) What imaging or other diagnostic techniques are recommended before Memokath-051 is inserted (in the UK)?	*The diagnosis of an obstruction is the same regardless of the treatment used, e.g. via ultrasound or other imaging technique (dependent on surgeon). No additional imaging or diagnosis was reported.*	Noted with thanks

Overall	17) In addition to the Memokath 051 stent, what additional consumables are required to complete a procedures and do these differ between the Memokath 051 and comparator products?	*Ureter catheters and balloon catheters are required (unclear if these are needed for comparator products). The procedure should occur in a room that has a fluoroscopy machine.*	Noted with thanks
Overall	18) Please advise on the length of time from entry to leaving theatre for patients a) Receiving a Memokath 051 b) Having a Memokath 051 removed c) c) Having a Memokath 051 exchanged	*a) Start to end 20 minutes* *b) Start to end 15 minutes* *c) 35 minutes to an hour*	Noted with thanks
Overall	19) Will these times be the same for relevant comparators? If not, please explain the differences.	*No, times for removal or exchange would be different. Removal very difficult for most other metal stents apart from Memokath-051. Would typically only be put in if patient were to die before removal needed.*	Noted with thanks
Overall	20) What postoperative aftercare do you recommend should be provided in the UK, including use of medication and follow-up to check patency (e.g. X-rays)?	*PNN medial recommend that the patient is seen at 1 week, 1 month and then every 3-6 months. They will be asked if they have any symptoms and if so will have an x-ray. If problems are identified, they will go on to have intravenous flowography. However, there is variation amongst clinicians regarding follow-up.*	Noted with thanks
Overall	21) Please advise if checking patency or any other post procedure follow-up differs between the Memokath 051 and other comparator products.	*There is not much information on competitors, except double J stents that are removed after 6 months.*	Noted with thanks

Overall	22) What are the most common reasons for stent replacement with Memokath 051 and comparator products?	*Migration occurs in an average of 8% of patients at 4 years follow-up. This would require removal of the stent* *Incrustation occurs in an average of 12% of patients at 4 years follow-up. In many countries the stent is not removed, just cleaned.*	Noted with thanks
Overall	23) What resources are associated with managing stent related infections (e.g. removing and replacing the stent, other procedures, materially longer length of stay, use of IV antibiotics)?	*Infections occur in around 3-5% of patients and treated like normal UTI (using antibiotics). Rare to have to remove the stent.*	Noted with thanks
Overall	24) We understand that Memokath 051 has the potential to be inserted under local anaesthesia. As far as you know, does this occur in practice in the UK? Where would this take place?	*No, in UK is it used under general anaesthetic. In Italy and South Africa it is inserted under local anaesthetic.*	Noted with thanks
Overall	25) Please describe the training required to use Memokath-051 including: • Who provides the training; • How long the training takes; • Which clinical staff would be trained (within the UK NHS); • How many staff would be trained per device; • The cost of the training is and who pays for it; • Any ongoing training.	*"See one, do one" technique. Product specialists attend operation. IFU in every stent. Specialist does everything in front of doctors. Supply also with IFU To keep in operating room. Assistant (nurse) trained on when to inject water, what help might be needed. If second round of training needed they provide it. Training provided by company at no charge.* *Takes about 5 mins longer to do the procedure before being trained up. No specialist skills are needed as insertion is similar to double J stents.*	Noted with thanks

Overall	26) Are you aware of any other metals stents that are available within the UK NHS?	*Korean stent – UVENTA (may be available)* *Cook metal stent. Stays in body only 1 year. Has to be removed before 1 year.* [Further information received 05/05/17] *To our knowledge the Cook stent (Resonance) and Allium stent have been used before in UK but as other places outside UK the use is very limited and there is no good data about these at the moment.* *The main comparator is JJ stents as no one is able to produce a stent which can stay insitu for long time and at the same time can be removed easy and safe except for MK051*	Noted with thanks
Overall	27) Are you aware of any studies that have directly compared the Memokath 051 with other metal stents? Are you aware of any high quality studies published on other metal stents for this indication?	*There is one study in Korea Memokath-051 vs. UVENTA.*	Noted with thanks. This study is included in the topic briefing.
Overall	28) Compared with other metal stents, what would you consider was the main "unique selling point" (USP) of Memokath 051?	*(1) Easily removable, there have been no complaints about this and few complications. This gives patients piece of mind.* *(2) Long life span in the body.*	Noted with thanks

Overall	29) Lastly, could we ask some advance questions on what to expect from the economic model? a. What software will it be written on? b. Will it use double J stents as a sole comparator? c. Will it include any of the subgroups stated in the PICO analysis (decision problem) outlined in the scope? d. Will it incorporate sensitivity analysis?	a. [PNN to advise at a later date] *b. Double J stents will be included. Competitor stents not widely used so not much data, their inclusion to be determined. Outside of the UK, competitor stents seem to have very similar costs (10% more or less thank Memokath-051).* *c. Will look at the overall population (and length of time a stent is required for) rather than subgroups.* *d. Yes, expect that it will.*	Response to part a not received, but no longer relevant.

	On 05/05/17 EAC emailed Jakob Sandersen of PNN medical with 2 further queries regarding the clinical submission: 1) We had one further point that we wanted to clarify relating to your Table A1 within your submission. We note the column "Scope issued by NICE" within this table is not fully aligned with the final scope issued by NICE. Rather, it is aligned with the draft scope. Please could you confirm that this table was based on the draft rather than the final scope? 2) Secondly, please could you provide rationale where there were differences between the scope and your selection criteria (i.e. tables A1 and B1 within your submission)?	**Response received from Jakob Sandersen on 09/05/17:** 1) *I confirm that the table was based on the draft rather than the final scope. Please correct it or let us know if we should submit a new version.* 2) *For B1 table, this is the criteria we have chosen for the submission. We believe it is totally in alignment with the scope for the following reasons:* o *Over 20 years of business, we have never found any comparison of the MK51 stents with conventional surgeries. The comparison was/is always with JJ stents in chronic cases* o *The very specific indication of MK51 in cases of malignant cases, surgeries are not even indicated. It is only stents.* o *The purpose of surgeries is mainly the complete cure of the patients, while the main purpose of stents generally is to relief the symptoms and preserve the kidney function. But due to the fact that these surgeries are special skills surgeries, very difficult ones, and due to the fact that there are many cases who are not fit for such operations such are malignancies and cardiac patients or patients on anti coagulants or patients who are not willing to have a major*	EAC responded 09/05/17 stating that there was no need to submit an updated table, but following discussion with NICE the company were invited to submit an updated table.

		surgery and finally due to cost restrictions in many cases, then the stents have a very important role for these patients. *Based on the above, we decided to make the submission as close as possible to reality and practicality on the ground as we see in practice and focus of the value of MK51 in the nearest indicated cases.*	
	On 10/05/17 EAC emailed Jakob Sandersen of PNN medical inviting the company to resubmit table A1 of the clinical submission, as agreed with NICE	**Response received from Jakob Sandersen on 17/05/17, with the updated table A1**	Noted with thanks
	On 11/05/2017, a list of eight questions were sent by the EAC to 5 Expert Advisors named by NICE for this project	**Responses received by EAC were collated into a single documented response: See Appendix 3.** 11/05/2017 – response received from Ms Daniela Andrich confirming that she would respond to the questions in due course 19/05/2017 – answers received from Mr Ranan DasGupta 19/05/2017 – answers received from Mr Matthew Shaw [Mr Shaw added: *Please note we have all but stopped using Memokath stents due to what we think is the superior performance of other stent types.*]	Due to cyber attacks on the NHS in the week of 08/05/17, EAC re-sent questions to the 4 expert advisers who had not responded and followed up with Daniela Aldrich on 19/05/17 Responses were noted with thanks To inform EAC report

	On 16/05/2017, EAC made an FOI request to NHS Business Services Authority requesting the following: *Please can I request the quantities sold per year for the past 5 years of the following items* *listed on the NHS supply chain: FAL5758: Ureteral stent Resonance metallic ureteral stent* *set 6fr 20cm, MPC: RMS-060020 FAL5759:Ureteral stent Resonance metallic ureteral stent and introducer 6fr 20cm, MPC: RMS-060020-R FAL5760: Ureteral stent Resonance metallic ureteral stent set 6fr 22cm, MPC: RMS-060022 FAL5761: Ureteral stent Resonance metallic ureteral stent and introducer 6fr 22cm, MPC: RMS-060022-R FAL5762: Ureteral stent Resonance metallic ureteral stent set 6fr 24cm, MPC: RMS-060024 FAL5763: Ureteral stent Resonance metallic ureteral stent and introducer 6fr 24cm, MPC: RMS-060024-R FAL5764: Ureteral stent Resonance metallic ureteral stent set 6fr x 26cm, MPC: RMS-060026 FAL5765: Ureteral stent Resonance metallic ureteral stent and introducer 6fr 26cm, MPC: RMS-060026-R FAL5766: Ureteral stent Resonance metallic ureteral stent set 6fr 28cm, MPC: RMS-060028 FAL5767: Ureteral stent Resonance metallic ureteral stent and introducer 6fr 28cm, MPC: RMS-060028-R FAL5768: Ureteral stent Resonance metallic ureteral stent set 6fr 30cm, MPC: RMS-060030 FAL5668: Ureteral stent Resonance metallic ureteral stent and introducer 6fr 30cm, MPC: RMS-060030-R**	**A response was received on 12/06/2017 and the information provided is shown in Appendix 4.**	Noted with thanks

	On 26/05/2017, EAC contacted the manufacturers of the UVENTA (contact@stent.net) and Allium (info@allium-medical.com) stents requesting UK list prices to inform the economic model	**Response received from Lea Oh at Taewoong Medical on 31/05/2017 introducing the UK distributor of UVENTA stents, Gareth Longden of Macromed Ltd** **No response received from Allium Medical**	Gareth Longden of Macromed Ltd contacted
	On 01/06/2017, EAC contacted Gareth Longden of Macromed Ltd requesting the UK list price for the UVENTA stent	**Response received from Gareth Longden of Macromed Ltd on 01/06/2017:** *The UK list price is £1500.00 per unit for the Uventa stent.*	To inform EAC report on the Economic Evidence Submission
	On 02/06/2017, a further list of twelve questions were sent by the EAC to the 5 Expert Advisors named by NICE for this project	**No responses were received**	To inform EAC report on the Economic Evidence Submission
	On 07/06/2017, EAC followed up with the 5 Expert Advisors regarding the list of twelve questions as no responses had been received	**No responses were received**	
	On 07/06/2017, EAC contacted Ossama Abuldahab of PNN Medical with the following question: *Specifically, could you tell us the number of hospitals using Memokath-051 in England and the nature of these hospitals. For instance, are they tertiary centres or district general hospitals?*	**Response is reported below (page 29)**	

	On 08/06/2017, EAC contacted Nik Levey of Sigmacon Surgical Systems, the UK distributor of the Allium ureteral stent, requesting the UK list price for the device.	**Response received from Nik Levey of Macromed Ltd on 01/06/2017:** *£1,700 ex VAT per stent.*	To inform EAC report on the Economic Evidence Submission
	On 12/06/2017, EAC contacted Gareth Longden of Macromed Ltd and Nik Levey of Sigmacon Surgical Systems, with a further question regarding the UVENTA and Allium stents: *Are you aware of any sources that report whether a passport balloon catheter is used during stent insertion or replacement?*	**Response received from Simon Angove of Sigmacon Surgical Systems Ltd on 13/06/2017:** *Regarding your request for use of Allium stent using the Passport Balloon dilator it would be possible however the dilator only dilates to a maximum of 12 French. Allium Medical request that the ureter is ideally dilated to 14 French prior to insertion of the Allium stent. In my experience balloon dilators are also fairly short in length and thus the dilator needs to be inflated several times to encompass the whole of the stricture. This often leads to the dilator not inflating completely or distorting after a couple of uses. Also the section of the ureter which is dilated first often closes up thus making deployment of the Allium stent more difficult.* *The simplest and often cheapest way is to use a stepped Nottingham type dilator set, dilating to 14 French. The Allium introducing catheter is 10 French but the stent requires a few extra French to deploy correctly and expand.*	To inform EAC report on the Economic Evidence Submission

	On 12/06/2017, EAC contacted Ossama Abuldahab of PNN Medical with a further 3 questions:
	
	1. *Can you please advise on the proportion of stent insertions that are conducted within the English NHS as a:*
	  o *Day case procedure*
	  o *Inpatient procedure*
	  o *Patients who are already in hospital for another reason.*
	2. *We note that in your economic submission you included the cost of a 'passport' (presumably a catheter passport) for Memokath-051 patients. Is this passport also required within the English NHS for patients with double J stents or other metallic/nickel stents?*
	3. *Could you tell us the number of hospitals using Memokath-051 in England and the nature of these hospitals. For instance, are they tertiary centres or district general hospitals?*
		Response received from Ossama Abuldahab on 19/06/2017:
		
		1. *All hospitals –up to the best of our knowledge – deal with MK51 cases as day case procedure*
		2. *In our economical study we considered using the passport catheter for dilatation of ureter, this is not needed for either MK51 or JJ stent insertion. In some difficult cases, it is used to dilate the ureter regardless the type of stent the surgeon is going to use. Meaning, it is mainly used in very tight stricture cases to pass a stent whatever its type. That is why we decided to put it as a precaution to cover worst case scenario and highest cost*
		3. *For the hospitals used MK51, please find attached the list of hospitals which used MK51 in the last 2 years. We have sent before a list of our hospitals that use the stents regular but this is a list of hospitals used the stent even once.*	

	On 12/06/2017, EAC followed up with the 5 Expert Advisors by email as no answers had been received to the questions sent on 02/06/2017. A list of 7 key questions was sent to each advisor.	**Responses received by EAC were collated into a single documented response: See Appendix 3.** 12/06/2017 – answers received from Ms Daniela Andrich 13/06/2017 – answers received from Mr Mahmoud Elfar	To inform EAC report on the Economic Evidence Submission
	On 13/06/2017, EAC had a phone conversation with Daniela Andrich, one of the NICE ratified experts to further discuss questions on the economic submission. **Immediately after this call, the EAC sent a follow-up email to Daniela with a further question:** *As discussed, a further question was in response to your query in our earlier email regarding the use of a foley catheter. We were referring to a passport balloon catheter which I understand is used to dilate the ureter prior to insertion of a stent. Given that this is a relatively expensive surgical consumable we are trying to establish if it is required for the insertion of all stents or specifically for insertion of the Memokath stent. Are you aware of it being required to dilate the ureter prior to the insertion of a double J stent?*	**Daniela Andrich provided clinical context to the decision problem outlined in the topic briefing and provided clarification of her responses to one of the written economic questions, confirming that no balloon catheter is required for insertion of Memokath-051.** Daniela expressed concern that the comparison between Memokath-051, Double J stents and reconstructive surgery was flawed, as all are indicated in different patient groups. **A response to the question sent by email was received on 13/06/2017:** *No, you don't have to dilate the ureter for J-J stent insertion.*	To inform EAC report on the Economic Evidence Submission

	On 19/06/2017, EAC contacted Ossama Abuldahab of PNN Medical with 1 further question: *Within your submission you report on the NCT00166361 study which was part funded by PNN Medical. I wondered if you could confirm whether or not the abstract by Granberg 2010 is also reporting on the same study (i.e. NCT00166361)?*	**A response was received on 20/06/2017:** *Actually yes I confirm it is the same study. it is the only study run for MK 51 in USA till the moment.* *Please be aware that the 95 stent exchange and 425000 USD saving compared with JJ stents was done with US prices for JJ stents and our European prices for MK51 as it is not priced officially in US till date. So the 95 exchanges is medically confirmed but we didn't use the money savings in our arguments for the above reasons to be as honest as we can.*	Noted with thanks

Appendix 1

Appendix 1 - Additional answers

Appendix 2

Appendix 2 - Additional answers

Appendix 3

Appendix 3 - COLLATED RESPONS

Appendix 4

Appendix 4 - FOI_Request_(06907

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Medical Technologies Evaluation Programme

Sponsor submission of evidence:

Evaluation title: The Memokath-051 stent for the treatment of ureteric obstruction

Sponsor: PNN medical

Date sections A and B submitted: 21 April 2017

Date section C submitted: 22 May 2017

August 2011 (Version 1.1)

Contents

Instructions for sponsors

This is the template for submission of evidence to the National Institute for Health and Care Excellence (NICE) as part of the Medical Technologies Evaluation Programme process for developing NICE medical technologies guidance. Use of the submission template is mandatory.

The purpose of the submission is for the sponsor to collate, analyse and present all relevant evidence that supports the case for adoption of the technology into the NHS in England, within the scope defined by NICE. Failure to comply with the submission template and instructions could mean that the NICE cannot issue recommendations on use of the technology.

The submission should be completed after reading the 'Medical Technologies Evaluation Programme Methods guide' and the 'Medical Technologies Evaluation Programme Process guide' available at www.nice.org.uk/mt. After submission to, and acceptance by, NICE, the submission will be critically appraised by an External Assessment Centre appointed by NICE.

Under exceptional circumstances, unpublished evidence is accepted under agreement of confidentiality. Such evidence includes 'commercial in confidence' information and data that are awaiting publication ('academic in confidence'). When data are 'commercial in confidence' or 'academic in confidence', it is the sponsor's responsibility to highlight such data clearly. For further information on disclosure of information, submitting cost models and equality issues, users should see section 11 of this document 'Related procedures for evidence submission'.

The submission should be concise and informative. The main body of the submission should not exceed 100 pages (excluding the pages covered by the template and appendices). The submission should be sent to NICE electronically in Word or a compatible format, not as a PDF file.

The submission must be a stand-alone document. Additional appendices may only be used for supplementary explanatory information that exceeds the level of detail requested, but that is considered to be relevant to the case for adoption. Appendices will not normally be presented to the Medical Technologies Advisory Committee when developing its recommendations. Any additional appendices should be clearly referenced in the body of the submission. Appendices should not be used for core information that has been requested in the specification. For example, it is not acceptable to attach a key study as an appendix and to complete the economic evidence section with 'see appendix X'.

All studies and data included in the submission must be referenced. Identify studies by the first author or trial ID, rather than by relying on numerical referencing alone (for example, 'Trial 123/Jones et al.[126], rather than 'one trial[126]').Please use a recognised referencing style, such as Harvard or Vancouver.

The sponsor should provide a PDF copy of full journal articles or reports – in electronic or hard copy form – included in the submission, if the sponsor is either the copyright owner or has adequate copyright clearance to permit the intended use by NICE. This clearance must be wide enough to allow NICE to make further copies, store the article electronically for a limited period of time on a shared drive to be accessed by a limited number of staff. Additionally, any full article obtained and submitted in electronic format must be done so in a manner compliant with the relevant contractual terms of use permitting the sponsor electronic access to the article. If the sponsor does not have sufficient copyright clearance, they are asked to submit references or links only, or details of contacts for unpublished research. NICE will then itself obtain full copies of all relevant papers or reports, paying a copyright fee where necessary. For unpublished studies for which a manuscript is not available, provide a structured abstract about future journal publication. If a structured abstract is not available, the sponsor must provide a statement from the authors to verify the data provided.

If a submission is based on preliminary regulatory recommendations, the sponsor must advise NICE immediately of any variation between the preliminary and final approval.

Document key

Boxed text with a grey background provides specific and/or important guidance for that section. This should not be removed.

Information in highlighted black italic is to help the user complete the submission and may be deleted.

The user should enter text at the point marked 'Response' or in the tables as appropriate. 'Response' text may be deleted.

Glossary of terms

Term	Definition
NHS	National health service
MK 51	Memokath® model 51
QOL	Quality of life

Section A – Decision problem

Section A describes the decision problem, the technology and its clinical context. There is also information about ongoing studies, regulatory information and equality issues.

Sponsors should submit section A before the full submission (for details on timelines, see the NICE document 'Guide to the Medical Technologies Evaluation Programme process', available from www.nice.org.uk/mt

1 Statement of the decision problem

The decision problem is specified in the final scope issued by NICE. The decision problem states the key parameters that should be addressed by the information in the evidence submission. All statements should be evidence based and directly relevant to the decision problem.

Table A1 Statement of the decision problem

	Scope issued by NICE	Variation from scope	Rationale for variation
Population	Patients with ureteric obstruction as a result of malignant or benign strictures.	None	
Intervention	The Memokath-051	None	
Comparator(s)	• Double J stents • Nephrostomy • Reconstructive surgery • Metallic and alloy stents (including nitinol stents)	There is no direct comparative evidence between MK51 and all of the comparators.	It is a patient to patient varation to decide each treatment is better for the patient
Outcomes	The outcome measures to consider include: • Number and rate of replacement stents • Number and rate of repeat procedures requiring anaesthesia and surgery • Theatre time and hospital stay • Quality of life including patient tolerability and comfort • Length of time stent remains in situ • Clinical success rate (e.g. improved renal function, no obstruction) • Frequency of stent removal/reversal • Device-related adverse events including procedure related complications and information pertaining to the resource use associated with these adverse events • Frequency of follow-up visits • Pain scores including from subsequent bladder irritation		
Cost analysis	Comparator(s): • Double J stents • Nephrostomy • Reconstructive surgery • Metal and alloy stents Costs will be considered from an NHS and personal social services perspective. The time horizon for the cost analysis will be sufficiently long to reflect any differences in costs and consequences between the technologies being compared. Sensitivity analysis will be undertaken to address uncertainties in the model parameter.		
Subgroups to be considered	• Patients unfit for surgery • Malignant or benign stricture • Antegrade or retrograde insertion (including the procedure performed either by an interventional radiologist or a urologist)		

Special considerations, including issues related to equality	Some ureteric obstructions are a result of malignancy - all people with cancer are protected under the Equality Act from the point of diagnosis. People with ureteric strictures may benefit from Memokath-051 as an alternative to double J stents, as it may be associated with a reduced number of replacement procedures and reduced adverse events, which would improve their quality of life. Memokath-051 may also provide an alternative treatment for people with ureteric strictures who cannot tolerate or who have had failed conventional stents, who would otherwise be nephrostomy- dependent and are likely to be classed as disabled under the Equality Act.		

2 Description of technology under assessment

2.1 Give the brand name, approved name and details of any different versions of the same device.

Memokath™ 051, Memokath™ 028, Memokath™ 044 and Memokath™ 045

All devices are approved in different sizes from 5 mm to 250 mm with minimum 5 mm jump between. The devices can be either single cone or double cone.

2.2 What is the principal mechanism of action of the technology?

The concept of inserting a stent to keep a blocked conduit open is attractive and urologists have historically been far ahead with applying this idea in clinical practice. The first reported use of a ureter stent dates back to the 19th century, Kulkarni R[1].

The Memokath™ nitinol (nickel-titanium) urological stents have been used clinically since the early 1990's. Over 70,000 Memokath™ stents have been implanted in urinary system since 1991. The Memokath51™ stent is an alternative to the conventional double-J stent, which is associated with pain, irritation, bleeding, reflux, obstruction, migration and reduced quality of life scores, Joshi HB et al. 2003[2].

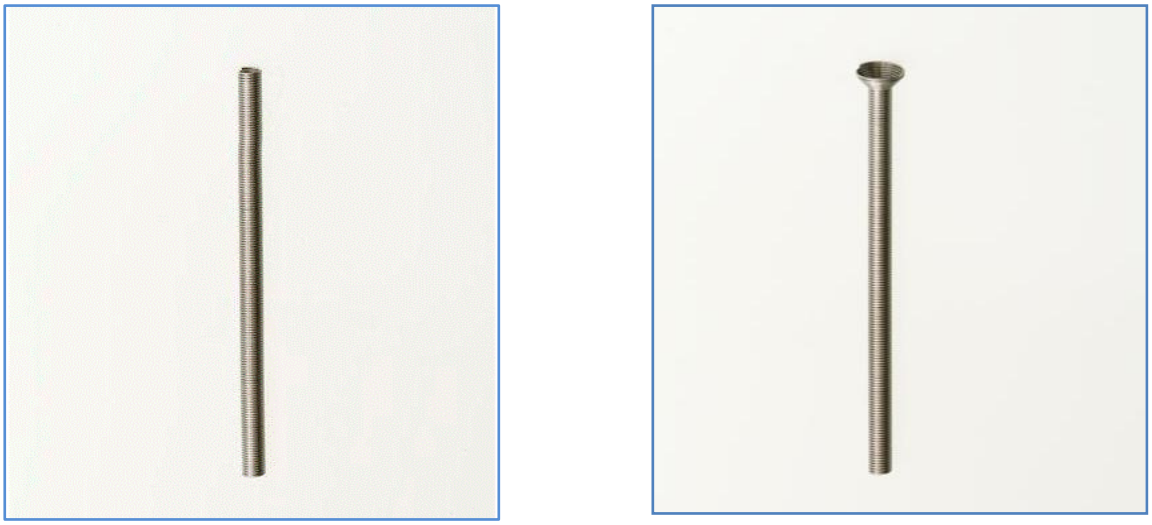
Memokath™ stents are thermo-expandable nickel-titanium alloy spiral stents, Staios D et al.[3] Nickel-Titanium exists in two states depending upon temperature. The structure of one of these states is floppy (soft) and the other is rigid, resulting in a thermo-sensitive "shape memory". A preformed piece of alloy is restored to its original shape by increased temperatures. More specifically, this alloy softens at temperatures below 7°C (45°F) and returns to a pre-formed shape when warmed to a temperature above 50ºC (122°F). When a Memokath™ stent is inserted in its correct place, it is flushed with warm, sterile fluid. This causes the distal part(s) of it to expand and to become anchored in the desired position. This is achieved by injecting 60°C-65°C (140-149°F) warm water into the insertion system. The temperature drops an estimated 8°C (18°F) during the passage through the insertion system.

Memokath™ stents have a tight spiral structure that prevents urothelial in-growth between the coils. The spiral design allows the Memokath™ stents to conform and adapt to the natural curves of the urinary tract. There is no outward pressure which minimizes or eliminates the risk of

secondary ischemic injury to the urothelium. The above-mentioned characteristics allow easy insertion and removal of Memokath™ stents.

The Memokath™051 stent is available in lengths from 30 mm to 250 mm. The inside diameter is CH8.1 and the outside is CH10.5 before expansion. The initial 12 coils expand upon instillation of hot, sterile fluid into a cone shape with the last coils becoming CH20 (Figure 1).

Figure 1: The Memokath™051 ureteral stent. The proximal end expands into a cone upon instillation of warm water, which anchors the stent (picture to the right).

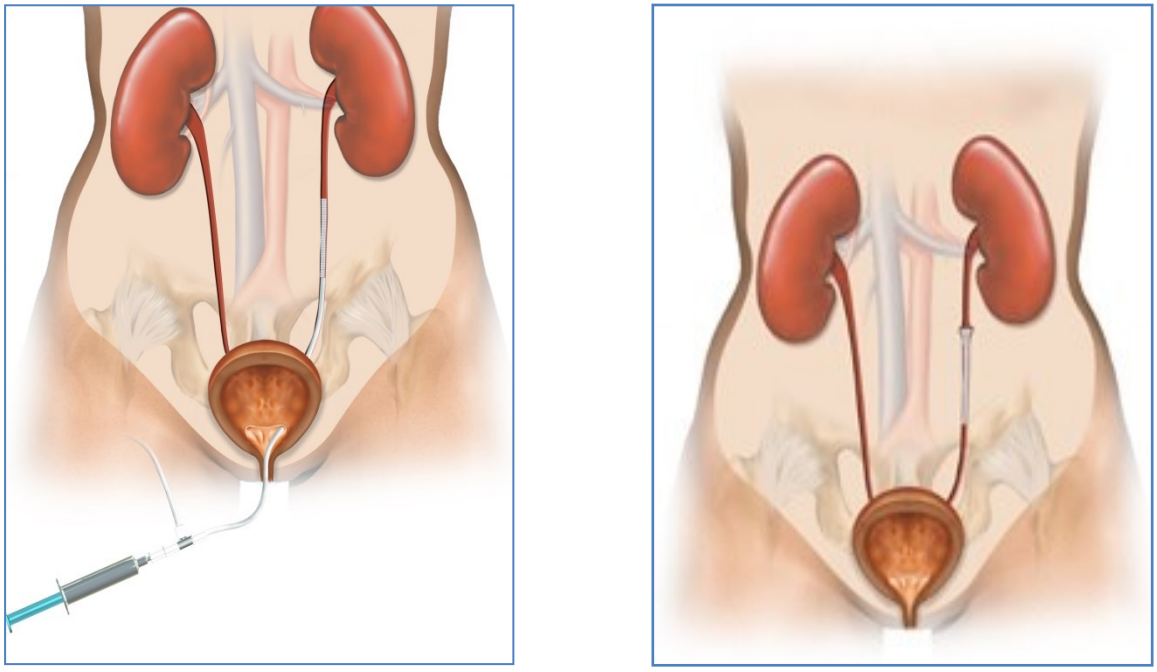


Endoscopically placed ureteral stents are the primary method of managing ureteral obstruction secondary to benign stricture processes or abdominal and pelvic malignancies.

Metallic stents for the ureter were first reported by Gort et al. in 1990[4], when a 6 mm diameter Wallstent™ was percutaneously placed in a ureter stricture and showed good results at the follow-up after 6 months. The Wallstent™ is placed either cystoscopically or through a percutaneous nephrostomy tube. It is made from a stainless cobalt-based mesh, which expands when deployed and thereby exerts radial forces that keep the ureteral lumen patent, Barbalias, GA et al. 2000[5]. Results from these stents have been varying, including clinical studies reporting durable long-term relief of extrinsic obstruction from pelvic malignancies or malignant ureteral obstruction, Pauer, W et al. 1992[6], Diaz-Lucas, EF et al. 1997[7]. Like the double-J stents, the Wallstents™ are subject to migration and encrustation, and the large gaps between the wires allow endoluminal protrusion of

edema and inflammatory tissue as well as later growth of obstructing fibrotic scar tissue or tumour into the stent lumen, causing recurrent obstruction. However, the major drawback of these metallic stents is that once placed, they cannot be easily removed as they are incorporated into the ureteral wall.

Figure 2: Drawings of a Memokath™051 stent in situ.



The Memokath™051 ureteral stent was developed to exploit the advantages of a permanent ureteral drainage device, while circumventing some of the major technical drawbacks of the Wallstent™ and double J stents. The Memokath™051 is designed to resist tissue ingrowths when placed endoluminally in the urinary system and to be removable even after long-term indwelling. The Memokath™051 has been on the market since 1996. The patient exposure is -based upon sales figures- estimated to be more than 10.000.

3 Clinical context

3.1 Provide a brief overview of the disease or condition for which the technology is being considered in the scope issued by NICE.

A ureteral stricture is characterized by a narrowing of the ureteral lumen, causing functional obstruction[8]. Common etiologies of ureteral strictures include ischemia, surgical and non surgical trauma, periureteral fibrosis, malignancy or congenital[9].

The exact incidence of chronic ureteral strictures is very difficult to determine. RJ Cetti et al showed incidence of 8% ureteric strictures following rigid and flexible upper renal scopes (URS)10 Philip May et al[11] - in a study with lage number of patients (270,008), published in The Journal of Urology Vol. 195, No. 4S, Supplement, Sunday, May 8, 2016- showed incidence of 2-3% of strictures following URS and SWL[12]. Many studies else mentioned overall 3-11% strictures following URS and SWL[13]..

3.2 Give details of any relevant NICE or other national guidance or expert guidelines for the condition for which the technology is being used. Specify whether the guidance identifies specific subgroups and make any recommendations for their treatment. If available, these should be UK based guidelines.

In the NHS in England in 2014-15, there were 7,674 retrograde insertions and 2,733 retrograde removals of ureteric stents, but the type of stent (plastic or metallic), or the reason for insertion was not specified. There were 80 cases of percutaneous insertions and 22 replacements of ureteric metallic stents.

People with complete ureteric obstruction require urgent referral and treatment to relieve the blockage and avoid the development of obstructive renal failure. The relief of ureteric obstruction can be achieved either by stenting the ureter or by creating a nephrostomy. The NICE guideline for acute kidney injury (CG169)[14] (AKI) includes recommendations for the detection and management of AKI, which includes people with ureteric strictures. The guideline states that all people with upper urinary tract obstruction should be referred to an urologist, and that when nephrostomy or stenting is undertaken, it should be done as soon as possible and certainly within 12 hours of diagnosis.

3.3 For people with malignant ureteric strictures, there are specific recommendations for those with prostate or bladder cancer (CG175)[15]. In the NICE guideline for prostate cancer, decompression of the upper urinary tract is recommended by nephrostomy or by insertion of a double J stent for men with obstructive uropathy secondary to hormone-relapsed prostate cancer. In the NICE guideline for bladder cancer[16], nephrostomy or retrograde stenting is recommended (if technically feasible) for people with locally advanced or metastatic bladder cancer with ureteric obstruction who need treatment to relieve pain, treat

AKI or improve renal function before undergoing further therapy. Describe the clinical pathway of care that includes the proposed use of the technology.

Up to the best of our knowledge, NICE guidelines did not discuss ureteric strictures as a separate title disease for management. For people with malignant ureteric strictures, there are specific recommendations for those with prostate or bladder cancer (CG175)[17] as follows:

In Metastatic prostate Cancer, Pelvic-targeted therapies[18]

1.5.20 Offer decompression of the upper urinary tract by percutaneous nephrostomy or by insertion of a double J stent to men with obstructive uropathy secondary to hormone-relapsed prostate cancer. **[2008]**

1.5.21 The option of no intervention should also be discussed with men with obstructive uropathy secondary to hormone-relapsed prostate cancer and remains a choice for some. **[2008]**

Campbell-Walsh discussed endourologic options for intervention of stirctures of ureter as follows[19]:

- Ureteral stent placement and percutaneous nephrostomy: as a first line of treatment for ureter decompression. Percutaneous nephrostomy tubes, although up to 98% successful in establishing upper tract drainage, are easily dislodged and have also been associated with a 4% significant complication rate including almost certain colonization, infection, haemorrhage, and urine leak, Stables DP et al. 1978[20], Protzel C et al. 2001[21], Allen DJ 2010[22].

- Ureteral stent placement in chronic cases: Welzener et al, 2008 reported very good results of success (88% with 26 month follow up) of using stents in intrinsic ureteral strictures[23] . specifically, Campbell-Walsh mentioned the use of Metal stents and its positive results in treating chronic ureteral strictures. There was two paper mentioned in this context: Borin et al, 2006, reported their positive first experience with the metallic stent[24]. The second study was by liatsikos et al, 2010 which reported treating 50 patients with metallic stents with 12 month interval of change and recommended metallic stents as the best treatment for malignant strictures[25]

- Retrograde and antegrade balloon dilatation: it was only recommended with strictures less than 2 cm in length with success rates ranging from 50 % to 75% (King et al 1984b, chang et al, 1987, Netto et al, 1990 and Gerber 1997)

- Endureterotomy: Endoluminal ureteral incision is considered a logical extension of balloon dilatation. Hibi et al 2003[26] suggested that Percutaneous ureteral incision for ureteroenteroanastomotic stricture using the holmium laser was associated with a good outcome.

They recommended that this procedure be considered initially because it is markedly less invasive and has a favourable outcome.

- Surgical repair:
    - Open uteroureterostomy: it is mostly indicated for a short upper or middle ureter stricture[27]. On the other hand, a lower ureter stricture stricture is usually best managed ureterorenocystostomy with or without psoas hitch or Boari flap.
    - Laparoscopic and open ureteroureterostomy: it is mentioned in many articles without a sustainable long term follow up results
    - Laparoscopic ureteroreneocystosmy: many case studies like Yohannes et al28 described the technique and suggested the success of it.
    - Open and laparoscopic Psoas Hitch
    - Open and laparoscopic Boari flap
    - Open and laparoscopic transureteroureterostomy
    - Open and laparoscopic ileal ureteral substitution
    - Autotransplantation
- Surgical repair in General is a high skilled operation and results and success rates varies greatly from center to center and country to country

3.4 Describe any issues relating to current clinical practice, including any uncertainty about best practice.

As mentioned above, there is no specific recommendation for stricture ureter desease. Adding to that, it is only mentioned in CG175 in metastatic prostate cancer for decompression of the ureter.

This is leaving a space for drawbacks:

- Non putting a solid strategy for ureter decompression for benign and malignant cases opens the possibilities for choosing treatments which can be more costly and more skill dependant and maybe less in effectiveness and QOL of patients

- Indwelling double-J stents can be associated with significant morbidity including hematuria, irritative symptoms, flank pain, stent migration, reduced quality of life, and stent fragmentation. Therefore, there was a clear need for a stent which can be left in situ for prolonged periods without the inevitable morbidity encountered with the double-J stents; Leroy AJ et al. 1986[29], Maan Z et al. 2009[30], Sountoulides P et al. 2010[31].

- Stent exchange requires hospitalization and anaesthesia. Stent exchange can be technically difficult, can possibly fail or cause complications with added morbidity and decreased quality of life.

- Patient satisfaction rate with Memokath 051 in situ is much higher than the traditional Double J stents Maan Z et al. 2010[32], Bonniol R et Al[33], Azizi A1[34]

- Repeated change of double J stents is more cost on the patient and/or NHS on the long term compared with the cost of Memokath 051 which lasts much more inside the bodyPapatsoris A et al[35]

3.5 Describe the new pathway of care incorporating the new technology that would exist if the technology was adopted by the NHS in England.

Memokath 051 should be considered the first line of treatment for all cases of chronic ureteric strictures due to benign or malignant diseases

3.6 Describe any changes to the way current services are organised or delivered as a result of introducing the technology.

putting Memokath 051 as the corner stone treatment for chronic ureteric stricturs will lead to:

- Less waiting list of patient due to avoidance of recurrent admission for double j

- Less waiting list of patients due to avoidance of recurrent infections due to nephrostomies

- Much less cost and time waste specially for cancer patients whom other treatments fail to protect their ureters

3.7 Describe any additional tests or investigations needed for selecting or monitoring patients, or particular administration requirements, associated with using this technology that are over and above usual clinical practice.

No additional tests or investigations are needed

3.8 Describe any additional facilities, technologies or infrastructure that need to be used alongside the technology under evaluation for the claimed benefits to be realised.

No additional facilities, technologies or infrastructure are needed

3.9 Describe any tests, investigations, interventions, facilities or technologies that would no longer be needed with using this technology.

ND

3.10 Describe how the NHS in England can disinvest from tests, investigations, interventions, facilities or technologies described in section 3.9 that would no longer be needed with using this technology.

ND

4 Regulatory information

4.1 Provide PDF copies of the following documents:

- instructions for use
- CE mark certificate or equivalent UK regulatory approval such as EC declaration of conformity
- quality systems (ISO 13485) certificate (if required).

4.2 Does the technology have CE mark for the indication(s) specified in the scope issued by NICE? If so, give the date that authorisation was received. If not, state current UK regulatory status, with relevant dates (for example, date of application and/or expected approval dates).

Yes Memokath have CE mark for the indication specified in the scope issued by NICE. Memokath were authorized 29th October 1997 in EU

4.3 Does the technology have regulatory approval outside the UK? If so, please provide details.

Yes the technology have regulatory approval Eire, France, Germany, Switzerland, China, Japan, Midle East, Sweden, Norway, Spain, Portugal, Denmark, Australia, Egypt, India and South Africa

4.4 If the technology has not been launched in the UK provide the anticipated date of availability in the UK.

The product has been on the UK market for more than 20 years

4.5 If the technology has been launched in the UK provide information on the use in England.

The technology is being used at UCLH, Charing Cross, Ealing, Luton, Hillingdon, Salisbury, Princess Alexander, Princess of Wales, Kettering, Whipps Cross, Eastbourne, Bristol, Royal Devon and Exeter, Kings and Epsom, Ashford, St. Peters, Broomfield, Maidstone, Coventry, Broomfield, Ipswich, Q/E Birmingham, BUPA, BMI, Nuffield, Forth Valley Hosp, Western General Edinburg, Freeman hosp., Bradford royal and University of Aintree.

5 Ongoing studies

5.1 Provide details of all completed and ongoing studies on the technology from which additional evidence relevant to the decision problem is likely to be available in the next 12 months.

NA

5.2 If the technology is, or is planned to be, subject to any other form of assessment in the UK, please give details of the assessment, organisation and expected timescale.

NA

6 Equality

NICE is committed to promoting equality of opportunity and eliminating unlawful discrimination on the grounds of age, disability, gender reassignment, race, religion or belief, sex, and sexual orientation, and to comply fully with legal obligations on equality and human rights.

Equality issues require special attention because of NICE's duties to have due regard to the need to eliminate unlawful discrimination, promote equality and foster good relations between people with a characteristic protected by the equalities legislation and others.

Any issues relating to equality that are relevant to the technology under assessment should be described. This section should identify issues described in the scope and also any equality issues not captured in the final scope.

Further details on equality may be found in section 11.3 of this document.

6.1.1 Describe any equality issues relating to the patient population and condition for which the technology is being used.

NA

6.1.2 Describe any equality issues relating to the assessment of the technology that may require special attention.

NA

6.1.3 How will the submission address these issues and any equality issues raised in the scope?

NA

Section B – Clinical evidence

7 Published and unpublished clinical evidence

7.1 Identification of studies

Published studies

7.1.1 Describe the strategies used to retrieve relevant clinical data from the published literature. Exact details of the search strategy used should be provided in section 10, appendix 1.

Stenting of the ureter is not a new technique and it goes beyond the Memokath™051 stent. The outcomes and complications of stent placement have been well described in the literature. High success rates, defined as the ability to re-establish urinary flow, have been reported in general with stenting of ureter. Complications include urinary tract infections, sepsis, stent encrustation, stent obstruction and stent migration.

Most of studies did not focus on comparison rather than the sole results and value of MK51. It is true there are some comparisons with JJ stents, but we have seen that it will not give the complete concept, coverage and description of MK51

A number of articles has been published in peer reviewed journals specifically on Memokath™051 since the introduction of the Memokath™051 stent. Relevant findings from identified articles and abstracts are summarized too.

All identified articles were included to prevent selection bias. Abstracts from congresses were only exceptionally included because they contain limited information.

Pnn Medical A/S has no information or reason to suspect that studies were conducted but not published. Thus, there is no indication of publication bias.

The search strategy was created with the guide for manufacturers and notified bodies on clinical evaluation as a starting point. The search strategy is as follows:

Relevant keywords (“Memokath”, “Memokath 051”, “ureter Stents”,“Metal Stent(s)”,“Ureteric stricture”, “ureteral Stricture”, “Stenting Ureteral obstructions”, “Urinary Stenting”, “Stenting” “Complications”, “Adverse Events”, and “Urinary Stenting”) were identified from the literature mentioned earlier, and from the thesaurus MeSH. MeSH was used to find preferred and related terms in the PubMed-database, medline, , Campbell Urology tenth edition and the Cochrane library.

The search terms were then combined into search “blocks”, each consisting of the search term Memokath, and one or more of the other search terms. The terms were combined using the Boolean operator AND. A wildcard was used with the terms when appropriate.

No limits were placed on the language or type of literature in the search. A limit was placed on the publish date of the literature, specifying that it had to be published in 1991 or later. Then a refine for English language was done

Of the retrieved literature, articles with very small samples (<10 patients) were excluded from the present review.

Overall, there is no reason to believe that the identified data do not reflect current practice.

Unpublished studies

7.1.2 Describe the strategies used to retrieve relevant clinical data from unpublished sources.

Up to best of our knowledge, we do not know any studies or papers which have been finished or unfinished and were not published yet

7.2 Study selection

Published studies

7.2.1 Complete table B1 to describe the inclusion and exclusion criteria used to select studies from the published literature. Suggested headings are listed in the table below. Other headings should be used if necessary.

Table B1 Selection criteria used for published studies

Primary search

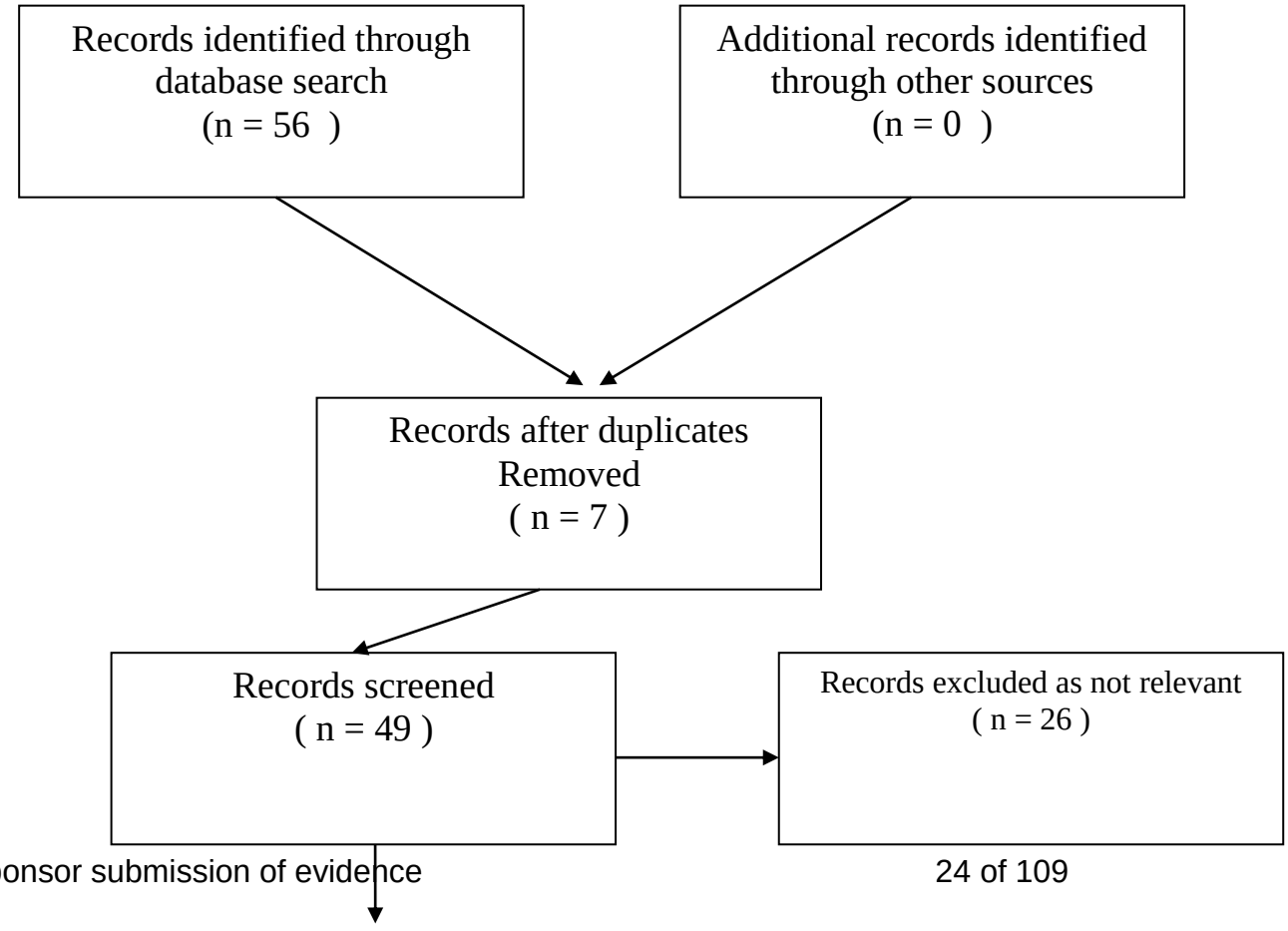
Inclusion criteria	
Population	Adult Patients (over 18) with ureteric obstruction due to benign and malignant reasons
Interventions	Memokath 051
Outcomes	Relief of back pressure, and/or improvement of QOL compared with JJ stents
Study design	None
Language restrictions	English
Search dates	1992-current
Number of patients	More than 20 patients
Exclusion criteria	
Population	Anything other than patients with ureteric obstruction due to both benign and malignant obstruction
Interventions	Anything other than Memokath 051
Outcomes	None
Study design	None
Language restrictions	Non English
Search dates	Prior to 1992
Number of patients	20 or less

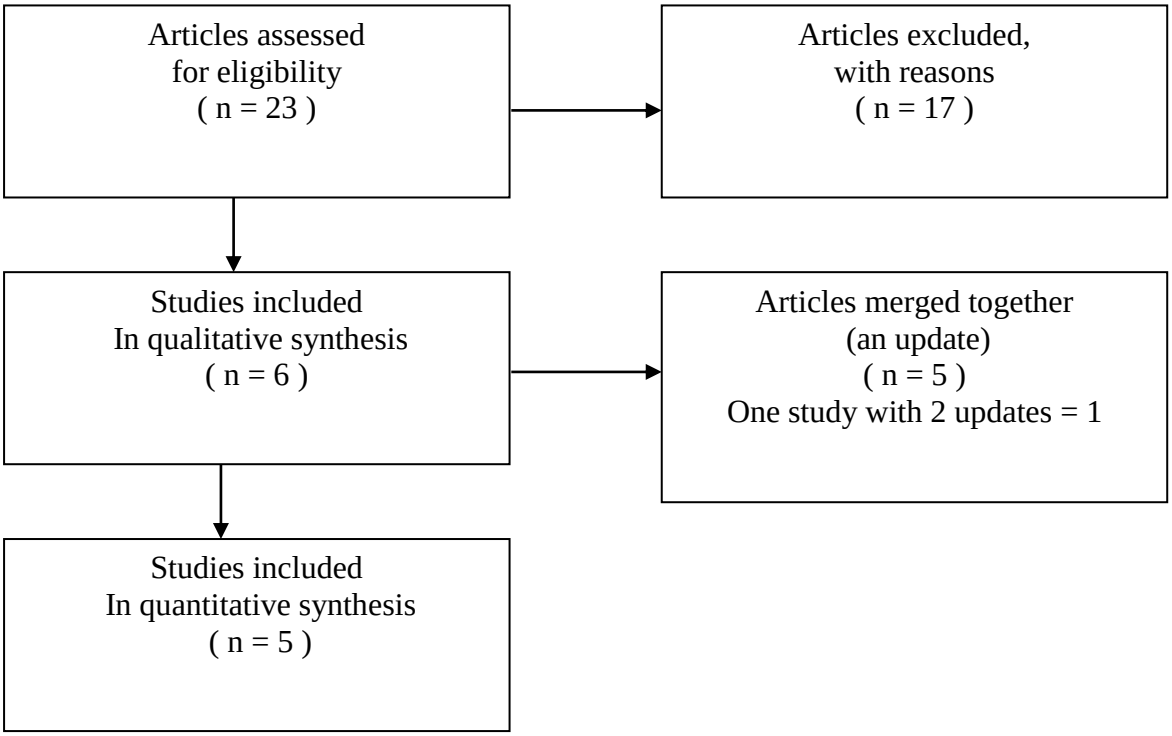
Secondary search: two arm comparison between Memokath 051 and Double J stents

Inclusion criteria	
Population	Adult Patients (over 18) with ureteric obstruction due to benign or malignant reasons with MK 51 insertion compared with JJ stents insertions
Interventions	Memokath 051 Double J stents
Outcomes	Relief of back pressure, and/or improvement of QOL
Study design	Double arm
Language restrictions	English
Search dates	1992-current
Exclusion criteria	
Population	Anything other than patients with ureteric obstruction due to both benign and malignant obstruction treated with both MK51 and JJ stents
Interventions	Anything other than Memokath 051 and JJ stents
Outcomes	None
Study design	Anything other than a double arm study
Language restrictions	Non English
Search dates	Prior to 1992

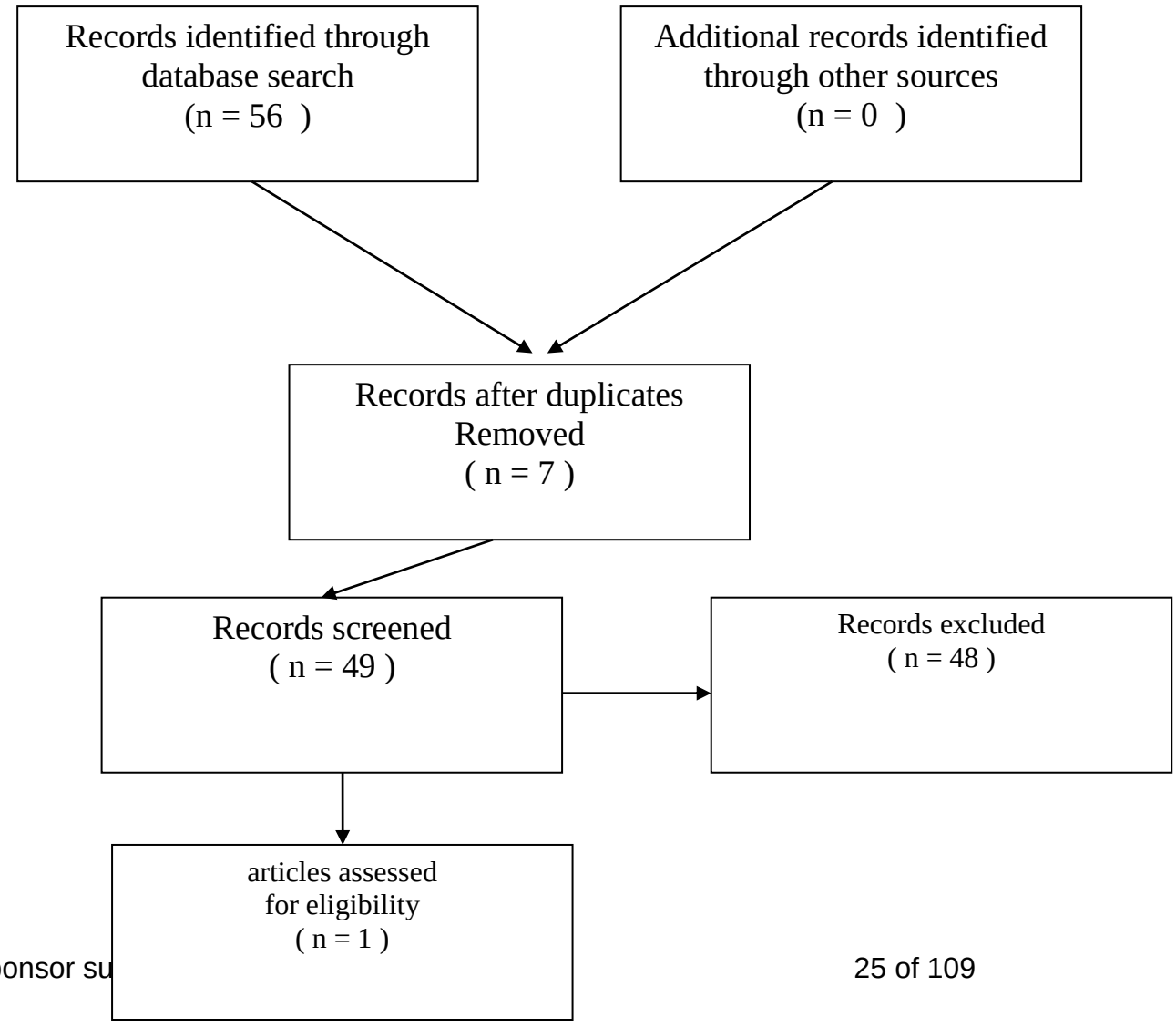
7.2.2 Report the numbers of published studies included and excluded at each stage in an appropriate format.

The following diagram represents the Primary search performed





The following diagram represents the Secondary search performed



Unpublished studies

7.2.3 Complete table B2 to describe the inclusion and exclusion criteria used to select studies from the unpublished literature. Suggested headings are listed in the table below. Other headings should be used if necessary.

No data

7.2.4 Report the numbers of unpublished studies included and excluded at each stage in an appropriate format.

No data

7.3 Complete list of relevant studies

Table B3 List of relevant published studies

Study reference	Population	Intervention	Comparator
A) First version: Kulkarni R, Bellamy EA. A new thermo-expandable shape-memory nickel-titanium alloy stent for the management of ureteric strictures. BJU Int 1999 May;83(7):755-9. B) <u>Update of same study</u> Kulkarni R, Bellamy E. Nickel-titanium shape memory alloy Memokath 051 ureteral stent for managing long-term ureteral obstruction: 4-year experience. J Urol 2001 Nov;166(5):1750-4.	Patients with ureteric obstruction due to malignant and benign strictures with age over 18 years	Memokath 051	Conventional Double J stents as per the common knowledge about them. No second arm
Agrawal S, Brown CT, Bellamy EA, Kulkarni R. The thermo-expandable	Same as above	Memokath 051	Conventional Double J stents as per the

metallic ureteric stent: an 11-year follow-up. BJU Int 2009 Feb 1;2009 Feb 103(3):372-6.			common knowledge about them. No second arm
Papatsoris A, Masood J, El-Husseiny T, Ndirika S, Junaid I, Buchholz NP. A novel long-term thermo-expandable ureteric metal stent: Memokath 051. BJU Int 2007;1-10.	Same as above	Memokath 051	Conventional Double J stents as per the common knowledge about them. No second arm
Characterising stent symptoms associated with a segmental thermo-expandable metallic stents using a validated stent symptom questionnaire Dharmesh Patel, Zafaar Maan et al	Data collection from patients who already inserted the MK51	Memokath 051	Double J stents as per other studies
Drainage of Malignant Extrinsic Ureteral Obstruction Using the Memokath Ureteral Sten Lance A. Mynderse, Mayo Clinic	Double arm non randomised study comparing Memokath051 and JJ stents outcome	Memokath 051	JJ stent

NB: for the studies which have been updated and published over years, we will handle as one study and include the last version in the analysis

Table B4 List of relevant unpublished studies

No data

7.3.1 State the rationale behind excluding any of the published studies listed in tables B3 and B4.

We didn't exclude any. Kulkarni R, Bellamy E study was published twice during follow up period, so we considered it one paper and considered the data of last update only.

7.4 Summary of methodology of relevant studies

7.4.1 Describe the study design and methodology for each of the published and unpublished studies using tables B5 and B6 as appropriate. A separate table should be completed for each study.

Table B5 Summary of methodology for randomised controlled trials

This is not implemented here as we have a lot of studies and non them is randomised

Table B6 Summary of methodology for observational studies

Study name	Kulkarni R, Bellamy E. Nickel-titanium shape memory alloy Memokath 051 ureteral stent for managing long-term ureteral obstruction: 4-year experience. J Urol 2001 Nov;166(5):1750-4.
Objective	4 years experience of using thermo-expandable MK51 stents. 2001
Location	Department of Urology and Radiology, Ashfrord and St. Peters Hospital, Ashford, Middlesex, UK
Design	Observational non randomised therapy, case series
Duration of study	4 years from November 1996 to November 2000
Patient population	Adult Patients with ureteric strictures due to benign and malignant causes
Sample size	37 stents in 28 patients
Inclusion criteria	Adult Patients with ureteric strictures due to benign and malignant causes
Exclusion criteria	NA
Intervention(s) (n =) and comparator(s) (n =)	Memokath 051
Baseline differences	NA
How were participants followed-up (for example, through pro-active follow-up or passively). Duration of follow-up, participants lost to follow-up	IVP, Renal function tests, urine microscopy at 6 weeks after insertion Ultrasound, Renal function tests and urine microscopy were done every three month after. Renography was done only in relevant cases 3-35 month follow up (mean 19.3)
Statistical tests	NA
Primary outcomes (including scoring methods and timings of assessments)	Upper urinary tract decompression proved by radiology, renal function test urine C&S. Urography intra-operative and other post operative
Secondary outcomes (including scoring methods and timings of assessments)	Complications – cost analysis compared with JJ stents

Study name	Agrawal S, Brown CT, Bellamy EA, Kulkarni R. The thermo-expandable metallic ureteric stent: an 11-year follow-up. BJU Int 2009 Feb 1;2009 Feb 103(3):372-6.
Objective	The thermo-expandable metallic ureteric stent: an 11-year follow-up, 2008
Location	Departments of Urology and *Radiology, St Peter's Hospital, Chertsey, UK
Design	Prospective. therapy, case series. Level of evidence 4
Duration of study	11 years

Patient population	Adult Patients with ureteric strictures due to benign and malignant causes,
Sample size	74 stents in 55 patients
Inclusion criteria	Adult Patients with ureteric strictures due to benign and malignant causes, and same patients who failed JJ stents and palliative treatment and where significant comorbidity limited repetitive stent changes
Exclusion criteria	Pre-existing fungal infection. Chronic kidney disease. Diabetes mellitus. Concurrent immunosuppressive therapy. <15% DMSA split renal function on the affected side. Distal strictures involving the ureteric orifice. PUJ strictures
Intervention(s) (n =) and comparator(s) (n =)	Memokath 051
Baseline differences	NA
How were participants followed-up (for example, through pro-active follow-up or passively). Duration of follow-up, participants lost to follow-up	IVP, Renal function tests, urine microscopy at 6 weeks after insertion IVU and mid-stream sample testing at 6 weeks. Serial follow-up imaging 4 - 98 month follow up (mean 16)
Statistical tests	NA
Primary outcomes (including scoring methods and timings of assessments)	Relief of obstruction
Secondary outcomes (including scoring methods and timings of assessments)	Complications Cost analysis

Study name	Papatsoris A, Masood J, El-Husseiny T, Ndirika S, Junaid I, Buchholz NP. A novel long-term thermo-expandable ureteric metal stent: Memokath 051. BJU Int 2007;1-10.
Objective	Investigators have focused on the development of the “ideal” stent that would have friendly manoeuvrability to the user, stability after insertion, radiopacity, resistance to encrustation and infection, efficiency in relieving intrinsic and extrinsic obstruction, long-term patency and low cost. In an attempt to improve upon existing JJ stents, metallic versions were introduced such as the novel long-term indwelling thermo-expandable Memokath 051 stent.

Location	Department of Urology, Barts & The London NHS Trust, London, UK
Design	therapy, case series.
Duration of study	4 years
Patient population	Adult Patients with ureteric strictures due to benign and malignant causes,
Sample size	42 stents in 38 patients
Inclusion criteria	Adult Patients with ureteric strictures due to benign and malignant causes,
Exclusion criteria	NA
Intervention(s) (n =) and comparator(s) (n =)	Memokath 051
Baseline differences	NA
How were participants followed-up (for example, through pro-active follow-up or passively). Duration of follow-up, participants lost to follow-up	clinical examination, U&E's, X-ray KUB and US of kidneys after 2 weeks, 3 months and then every 6 months. IVU and renal isotope studies were performed if needed. In 2 patients a flexible ureteroscopy was performed after 1 year, which did not reveal any ureteric hyperplasia into the Memokath stent.
Statistical tests	NA
Primary outcomes (including scoring methods and timings of assessments)	Relief of obstruction Cost analysis
Secondary outcomes (including scoring methods and timings of assessments)	Complications

Study name	Characterising stent symptoms associated with a segmental thermo-expandable metallic stents using a validated stent symptom questionnaire Dharmesh Patel, Zafaar Maan et al. 2011
Objective	Using Ureter Stent Symptom Questionnaire (USSQ) done by Joshi et al[36] to measure stent related symptoms for MK51 and compare findings
Location	Department of Urology, Barts & The London NHS Trust, London, UK
Design	Prospective data collection, meta analysis
Duration of study	1 year
Patient population	All patients who had undergone MK51 stents over one year
Sample size	23 patients
Inclusion criteria	NA

Exclusion criteria	NA
Intervention(s) (n =) and comparator(s) (n =)	Memokath 051 JJ stents
Baseline differences	NA
How were participants followed-up (for example, through pro-active follow-up or passively). Duration of follow-up, participants lost to follow-up	No follow up 5 patients did not answer the questionnaire
Statistical tests	NA
Primary outcomes (including scoring methods and timings of assessments)	Symptom analysis
Secondary outcomes (including scoring methods and timings of assessments)	

Study name	Mynderse L, Grandberg C. Long term drainage of malignant extrinsic ureteral obstruction secondary to inoperable pelvic or abdominal malignancies using the memokath 051 ureteral stent. 2010. AUA 2010.
Objective	The purpose of this study is to evaluate the safety and efficacy of the Memokath 051 ureteral stent as a long-term temporary and minimally invasive means of providing ureteral drainage in the setting of malignant extrinsic ureteral obstruction secondary to inoperable abdominal or pelvic malignancies.
Location	Department of urology, Mayo clinic Rochester, Minnesota, United States, 55905
Design	Allocation: Non-Randomized Intervention Model: Single Group Assignment Masking: Open Label Primary Purpose: Treatment
Duration of study	Started September 12, 2005 Last updated: June 19, 2014
Patient population	Adult patients who have ureteric obstruction due to extrinsic malignancy
Sample size	15 patients received MK51 10 Patients received JJ stents
Inclusion criteria	Inclusion Criteria: 1. Presence of extrinsic ureteral obstruction a. secondary to inoperable pelvic or abdominal malignancy or b. secondary to changes caused by surgery, chemotherapy, or radiation for pelvic and/or abdominal malignancies who have had >2 standard double J stent exchanges with no prospect of being stent-free

	2. Life expectancy greater than 4 months 3. Adult patient (18 years of age or older) 4. Preoperative medical examination clearing the patient for general anaesthesia 5. No active urinary tract infection by urinalysis and urine culture.
Exclusion criteria	1. Ureteral obstruction of a benign or intrinsic aetiology 2. Lower urinary tract abnormality precluding cystoscopic stent placement 3. Patients with a solitary kidney 4. Patients not willing or unable to receive their post-operative follow-up at the Mayo Clinic in Rochester, Minnesota 5. Pregnant female patient.
Intervention(s) (n =) and comparator(s) (n =)	Memokath 051 = 15 patients JJ stents = 10 stents
Baseline Measures	Please check the below table
How were participants followed-up (for example, through pro-active follow-up or passively). Duration of follow-up, participants lost to follow-up	Active follow up 5 patients did not answer the questionnaire
Statistical tests	NA
Primary outcomes (including scoring methods and timings of assessments)	Treatment
Secondary outcomes (including scoring methods and timings of assessments)	

Baseline measures:

	MK51	JJ stents	Total
Overall participants analysed	14	10	24
Age 1. Less than 18 years 2. 18 to 65 3. More than 65	 0 9 5	 0 0 10	 0 9 15
Gender			

• Male • Female	3 11	3 7	6 18
Region of enrolment USA	14	10	24

7.4.2 Provide details on data from any single study that have been drawn from more than one source (for example a poster and unpublished report) and/or when trials are linked this should be made clear (for example, an open-label extension to randomised controlled trial).

The following study was published as a first version results then republished with more results and more follow up:

First version:

Kulkarni R, Bellamy EA. A new thermo-expandable shape-memory nickel-titanium alloy stent for the management of ureteric strictures. BJU Int 1999 May;83(7):755-9.

Update of same study

Kulkarni R, Bellamy E. Nickel-titanium shape memory alloy Memokath 051 ureteral stent for managing long-term ureteral obstruction: 4-year experience. J Urol 2001 Nov;166(5):1750-4

7.4.3 Highlight any differences between patient populations and methodology in all included studies.

No differences between patient population in all studies except in study Agrawal S, Brown CT, Bellamy EA, Kulkarni R which excluded patients with PUJ as an exclusion criteria.

7.4.4 Provide details of any subgroup analyses that were undertaken in the studies included in section 7.4.1. Specify the rationale and state whether these analyses were pre-planned or post-hoc.

No subgroups

7.4.5 If applicable, provide details of the numbers of patients who were eligible to enter the study(s), randomised, and allocated to each treatment in an appropriate format.

All studies mentioned are not randomised. Numbers of patients are mentioned above

If applicable provide details of and the rationale for, patients that were lost to follow-up or withdrew from the studies. Study reference	Number of patients	Number of those who lost follow up	Reason if any
Kulkarni R, Bellamy E. Nickel-titanium shape memory alloy Memokath 051 ureteral stent for managing long-term ureteral obstruction: 4-year experience. J Urol 2001 Nov;166(5):1750-4.	34 stents in 28 patients	0	8 patients died with the stent functioning insitu but they were included with the mean follow up time
Agrawal S, Brown CT, Bellamy EA, Kulkarni R. The thermo-expandable metallic ureteric stent: an 11-year follow-up. BJU Int 2009 Feb 1;2009 Feb 103(3):372-6.	74 stents in 55 patients	Not mentioned	Not mentioned
Papatsoris A, Masood J, El-Husseiny T, Ndirika S, Junaid I, Buchholz NP. A novel long-term thermo-expandable ureteric metal stent: Memokath 051. BJU Int 2007;1-10.	42 stents in 38 patients	0	
Characterising stent symptoms associated with a segmental thermo-expandable metallic stents using a validated stent symptom questionnaire Dharmesh Patel, Zafaar Maan et al	Data collection from 23 patients	5 patients	Not willing to answer the questionnaire in full
Drainage of Malignant Extrinsic Ureteral Obstruction Using the Memokath Ureteral Stent Lance A. Mynderse, Mayo Clinic	Double arm non randomised study comparing Memokath051 and JJ stents outcome	5 patients were excluded as they didn't answer the questionnaire	JJ stent

7.5 Critical appraisal of relevant studies

7.5.1 Complete a separate quality assessment table for each study. A suggested format for the quality assessment results is shown in tables B7 and B8.

Table B7 Critical appraisal of randomised control trials All studies are not randomised

Table B8 Critical appraisal of observational studies

Table 8.1: Appraisal criteria for suitability applied to the studies in Table 3 (GHTF guideline).

Suitability Criteria	Description	Grading System
Appropriate device	Were the data generated from the device in question?	D1 - Actual device D2 - Comparable device D3 - Other device
Appropriate device Application	Was the device used for the same intended use (e.g., methods of deployment, application, etc.)?	A1 - Same use A2 - Minor deviation A3 - Major deviation
Appropriate patient group	Were the data generated from a patient group that is representative of the intended treatment population (e.g., age, sex, etc.) and clinical condition (i.e., disease, including state and severity)?	P1 - Applicable P2 - Limited P3 - Different population
Acceptable report / data collation	Do the reports or collations of data contain sufficient information to be able to undertake a rational and objective assessment?	R1 - High quality R2 - Minor deficiencies R3- Insufficient information

Table 8.2: Continued sample appraisal criteria for data contribution applied to the studies in Table 1.

Data Contribution Criteria	Description	Grading System
Grading System	Was the design of the study appropriate?	T1 - Yes T2 – No
Outcome measures	Does the outcome measures reported reflect the intended performance of the device?	O1 – Yes O2 - No
Follow up	Is the duration of follow-up long enough to assess whether	F1 – Yes F2 – No

	duration of treatment effects and identify complications?	
Statistical significance	Has a statistical analysis of the data been provided and is it appropriate?	S1 – Yes S2 – No
Clinical significance	Was the magnitude of the treatment effect observed clinically significant?	C1 – Yes C2 – No

Table 8.3: Overview of publications specifically on Memokath^{TM}051

Author	**Number studied patients**	**Appraisal**	**Comments/ Limitations**
Kulkarni, R and Bellamy, E. 2001	28 (prospective study)	D1, A1, P1, R1,T1, O1, F1, S2,C:NA	Descriptive study, No comparator, Limited statistical considerations
Agrawal, S et al. 2008	55 (prospective study)	D1, A1, P1, R1,T1, O1, F1, S2,C:NA	Decent number of patients included. Descriptive study, No comparator, Limited statistical considerations.
Papatsoris, A et al. 2007	28 (prospective)	D1, A1, P:NA, R1,T1, O1, F1, S2,C:NA	Descriptive study, No comparator, Limited statistical considerations.
Maan Z et al. 2010	23(questionnaire)	D1, A1, P1, R1,T1, O1, F1, S1,C1.	Decent size study based upon validated questionnaire.
Mynderse, L et al. 2010 (31) See: **Error! Reference source not found.**	15 (prospective study)	D1, A1, P1, R1,T1 O1, F1, S2,C:NA	Limited number of patients. Congress presentation; Abstract

7.6 Results of the relevant studies

7.6.1 Complete a results table for each study with all relevant outcome measures pertinent to the decision problem. A suggested format is given in table B9.

Table B9 Outcomes from published and unpublished studies

Study name		Kulkarni R, Bellamy E. Nickel-titanium shape memory alloy Memokath 051 ureteral stent for managing long-term ureteral obstruction: 4-year experience. J Urol 2001 Nov;166(5):1750-4.
Size of study groups	**Treatment**	37 stents in 28 patients
Study duration	**Time unit**	4 years
Folllow up		3 -35 months. Mean 19.3 Month
Type of analysis	**Intention-to -treat/per protocol**	Treatment
Outcome		
immediate outcome postoperative		Upper urinary trach decompression happened in all patients except two due to non optimal stent positioning. The two stents were replaced in the same session and decompression happened
Primary outcome		At a mean follow-up of 19.3 months, 15 stents were in place and functioning in 13 patients. Eight patients had died from their primary disease with functioning stents in place. Thereby, the success rate was considered to be 75% in this study
AD HOC Outcome		4 cases stent migrated after treatment of underlying malignancy. Upper urinary tract decompression was maintained due to resolve of stricture
Comments		• By comment of the publisher: 21 patients benifited from stent insertion without the side effects usually associated with JJ stents • No statistics were done due to low number of patients, so the paper used the real numbers
Conclusion		We have placed MK51 stent for a wide variety of indications with a reasonably good results. We believe it represents an alternative in patients with long term uretertic obstruction, which is particulary important in those with malignant disease in whom long term survival or cure is expected We believe that those patients have benefited by improved quality of life due to decreased hospital admissions and decreased stent related complications. The

	stent also proved promising for managing some benign strictures

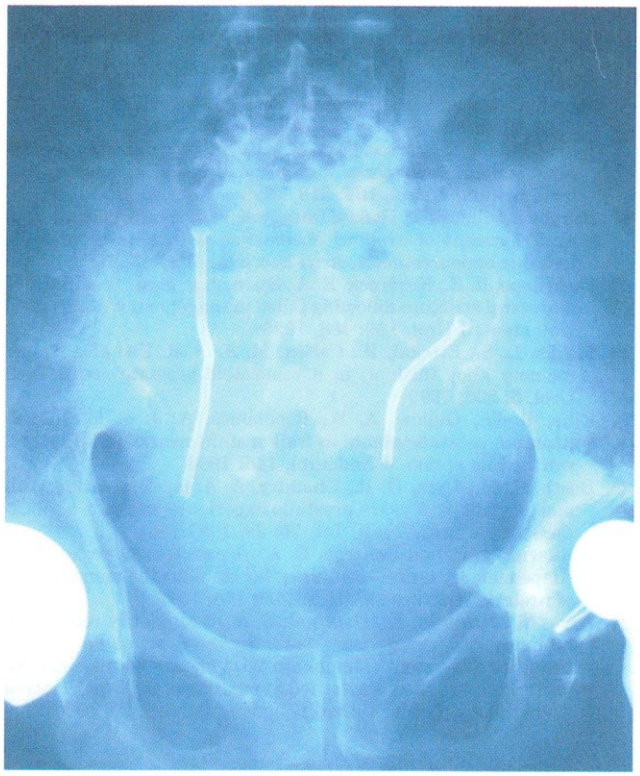


FIG. 5. Bilateral, simultaneously inserted stents

as well as in the delivery system since the original version was used in November 1996. The original design had a shaft diameter of 9.5Fr and its upper fluted end expanded to 14Fr.

TABLE 1. *Indications for stent insertion*

	No. Pts.
Malignant disease:	
Recurrent colorectal/anal Ca	6
Prostate Ca retroperitoneal spread	1
Breast Ca retroperitoneal spread	2
Bladder transitional cell Ca	2
Lymphoma	1
Vaginal Ca pelvic extension	1
Vulval Ca pelvic extension	1
Cervical Ca	3
Uterine body Ca	1
Total	18
Benign disease:	
Ischemic (ureteroileal)	2
Post-radiotherapy	2
Iatrogenic	1
Benign retroperitoneal fibrosis	1
Post-transplant stricture	1
Ureteropelvic junction obstruction	1
Endometriosis	1
Idiopathic	1
Total	10

TABLE 2. *Current status*

Status	No. Pts.	No. Stents
Functional stent:		
Alive	13	15 (1 bilat., 1 reinsertion)
Dead	8	13 (2 bilat., 3 migrations)
Totals	21	28
No. stent:		
Resolved stricture	4	4
Cystectomy, nephroureterectomy	1	2
Nephrectomy	1	2
Progressive renal failure	1	1
Totals	7	9

Study name		Agrawal S, Brown CT, Bellamy EA, Kulkarni R. The thermo-expandable metallic ureteric stent: an 11-year follow-up. BJU Int 2009 Feb 1;2009 Feb 103(3):372-6.
Size of study groups	**Treatment**	74 stents in 55 patients
Study duration	**Time unit**	11 years
Folllow up		3 -35 months. Mean 16 Month (4-98)
Type of analysis	**Intention-to-treat/per protocol**	Treatment, prospective data collection
Outcome		
immediate outcome postoperative		Imaging after insertion showed normal or improved functional drainage in all but three patients
Primary outcome		• In 28 patients, the obstruction was caused by malignancy, whereas in 27 patients it was caused by benign disease. • No tissue in-growth (a problem with other metallic stents) was reported in the present series • 7 patients had functioning stents at the end of study • 29 patients died with the stent functioning insitu • 18 patients showed complications (will be discussed later, 14 of them had re-insertion
AD HOC Outcome		• Cost is additional important issue. The Memokath 051 stent costs £1495 (1945 Euro) compared with £80 (108 Euro) for a conventional JJ stent. In our centre standard JJ stenting, including hospital admission, costs £3220, and the equivalent Memokath 051 cost is £6295. However, these costs are offset if the Memokath stent remains in situ for > 8–12 months. • An added benefit might be an overall reduction in inpatient stay and the reduced morbidity of repeated procedures
Comments		• Data were collected prospectively from all patients who had a Memokath™051 ureteral stent inserted between November 1996 and November 2007 • All stents were inserted by the same surgeon following a standard protocol • The mean hospital stay was 1.43 (0-7) days. • Indications for metallic stenting included primary stenting for malignancy, failed conventional open and endoscopic techniques, palliation, and where significant comorbidity limited repetitive stent changes.

Conclusion	In conclusion, a clear benefit from the Memokath stent has emerged over the past 11 years. However, there are still limitations and patient selection remains paramount. Our current protocol and relative contraindications are shown in Table 4. Overall, the thermo-expandable metallic Memokath 051 ureteric stent offers effective and durable long-term relief from ureteric obstruction, and is a safe alternative to conventional JJ stenting. Further studies are required to evaluate stricture resolution and the emerging role in palliation and the primary management of strictures.

TABLE 1 The indications for stent insertion

Stricture (*N* patients)			
Malignant		Recurrent benign	
Colorectal carcinoma	10	Ileal conduit	4
Carcinoma of anal canal	2	Radiation-induced	8
Prostate adenocarcinoma	2	Iatrogenic	5
TCC bladder	2	PUJ obstruction	2
Carcinoma of cervix	3	Endometriosis	2
Carcinoma of vagina	1	Retroperitoneal fibrosis	2
Carcinoma of vulva	1	Transplant	1
Carcinoma of uterus	1	Idiopathic	1
Carcinoma of breast (retroperitoneal spread)	2	After abdominal aortic aneurysm	2
Carcinoma of pancreas	1		
Lymphoma	2		
TCC ureter	1		
Total	28		27

TABLE 4 A summary of indications, contraindications and recommended protocol for the Memokath stent

Procedure	Details
Protocol	Preoperative assessment of renal function (urea and electrolytes, DMSA) and mid-stream urine sample testing.
	Evaluate the stricture ch3aracteristics; IVU, retrograde study.
	Stent insertion under general anaesthesia.
	Gentamicin during insertion and 5 days of norfloxacin.
	IVU and mid-stream sample testing at 6 weeks.
	Serial follow-up imaging.
Indications	Primary stenting for malignancy.
	Failed conventional open and endoscopic techniques.
	Palliation.
	In patients who have significant comorbidity limiting repetitive stent changes.
Relative contraindications	Pre-existing fungal infection.
	Chronic kidney disease.
	Diabetes mellitus.
	Concurrent immunosuppressive therapy.
	<15% DMSA split renal function on the affected side.
	Distal strictures involving the ureteric orifice.
	PUJ strictures

Study name		Papatsoris A, Masood J, El-Husseiny T, Ndirika S, Junaid I, Buchholz NP. A novel long-term thermo-expandable ureteric metal stent: Memokath 051. BJU Int 2007;1-10.
Size of study groups	**Treatment**	55 stents in 38 patients
Study duration	**Time unit**	44 month
Folllow up		17 month. Mean 16 Month (1-44)
Type of analysis	**Intention-to-treat/per protocol**	Treatment, personal clinical experience
Outcome		
immediate outcome postoperative		Imaging after insertion showed normal or improved functional drainage in all patients
Primary outcome		• In 36 (86%) cases no Memokath exchange took place • while in 3 (8%) cases we performed one exchange, in 1 (2%) case two exchanges and in 2 (4%) cases we performed three exchanges • A total of 16 complications were revealed after the insertion of the 55 Memokaths (29%) (will be discussed later)
AD HOC Outcome		• In 2 patients a flexible ureteroscopy was performed after 1 year, which did not reveal any ureteric hyperplasia into the Memokath stent • 8 patients showed spontaneous resolution of stricture after average of 8 month • For the UK health system, we have developed a cost-comparison model between JJ and Memokath stent insertion. o A JJ stent insertion including all costs (material, hospital services, theatre, recovery etc.) o comes to ~ 3000 €. Assuming 6-monthly stent changes and 2 outpatient follow-ups with Xray per year, the total costs to treat a ureteric stricture with JJ stents is ~ 6600 €/ year. o Insertion of a Memokath 051 TM requires roughly the same infrastructure. Additional costs arise from the stent itself at ~ 2300 €. o Therefore, Memokath 051 insertion comes to ~ 5300 €. Together with 3 follow-up visits in the first year with Xray the total cost is ~ 5700€. o Therefore, in the first year, the Memokath 051 is with ~ 900 €

	slightly less expensive than treatment with regular exchanges of JJ stent. o However, from the 2nd year Memokath patients will only require 2 yearly follow-up visits with X-ray KUB at ~ 500 €. o Therefore, from the 2nd year after stent insertion, the annual savings through Memokath 051 TM is ~ 6000 €. o These calculations do not take into account any time off work or complications and resulting costs
Comments	• The average hospital stay was 1.5 days and patients were discharged with antibiotics for 5 days • 42 renal units in 38 patients (20 females and 18 males), aged 23-84 years (median age 55.7) with Memokath 051 TM. Strictures were benign in 29 cases and malignant in 9 cases (table 1), and bilateral in 4 patients • follow-up included clinical examination, U&E's, X-ray KUB and US of kidneys after 2 weeks, 3 months and then every 6 months. IVU and renal isotope studies were performed if needed
Conclusion	The Memokath051TM stent seems to be an attractive cost effective treatment option for both benign and malignant ureteric strictures. It has the advantages of immediate decompression and relief of obstructive uropathy symptoms. It bears minimal risk for bladder irritation, reflux and flank pain. Insertion, removal and/or exchange of the Memokath051TM stent is easy and it can be easily removed with a balloon catheter even if it migrated into the kidney in contrast with previously used mesh metallic stents. It is well tolerated by patients, who do not experience lower urinary tract symptoms or loin pain. With the Memokath 051TM stent there is no need for frequent replacement such as every three-six months. From our own experience, we discourage its usage in active stone formers as well as the use of

	holmium laser in case of Memokath encrustation. Interestingly, a 20% rate of spontaneous stricture resolution could be related with the insertion of the Memokath stent, but further studies are warranted to prove this

Benign strictures (29)

○	Iatrogenic (post stone manipulation)	4
○	Gynaecologic injury	3
▪	Uretero-vaginal fistula	2
○	Pelvic inflammatory disease (BIL)	1
○	Retroperitoneal/ para-aortic fibrosis	2
○	Pelvic endometriosis	1
○	Crohn's disease	1
○	Simple (idiopathic) strictures	12
▪	in transplant kidney	1
○	Vesico-ureteric anastomosis stricture	5
▪	in transplant kidneys	4
▪	Bilateral after re-implantation	1
○	Single kidneys	3
○	Bilateral strictures	4

Malignant strictures (9)

○	Rectum CA	2
○	Cervix CA	3
○	Prostate CA	2
○	Colon CA	1
○	Breast CA (retroperitoneal lymphadenopathy)	1

Study name		Characterising stent symptoms associated with a segmental thermo-expandable metallic stents using a validated stent symptom questionnaire Dharmesh Patel, Zafaar Maan et al
Size of study groups	**Treatment**	23 patients
Study duration	**Time unit**	One year
Folllow up		Not a follow up study. data collection and analysis
Type of analysis	**Intention-to-treat/per protocol**	Data collection. Comparison according to USSQ
Outcome		
immediate outcome postoperative		ND
Primary outcome		See below tables
AD HOC Outcome		ND
Comments		ND
Conclusion		Also study population is small, our results indicate that MK051 stents are well tolerated by patients in terms of quality of life. The study provides important information about stent related symptoms

Table 2. Urinary symptom domain

Patient	Gender	Age	Reason for stent	Length, Stent mm	position	Side	Frequency of urine	Nocturia	Urgency	Urge incontinence	Incontinence	Residual	Dysuria	Frequency of hematuria	Severity of hematuria	Bothersome	Overall urinary symptoms	Urinary symptom index
1	male	81	after abdominal aortic aneurysm	30	lower ureter	left	3 hourly	1	never	occasionally	never	never	never	never	no blood	not at all	delighted	15
2	male	53	repair retroperitoneal fibrosis	r: 150, l: 100	r: upper & mid, l: mid	bilateral	–	3	never	never	never	occasionally	most times	most times	heavily blood stained	moderate	pleased	–
3	male	79	surgery diverticulitis	r: 150, l: 150	r: upper & mid, l: mid & lower	bilateral	hourly	>4	never	never	never	never	occasionally	never	no blood	moderate	pleased	24
4	male	68	radiation	100	mid ureter	right	hourly	>4	some times	some times	occasionally	some times	some times	never	no blood	quite a bit	unhappy	41
5	male	44	fibrosis horseshoe	200	whole ureter	left	4 hourly	>4	all times	some times	all times	some times	all times	all times	clots	quite a bit	mostly dissatisfied	50
6	male	37	kidney recurrent stone disease	60	mid ureter	left	<1 hourly	>4	all times	all times	all times	all of the time	all times	most times	slightly blood stained	extreme	terrible	60
7	male	82		100	lower ureter	right	4 hourly	none	never	never	never	never	never	never	no blood	not at all	delighted	12
8	male	75	prostate cancer	100	lower ureter	left	3 hourly	>4	never	never	never	never	occasionally	never	no blood	moderate	mostly satisfied	24
9	male	76	prostate cancer	30	lower ureter	right	4 hourly	2	sometimes	sometimes	never	occasionally	never	never	no blood	little bit	mostly satisfied	24
10	male	83	prostate cancer	r: 60, l: 30	r: lower, l: lower	bilateral	2 hourly	3	never	never	occasionally	never	sometimes	sometimes	slightly blood stained	little bit	pleased	26
11	male	71		60	lower ureter	left	3 hourly	none	never	never	never	sometimes	never	never	no blood	not at all	pleased	17
12	female	42	idiopathic	150	upper ureter	left	3 hourly	>4	sometimes	most times	sometimes	all times	never	never	no blood	quite a bit	terrible	43
13	female	47	idiopathic radiation	100	lower ureter	right	2 hourly	1	occasionally	occasionally	never	occasionally	never	never	no blood	not at all	delighted	18
14	female	40	fibrosis recurrent stone	100	upper ureter	right	hourly	2	occasionally	occasionally	occasionally	never	never	never	no blood	not at all	pleased	22
15	female	35	disease radiation fibrosis	100	lower ureter	left	3 hourly	3	occasionally	never	never	occasionally	sometimes	sometimes	slightly blood stained	quite a bit	unhappy	37
16	female	60	radiation fibrosis	r: 150, l: 30	r: mid & ureter, l: lower	bilateral	3 hourly	2	sometimes	never	never	–	never	never	no blood	not at all	–	–
17	female	29	pelviureteric junction	150	upper ureter	right	4 hourly	2	never	never	never	sometimes	never	never	no blood	little bit	mostly satisfied	21
18	female	55	double kidney lymphoma	60	lower ureter	right	hourly	3	most times	most times	all times	most times	never	most times	slightly blood stained	quite a bit	terrible	50

Most times: >2/3 of time; Sometimes: 1/3–2/3 time; Occasionally: <1/3 time.

Table 3. Pain domain

Patient	Gender	Age	Pain	Activities	Sleep	Pain on voiding	Loin pain	Analgesia	Pain	Pain on light	Pain with heavy
1	male	81	no	–	–	–	–	–	–	none	don't do for other
2	male	53	no	–	–	–	–	–	–	none	no difficulty
3	male	79	no	–	–	–	–	–	–	none	abstain due to stent
4	male	68	yes	basic activity	occasionally	sometimes	no	occasionally	quite a bit	none	some difficulty
5	male	44	yes	pain at rest	most times	all times	–	all times	extreme	much	–
6	male	37	yes	pain at rest	all times	all times	yes	all times	extreme	some	much difficulty
7	male	82	no	–	–	–	–	–	–	none	no difficulty
8	male	75	no	–	–	–	–	–	–	–	–
9	male	76	no	–	–	–	–	–	–	none	don't do for other
10	male	83	no	–	–	–	–	–	–	none	much difficulty
11	male	71	no	–	–	–	–	–	–	none	no difficulty
12	female	42	yes	moderate activity	most times	sometimes	yes	sometimes	moderate	some	some difficulty
13	female	47	no	–	–	–	–	–	–	none	abstain due to stent
14	female	40	yes	no pain	sometimes	never	no	sometimes	–	none	no difficulty
15	female	35	yes	vigorous activity	occasionally	occasionally	yes	sometimes	moderate	none	no difficulty
16	female	60	no	–	–	–	–	–	–	some	some difficulty
17	female	29	no	–	–	–	–	–	–	none	some difficulty
18	female	55	yes	pain at rest	most times	occasionally	yes	all times	quite a bit	some	much difficulty

Most times: >2/3 of time; Sometimes: 1/3–2/3 time; Occasionally: <1/3 time.

Table 4. Social life and sex life domain

Patient	Gender	Age	Lethargy	Calm	Social	Help	Sex life	No sex life	No sex life reason	Dyspareunia	Sex satisfaction
1	male	81	occasionally	all times	all times	never	no	–	–	–	–
2	male	53	sometime	most	all times	never	yes	–	–	mild	satisfied
3	male	79	occasionally	sometime	all times	most times	no	–	–	–	–
4	male	68	never	most	most	never	no	after stent	no attempt (other reason)	–	–
5	male	44	sometime	never	never	never	yes	–	–	severe	dissatisfied
6	male	37	all times	never	occasionally	all times	no	before stent	–	–	–
7	male	82	occasionally	never	all times	never	no	–	–	–	–
8	male	75	–	–	–	–	no	before stent	no attempt (other reason)	–	–
9	male	76	sometime	most	sometime	sometime	no	–	–	–	–
10	male	83	sometime	some time	all times	most times	no	before stent	–	–	–
11	male	71	never	all times	–	never	yes	–	–	no	satisfied
12	female	42	sometime	occasionally	sometime	sometime	no	before stent	no attempt (other reason)	–	–
13	female	47	never	all times	all times	never	yes	–	–	severe	satisfied
14	female	40	most times	most	most	occasionally	yes	–	–	none	unsure
15	female	35	occasionally	most	most	occasionally	yes	–	–	mild	dissatisfied
16	female	60	all times	sometimes	occasionally	most times	no	–	–	–	–
17	female	29	sometime	sometimes	most	occasionally	yes	–	–	mild	satisfied
18	female	55	all times	occasionally	occasionally	sometimes	no	before stent	no attempt (other reason)	–	–

Most times: >2/3 of time; Sometimes: 1/3–2/3 time; Occasionally: <1/3 time.

Table 5. Employment domain

Patient	Gender	Age	Employment	Bed	Reduction of activities	Employment type	Breaks	Workstyle	Regular hours
1	male	81	not working (other reason)	–	–	–	–	–	–
2	male	53	full-time	1	2	employee	never	all of the time	never
3	male	79	retired (another reason)	0	–	–	–	–	–
4	male	68	retired (ill-health)	14	–	–	–	–	–
5	male	44	part-time	–	30	employee	all of the time	never	all the time
6	male	37	not working (other reason)	14	14	–	–	–	–
7	male	82	not working (other reason)	–	–	–	–	–	–
8	male	75	–	–	–	–	–	–	–
9	male	76	retired (another reason)	1	1	–	–	–	–
10	male	83	retired (another reason)	–	–	–	–	–	–
11	male	71	not working (other reason)	0	0	–	–	–	–
12	female	42	part-time	5	11	employee	most of the time	occasionally	never
13	female	47	full-time	1	6	employee	never	all of the time	all the time
14	female	40	unemployed (looking for work)	–	–	–	–	–	never
15	female	35	full-time	5	10	self employed	occasionally	most of the time	most
16	female	60	not working (other reason)	–	–	–	–	–	–
17	female	29	full-time	1	3	employee	never	never	all the time
18	female	55	full-time	–	–	employee	most of the time	occasionally	sometimes

Most times: >2/3 of time; Sometimes: 1/3–2/3 time; Occasionally: <1/3 time; Bed: number of days in bed if time taken off work; Reduction of activities: number of hours where activity was less than usual.

Table 6. Additional symptoms domain

Patient	Gender	Age	UTI	Antibiotics	HCP	Hospital	Future stent
1	male	81	never	none	never	never	delighted
2	male	53	never	none	never	never	pleased
3	male	79	sometimes	none	never	never	mixed feelings
4	male	68	sometimes	>3	–	>3	mixed feelings
5	male	44	all of the time	none	>3	>3	unhappy
6	male	37	all of the time	>3	>3	once	terrible
7	male	82	never	none	never	never	delighted
8	male	75	never	none	never	never	mostly satisfied
9	male	76	never	none	never	never	mixed feelings
10	male	83	occasionally	1	never	never	mostly satisfied
11	male	71	never	none	once	never	pleased
12	female	42	most of the time	>3	>3	twice	unhappy
13	female	47	occasionally	1	once	never	pleased
14	female	40	never	none	–	never	mixed feelings
15	female	35	sometimes	>3	>3	twice	mixed feelings
16	female	60	most of the time	>2	never	never	delighted
17	female	29	occasionally	1	once	once	mostly satisfied
18	female	55	sometimes	>3	>3	>3	mixed feelings

Most times: >2/3 of time; Sometimes: 1/3–2/3 time; Occasionally: <1/3 time; Antibiotics: number of prescriptions; HCP: number of times sought help from health care professional; Hospital: number of hospital visits.

Study name		Mynderse L, Grandberg C. Long term drainage of malignant extrinsic ureteral obstruction secondary to inoperable pelvic or abdominal malignancies using the memokath 051 ureteral stent. 2010. AUA 2010.	
Size of study groups	**Treatment**	15 patients received MK51 10 Patients received JJ stents	
Study duration	**Time unit**	Started September 12, 2005 Last updated: June 19, 2014	
Folllow up		Baseline to 59 month	
Type of analysis	**Intention-to-treat/per protocol**	Treatment, comparison between MK051 and JJ outcomes	
Outcome			
Mean stent Dwell time		MK 1-59 month mean 17	JJ 2.56 to 5.36 mean 3.97

7.6.2 Justify the inclusion of outcomes in table B9 from any analyses other than intention-to-treat.

No Data

7.7 Adverse events.

7.7.1 Using the previous instructions in sections 7.1 to 7.6, provide details of the identification of studies on adverse events, study selection, study methodologies, critical appraisal and results.

No Data

7.7.2 Provide details of all important adverse events reported for each study. A suggested format is shown in table B10.

Table B10 Adverse events across patient groups

Kulkarni R, Bellamy E. Nickel-titanium shape memory alloy Memokath 051 ureteral stent for managing long-term ureteral obstruction: 4-year experience. J Urol 2001 Nov;166(5):1750-4.		
Total number of patients	37 stents in 28 patients	Some bilateral insertions
Immediate side effects	0	

Immediate non complete resolution of obstruction	2	Replacement with a longer stent was done in same session. Then complete evacuation happened
Migration	3 stents	2 patients replacement 1 patient didn't need as ureter continued to be potent
Re blockage of ureter	1	Replaced with a longer stent to cover the new formed stricture due to advancement of cancer

Agrawal S, Brown CT, Bellamy EA, Kulkarni R. The thermo-expandable metallic ureteric stent: an 11-year follow-up. BJU Int 2009 Feb 1;2009 Feb 103(3):372-6.		
Total number of patients	74 stents in 55 patients	Some bilateral insertions
Immediate side effects • Urinary extravasation • Poor expansion • Equipment failure	 1 1 1	All cases have been treated by replacement of stent
Stent migration	13	
Encrustation	2 stents	
Infection	2	Treated by antibiotics
Re-blockage due to stricture progression	3	Re-insertion of a longer stent was done

expandable ureteric metal stent: Memokath 051. BJU Int 2007;1-10.		
Total number of patients	42 stents in 38 patients	Some bilateral insertions
Immediate side effects	0	
Stent migration	6 (11%)	
Encrustation	4 stents (7%)	
Infection	6	Treated by antibiotics

Characterising stent symptoms associated with a segmental thermo-expandable metallic stents using a validated stent symptom questionnaire Dharmesh Patel, Zafaar Maan et al. 2011		
Total number of patients	23	
Immediate side effects	0	
Dysiuria	28%	
Frequency	6%	
Nocturia	43%	
Urgency	72%	
Urge incontinence	43%	
Heamaturia	29%	
Lethargy	23%	

Comment: most of the above side effects was noticed over the path of having the stent inserted but not all over the indwelling time

Mynderse L, Grandberg C. Long term drainage of malignant extrinsic ureteral obstruction secondary to inoperable pelvic or abdominal malignancies using the memokath 051 ureteral stent. 2010. AUA 2010.		
Total number of patients	23	

Serious Adverse Events

	Memokath 051 Ureteral Stent	JJ Stent
Total, Serious Adverse Events		
# participants affected / at risk	12/14 (85.71%)	2/10 (20.00%)
Blood and lymphatic system disorders		
Hypokalemia †		
# participants affected / at risk	1/14 (7.14%)	0/10 (0.00%)
# events	1	0
Acute Chronic Anemia †		
# participants affected / at risk	1/14 (7.14%)	0/10 (0.00%)
# events	1	0
Pulmonary embolism †		
# participants affected / at risk	1/14 (7.14%)	0/10 (0.00%)
# events	1	0
Cardiac disorders		
Carcinoid heart disease †		
# participants affected / at risk	1/14 (7.14%)	0/10 (0.00%)
# events	1	0
Heart failure related to underlying disease †		
# participants affected / at risk	1/14 (7.14%)	0/10 (0.00%)
# events	1	0
Gastrointestinal disorders		
Surgery related to underlying disease †		
# participants affected / at risk	1/14 (7.14%)	0/10 (0.00%)
# events	1	0
Bowel Obstruction †		

# participants affected / at risk	4/14 (28.57%)	0/10 (0.00%)
# events	4	0
General disorders		
Dehydration † [2]		
# participants affected / at risk	1/14 (7.14%)	0/10 (0.00%)
# events	1	0
Hospitalization for sepsis †		
# participants affected / at risk	0/14 (0.00%)	2/10 (20.00%)
# events	0	2
Injury, poisoning and procedural complications		
Stent encrustation/obstruction †		
# participants affected / at risk	4/14 (28.57%)	0/10 (0.00%)
# events	6	0
Hospitalization for fractured ankle †		
# participants affected / at risk	1/14 (7.14%)	0/10 (0.00%)
# events	1	0
Trouble with stent placement due to faulty guide wire †		
# participants affected / at risk	1/14 (7.14%)	0/10 (0.00%)
# events	1	0
Renal and urinary disorders		
Ureteral Obstruction †		
# participants affected / at risk	7/14 (50.00%)	0/10 (0.00%)
# events	7	0
Hematuria †		
# participants affected / at risk	1/14 (7.14%)	0/10 (0.00%)
# events	2	0
Hospitalization due to disease progression †		
# participants affected / at risk	3/14 (21.43%)	0/10 (0.00%)
# events	3	0
Edema of ureter †		
# participants affected / at risk	2/14 (14.29%)	0/10 (0.00%)

# events	2	0
Acute renal failure † [2]		
# participants affected / at risk	1/14 (7.14%)	0/10 (0.00%)
# events	1	0
Hydroureteronephrosis †		
# participants affected / at risk	3/14 (21.43%)	0/10 (0.00%)
# events	3	0
Atrophy of the kidney †		
# participants affected / at risk	1/14 (7.14%)	0/10 (0.00%)
# events	1	0
Nephrectomy †		
# participants affected / at risk	0/14 (0.00%)	1/10 (10.00%)
# events	0	1
Partial ureterectomy †		
# participants affected / at risk	0/14 (0.00%)	1/10 (10.00%)
# events	0	1
Hospitalization for urinary tract infection (UTI) †		
# participants affected / at risk	0/14 (0.00%)	1/10 (10.00%)
# events	0	1
Respiratory, thoracic and mediastinal disorders		
Acute respiratory failure †		
# participants affected / at risk	1/14 (7.14%)	0/10 (0.00%)
# events	1	0
Surgical and medical procedures		
Stent migrated into bladder †		
# participants affected / at risk	1/14 (7.14%)	0/10 (0.00%)
# events	2	0

† Events were collected by systematic assessment

[2] due to bowel obstruction

Other Adverse Events

	Memokath 051 Ureteral Stent	JJ Stent

Total, Other (not including serious) Adverse Events		
# participants affected / at risk	10/14 (71.43%)	8/10 (80.00%)
Cardiac disorders		
Essential hypertension †		
# participants affected / at risk	1/14 (7.14%)	0/10 (0.00%)
# events	1	0
Gastrointestinal disorders		
Abdominal pain †		
# participants affected / at risk	4/14 (28.57%)	1/10 (10.00%)
# events	4	1
Iliac pain †		
# participants affected / at risk	0/14 (0.00%)	1/10 (10.00%)
# events	0	1
Acid reflux †		
# participants affected / at risk	1/14 (7.14%)	0/10 (0.00%)
# events	1	0
Ascites †		
# participants affected / at risk	1/14 (7.14%)	0/10 (0.00%)
# events	1	0
Constipation †		
# participants affected / at risk	1/14 (7.14%)	0/10 (0.00%)
# events	1	0
Diarrhea †		
# participants affected / at risk	2/14 (14.29%)	0/10 (0.00%)
# events	2	0
Difficulty eating †		
# participants affected / at risk	1/14 (7.14%)	0/10 (0.00%)
# events	1	0
Nausea †		
# participants affected / at risk	8/14 (57.14%)	0/10 (0.00%)
# events	10	0

Vomiting †		
# participants affected / at risk	6/14 (42.86%)	0/10 (0.00%)
# events	7	0
General disorders		
Chest pain †		
# participants affected / at risk	1/14 (7.14%)	0/10 (0.00%)
# events	1	0
Groin pain †		
# participants affected / at risk	3/14 (21.43%)	3/10 (30.00%)
# events	3	5
Left lower quadrant pain †		
# participants affected / at risk	3/14 (21.43%)	0/10 (0.00%)
# events	4	0
Right lower quadrant pain †		
# participants affected / at risk	0/14 (0.00%)	1/10 (10.00%)
# events	0	3
Chills †		
# participants affected / at risk	1/14 (7.14%)	1/10 (10.00%)
# events	1	1
Deydration †		
# participants affected / at risk	1/14 (7.14%)	0/10 (0.00%)
# events	1	0
Flu like symptoms †		
# participants affected / at risk	3/14 (21.43%)	1/10 (10.00%)
# events	4	1
Fever †		
# participants affected / at risk	3/14 (21.43%)	2/10 (20.00%)
# events	4	2
Fragility †		
# participants affected / at risk	2/14 (14.29%)	0/10 (0.00%)
# events	2	0
Headache †		
# participants affected / at risk	1/14 (7.14%)	0/10 (0.00%)

# events	5	0
Insomnia †		
# participants affected / at risk	1/14 (7.14%)	0/10 (0.00%)
# events	1	0
Knee weakness †		
# participants affected / at risk	1/14 (7.14%)	0/10 (0.00%)
# events	1	0
Night Sweats †		
# participants affected / at risk	1/14 (7.14%)	0/10 (0.00%)
# events	1	0
Weight Loss †		
# participants affected / at risk	1/14 (7.14%)	0/10 (0.00%)
# events	1	0
Tiredness/fatigue †		
# participants affected / at risk	2/14 (14.29%)	0/10 (0.00%)
# events	3	0
Weakness †		
# participants affected / at risk	2/14 (14.29%)	0/10 (0.00%)
# events	2	0
Injury, poisoning and procedural complications		
Fall resulting in fractured ribs †		
# participants affected / at risk	1/14 (7.14%)	0/10 (0.00%)
# events	1	0
Musculoskeletal and connective tissue disorders		
Back Pain †		
# participants affected / at risk	2/14 (14.29%)	1/10 (10.00%)
# events	2	1
Hip pain †		
# participants affected / at risk	1/14 (7.14%)	0/10 (0.00%)
# events	1	0
Leg pain †		

# participants affected / at risk	2/14 (14.29%)	0/10 (0.00%)
# events	2	0
Thigh pain †		
# participants affected / at risk	1/14 (7.14%)	0/10 (0.00%)
# events	1	0
Nervous system disorders		
Migraine †		
# participants affected / at risk	1/14 (7.14%)	0/10 (0.00%)
# events	1	0
Vasovagal episode †		
# participants affected / at risk	1/14 (7.14%)	0/10 (0.00%)
# events	1	0
Renal and urinary disorders		
Flank pain †		
# participants affected / at risk	6/14 (42.86%)	3/10 (30.00%)
# events	8	4
Bladder spasms †		
# participants affected / at risk	0/14 (0.00%)	1/10 (10.00%)
# events	0	2
Decreased renal function †		
# participants affected / at risk	1/14 (7.14%)	0/10 (0.00%)
# events	1	0
Hematuria †		
# participants affected / at risk	1/14 (7.14%)	3/10 (30.00%)
# events	1	3
Hydronephrosis †		
# participants affected / at risk	7/14 (50.00%)	0/10 (0.00%)
# events	8	0
Renal colic †		
# participants affected / at risk	1/14 (7.14%)	0/10 (0.00%)
# events	1	0
Ureterectasis †		

# participants affected / at risk	2/14 (14.29%)	0/10 (0.00%)
# events	2	0
Urinary tract infections (UTI) †		
# participants affected / at risk	9/14 (64.29%)	4/10 (40.00%)
# events	19	7
Urine leakage †		
# participants affected / at risk	0/14 (0.00%)	3/10 (30.00%)
# events	0	6
Burning when urinating †		
# participants affected / at risk	0/14 (0.00%)	2/10 (20.00%)
# events	0	2
Urinary urgency †		
# participants affected / at risk	0/14 (0.00%)	1/10 (10.00%)
# events	0	1
Respiratory, thoracic and mediastinal disorders		
Dyspnoea †		
# participants affected / at risk	1/14 (7.14%)	0/10 (0.00%)
# events	2	0

† Events were collected by systematic assessment

7.7.3 Describe all adverse events and outcomes associated with the technology in national regulatory databases such as those maintained by the MHRA and FDA (Maude).

No data

7.7.4 Provide a brief overview of the safety of the technology in relation to the scope.

The complications described in the literature primarily concern migration, encrustation, and infections. Migrations seem to be dependent upon disease progress (change of anatomy as e.g. healing of strictures) and correct procedures during implantation of the stent (as e.g. correct expansion of proximal end of stent above the stricture; See figure below). Based upon the overview, the migration rate is estimated to 10-17% in the average patient. Migration is usually caused by the propulsion of the peristalsis along the ureter towards the bladder. Migration against peristalsis into the kidney has been observed but is unusual; Siddique, KA et al. 2006[37]. Migration

has been suggested to be the result of stricture healing by more investigators e.g. Bach et al. 2011.

Migration also occurs with double-J stents. Thus, migration rates of 3-10 % were reported in the literature; Pearle et al. 2004[38].

Encrustation is dependent upon the individual patients' tendency to form stones. Encrustation rates of 0% to 27% were reported. Encrustation also occurs with double-J stents. Thus, encrustation rates of 9-76% (varying with indwell duration) were reported in the literature [39].

The studies reported urinary infection rates in the range of 0%-11.3%. Infection also occurs with double-J stents. Thus, infection rates of 6.8-38% percent were reported in the literature (39).

Figure: The Memokath™051 ureteral stent. The proximal end expands into a cone upon instillation of warm water, which anchors the stent (picture to the right).

Author	Number of Studied Patients	Migration	Encrustation	Urinary Infection
Kulkarni, R and Bellamy, E 2001	28 (prospective study)	10%	No reported	None reported
Agrawal, S et al. 2009 (19)	55 (prospective study)	11%	3% (2/75 stents)	4%
Papatsoris, A et al. 2007 (27)	38 (prospective)	17%	19%	5% (2/38 patients)
Mynderse, L et al. 2010 (31)	15 (prospective)	13%	13%	0%

7.8 Evidence synthesis and meta-analysis all this one is very difficult to handle

7.8.1 Describe the technique used for evidence synthesis and/or meta-analysis. Include a rationale for the studies selected, details of the methodology used and the results of the analysis.

MK051 is a great alternative for maintaining ureter potent in all chronic ureteric obstruction cases. The technique depended on selection of all published or unpublished which cover the above indication. Exclusion of papers which contained only benign or malignant stricture was done to avoid any false impressions.

Double J stents is very well known to all healthcare personnel, this is including indications , contraindications, average indwelling time and complications. It is noticed that most of the studies made a focus on MK051 without making a direct comparison as the results of JJ stents is already well known

Due to small number of patient samples of most papers, statistics were disregarded and most of the mentioned the direct numbers.

7.8.2 If evidence synthesis is not considered appropriate, give a rationale and provide a qualitative review. The review should summarise the overall results of the individual studies with reference to their critical appraisal.

Already mentioned in clinical appraisal

7.9 Interpretation of clinical evidence

7.9.1 Provide a statement of principal findings from the clinical evidence highlighting the clinical benefit and any risks relating to adverse events from the technology.

The MemokathTM051 was investigated and/or discussed in a total of 26 publications presenting data of more than 650 patients. The studies were to a large extent descriptive, uncontrolled studies of which some were relatively small. The knowledge about the stent does indeed accumulate because of the high number of studies. Added knowledge about the Memokath™051 product is available from experience with other Memokath™ stents which are inserted in the urethra. Considerable experience with the product is also accumulating simply because Memokath™ stents – including Memokath™051- have been on the market throughout the world

since the early 1990. Thus, an estimated 5,000 patients were exposed to Memokath™051. More than 30,000 patients were exposed to either stent of the Memokath™ portfolio.

Concerning duration of indwell, the different studies of Memokath™051 yielded different values. Mean indwell durations of more than one year were reported in several studies. Very long indwells of years' duration were reported in some studies. The maximum reported indwell of Memokath™051 is 59 month.

Based upon this Pnn Medical A/S concludes that the average patient can expect indwell durations of 10-30 months. However, individual variations must be expected and some patients may have their stents for years. Since it is hard to predict which patients qualify for long indwells, it is recommended that patients are followed-up regularly usually with X-ray to ensure continued stent function.

Double-J stents are associated with high frequencies of adverse events. Thus, up to 80% of patients with double-J stents may experience some degree of stent related urinary tract symptoms (dysuria, frequency, urgency, hematuria and/or flank pain). In 42% of the patients the symptoms are sufficiently severe to reduce daily activities with 50% (Mendez-Probst, CE et al, 2010[40]; Joshi, HB et al. 2003 (38). The aetiology of the symptoms is not completely understood but vesico-ureteral reflux and/or physical irritation of the mucosa are suggested mechanism for some of the symptoms (40).

Memokath™051 does not extend into the renal pelvis and the bladder. This confines the physical irritation to the ureter. Since Memokath™051 is confined to the ureter, there is no reflux. Fact is that some of these symptoms occur rarely or not at all with Memokath™051. Overall, it can be concluded that since the stent only covers the stricture inside the ureter few side-effects occur. This is in distinction to the double-J stents that span the entire length of ureter irrespective of the length of the stricture and further extends into the renal pelvis and the bladder.

Migration is described in several studies. Migration in this context concerns movement of the stent –usually distally- within the urinary system. It has never been described that the stent moved to other parts of the body outside the urinary system. It cannot be described based upon the studies whether migration concerned clinically insignificant movements of few millimetres or clinically significant relocations of the stent.

Pnn Medical A/S considers an overweight towards clinically significant relocations likely to being reported in the literature. The range of reported migration frequencies varies from a low 8% up to a high 20%.. This is higher than migration rates of double J stents. (20). The difference is that double-J stents are anchored solidly in the renal pelvis and the bladder by the so called "pigtails". See
Figure. This is however also the likely reason for the difference in side-effects. Bladder irritation and flank pain are associated with double-J stents while this is not an expected side-effect with Memokath™051

Figure: The "pigtails" of double J stents. One end is positioned in the renal pelvis and the other end is in the bladder.

Based upon similar considerations the clinically significant encrustation rate is assessed to be 5-15% in the average patient

Pnn Medical A/S assesses the urinary infection rate to be 5-10% . However, limited data are available on urinary infection rates.

Encrustations and urinary infections are expected to occur with relatively high frequencies with all ureter stents (Agarwal et al. 2009[41], Mendez-Probst et al. 2010[42]. There are no controlled trials available for direct comparison of Memokath™051 with double-J stents. Concerning encrustation it is reasonable to expect that high percentage of stents eventually will encrust if left in situ. Therefore, it is questionable whether it is actually reasonable to discuss an encrustation rate. Time to encrustation – or encrustation rates at specific points in time - may be more appropriate. Memokath™051 is likely to reach the level of clinically significant encrustations later than double-J stents as evidenced by the longer functional indwell time.

If the low Memokath™051 rates of urinary infection of 5-10% reflect true figures, Memokath™051 would carry a low risk of urinary tract infections (UTIs) compared to other ureteral stents. Mendez-Probst et al. 2010 (42) stated that UTIs are very frequent in stented patients. Thus, 100% of patients with malignancies and long-term ureter stenting will have UTIs. Patients with diabetes and renal insufficiency will also have high rates of UTIs. The risk increases with duration of stent indwell.

7.9.2 Provide a summary of the strengths and limitations of the clinical-evidence base of the technology.

The studies used for analysis are generated in different place in the world. Mostly descriptive and designed for treating patients. The main focus was MK051 evaluation. Studies are describing a long history of success of MK051 in the market.

Limitations include non randomisation, mainly because the stent is designed for certain category of patients.

7.9.3 Provide a brief statement on the relevance of the evidence base to the scope. This should focus on the claimed patient- and system-benefits described in the scope.

Stenting of the urinary system is a well established procedure. The Memokath™051 stent was introduced in 1996 and experience with its use accumulated since. The Memokath™051 was designed for the treatment of patients with a variety of benign and malignant diseases causing obstruction of one or both ureters.

High success rates (93%) can be expected upon correct insertion of the stent. The Memokath™051 has the important advantage that it does not embed itself into the tissue and it is removable even after long-term indwelling.

The stent may stay in situ for several years but the average time indwelling is 10-30 months in the average patient. This is four to eight times longer than double-J stents that usually remain in situ for 3 to 4 months. Hence, the Memokath™051 has been suggested to lead to fewer surgical sessions, better quality of life and to be cheaper in the long run compared to the double-J stent.

Encrustation is seen with all urological stents including double-J stents. Eventually, a high percentage of ureter stents will encrust. In case encrustation occurs, Memokath™051 will reach the level of clinically significant encrustation later than double-J stents as evidenced by the significantly long duration of functional indwell time.

The commonly observed adverse effects of double-J stents, i.e. pain, irritation, bleeding and reflux are rare with Memokath™051. In conclusion, higher quality of life scores may be expected with Memokath™051 compared to the double-J stent.

The benefit/ risk profile of Memokath™051 is considered favourable and better than double-J stents.

7.9.4 Identify any factors that may influence the external validity of study results to patients in routine clinical practice.

It was noticed that all studies avoided PUJ strictures. Those who involved them, found a higher migration rate related to such cases

One other side, all studies avoided this type of stenting in below 18 of age

7.9.5 Based on external validity factors identified in 7.9.4 describe any criteria that would be used in clinical practice to select patients for whom the technology would be suitable.

Indication: any type of chronic ureteric obstruction due to either benign or malignant strictures with remarkable protection of ureter in cases of malignant strictures

Contraindications:

- PUJ cases
- Children
- Active infection

Section C – Economic evidence

Section C requires sponsors to present economic evidence for their technology.

All statements should be evidence-based and directly relevant to the decision problem.

The approach to the de novo cost analysis expected to be appropriate for most technologies is cost-consequence analysis. Sponsors should read section 7 of the Medical Technologies Evaluation Programme Methods guide on cost-consequences analysis, available from www.nice.org.uk/mt

Sponsors are requested to submit section C with the full submission. For details on timelines, see the NICE document 'Guide to the Medical Technologies Evaluation Programme process', available from www.nice.org.uk/mt

8 Existing economic evaluations

8.1 Identification of studies

The review of the economic evidence should be systematic and transparent and a suitable instrument for reporting such as the PRISMA statement (www.prisma-statement.org/statement.htm).

A PDF copy of all included studies should be provided by the sponsor.

8.1.1 Describe the strategies used to retrieve relevant health economics studies from the published literature and to identify all unpublished data. The search strategy used should be provided as in section 10, appendix 3.

Search was done in the following sites:

- Medline, pubmed
- Embase
- Clinicaltrials.com
- General internet google search
- Our in-company studies related to cost evaluation

We have done search using word Memokath alone, then Memokath 051, Memokath 51.
The next step was to indentify Memokath 51 related studies
Then the search was for the cost related studies.

Health economics studies should include all types of economic evaluation and cost studies, including cost analyses and cost-effectiveness and budget-impact analyses. The methods used should be justified with reference to the decision problem.

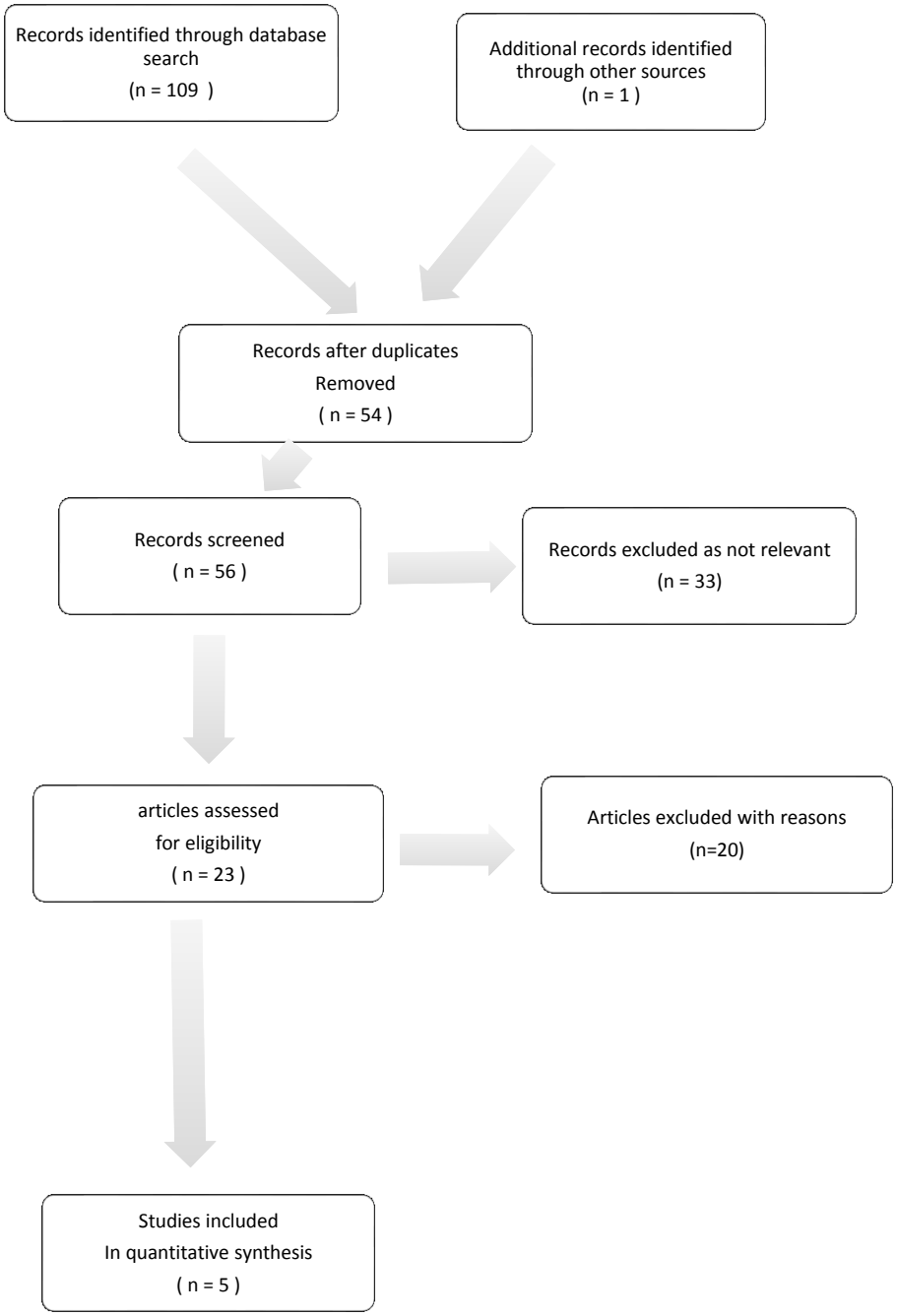
Sufficient detail should be provided to enable the methods to be reproduced (the External Assessment Centre must be able to reproduce the search), and the rationale for any inclusion and exclusion criteria regarding search terms should be used.

8.1.2 Describe the inclusion and exclusion criteria used to select studies from the published and unpublished literature. Suggested headings are listed in the table below. Other headings should be used if necessary.

Table C1 Selection criteria used for health economic studies

Inclusion criteria	
Population	Adult Patients (over 18) with ureteric obstruction due to benign or malignant reasons
Interventions	Memokath 051
Outcomes	Health economics, cost effective analysis, cost analysis
Study design	None
Language restrictions	English
Search dates	1992-current
Exclusion criteria	
Population	Anything other than adult patients with ureteric obstruction due to benign or malignant reasons
Interventions	Anything other than Memokath 051
Outcomes	None
Study design	None
Language restrictions	Non English
Search dates	Prior to 1992

8.1.3 Report the numbers of published studies included and excluded at each stage in an appropriate format.



It is recommended that the number of published studies included and excluded at each stage is reported using the PRISMA statement flow diagram (available from *www.prisma-statement.org/statement.htm*)

8.2 Description of identified studies

8.2.1 Provide a brief review of each study, stating the methods, results and relevance to the scope. A suggested format is provided in table C2.

Outcome measures should be included if applicable. Patient outcomes could include gains in life expectancy, improved quality of life, longer time to recurrence, and comparative costs.

Table C2 Summary list of all evaluations involving costs

Study reference	Population	Intervention	Comparator
Agrawal S, Brown CT, Bellamy EA, Kulkarni R. The thermo-expandable metallic ureteric stent: an 11-year follow-up. BJU Int 2009 Feb 1;2009 Feb 103(3):372-6.	Patients with ureteric obstruction due to malignant and benign strictures with age over 18 years	Memokath 051	Conventional Double J stents as per the common knowledge about them. No second arm. Cost is mentioned in the study without details
Papatsoris A, Masood J, El-Husseiny T, Ndirika S,	Same as above	Memokath 051	Conventional Double J stents as per the common

Junaid I, Buchholz NP. A novel long-term thermo-expandable ureteric metal stent: Memokath 051. BJU Int 2007;1-10.			knowledge about them. No second arm. Cost is analysed based on the price scheme of NHS
Cost analysis presentation made by Aintree hospital staff for audit approval (non published)	Cost analysis based on the prices in NHS	Memokath 051	JJ stent

8.2.2 Provide a complete quality assessment for each health economic study identified.

Table B8 Critical appraisal of observational studies

Table 8.1: Appraisal criteria for suitability applied to the studies in Table 3 (GHTF guideline).

Suitability Criteria	Description	Grading System
Appropriate device	Were the data generated from the device in question?	D1 - Actual device D2 - Comparable device D3 - Other device
Appropriate device Application	Was the device used for the same intended use (e.g., methods of deployment, application, etc.)?	A1 - Same use A2 - Minor deviation A3 - Major deviation
Appropriate patient group	Were the data generated from a patient group that is representative of the intended treatment population (e.g., age, sex, etc.) and clinical condition (i.e., disease, including state and severity)?	P1 – Applicable P2 - Limited P3 - Different population

Acceptable report / data collation	Do the reports or collations of data contain sufficient information to be able to undertake a rational and objective assessment?	R1 - High quality R2 - Minor deficiencies R3- Insufficient information

Table 8.2: Continued sample appraisal criteria for data contribution applied to the studies in Table 1.

Data Contribution Criteria	Description	Grading System
Grading System	Was the design of the study appropriate?	T1 – Yes T2 – No
Outcome measures	Does the outcome measures reported reflect the intended performance of the device?	O1 – Yes O2 - No
Follow up	Is the duration of follow-up long enough to assess whether duration of treatment effects and identify complications?	F1 – Yes F2 – No
Statistical significance	Has a statistical analysis of the data been provided and is it appropriate?	S1 – Yes S2 – No
Clinical significance	Was the magnitude of the treatment effect observed clinically significant?	C1 – Yes C2 – No

Table 8.3: Overview of publications specifically on MemokathTM051

Author	Number studied patients	Appraisal	Comments/ Limitations
Agrawal, S et al. 2008	55 (prospective study)	D1, A1, P1, R1,T1, O1, F1, S2,C:NA	Decent number of patients included. Descriptive study, No comparator, Limited statistical considerations.
Papatsoris, A et al. 2007	28 (prospective)	D1, A1, P:NA, R1,T1, O1, F1, S2,C:NA	Descriptive study, No comparator, Limited statistical considerations.
Cost analysis presentation made by Aintree hospital staff for audit approval (non published**)**	It is not a typical study. it is a presentation made by Aintree hospital staff. We have put it as it discusses the cost effectiveness from the prospect of NHS staff		

9 De novo cost analysis

Section 9 requires the sponsor to provide information on the de novo cost analysis.

The de novo cost analysis developed should be relevant to the scope.

All costs resulting from or associated with the use of the technology should be estimated using processes relevant to the NHS and personal social services.

Note that NICE cites the price of the product used in the model in the Medical Technology guidance.

9.1 Description of the de novo cost analysis

9.1.1 Provide the rationale for undertaking further cost analysis in relation to the scope.

The cost analysis is made based on the following factors

1. Price sources were taken from the Papatsoris, A et al. 2007 sudy (43) and the presentation of eintree hospital and the most recent market price of MK51 in UK

2. The comparison is based on the MK51 price Vs expected insitu time compared with traditional JJ stents. Other comparators are not put in the study due to the fact that these procedures are more related to medical intervention decision and not the price or time factors.

3. The analysis also put in consideration that all side effects or failures related to MK51 or JJ are mainly treated by exchange of stents. there is no patient long term complications

4. To take the maximum side of just, we considered JJ stents exchange every 6 month with zero complication factor. It is known that many JJ stents need to be change after 3-4 month but we wanted to show the results even with securing all factors for comaparator

On the other side, we took the average failure rate of most of MK51 studies on 2 years range (nearly 25 %) and we used it as a risk factor for MK51 cost analysis calculation.

Patients

9.1.2 What patient group(s) is (are) included in the cost analysis?

All patients of chronic ureteric strictures (obstruction) due to both benign and malignant causes

The patient group(s) included in the cost analysis must reflect the licensed indication/CE mark/marketing authorisation and be relevant to the scope.

The sponsor should not deviate from the scope.

Technology and comparator

9.1.3 Provide a justification if the comparator used in the cost analysis is different from the scope.

Not applicable. The comparator is the same in the scope

If the choice of comparator used in the cost analysis is different from the scope an explanation must be provided.

Model structure

9.1.4 Provide a diagram of the model structure you have chosen.

Attached

The model structure must be supplied to NICE in a legible format when printed on A4 paper.

9.1.5 Justify the chosen structure in line with the clinical pathway of care identified in response to question 3.3.

The chosen structure goes in alignment with the clinical pathway mentioned in response to question number 3

Consider how the model structure captures the main aspects of the condition for patients and the NHS. What was the underlying disease progression implemented in the model? Or what treatment was assumed to reflect underlying disease progression? Cross-reference to section 3.3.

9.1.6 Provide a list of all assumptions in the cost model and a justification for each assumption.

Assumption	justification
All patients with JJ insertions have no early removal or early complication	This is to make it more easy for any evaluator to see the value of MK even with putting the comparator in an ideal situation
No complications require any surgical interference or long term side effects	99% of complications for both MK51 and JJ stents are only treated by exchange
Risk factor of early exchange of MK51 is 25%	The study is based on 2.5 years follow up. While the overall success rate of MK 51 was about 75% in 4 years and more[43]

9.1.7 Define what the model's health states are intended to capture.

It is intended to capture the fact that despite that the first insertion of MK 51 will cost more than the comparator, but the cost is nearly equal after one year. Then after more than one year, the cost goes nearly half in second year and so on. So the more the time goes, the more the cost is less on NHS to use MK51 for chronic patientse

9.1.8 Describe any key features of the cost model not previously reported. A suggested format is presented below.

Table C4 Key features of model not previously reported

Factor	Chosen values	Justification	Reference
Time horizon of model	2.5 years	The follow up studies for MK 51 are up to 11 years so we just wanted to show the cost benefit over a much shorter period and it goes without saying that the longer the stent insitu will be even more cost effective	
Discount of 3.5% for costs	No discount was calculated		
Perspective (NHS/PSS)			
Risk factor for complications	25% on MK 51	As explained before, we only put it on MK 51 based on the average success rate in different papers over 4 years and avoided it on JJ stents for securing max. Success for comparator	
NHS, National Health Service; PSS, Personal Social Services			

9.2 Clinical parameters and variables

When relevant, answers to the following questions should be derived from, and be consistent with, the clinical evidence section of the submission (section 7). Cross-references should be provided. If alternative sources of evidence have been used, the method of identification, selection and synthesis should be provided as well as a justification for the approach.

9.2.1 Describe how the data from the clinical evidence were used in the cost analysis.

All cost analysis is derived from the same clinical papers mentioned in the clinical submission. Added to that is the audit report from Aintree hospital (attached) as it is one big hospital in UK and directly related to NHS

In addition, if transition probabilities have been used in the model, explain how they were calculated from the clinical data. If appropriate, provide the

transition matrix, details of the transformation of clinical outcomes or other details here. If the (transition) probabilities vary over time for the condition or disease, state how this has this been included in the evaluation and if it has not been included, provide an explanation of why it has been excluded. If transition probabilities have not been used, explain how the results of the clinical evidence were incorporated into the model.

9.2.2 Are costs and clinical outcomes extrapolated beyond the study follow-up period(s)? If so, what are the assumptions that underpin this extrapolation and how are they justified?

No. It is all coming within the normal follow up periods in clinical submission

In particular, consider what assumption was used regarding the longer term difference in effectiveness between the technology and its comparator.

Were any assumptions and/or techniques used for the extrapolation of longer term differences in clinical outcomes between the technology and its comparator?

9.2.3 Were intermediate outcome measures linked to final outcomes (for example, was a change in a surrogate outcome linked to a final clinical outcome)? If so, how was this relationship estimated, what sources of evidence were used and what other evidence is there to support it?

The calculation is very direct and simple in our case, it is directly related to the prices of the MK51 and JJ. Fortunately, even the insertion prices are nearly the same. So the only variables are time of stent insitu and basic price of each stents

9.2.4 Were adverse events such as those described in section 7.7 included in the cost analysis? If appropriate, provide a rationale for the calculation of the risk of each adverse event.

Yes all adverse effects are calculated with percent of risk of 25%. It is the average of failure rate of the clinical papers mentioned in the clinical submission

9.2.5 Provide details of the process used when the sponsor's clinical advisers assessed the applicability of available or estimated clinical model parameter and inputs used in the analysis.

There was no advisers, it is all based on clinical study cost analysis and audit report from actual life big hospital (Aintree)

This is a critical step and the names and professional titles of the clinical advisers should be included along with the following[1]:

- *the criteria for selecting the experts*
- *the number of experts approached*
- *the number of experts who participated*
- *declaration of potential conflict(s) of interest from each expert or medical speciality whose opinion was sought*
- *the background information provided and its consistency with the totality of the evidence provided in the submission*
- *the method(s) used to collect and collate the opinions*
- *the medium used to collect opinions (for example, was information gathered by direct interview, telephone interview or self-administered questionnaire?)*
- *the questions asked*
- *whether iteration was used in the collation of opinions and if so, how it was used*

[1] Adapted from Pharmaceutical Benefits Advisory Committee (2008) Guidelines for preparing submissions to the Pharmaceutical Benefits Advisory Committee (Version 4.3). Canberra: Pharmaceutical Benefits Advisory Committee.

- *the uncertainly around these values should be addressed in the sensitivity analysis.*

9.2.6 Summarise all the variables included in the cost analysis. Provide cross-references to other parts of the submission.

One variable, we updated the prices from the clinical study according to current market price of the stent and changed the currency from euro to sterling according to the audit report from Aintree hospital

All parameters used to estimate cost should be presented clearly and include details of data sources. For continuous variables, mean values should be presented and used in the analyses. For all variables, measures of precision should be detailed.

Details should also include the values used, range (and distribution) and source.

9.3 Resource identification, measurement and valuation

NHS costs

9.3.1 Describe how the clinical management of the condition is currently costed in the NHS in terms of reference costs and the payment by results (PbR) tariff.

The prices of current used practice which is the JJ insertion is described in details in the cost analysis sheet

Provide Healthcare Resource Groups (HRG) and PbR codes and justify their selection.

9.3.2 State the Office of Population, Censuses and Surveys Classification of Surgical Operations and Procedures (OPCS) codes for the operations, procedures and interventions relevant to the use of the technology for the clinical management of the condition.

NO data

Resource identification, measurement and valuation studies

9.3.3 Provide a systematic search of relevant resource data for the NHS in England. Include a search strategy and inclusion criteria, and consider published and unpublished studies.

We couldn't reach any systematic data for costs in NHS site, so we were depending on the sources mentioned above

9.3.4 Provide details of the process used when clinical advisers assessed the applicability of the resources used in the model[2].

No data

The details of the process should include:

- *the criteria for selecting the experts*
- *the number of experts approached*
- *the number of experts who participated*
- *declaration of potential conflict(s) of interest from each expert or medical speciality whose opinion was sought*
- *the background information provided and its consistency with the totality of the evidence provided in the submission*
- *the method(s) used to collect and collate the opinions*
- *the medium used to collect opinions (for example, was information gathered by direct interview, telephone interview or self-administered questionnaire?)*
- *the questions asked*
- *whether iteration was used in the collation of opinions and if so, how it was used*
- *the uncertainty around these values should be addressed in the sensitivity analysis.*

[2] Adapted from Pharmaceutical Benefits Advisory Committee (2008) Guidelines for preparing submissions to the Pharmaceutical Benefits Advisory Committee (Version 4.3). Canberra: Pharmaceutical Benefits Advisory Committee.

Technology and comparators' costs

9.3.5 Provide the list price for the technology.

1690 Sterling

9.3.6 If the list price is not used in the de novo cost model, provide the alternative price and a justification.

Same price is used

A rationale must be provided for the choice of values used in the cost model. All prices should be referenced. Any uncertainty around prices should be addressed by sensitivity analysis. All costs must be cross-referenced to other sections of the submission if possible.

9.3.7 Summarise the annual costs associated with the technology and the comparator technology (if applicable) applied in the cost model. A suggested format is provided in tables C6

Table C6 Costs per treatment/patient associated with the technology in the cost model

Items	Values for MK 51	Values for JJ stents	Source
Theatre staff costs	**1,159.93**	**1,159.93**	**The clinical study mentioned above and the Aintree audit report**
Theatre consumable costs	**1,874.16**	**109.44**	**Same**
Procedure code/surgery tariff	**34**	**138 - 407**	**Same**
2x Patient F/U OPD **X-Rray 1st 6/12** **NM Renogram 2nd 6/12**	**285** **(included 1st year and later on after insertion)**	**100 for 2 X ray follow up every 6 months**	**Same**
Total for first year	**3,353.09 / year**	**1,776.37 / 6 months** **3,552.74/year**	**Same**
Total for second year	**285**	**3552.74**	**Same**
Total for last 6 month	**142.5**	**1776.37**	**Same**
Total cost per treatment/patient over 2.5 years	**3,780.59**	**8881.85**	**Same**
Risk factor 25%	**945.15**	**0**	
Total cost per treatment/patient over 2.5 years with calculation of risk	**4,725.74**	**8881.85**	

When completing tables C6 the price of the technology should refer to the list price stated in 9.3.4 unless a justification for using an alternative price has been provided in 9.3.5. If a technology is not for single use and consumables are needed to provide a treatment, these must be itemised and a breakdown of prices presented.

For all costs presented a source of the data must be stated.

Health-state costs

9.3.8 If the cost model presents health states, the costs related to each health state should be presented in table C8. The health states should refer to the states in section 9.1.7. Provide a rationale for the choice of values used in the cost model.

Table C8 List of health states and associated costs in the economic model

Items	Values for MK 51	Values for JJ stents	Source
Theatre staff costs	**1,159.93**	**1,159.93**	**The clinical study mentioned above and the Aintree audit report**
Theatre consumable costs	**1,874.16**	**109.44**	**Same**
Procedure code/surgery tariff	**34**	**138 - 407**	**Same**
2x Patient F/U OPD **X-Rray 1st 6/12** **NM Renogram 2nd 6/12**	**285** **(included 1st year and later on after insertion)**	**100 for 2 X ray follow up every 6 months**	**Same**
Total for first year	**3,353.09 / year**	**1,776.37 / 6 months** **3,552.74/year**	**Same**
Total for second year	**285**	**3552.74**	**Same**
Total for last 6 month	**142.5**	**1776.37**	**Same**
Total cost per treatment/patient over 2.5 years	**3,780.59**	**8881.85**	**Same**

Adverse-event costs

9.3.9 Complete table C9 with details of the costs associated with each adverse event referred to in 9.2.4 included in the cost model. Include all adverse events and complication costs, both during and after longer-term use of the technology.

All adverse effects for both techniques are the same and treated by exchange. We have put it only on MK51 for more clearance of the cost effectiveness off the product

Miscellaneous costs

9.3.10 Describe any additional costs and cost savings that have not been covered anywhere else (for example, PSS costs, and patient and carer costs). If none, please state.

No additional

9.3.11 Are there any other opportunities for resource savings or redirection of resources that it has not been possible to quantify?

no

Include a justification as to why it has not possible to quantify the resource use and/or costs.

9.4 Approach to sensitivity analysis

Section 9.4 requires the sponsor to carry out sensitivity analyses to explore uncertainty around the structural assumptions and parameters used in the analysis. All inputs used in the analysis will be estimated with a degree of imprecision. For technologies whose final price/acquisition cost has not been confirmed, sensitivity analysis should be conducted over a plausible range of prices.

Analysis of a representative range of plausible scenarios should be presented and each alternative analysis should present separate results.

9.4.1 Has the uncertainty around structural assumptions been investigated? State the types of sensitivity analysis that have been carried out in the cost analysis.

No sensitivity analysis needed for the product

9.4.2 Was a deterministic and/or probabilistic sensitivity analysis undertaken? If not, why not? How were variables varied and what

was the rationale for this? If relevant, the distributions and their sources should be clearly stated.

No data

All scenarios and/or ranges of variables must be justified.

9.4.3 Complete table C10.1, C10.2 and/or C10.3 as appropriate to summarise the variables used in the sensitivity analysis.

No data

9.4.4 If any parameters or variables listed in section 9.2.6 were omitted from the sensitivity analysis, provide the rationale.

No data

It is acknowledged that some model parameters may be excluded from sensitivity analysis considerations, for example, because they can be considered 'constant' or because evidence exists about unbiased and accurate measurement.

9.5 Results of de novo cost analysis

Section 9.5 requires the sponsor to report the de novo cost analysis results. These should include the following:

- costs
- disaggregated results such as costs associated with treatment, costs associated with adverse events, and costs associated with follow-up/subsequent treatment
- a tabulation of the mean cost results
- results of the sensitivity analysis.

Base-case analysis

9.5.1 Report the total costs associated with use of the technology and the comparator(s) in the base-case analysis. A suggested format is presented in table C11.

Table C11 Base-case results

	Total per patient cost (£)
Technology	4870
Comparator 1	8881.85
...	

9.5.2 Report the total difference in costs between the technology and comparator(s).

4011.85

9.5.3 Provide details of the costs for the technology and its comparator by category of cost. A suggested format is presented in table C12.

Table C12 Summary of costs by category of cost per patient

Items	Values for MK 51	Values for JJ stents	Source
Theatre staff costs	**1,159.93**	**1,159.93**	**The clinical study mentioned above and the Aintree audit report**
Theatre consumable costs	**1,874.16**	**109.44**	**Same**
Procedure code/surgery tariff	**34**	**138 - 407**	**Same**
2x Patient F/U OPD **X-Rray 1st 6/12** **NM Renogram 2nd 6/12**	**285** **(included 1st year and later on after insertion)**	**100 for 2 X ray follow up every 6 months**	**Same**
Total for first year	**3,326.09 / year**	**1,776.37 / 6 months** **3,552.74/year**	**Same**
Total for second year	**285**	**3552.74**	**Same**
Total for last 6 month	**285**	**1776.37**	**Same**
Total cost per treatment/patient over 2.5 years	**3896.09**	**8881.85**	**Same**
Risk factor	**974**	**0**	
Total cost per treatment/patient over 2.5 years with calculation of risk	**4870**	**8881.85**	
Adapted from Pharmaceutical Benefits Advisory Committee (2008) Guidelines for preparing submissions to the Pharmaceutical Benefits Advisory Committee (Version 4.3). Canberra: Pharmaceutical Benefits Advisory Committee			

9.5.4 If appropriate, provide details of the costs for the technology and its comparator by health state. A suggested format is presented in table C13.

Table C13 Summary of costs by health state per patient

Items	Values for MK 51	Values for JJ stents	Source
Theatre staff costs	**1,159.93**	**1,159.93**	**The clinical study mentioned above and the Aintree audit report**
Theatre consumable costs	**1,874.16**	**109.44**	**Same**
Procedure code/surgery tariff	**34**	**138 - 407**	**Same**
2x Patient F/U OPD **X-Rray 1st 6/12** **NM Renogram 2nd 6/12**	**285** **(included 1st year and later on after insertion)**	**100 for 2 X ray follow up every 6 months**	**Same**
Total for first year	**3,326.09 / year**	**1,776.37 / 6 months** **3,552.74/year**	**Same**
Total for second year	**285**	**3552.74**	**Same**
Total for last 6 month	**285**	**1776.37**	**Same**
Total cost per treatment/patient over 2.5 years	**3896.09**	**8881.85**	**Same**
Risk factor	**974**	**0**	
Total cost per treatment/patient over 2.5 years with calculation of risk	**4870**	**8881.85**	

Adapted from Pharmaceutical Benefits Advisory Committee (2008) Guidelines for preparing submissions to the Pharmaceutical Benefits Advisory Committee (Version 4.3). Canberra: Pharmaceutical Benefits Advisory Committee

9.5.5 If appropriate, provide details of the costs for the technology and its comparator by adverse event. A suggested format is provided in table C14.

All adverse events are treated by exchange and calculated above

Sensitivity analysis results

9.5.6 Present results of deterministic one-way sensitivity analysis of the variables described in table C10.1.

No datacost

9.5.7 Present results of deterministic multi-way scenario sensitivity analysis described in table C10.2.

No data

9.5.8 Present results of the probabilistic sensitivity analysis described in table C10.3.

No data

9.5.9 What were the main findings of each of the sensitivity analyses?

No data

9.5.10 What are the key drivers of the cost results?

The key drivers are the cost of stents vs the insitu time

Miscellaneous results

9.5.11 Describe any additional results that have not been specifically requested in this template. If none, please state.

No data

9.6 Subgroup analysis

For many technologies, the capacity to benefit from treatment will differ for patients with differing characteristics. Sponsors are required to complete section 9.6 in accordance with the subgroups identified in the scope and for any additional subgroups considered relevant.

Types of subgroups that are not considered relevant are those based solely on the following factors.

- Subgroups based solely on differential treatment costs for individuals according to their social characteristics.
- Subgroups specified in relation to the costs of providing treatment in different geographical locations within the UK (for example, if the costs of facilities available for providing the technology vary according to location).

9.6.1 Specify whether analysis of subgroups was undertaken and how these subgroups were identified. Cross-reference the response to the decision problem in table A1 and sections 3.2 and 7.4.4.

No subgroups in our case, it is for all chronic ureter obstruction cases with no subgroups

Consider if these subgroups were identified on the basis of a hypothesised expectation of differential clinical benefit or cost because of known, biologically plausible, mechanisms, social characteristics or other clearly justified factors.

9.6.2 Define the characteristics of patients in the subgroup(s).

Not applicable

9.6.3 Describe how the subgroups were included in the cost analysis.

Not applicable

9.6.4 What were the results of the subgroup analysis/analyses, if conducted? The results should be presented in a table similar to that in section 9.5.1 (base-case analysis).

Not applicable

9.6.5 Were any subgroups not included in the submission? If so, which ones, and why were they not considered?

Not applicable

9.7 Validation

9.7.1 Describe the methods used to validate and cross-validate (for example with external evidence sources) and quality-assure the model. Provide references to the results produced and cross-reference to evidence identified in the clinical and resources sections.

The model structure was designed to emulate the clinical pathways derived from a published study and an audit report for NHS. Transition probabilities were primarily sourced from the results of the clinical and economic evidence searches performed for sections 7 and 8. Unit costs were primarily referenced from NHS data sources

9.8 Interpretation of economic evidence

9.8.1 Are the results from this cost analysis consistent with the published economic literature? If not, why do the results from this evaluation differ, and why should the results in the submission be given more credence than those in the published literature?

There is no difference except the update of current market prices the MK51

9.8.2 Is the cost analysis relevant to all groups of patients and NHS settings in England that could potentially use the technology as identified in the scope?

Yes

9.8.3 What are the main strengths and weaknesses of the analysis? How might these affect the interpretation of the results?

The product is very simple so there is no deep analysis for the cost related issues. That is why we tried to use the max safety for calculations to show the maximum cost effectiveness over time compared with comparator

9.8.4 What further analyses could be undertaken to enhance the robustness/completeness of the results?

Getting back to NHS files and renewal of calculation according the last price figures can be of great value

References

Please use a recognised referencing style, such as Harvard or Vancouver.

1 Kulkarni R. Metallic ureteric stents: the current situation. BJU Int 2003 Aug;92(3):188-9.
1 Joshi HB, Stainthorpe A, MacDonagh RP, Keeley FX, Jr., Timoney AG, Barry MJ. Indwelling ureteral stents: evaluation of symptoms, quality of life and utility. J Urol 2003 Mar;169(3):1065-9
1 Staios D, Shergill I, Thwaini A, Junaid I, Buchholz NP. The Memokath stent. Expert Rev Med Devices 2007 Mar;4(2):99-101.
1 Gort HB, Mali WP, van Waes PF, Kloet AG. Metallic self-expandible stenting of a ureteroileal stricture. AJR Am J Roentgenol 1990 Aug;155(2):422-3.
1 Barbalias GA, Liatsikos EN, Kalogeropoulou C, Karnabatidis D, Siablis D. Metallic stents in gynecologic cancer: an approach to treat extrinsic ureteral obstruction. Eur Urol 2000 Jul;38(1):35-40
1 Pauer W, Lugmayr H. Metallic Wallstents: a new therapy for extrinsic ureteral obstruction. J Urol 1992 Aug;148(2 Pt 1):281-4.
1 Diaz-Lucas EF, Martinez-Torres JL, Fernandez MJ, Carazo MO, de la Fuente SA,Zuluaga GA. Self-expanding wallstent endoprosthesis for malignant ureteral obstruct. J Endourol 1997 Dec;11(6):441-7.
1 http://emedicine.medscape.com/article/442469-overview#a1
1 Campbell-Walsh Urology, Tenth Edition. Chapter 41. Page 1149. Ureteral stricture desease
1 RJ Cetti, S Biers, and SR Keoghane\South Coast Stone Centre, Department of Urology, Queen Alexandra Hospital, Portsmouth, UK. 2011 by the Annals of The Royal College of Surgeons of England
1 RATE OF URETERAL STRICTURE FOLLOWING URETEROSCOPY FOR NEPHROLITHIASIS USING A NATIONAL DATABASE OF INSURED PATIENTS Philip May*, Sarah Holt, Joshua Calvert, Jonathan Harper, Seattle, WA
1 http://www.jurology.com/article/S0022-5347(16)00753-9/pdf
1 https://urologysurgery.wordpress.com/2009/01/01/ureteral-stricture/
1 https://www.nice.org.uk/guidance/cg169/chapter/1-Recommendations#managing-acute-kidney-injury
1 https://www.nice.org.uk/guidance/CG175
1 https://www.nice.org.uk/guidance/ng2
1 https://www.nice.org.uk/guidance/CG175
1 https://www.nice.org.uk/guidance/cg175/chapter/1-Recommendations#assessment-2
1 Cambpell-Walsh Urology, Tenth Edition, https://books.google.com.eg/books?id=fu3BBwAAQBAJ&pg=PA1149&lpg=PA1149&dq=ureteral+stricture+campbell&source=bl&ots=Z0DAaVgjcG&sig=aZTR85U0CE_7eh9i2C-guV-rDn0&hl=en&sa=X&ved=0ahUKEwjbiceTsuLSAhWF3SYKHW64Bh4Q6AEIJzAC#v=onepage&q=ureteral%20stricture&f=false
1 Stables DP, Ginsberg NJ, Johnson ML. Percutaneous nephrostomy: a series and review of the literature. AJR Am J Roentgenol 1978 Jan;130(1):75-82
1 Protzel C, Dahm JB, Klebingat KJ. High frequency rotablation as a new therapeutic procedure for obstructed metallic ureter stents. J Urol 2001 Oct;166(4):1399-400.
1 Allen DJ, Longhorn SE, Philp T, Smith RD, Choong S. Percutaneous urinary drainage and ureteric stenting in malignant disease. Clin Oncol (R Coll Radiol) 2010 Nov;22(9):733-9.
1 J Endourol. 2008 Feb;22(2):295-9. doi: 10.1089/end.2007.0201.Success of ureteral stents for intrinsic ureteral obstruction.Wenzler DL1, Kim SP, Rosevear HM, Faerber GJ, Roberts WW, Wolf JS Jr.Department of Urology, University of Michigan, Ann Arbor, Michigan, USA.
1 Initial Experience with Full-Length Metal Stent to Relieve Malignant Ureteral Obstruction James F. Borin, Ori Melamud, and Ralph V. Clayman. Journal of Endourology. May 2006
1 Ther Adv Urol. 2013 Dec; 5(6): 354–365.Current status of minimally invasive endoscopic management of ureteric strictures. Stefanos Kachrilas, Andreas Bourdoumis, Theocharis Karaolides, Stavroula Nikitopoulou, George Papadopoulos, Noor Buchholz, and Junaid Masood
1 JSLS. 2003 Apr-Jun;Percutaneous Ureteral Incision With a Small-Caliber Flexible Ureteroscope

Hatsuki Hibi, MD, Yoshiaki Yamada, MD, Hitoshi Nonomura, MD, Yukio Hatano, MD, Kenji Mitsui, MD, Tomohiro Taki, MD, Nobuaki Honda, MD, and Hidetoshi Fukatsu, MD
Hatsuki Hibi, Department of Urology, Aichi Medical University School of Medicine, Nagakute, Japan.
1 Campbell-Walsh Urology, Tenth Edition. Section IX. Upper Urinary Tract Obstruction and Trauma. Page 1154
1 Paulos Yohannes, David Gershbaum, Paul E. Rotariu, Arthur D. Smith, and Benjamin R. Lee. Journal of Endourology. July 2004, Management of Ureteral Stricture Disease during Laparoscopic Ureteroneocystostomy
1 Staios D, Shergill I, Thwaini A, Junaid I, Buchholz NP. The Memokath stent. Expert Rev Med Devices 2007 Mar;4(2):99-101.
1 Maan Z, Patel D, Moraitis K, El-Husseiny T, Papatsoris AG, Buchholz NP, et al. Comparison of stent-related symptoms between conventional Double-J stents and a new-generation thermoexpandable segmental metallic stent: a validated-questionnaire-based study. J Endourol2010(4):589-93
1 Sountoulides P, Kaplan A, Kaufmann OG, Sofikitis N. Current status of metal stents for managing malignant ureteric obstruction. BJU Int 2010 Jan 8;(105):1066-72.
1 Maan Z, Patel D, Moraitis K, El-Husseiny T, Papatsoris AG, Buchholz NP, et al. Comparison of stent-related symptoms between conventional Double-J stents and a new-generation thermoexpandable segmental metallic stent: a validated-questionnaire-based study. J Endourol2010(4):589-93.
1 Prog Urol. 2011 Jun;21(6):397-404. doi: 10.1016/j.purol.2010.11.008. Epub 2011 Jan 26.The thermoformable spiral metallic stents in the treatment of localized ureteral stenosis: an alternative to JJ stent? Prospective multicenter study. Bonniol R1, Meria P, Safsaf A, Albouy B, Sibert L.Service d'urologie, hôpital Charles-Nicolle, Rouen,
1 Urol. 2012 May;22.Tolerance and effectiveness of Memokath® 051 ureteral stents : a prospective 3 year follow-up study].Azizi A1, Pasticier G, Bénard A, Lapouge O, Ferrière JM, Ballanger P, Robert G Service d'urologie, CHU de Bordeaux, université Bordeaux-Segalen, place Amélie-Raba-Léon, 33000 Bordeaux, France
1 Papatsoris A, Buchholz N. A novel thermo-expandable ureteric metal stent for the minimally invasive management of ureteral strictures. Journal of Endourology 2010 Mar 1;24(3):487-91Efficacy in benign and malignant cases together with a prove that MK51 is more cost effective than JJ stents on the long term Usage. UK
1 Characterization of Urinary Symptoms in Patients With Ureteral Stents
HB Joshi et al. Urology 59 (4), 511-516. 4 2002
https://www.ncbi.nlm.nih.gov/labs/articles/11927301/

1 Siddique KA, Zammit P, Bafaloukas N, Albanis S, Buchholz NP. Repositioning and removal of an intra-renal migrated ureteric Memokath stent. Urol Int 2006;77(4):297-300.

1 Pearle M, Watson G. Optimal drainage of the obstructed kidney: stent versus nephrostomy. In: Yachia D, Paterson P, editors. Stenting the Urinary System. 2004. p. 139-42.
1 Pearle M, Watson G. Optimal drainage of the obstructed kidney: stent versus nephrostomy. In: Yachia D, Paterson P, editors. Stenting the Urinary System. 2004. p. 139-42.
1 Mendez-Probst CE, Fernandez A, Denstedt JD. Current status of ureteral stent technologies: comfort and antimicrobial resistance. Curr Urol Rep 2010 Mar;11(2):67-73.
1 Agarwal MM, Singh SK, Mandal AK, Bhalla V, Acharya NC, Kumar S. Endourologic management of forgotten encrusted ureteral stents: can ureteroscopic lithotripsy be avoided? Surg Laparosc Endosc Percutan Tech 2009 Feb;19(1):72-7.
1 Mendez-Probst CE, Fernandez A, Denstedt JD. Current status of ureteral stent technologies: comfort and antimicrobial resistance. Curr Urol Rep 2010 Mar;11(2):67-73.
1 The thermo-expandable metallic ureteric stent: an 11-year follow-up Sachin Agrawal, Christian T. Brown, Elizabeth A. Bellamy* and Ravi Kulkarni Departments of Urology and *Radiology, St Peter's Hospital, Chertsey, UK
Accepted for publication 6 June 2008
Kulkarni R, Bellamy E. Nickel-titanium shape memory alloy Memokath 051 ureteral stent for managing long-term ureteral obstruction: 4-year experience. J Urol 2001 Nov;166(5):1750-4.
Papatsoris A, Masood J, El-Husseiny T, Ndirika S, Junaid I, Buchholz NP. A novel long-term

thermo-expandable ureteric metal stent: Memokath 051. BJU Int 2007;1-10

10 Appendices

10.1 Appendix 1: Search strategy for clinical evidence (section 7.1.1)

The following information should be provided:

10.1.1 The specific databases searched and the service provider used (for example, Dialog, DataStar, OVID, Silver Platter), including at least:

- Medline
- Embase
- Medline (R) In-Process
- The Cochrane Library.

Response

10.1.2 The date on which the search was conducted.

Response

10.1.3 The date span of the search.

Response

10.1.4 The complete search strategies used, including all the search terms: textwords (free text), subject index headings (for example, MeSH) and the relationship between the search terms (for example, Boolean).

Response

10.1.5 Details of any additional searches, such as searches of company or professional organisation databases (include a description of each database).

Response

10.1.6 The inclusion and exclusion criteria.

Response

10.1.7 The data abstraction strategy.

Response

10.2 Appendix 2: Search strategy for adverse events (section 7.7.1)

The following information should be provided.

10.2.1 The specific databases searched and the service provider used (for example, Dialog, DataStar, OVID, Silver Platter), including at least:

- Medline
- Embase
- Medline (R) In-Process
- The Cochrane Library.

Response

10.2.2 The date on which the search was conducted.

Response

10.2.3 The date span of the search.

Response

10.2.4 The complete search strategies used, including all the search terms: textwords (free text), subject index headings (for example, MeSH) and the relationship between the search terms (for example, Boolean).

Response

10.2.5 Details of any additional searches (for example, searches of company databases [include a description of each database]).

Response

10.2.6 The inclusion and exclusion criteria.

Response

10.2.7 The data abstraction strategy.

Response

10.3 Appendix 3: Search strategy for economic evidence (section 8.1.1)

The following information should be provided.

10.3.1 The specific databases searched and the service provider used (for example, Dialog, DataStar, OVID, Silver Platter), including at least:

- Medline
- Embase
- Medline (R) In-Process
- EconLIT
- NHS EED.

Response

10.3.2 The date on which the search was conducted.

Response

10.3.3 The date span of the search.

Response

10.3.4 The complete search strategies used, including all the search terms: textwords (free text), subject index headings (for example,

MeSH) and the relationship between the search terms (for example, Boolean).

Response

10.3.5 Details of any additional searches (for example, searches of company databases [include a description of each database]).

Response

10.4 Appendix 4: Resource identification, measurement and valuation (section 9.3.2)

The following information should be provided.

10.4.1 The specific databases searched and the service provider used (for example, Dialog, DataStar, OVID, Silver Platter), including at least:

- Medline
- Embase
- Medline (R) In-Process
- NHS EED
- EconLIT.

Response

10.4.2 The date on which the search was conducted.

Response

10.4.3 The date span of the search.

Response

10.4.4 The complete search strategies used, including all the search terms: textwords (free text), subject index headings (for example, MeSH) and the relationship between the search terms (for example, Boolean).

Response

10.4.5 Details of any additional searches (for example, searches of company databases [include a description of each database]).

Response

10.4.6 The inclusion and exclusion criteria.

Response

10.4.7 The data abstraction strategy.

Response

11 Related procedures for evidence submission

11.1 Cost models

An electronic executable version of the cost model should be submitted to NICE with the full submission.

NICE accepts executable cost models using standard software – that is, Excel, TreeAge Pro, R or WinBUGs. If you plan to submit a model in a non-standard package, NICE should be informed in advance. NICE, in association with the External Assessment Centre, will investigate whether the requested software is acceptable, and establish if you need to provide NICE and the External Assessment Centre with temporary licences for the non-standard software for the duration of the assessment. NICE reserves the right to reject cost models in non-standard software. A fully executable electronic copy of the model must be submitted to NICE with full access to the programming code. Care should be taken to ensure that the submitted versions of the model programme and the written content of the evidence submission match.

NICE may distribute the executable version of the cost model to a consultee if they request it. If a request is received, NICE will release the model as long as it does not contain information that was designated confidential by the model owner, or the confidential material can be redacted by the model owner without producing severe limitations on the functionality of the model. The consultee will be advised that the model is protected by intellectual property rights, and can be used only for the purposes of commenting on the model's reliability and informing comments on the medical technology consultation document.

Sponsors must ensure that all relevant material pertinent to the decision problem has been disclosed to NICE at the time of submission. NICE may request additional information not submitted in the original submission of evidence. Any other information will be accepted at NICE's discretion.

When making a full submission, sponsors should check that:

- an electronic copy of the submission has been given to NICE with all confidential information highlighted and underlined
- a copy of the instructions for use, regulatory documentation and quality systems certificate have been submitted
- an executable electronic copy of the cost model has been submitted
- the checklist of confidential information provided by NICE has been completed and submitted.

- A PDF version of all studies (or other appropriate format for unpublished data, for example, a structured abstract) included in the submission have been submitted

11.2 Disclosure of information

To ensure that the assessment process is as transparent as possible, NICE considers it highly desirable that evidence pivotal to the Medical Technologies Advisory Committee's decisions should be publicly available at the point of issuing the medical technology consultation document and medical technology guidance.

Under exceptional circumstances, unpublished evidence is accepted under agreement of confidentiality. Such evidence includes 'commercial in confidence' information and data that are awaiting publication ('academic in confidence').

When data are 'commercial in confidence' or 'academic in confidence', it is the sponsor's responsibility to highlight such data clearly, and to provide reasons why they are confidential and the timescale within which they will remain confidential. The checklist of confidential information should be completed: if it is not provided, NICE will assume that there is no confidential information in the submission. It is the responsibility of the manufacturer or sponsor to ensure that the confidential information checklist is kept up to date.

It is the responsibility of the sponsor to ensure that any confidential information in their evidence submission is clearly underlined and highlighted

correctly. NICE is assured that information marked ‘academic in confidence’ can be presented and discussed during the public part of the Medical Technologies Advisory Committee meeting. NICE is confident that such public presentation does not affect the subsequent publication of the information, which is the prerequisite allowing for the marking of information as ‘academic in confidence’.

Please therefore underline all confidential information, and highlight information that is submitted under ‘commercial in confidence’ in blue and information submitted under ‘academic in confidence’ in yellow.

NICE will ask sponsors to reconsider restrictions on the release of data if there appears to be no obvious reason for the restrictions, or if such restrictions would make it difficult or impossible for NICE to show the evidential basis for its guidance. Information that has been put into the public domain, anywhere in the world, cannot be marked as confidential.

Confidential information submitted will be made available for review by the External Assessment Centre and the Medical Technologies Advisory Committee. NICE will at all times seek to protect the confidentiality of the information submitted, but nothing will restrict the disclosure of information by NICE that is required by law (including in particular, but without limitation, the Freedom of Information Act 2000).

The Freedom of Information Act 2000, which came into force on 1 January 2005, enables any person to obtain information from public authorities such as NICE. The Act obliges NICE to respond to requests about the recorded information it holds, and it gives people a right of access to that information. This obligation extends to submissions made to NICE. Information that is designated as ‘commercial in confidence’ may be exempt under the Act. On receipt of a request for information, the NICE secretariat will make every effort to contact the designated company representative to confirm the status of any information previously deemed ‘commercial in confidence’ before making any decision on disclosure.

11.3 Equality

NICE is committed to promoting equality and eliminating unlawful discrimination, including paying particular attention to groups protected by equalities legislation. The scoping process is designed to identify groups who are relevant to the evaluation of the technology, and to reflect the diversity of the population. NICE consults on whether there are any issues relevant to equalities within the scope of the evaluation, or if there is information that could be included in the evidence presented to the Medical Technologies Advisory Committee to enable them to take account of equalities issues when developing guidance.

Evidence submitters are asked to consider whether the chosen decision problem could be impacted by NICE's responsibility in this respect, including when considering subgroups and access to recommendations that use a clinical or biological criterion.

For further information, please see the NICE website (www.nice.org.uk/aboutnice/howwework/NICEEqualityScheme.jsp).

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[1] Kulkarni R. Metallic ureteric stents: the current situation. BJU Int 2003 Aug;92(3):188-9.
2 Joshi HB, Stainthorpe A, MacDonagh RP, Keeley FX, Jr., Timoney AG, Barry MJ. Indwelling ureteral stents: evaluation of symptoms, quality of life and utility. J Urol 2003 Mar;169(3):1065-9
[3] Staios D, Shergill I, Thwaini A, Junaid I, Buchholz NP. The Memokath stent. Expert Rev Med Devices 2007 Mar;4(2):99-101.
4 Gort HB, Mali WP, van Waes PF, Kloet AG. Metallic self-expandible stenting of a ureteroileal stricture. AJR Am J Roentgenol 1990 Aug;155(2):422-3.
5 Barbalias GA, Liatsikos EN, Kalogeropoulou C, Karnabatidis D, Siablis D. Metallic stents in gynecologic cancer: an approach to treat extrinsic ureteral obstruction. Eur Urol 2000 Jul;38(1):35-40
[6] Pauer W, Lugmayr H. Metallic Wallstents: a new therapy for extrinsic ureteral obstruction. J Urol 1992 Aug;148(2 Pt 1):281-4.
[7] Diaz-Lucas EF, Martinez-Torres JL, Fernandez MJ, Carazo MO, de la Fuente SA,Zuluaga GA. Self-expanding wallstent endoprosthesis for malignant ureteral obstruct. J Endourol 1997 Dec;11(6):441-7.
8 http://emedicine.medscape.com/article/442469-overview#a1
[9] Campbell-Walsh Urology, Tenth Edition. Chapter 41. Page 1149. Ureteral stricture desease
[10] RJ Cetti, S Biers, and SR Keoghane\South Coast Stone Centre, Department of Urology, Queen Alexandra Hospital, Portsmouth, UK. 2011 by the Annals of The Royal College of Surgeons of England
[11] RATE OF URETERAL STRICTURE FOLLOWING URETEROSCOPY FOR NEPHROLITHIASIS USING A NATIONAL DATABASE OF INSURED PATIENTS Philip May*, Sarah Holt, Joshua Calvert, Jonathan Harper, Seattle, WA
[12] http://www.jurology.com/article/S0022-5347(16)00753-9/pdf
[13] https://urologysurgery.wordpress.com/2009/01/01/ureteral-stricture/
[14] https://www.nice.org.uk/guidance/cg169/chapter/1-Recommendations#managing-acute-kidney-injury
[15] https://www.nice.org.uk/guidance/CG175
[16] https://www.nice.org.uk/guidance/ng2
[17] https://www.nice.org.uk/guidance/CG175
[18] https://www.nice.org.uk/guidance/cg175/chapter/1-Recommendations#assessment-2

[19] Cambpell-Walsh Urology, Tenth Edition, https://books.google.com.eg/books?id=fu3BBwAAQBAJ&pg=PA1149&lpg=PA1149&dq=ureteral+stricture+campbell&source=bl&ots=Z0DAaVgjcG&sig=aZTR85U0CE_7eh9i2C-guV-rDn0&hl=en&sa=X&ved=0ahUKEwjbiceTsuLSAhWF3SYKHW64Bh4Q6AEIJzAC#v=onepage&q=ureteral%20stricture&f=false

[20] Stables DP, Ginsberg NJ, Johnson ML. Percutaneous nephrostomy: a series and review of the literature. AJR Am J Roentgenol 1978 Jan;130(1):75-82

[21] Protzel C, Dahm JB, Klebingat KJ. High frequency rotablation as a new therapeutic procedure for obstructed metallic ureter stents. J Urol 2001 Oct;166(4):1399-400.

[22] Allen DJ, Longhorn SE, Philp T, Smith RD, Choong S. Percutaneous urinary drainage and ureteric stenting in malignant disease. Clin Oncol (R Coll Radiol) 2010 Nov;22(9):733-9.

[23] J Endourol. 2008 Feb;22(2):295-9. doi: 10.1089/end.2007.0201.Success of ureteral stents for intrinsic ureteral obstruction.Wenzler DL1, Kim SP, Rosevear HM, Faerber GJ, Roberts WW, Wolf JS Jr.Department of Urology, University of Michigan, Ann Arbor, Michigan, USA.

24 Initial Experience with Full-Length Metal Stent to Relieve Malignant Ureteral Obstruction James F. Borin, Ori Melamud, and Ralph V. Clayman. Journal of Endourology. May 2006

[25] Ther Adv Urol. 2013 Dec; 5(6): 354–365.Current status of minimally invasive endoscopic management of ureteric strictures. Stefanos Kachrilas, Andreas Bourdoumis, Theocharis Karaolides, Stavroula Nikitopoulou, George Papadopoulos, Noor Buchholz, and Junaid Masood

[26] JSLS. 2003 Apr-Jun;Percutaneous Ureteral Incision With a Small-Caliber Flexible Ureteroscope Hatsuki Hibi, MD, Yoshiaki Yamada, MD, Hitoshi Nonomura, MD, Yukio Hatano, MD, Kenji Mitsui, MD, Tomohiro Taki, MD, Nobuaki Honda, MD, and Hidetoshi Fukatsu, MD
Hatsuki Hibi, Department of Urology, Aichi Medical University School of Medicine, Nagakute, Japan.

[27] Campbell-Walsh Urology, Tenth Edition. Section IX. Upper Urinary Tract Obstruction and Trauma. Page 1154

28 Paulos Yohannes, David Gershbaum, Paul E. Rotariu, Arthur D. Smith, and Benjamin R. Lee. Journal of Endourology. July 2004, Management of Ureteral Stricture Disease during Laparoscopic Ureteroneocystostomy

[29] Staios D, Shergill I, Thwaini A, Junaid I, Buchholz NP. The Memokath stent. Expert Rev Med Devices 2007 Mar;4(2):99-101.

[30] Maan Z, Patel D, Moraitis K, El-Husseiny T, Papatsoris AG, Buchholz NP, et al. Comparison of stent-related symptoms between conventional Double-J stents and a new-generation thermoexpandable segmental metallic stent: a validated-questionnaire-based study. J Endourol2010(4):589-93

31 Sountoulides P, Kaplan A, Kaufmann OG, Sofikitis N. Current status of metal stents for managing malignant ureteric obstruction. BJU Int 2010 Jan 8;(105):1066-72.

[32] Maan Z, Patel D, Moraitis K, El-Husseiny T, Papatsoris AG, Buchholz NP, et al. Comparison of stent-related symptoms between conventional Double-J stents and a new-generation thermoexpandable segmental metallic stent: a validated-questionnaire-based study. J Endourol2010(4):589-93.

[33] Prog Urol. 2011 Jun;21(6):397-404. doi: 10.1016/j.purol.2010.11.008. Epub 2011 Jan 26.The thermoformable spiral metallic stents in the treatment of localized ureteral stenosis: an alternative to JJ stent? Prospective multicenter study. Bonniol R1, Meria P, Safsaf A, Albouy B, Sibert L.Service d'urologie, hôpital Charles-Nicolle, Rouen,

[34] Urol. 2012 May;22.Tolerance and effectiveness of Memokath® 051 ureteral stents : a prospective 3 year follow-up study].Azizi A1, Pasticier G, Bénard A, Lapouge O, Ferrière JM, Ballanger P, Robert G Service d'urologie, CHU de Bordeaux, université Bordeaux-Segalen, place Amélie-Raba-Léon, 33000 Bordeaux, France

[35] Papatsoris A, Buchholz N. A novel thermo-expandable ureteric metal stent for the minimally invasive management of ureteral strictures. Journal of Endourology 2010 Mar 1;24(3):487-91***E***fficacy in benign and malignant cases together with a prove that MK51 is more cost effective than JJ stents on the long term Usage. UK

[36] **Characterization of Urinary Symptoms in Patients With Ureteral Stents**

HB Joshi et al. Urology 59 (4), 511-516. 4 2002

https://www.ncbi.nlm.nih.gov/labs/articles/11927301/

[37] Siddique KA, Zammit P, Bafaloukas N, Albanis S, Buchholz NP. Repositioning and removal of an intra-renal migrated ureteric Memokath stent. Urol Int 2006;77(4):297-300.

[38] Pearle M, Watson G. Optimal drainage of the obstructed kidney: stent versus nephrostomy. In: Yachia D, Paterson P, editors. Stenting the Urinary System. 2004. p. 139-42.
[39] Pearle M, Watson G. Optimal drainage of the obstructed kidney: stent versus nephrostomy. In: Yachia D, Paterson P, editors. Stenting the Urinary System. 2004. p. 139-42.
[40] Mendez-Probst CE, Fernandez A, Denstedt JD. Current status of ureteral stent technologies: comfort and antimicrobial resistance. Curr Urol Rep 2010 Mar;11(2):67-73.
[41] Agarwal MM, Singh SK, Mandal AK, Bhalla V, Acharya NC, Kumar S. Endourologic management of forgotten encrusted ureteral stents: can ureteroscopic lithotripsy be avoided? Surg Laparosc Endosc Percutan Tech 2009 Feb;19(1):72-7.
[42] Mendez-Probst CE, Fernandez A, Denstedt JD. Current status of ureteral stent technologies: comfort and antimicrobial resistance. Curr Urol Rep 2010 Mar;11(2):67-73.

NICE National Institute for Health and Care Excellence

National Institute for Health and Care Excellence

Centre for Health Technology Evaluation

Pro-forma Response

External Assessment Centre Report factual check

The Memokath-051 stent for the treatment of ureteric obstruction

Please find enclosed the assessment report prepared for this assessment by the External Assessment Centre (EAC).

You are asked to check the assessment report from Newcastle upon Tyne Hospitals (NUTH) and York Health Economics Consortium (YHEC) External Assessment Centre (EAC) to ensure there are no factual inaccuracies contained within it. If you do identify any factual inaccuracies you must inform NICE by 12pm, 23 June 2017 using the below proforma comments table. All your comments on factual inaccuracies will receive a response from the EAC and when appropriate, will be amended in the EAC report. This table, including EAC responses will be presented to the Medical Technologies Advisory Committee and will subsequently be published on the NICE website with the Assessment report.

20 June 2017

NICE National Institute for Health and Care Excellence

Issue 1

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
Memokath-051 is estimated to be cost neutral compared with other metallic stents.	Memokath-051 is estimated to be more cost effective compared with other metallic stents.	There is no follow up study or experience of any other metallic stent. Specially followed by removal	Thank you for your comment. As this is not a factual error, no change has been made. This conclusion is based on cost modelling which utilised the clinical data identified in the clinical review and expert opinion.

Issue 2

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
The External Assessment Centre (EAC) expanded the selection criteria to include other comparators and identified 16 studies, including all those used by the company. These were 6 comparative studies, including 3 abstracts and 1 clinical trial record, comparing Memokath-051 to 1 of 5 comparators (reconstructive surgery, double-J stents, UVENTA stents, Allium stents and Resonance stents) and 10	We totally object expanding the crieteria	All studies related to other metallic stents is sponsored by other matellic stents manufacturers, all of them are very obviously biased and contain actions which show enormous weakness and insistence to go in certain direction. More and over, numbers are so small to measure on and follow up periods are designed to avoid long term follow up or removal after more than one year. No other competitor can prove that they can remove their stents after more than one year	Thank you for your comment. As this is not a factual error, no change has been made. Our selection criteria were expanded in line with the NICE final scope. This was developed following stakeholder consultation.

single-arm, observational studies.			

Issue 3

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
• In the clinical care pathway first point'' Older patients with malignant terminal illness who have a life expectancy of 1 year or over''	Patients with malignant illness who have life expectancy or 1 year or over	Patient to benefit from MK51 are not needed to be old or terminal. Actually younger patients with better life expectancy are in more need to protect their ureters during the long course of radiotherapy or chemotherapy. They also deserve a better chance to have full protection until their disease is over and this might take years	Thank you for your comment. This has been updated as suggested.

Issue 4

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC response
In exclusion criteria in pathway of clinincal care: • Those with progressive malignant disease where the ureter may become	Removing that point	Actually from testimonials of majority of doctors worldwide (and even with sense) MK51 might be the best solution for such patients provided that the longer one (20) cm is inserted. The reason is that it is metal with no spaces in-between. This means low or no filtration, also better protection	Thank you for your comment. We acknowledge that you do not agree with the criteria, but are directly citing the scoping report produced by NICE. We have made a note next to this bullet point stating that the company does not agree with the criterion.

blocked above or below the stent;		from outside pressure, so better result and outcome for patients.	

NICE National Institute for Health and Care Excellence

Medical Technologies Evaluation Programme

MT311 The Memokath-051 stent for ureteral obstruction

Expert Adviser Questionnaire Responses

Name of Expert Advisers	Job Title	Professional Organisation/ Specialist Society	Nominated by	Ratified
Mr Matthew Shaw	Consultant Urologist	British Association of Urological Surgeons	Sponsor	Yes
Mr Mahmoud Elfar	Consultant Urologist	British Association of Urological Surgeons	Sponsor	Yes
Mr Peter Guy	Consultant Urologist	British Association of Urological Surgeons	NICE	Yes
Mr Ranan Das Gupta	Consultant Urologist	British Association of Urological Surgeons	Sponsor	Yes
Ms Daniela Andrich	Consultant Urological Surgeon	British Association of Urological Surgeons	Specialist Society	-

YOUR PERSONAL EXPERIENCE (IF ANY) WITH THIS TECHNOLOGY

Question 2: Please indicate your experience with this technology?

Expert Advisers	I have had direct involvement with this	I have referred patients for its use	I manage patients on whom it is used in another part of their care pathway	I would like to use this technology but it is not currently available to me
Mr Matthew Shaw Consultant Urologist	**Yes**	Blank	Blank	Blank
Mr Mahmoud Elfar Consultant Urologist	**Yes**	Blank	Blank	Blank
Mr Peter Guy Consultant Urologist	**Yes**	**Yes**	Blank	Blank
Mr Ranan Das Gupta Consultant Urologist	**Yes**	No	No	No
Ms Daniela Andrich Consultant Urological Surgeon	No	No	**Yes**	No

Any Comments?	
Mr Matthew Shaw Consultant Urologist	**I have inserted metallic stents into the ureter for 6 years.**
Mr Mahmoud Elfar Consultant Urologist	Blank
Mr Peter Guy Consultant Urologist	**I would only use this stent where the patient's life expectancy is > 6 months, where any malignancy is in complete remission or in benign strictures which cannot be "surgically" corrected**
Mr Ranan Das Gupta Consultant Urologist	**We are the main referral centre for this type of stent in our region**
Ms Daniela Andrich Consultant Urological Surgeon	Blank

Question 3: Have you been involved in any kind of research on this technology? If Yes, please describe?

Expert Advisers	Yes/No	Comment
Mr Matthew Shaw **Consultant Urologist**	No	Blank
Mr Mahmoud Elfar **Consultant Urologist**	No	Blank
Mr Peter Guy **Consultant Urologist**	No	Blank
Mr Ranan Das Gupta **Consultant Urologist**	**Yes**	**Only at preliminary discussion stages, with proposed project, not yet undertaken the basic science study planned. We have presented our clinical experience in a research forum, at the World Congress of Endourology**
Ms Daniela Andrich **Consultant Urological Surgeon**	No	Blank

THIS PRODUCT (TECHNOLOGY) AND ITS USE

Question 4: How would you best describe this technology?

Expert Advisers	It is a minor variation on existing technologies with little potential for different outcomes and impact	It is a significant modification of an existing technology with real potential for different outcomes and impact	It is thoroughly novel - different in concept and/ or design to any existing
Mr Matthew Shaw Consultant Urologist	Blank	Blank	**Yes**
Mr Mahmoud Elfar Consultant Urologist	Blank	Blank	**Yes**
Mr Peter Guy Consultant Urologist	**Yes**	Blank	Blank
Mr Ranan Das Gupta Consultant Urologist	No	**Yes**	**Yes**
Ms Daniela Andrich Consultant Urological Surgeon	No	**Yes**	No

Any Comments?	
Mr Matthew Shaw Consultant Urologist	**I write that this novel, however this stent has been around for several years. It is novel in that I know of no other similar technologies, but it has been in production and use for some considerable time.**
Mr Mahmoud Elfar Consultant Urologist	**It provide the same concept of insertion of stent to releive obstruction but it is a completely different technology, material and design**
Mr Peter Guy Consultant Urologist	**This ureteric stent has been available for a number of years with only minor mofication.**
Mr Ranan Das Gupta Consultant Urologist	**Well engineered technology, also confirmed by a bio-engineering Professor at our university, who has considerable experience in stent design of cardiovascular stents. This is a fairly unique type of option for ureteric stricture disease.**

Ms Daniela Andrich **Consultant Urological Surgeon**	Blank

Question 5: What is the most appropriate use (e.g. clinical indication) for the technology?

Expert Advisers	Comment
Mr Matthew Shaw **Consultant Urologist**	**This stent is used in the treatment of benign or malignant ureteric strictures. It can maintain ureteric patency and provide resistance to compressive tissue forces.**
Mr Mahmoud Elfar **Consultant Urologist**	**1- Ureteric obstruction secondary to extrensic maliganant disease** **2- Benign intrinsic ureteric strictures unsiutable for reconstructive surgery** **3- Extrensic ureteric obstruction caused by benign disease in patinets unfit/unwelling to have construsctive surgery (eg: retroperitoneal fibrosis).**
Mr Peter Guy **Consultant Urologist**	**Malignant or benign ureteric obstruction where definitive surgical correction is impossible or inappropriate. (Usually stricture excision and reanastomosis or implantation into the bladder or Boari Flap**
dMr Ranan Das Gupta **Consultant Urologist**	**Ureteric stricture, in the absence of stone disease; either benign or malignant aetiology of stricture. Regular stent not tolerable by patient**
Ms Daniela Andrich **Consultant Urological Surgeon**	**This product should ONLY be used for MALIGNANT ureteric strictures where the patient has limited life expectancy. In those circumstances, this technology is the least invasive way to preserve renal unit function and to maximise quality of life. This product should NOT be used in benign ureteric strictrues where reconstructive surgery is curative, unless the patient in unfit for major surgery.**

COMPARATORS (including both products in current routine use and also "competing products")

Question 6: Given what you stated is the appropriate indication (clinical scenario) for its use, what are the most appropriate "comparators" for this technology which are in routine current use in the NHS?

Expert Advisers	Comment
Mr Matthew Shaw Consultant Urologist	**Internal J-J ureteric stents (made by multiple manufacturers) and 'resonance' metallic ureteric stents made by Cook Medical.**
Mr Mahmoud Elfar Consultant Urologist	**polyurethane and modefied polyurethane JJ ureteric stents. needs replacement ervery 6-12 months.**
Mr Peter Guy Consultant Urologist	**Interventional radiological nephrostomy and antegrade stent placement where possible. Where not feasible, and in the context of palliative of ureteric malignant stricure formation, I personally now tend to use subcutaneous urinary diversion stents, mainly on cost grounds.**
Mr Ranan Das Gupta Consultant Urologist	**Regular JJ ureteric stents**
Ms Daniela Andrich Consultant Urological Surgeon	**J-J ureteric stents are most commonly used in the NHS, in both benign and malignant uretheric strictures, presumably because reconstructive urological services are located in Specialist Units and not every patient is referred for a specialist opinion.**

Question 7: "Competing products": Are you aware of any other products which have been introduced with the same purpose as this one?

Expert Advisers	Comment
Mr Matthew Shaw Consultant Urologist	**Covered nitinol stents such as Uventa and Allium stents. These are covered stents used in similar scenarios to the Memmokath stent, but do not require deployment or removal strategies that utilise hot or cold fluids.**
Mr Mahmoud Elfar Consultant Urologist	**The Allium Ureteral Stents are intended for temporary long or short-term use in malignant or benign chronic Ureteral Stenosis. Needs replacement each 12 months**
Mr Peter Guy Consultant Urologist	**I am not aware of other metallic stents**

Mr Ranan Das Gupta **Consultant Urologist**	**Metallic Resonance stents (Cook), which actually have a double-J component, and therefore potential similar problems as regular JJ stents**
Ms Daniela Andrich **Consultant Urological Surgeon**	**No**

POSSIBLE BENEFITS FOR PATIENTS

Question 8: ***What are the likely additional benefits for patients of using this technology, compared with current practice/ comparators?***

Expert Advisers	Comment
Mr Matthew Shaw **Consultant Urologist**	**The stent may give better patency than conventional J-J stents over the medium term, reducing the number of anaesthetics required by the patient in order to change the stents.**
Mr Mahmoud Elfar **Consultant Urologist**	**1- reduction of stent related symptoms** **2- less frequent change of stent** **3- less likely to obstruct by external compression** **4- less likely to encrus**
Mr Peter Guy **Consultant Urologist**	**Used only for long-term relief of ureteric obstruction. Although stent migration is not uncommon, it may be less likely to migrate or require replacement than the (cheaper) urinary diversion stent. Considerably more tolerable for patients than managing a long term nophrostomy.**
Mr Ranan Das Gupta **Consultant Urologist**	**Fewer anaesthetics for stent changes, as current practice. Potential for several year f/up without stent change. Well tolerated and fewer side-effects**
Ms Daniela Andrich **Consultant Urological Surgeon**	**As menitoned above, for malignant ureteric strictures in a patient with a short life expectancey, major reconstructive surgery may not be feasible or indicated. In those circumstances, this products seems to perform better than a J-J stent, which occludes quicker and has to be changed more frequently.**

Question 8.1: Is each additional benefit likely to be realised in practice? What are the likely obstacles?

Expert Advisers	Comment
Mr Matthew Shaw Consultant Urologist	These stents can still block or migrate. In addition, if placed for malignancy the disease process may advance to affect other areas of the ureter not treated by the stent.
Mr Mahmoud Elfar Consultant Urologist	yes benefits are easily realised in practice. The main obstacle is the initial price of the stent
Mr Peter Guy Consultant Urologist	N/A
Mr Ranan Das Gupta Consultant Urologist	Yes, these are already achieved, in my experience. Main obstacles are cost (expensive) and availability of technical expertise.
Ms Daniela Andrich Consultant Urological Surgeon	Blank

Question 8.2: How might these benefits be measured? What specific outcome measures would enable assessment of whether additional benefits for patients are being realised?

Expert Advisers	Comment
Mr Matthew Shaw Consultant Urologist	Patency rate can be assessed
Mr Mahmoud Elfar Consultant Urologist	1- stent questionair for stent symptoms 2- measuring readdmission rates with obstructed stents and stent related symptoms 3- patinets Quality of life asessment
Mr Peter Guy Consultant Urologist	RCT analysis of MemoKath 051 versus subcutaneous urinary diversion stent: ("Failure", frequency of replacement and cost benefit of each).
Mr Ranan Das Gupta Consultant Urologist	Subjective questionnaires and long-term prospective data collection

Ms Daniela Andrich **Consultant Urological Surgeon**	Blank

Question 8.3: How good is this evidence for each of these additional benefits?

Expert Advisers	Comment
Mr Matthew Shaw **Consultant Urologist**	**Moderate**
Mr Mahmoud Elfar **Consultant Urologist**	**Publication by Bart hospital London.**
Mr Peter Guy **Consultant Urologist**	**No RCTs. However, good evidence of effectiveness in case series studies.ne**
Mr Ranan Das Gupta **Consultant Urologist**	**Remains based on cohort series in individual centres.**
Ms Daniela Andrich **Consultant Urological Surgeon**	**I am not aware of good evidence apart from case series, but one has to bear in mind that in palliative care, this is very difficult to do.**

Question 8.4: Please add any further comment on the claimed benefits of the technology to patients, as you see applicable

Expert Advisers	Comment
Mr Matthew Shaw **Consultant Urologist**	Blank
Mr Mahmoud Elfar **Consultant Urologist**	Blank
Mr Peter Guy **Consultant Urologist**	**None**
Mr Ranan Das Gupta **Consultant Urologist**	**Warrants full evaluation and reporting of complications and revision rates**

Expert Advisers	Comment
Ms Daniela Andrich **Consultant Urological Surgeon**	**Blank**

POSSIBLE BENEFITS FOR THE HEALTHCARE SYSTEM

Question 9: What are the likely additional benefits for the healthcare system of using this technology, compared with current practice/ comparators?

Expert Advisers	Comment
Mr Matthew Shaw **Consultant Urologist**	**The stent may give better patency than conventional J-J stents over the medium term, reducing the number of anaesthetics and admission episodes required by the patient in order to change the stents.**
Mr Mahmoud Elfar **Consultant Urologist**	**Provide significant cost rreduction in long term (after 18 months)** **Free Theater sessions to be utilised by other cases**
Mr Peter Guy **Consultant Urologist**	**Much shorter patient and morbidity stay that open corrective surgery (whenever possible)**
Mr Ranan Das Gupta **Consultant Urologist**	**Cost-benefit analysis would require comparison with cost of repeat JJ stent changes**
Ms Daniela Andrich **Consultant Urological Surgeon**	**This devices gives clinicians additional armamentarium to treat their patients (with the correct indication).**

Question 9.1: Is each additional benefit likely to be realised in practice? What are the likely obstacles?

Expert Advisers	Comment
Mr Matthew Shaw **Consultant Urologist**	**These stents can still block or migrate. In addition, if placed for malignancy the disease process may advance to affect other areas of the ureter not treated by the stent.**
Mr Mahmoud Elfar **Consultant Urologist**	**Yes, The initial cost, The need to stock variable sizes and staff training**

Expert Advisers	Comment
Mr Peter Guy **Consultant Urologist**	**yes. Short patient stays universally reported about 1.5 days**
Mr Ranan Das Gupta **Consultant Urologist**	**Possibly realisable; obstacles include accurate measurement of theatre costs, and hospital stays, etc in a prospective standardised method**
Ms Daniela Andrich **Consultant Urological Surgeon**	**Blank**

Question 9.2: How might these benefits be measured? What specific outcome measures would enable assessment of whether additional benefits for the healthcare system are being realised?

Expert Advisers	Comment
Mr Matthew Shaw **Consultant Urologist**	**Patency rate can be assessed**
Mr Mahmoud Elfar **Consultant Urologist**	**audit initial insertion coast versus long term standard stent insertion cost + unplanned accident and emergency addmissions cost with Acute renal obstruction secondary to blocked stent and stent related symptoms**
Mr Peter Guy **Consultant Urologist**	**Already well reported**
Mr Ranan Das Gupta **Consultant Urologist**	**A national study, coordinated in dedicated centre(s) with experience of this technology, to fully evaluate the economic justification of an otherwise expensive technology**
Ms Daniela Andrich **Consultant Urological Surgeon**	**Blank**

Question 9.3: How good is this evidence for each of these additional benefits?

Expert Advisers	Comment
Mr Matthew Shaw Consultant Urologist	**Moderate**
Mr Mahmoud Elfar Consultant Urologist	**can be easily proven by audinting / comparing costs**
Mr Peter Guy Consultant Urologist	**Good case series, although no RCTs. All level 3 evidence**
Mr Ranan Das Gupta Consultant Urologist	**Currently restricted to audits from individual centres, some presented in national meetings**
Ms Daniela Andrich Consultant Urological Surgeon	Blank

Question 9.4: Please add any further comment on the claimed benefits of the technology to the healthcare system, as you see applicable

Expert Advisers	Comment
Mr Matthew Shaw Consultant Urologist	Blank
Mr Mahmoud Elfar Consultant Urologist	Blank
Mr Peter Guy Consultant Urologist	**Already "widely" used although all the case series report small numbers because of the uncommon nature of the condition and specific indcations.**
Mr Ranan Das Gupta Consultant Urologist	**N/A**
Ms Daniela Andrich Consultant Urological Surgeon	Blank

FACILITIES, TRAINING AND FUNCTIONING

Question 10: Are there any particular facilities or infrastructure which needs to be in place for the safe and effective use of this technology?

Expert Advisers	Comment
Mr Matthew Shaw Consultant Urologist	**It is likely that these stents would either be inserted by a sub-specialist endo urologist or by a urologist working with a radiologist. Radiology guidance is required. I would not envisage this service being offered by every urology department.**
Mr Mahmoud Elfar Consultant Urologist	**The facilities and infra-structure arre alresady in place in NHS theatres to insert traditional JJ polyurethane stents. this include Cystoscopy and C-arm Xray Unit. The additional cost will be for baby bottle wormer to heat the normal saline and fridge to keep cold saline if needed.**
Mr Peter Guy Consultant Urologist	**No**
Mr Ranan Das Gupta Consultant Urologist	**yes, should be within an Endourology unit with large experience of ureteroscopy/ureteric surgery (possibly allied to a cancer/reconstructive centre, in order to manage complications)**
Ms Daniela Andrich Consultant Urological Surgeon	**this product should fall within the competence spectrum of any endourological service**

Question 11: Is special training required to use this technology safely and effectively?

Expert Advisers	Comment
Mr Matthew Shaw Consultant Urologist	**Yes, specialist training is needed. The implanting surgeon will need skills in using x-ray based imaging**
Mr Mahmoud Elfar Consultant Urologist	**Yes. Initial training is needed to alow nursing staff to be failiar with the procedure and Urologist to be able to dilate the ureter and insert the stent safely**
Mr Peter Guy Consultant Urologist	**Yes**
Mr Ranan Das Gupta Consultant Urologist	**Attendance at training workshops currently the standard; no formal mentoring process established.**

Ms Daniela Andrich Consultant Urological Surgeon	**this product should fall within the competence spectrum of any endourological service**

Question 12: Please comment on any issues relating to the functioning, reliability and maintenance of this technology which may be important to consider if it is introduced

Expert Advisers	Comment
Mr Matthew Shaw Consultant Urologist	**Patients require follow-up to check on continued patency of the implanted metallic stent.**
Mr Mahmoud Elfar Consultant Urologist	**The manifacturer stated that the stent should be changed on 5 yearly basis (However, there are data showing patients ahving the Memokath stent for nearly 11 years without any complications or need to change)**
Mr Peter Guy Consultant Urologist	**Not complex. Reliable technology, but technical skill and judgement required in case selection and device deployment.**
Mr Ranan Das Gupta Consultant Urologist	**Need to define its suitability in the presence of stone disease (we have avoided this due to risk of encrustation)**
Ms Daniela Andrich Consultant Urological Surgeon	**stents can slip, patient follow up is required**

COSTS

Question 13: Please provide any comments on the likely cost consequences of introducing this technology. In particular, please comment on the implications of this technology replacing the comparator/s you have described above

Expert Advisers	Comment
Mr Matthew Shaw **Consultant Urologist**	**I have no specific cost knowledge**
Mr Mahmoud Elfar **Consultant Urologist**	**The main problems ar the initial cost and the need for training;** **Bart Hospital comparing study -2012 showed;** **JJ stent** **6 monthly exchanges of 41 JJ in 37 patient** **22 month period of time** **€ 490,200** **Memokath 051** **€ 282,200 + / 2 blocked and 5 migrated stents** **Total cost – savings with Memokath 051 stent € 208,000** **I have attached our own audit with the documents for futher information.**
Mr Peter Guy **Consultant Urologist**	**Cost of implantation is around £6.5K for Mempkath 051,No compared to £3.5K for non metallic stent placement**
Mr Ranan Das Gupta **Consultant Urologist**	**Potential benefit depends on longevity of the technology (ie how many regular stent changes are avoided in order to justify cost of this semi-permanent stent)**
Ms Daniela Andrich **Consultant Urological Surgeon**	**Can't comment**

GENERAL ADVICE BASED ON YOUR SPECIALIST KNOWLEDGE

Question 14: Is there controversy about any aspect of this technology or about the care pathway?

Expert Advisers	Comment
Mr Matthew Shaw Consultant Urologist	**Not particularly, although follow-up post implantation is not defined.**
Mr Mahmoud Elfar Consultant Urologist	**No**
Mr Peter Guy Consultant Urologist	**Blank**
Mr Ranan Das Gupta Consultant Urologist	**No**
Ms Daniela Andrich Consultant Urological Surgeon	**The controversy will arise depending on whom you ask for their opinion. Generally, one would assume, one recommends treatment one is familiar with. There are more general urologists competent to perform endourological procedures than reconstructive surgical procedures. Reconstrucitve surgeons can do both.**

Question 15: If NICE were to develop guidance on this technology, how useful would this be to you and your colleagues?

Expert Advisers	Comment
Mr Matthew Shaw Consultant Urologist	**Quite helpful, particularly if it included recommendations about follow-up.**
Mr Mahmoud Elfar Consultant Urologist	**Very useful as it will generate spefic giudelines for the use of the technology.**
Mr Peter Guy Consultant Urologist	**Given that these stents are placed in centres where "special interest" has developed, referral guidance would be very helpful.**
Mr Ranan Das Gupta Consultant Urologist	**Helpful to have formal recognition of the technology, and also a directive about its use in specilaised centres**

Ms Daniela Andrich **Consultant Urological Surgeon**	**Very useful**

Question 16: Do any subgroups of patients need special consideration in relation to the technology (for example, because they have higher levels of ill health, poorer outcomes, problems accessing or using treatments or procedures)? Please explain why

Expert Advisers	Comment
Mr Matthew Shaw **Consultant Urologist**	**Many people using this product will have malignant disease.**
Mr Mahmoud Elfar **Consultant Urologist**	**1- Anticoagulated patients who can not safely stop their anticoagulat medication may have prolonged haematuria if they have very tight stricture reqiuring significant dilatation** **2- Patinets with pelvi-ureteric junction obstruction as they may expereience significant risk of stent migration** **3- young patinets who should ideally have reconstruction surgery whenever possible.** **4- Recurrent stone former or patinets with hypercalcuria, patients with hyperparathyroidism will have higher level of stent encrustation. This will be applicable for both Polyurethan and Memokath stents.**
Mr Peter Guy **Consultant Urologist**	**Patients with actively malignant strictures and poor survival expectance <6months need special consideration with regard to cost benefit.**
Mr Ranan Das Gupta **Consultant Urologist**	**Renal stone patients - may have higher rates of encrustation**
Ms Daniela Andrich **Consultant Urological Surgeon**	**See above**

CONFLICTS OF INTEREST

Question 18.1: Do you or a member of your family have a personal financial interest? The main examples are as follows:

Expert Advisers	Consultancies or directorships	Clinicians receiving payment for a procedure	Fee-paid work	Shareholdings	Financial interest in a company's product	Expenses and hospitality	Funds	Personal non-pecuniary interest
Mr Matthew Shaw Consultant Urologist	No	No	**Yes**	No	No	No	No	No
Mr Mahmoud Elfar Consultant Urologist	No	No	No	No	No	No	No	No
Mr Peter Guy Consultant Urologist	No	No	No	No	No	No	No	No
Mr Ranan Das Gupta Consultant Urologist	No	No	No	No	No	No	No	No
Ms Daniela Andrich Consultant Urological Surgeon	No	No	No	No	No	No	No	No

If you have answered YES to any of the above statements please describe the nature of the conflict(s) below.

Mr Matthew Shaw Consultant Urologist	**I have received payment for the provision of educational services for Eli Lily, Astellas, Glaxo Smith Kline and Lumenis Surgical.**
Mr Mahmoud Elfar Consultant Urologist	Blank
Mr Peter Guy Consultant Urologist	Blank

Mr Ranan Das Gupta Consultant Urologist	Blank
Ms Daniela Andrich Consultant Urological Surgeon	Blank

Question 18.2: Do you have a non-personal interest? The main examples are as follows:

Expert Advisers	Grant for the running of a unit	Grant or fellowship for a post or member of staff	Commissioning of research	Contracts with or grants from NICE
Mr Matthew Shaw Consultant Urologist	No	No	No	No
Mr Mahmoud Elfar Consultant Urologist	No	No	No	No
Mr Peter Guy Consultant Urologist	No	No	No	No
Mr Ranan Das Gupta Consultant Urologist	No	No	No	No
Ms Daniela Andrich Consultant Urological Surgeon	No	No	No	No

If you have answered YES to any of the above statements please describe the nature of the conflict(s) below.

Mr Matthew Shaw Consultant Urologist	Blank
Mr Mahmoud Elfar Consultant Urologist	Blank
Mr Peter Guy Consultant Urologist	Blank

Mr Ranan Das Gupta **Consultant Urologist**	Blank
Ms Daniela Andrich **Consultant Urological Surgeon**	Blank

Question 18.3: ***Do you or your organisation or department have any links with, or funding from the tobacco industry?***

Expert Advisers	Yes or No?	*If you have answered YES to any of the above statements please describe the nature of the conflict(s) below.*
Mr Matthew Shaw **Consultant Urologist**	No	Blank
Mr Mahmoud Elfar **Consultant Urologist**	No	Blank
Mr Peter Guy **Consultant Urologist**	No	Blank
Mr Ranan Das Gupta **Consultant Urologist**	No	Blank
Ms Daniela Andrich **Consultant Urological Surgeon**	No	Blank

National Institute for Health and Care Excellence

Medical technologies evaluation programme

MT311 – Memokath-051 stent for the treatment of ureteric obstruction

Consultation comments table

Final guidance MTAC date: 17 November 2017

There were 19 consultation comments from 7 consultees (2 manufacturer, 1 healthcare (other), 1 specialist society, 2 private sector professionals, 1 other). The comments are reproduced in full, arranged in the following groups according to the main issue raised in the relevant comment (**some comments contain multiple issues**):

- Evidence
- Patient choice
- Resolution of stricture
- Clinician experience
- Advantages against reconstruction surgery
- Ease of stent removal
- Cost model
- General
- Registry (see letter)

Evidence

Com. no.	Consultee number and organisation	Sec. no.	Comments	Response
5a	4 Private Sector Professional	1.2	I disagree that Memokath 051 has equivalent success rates to JJ stents. MK is much better in terms of QoL, long term cost efficacy, risk of repeated anaesthesia and use of hospital resources.	Thank you for your comment. The recommendation in section 1.2 is based on the committee's view of the benefits of the technology taking into consideration the available evidence and expert advice. The committee considered this comment and decided not to change the guidance.
10	5 Healthcare industry (other)	1.2	it is mentioned that " Point Number 1.2 Memokath-051 stents when implanted by trained and experienced surgeons (see section 4.7) and in appropriate patients are associated with equivalent success rates to double-J stents and a better patient experience. Compared with double-J, using Memokath-051 stents may also reduce the number of stent replacements needed. Memokath-051 stents for the treatment of ureteric obstruction should be considered as an option" and I see this is not totally correct as all the studies, including the ones acknowledged by the report confirm that MK051 is far higher in results than JJ stents. this covers nearly all terms, symptoms, QOL, duration of stay insitu, long term cost and protection against cancer cells. so saying it is equal in results is not fair as it seems to me	Thank you for your comment. In the assessment report the EAC considered 6 comparative studies, including 3 abstracts and 1 clinical trial record, comparing Memokath-051 to 1 of 5 comparators (reconstructive surgery, double-J stents, UVENTA stents, Allium stents and Resonance stents) and 10 single-arm, observational studies were deemed eligible for inclusion in the evaluation. The studies were judged low quality evidence, primarily because of inadequate reporting of study design, patient characteristics and outcomes. Please see response to comment 5a.
13	5 Healthcare industry (other)	3.1	The total number that can be found for medical search websites like pubmed is 56 studies. The 16 studies are the ones who has been considered by the External report	Thank you for your comment. Section 3.1 has been amended.
7a	4 Private Sector Professional	3.4	The evidence for comparable stents Allium and Uventa is based on single studies. This is meager. As far as I know, Allium and Uventa are approved for one year. After that use is off label. MK has no such restriction and my longest case is 10+ years	Thank you for your comment. In this evaluation the EAC identified and reviewed all the relevant evidence associated with Memokath-051. The evidence base for the comparator technologies was not reviewed however the committee were aware that the evidence base for these technologies is limited. Allium ureteric stents can remain in situ for up to 3 years and the duration of the UVENTA stent is uncertain. The committee decided not to change the guidance.
14a	5 Healthcare industry (other)	3.4	comparison with UVENTA and ALLIUM based on a single study each which is sponsored by the competitor and/or issued in the country of origin of the competitor is not fair at all and will lead to false outcome. Here we should consider this factor and refer to as many doctors who used these stents and check thier	Thank you for your comment. The committee was aware that the evidence base for the UVENTA and Allium stents is limited. Of the comparative studies, all of the studies except 2 (Bolton et al., 2015, Nam et al., 2015) reported on their funding status. Of these, 3 received no funding or declared no competing financial

Com. no.	Consultee number and organisation	Sec. no.	Comments	Response
			experience. this because the papers and studies of competitors are too little.	interests (Akbarov et al., 2017, Kim et al., 2014, Maan et al., 2010). The remaining study was funded by both the Mayo Clinic and PNN Medical (i.e. the company) (NCT00166361, 2014). The committee decided not to change the guidance.
14b	5 Healthcare industry (other)	3.4	Also, to the best of our knowlege, Other metal stents are only approved for one year. any longer use is off label and upon company claims which is not supported scientifically. we totally believe that taking the information from companies recommendations is not a scientifically solid proof, otherwise you should do the same for MK051	Thank you for your comment. Please see response to comment 7a.
8a	4 Private Sector Professional	3.8	Whereas I agree with an average indwelling time for JJ stents of 6 months, a high incidence of reflux pain and lower urinary tract symptoms can hardly be seen as 100% success. Success cannot only be defined as patency of the ureter. We treat patients, not ureters.	Thank you for your comment. The committee makes recommendations after considering all of the relevant evidence including expert advice. In their review of the evidence the EAC noted that definitions of clinical success were inconsistent across the trials and it is not clear how long a stent must remain functioning and in place before it is classified as a clinical success in each trial. The frequency and duration of follow-up varied across the studies meaning the point at which clinical success was measured varied. The committee noted the quality of life benefits to patients from the technology in section 4.5. The committee decided not to change the guidance.
8b	4 Private Sector Professional	3.8	Data derived from company studies must be regarded as biased, as opposed to clinical studies from independent health care providers. Please consider.	Thank you for your comment. Please see response to comment 14a.
17	5 Healthcare industry (other)	-	there is a presentation in WCE in october this year discussed the durability, effectiveness and advanges of some metal stents compared with MK051. this was presented by Dr. Ravi Kulkarni from UK. I would like to refer you to that presentation which showed very clear that MK051 is far higher that the other competitors.	Thank you for your comment. This presentation occurred after the EAC conducted their searches. The EAC have reviewed the presentation and concluded that it does not report on any new data, but rather reports on data either already included within the assessment report or not suitable for inclusion (e.g. unpublished case studies) it does not appear to add to the evidence base. The committee decided not to change the guidance.

Patient choice

Com. no.	Consultee number and organisation	Sec. no.	Comments	Response
5b	4 Private Sector Professional	1.2	Especially in malignant cases with a limited life expectancy, less hospital stays/ visits mean a significant improvement of the patients QoL. Patients may choose not to undergo major reconstructive surgery and opt for a minimally invasive treatment with MK. This patient choice has nowhere been considered.	Thank you for your comment. The committee decided to amend the guidance in sections 1.2 and 4.3 to reflect patient choice.
11a	5 Healthcare industry (other)	1.2	Memokath-051 stents for the treatment of ureteric obstruction should be considered as an option in patients with: · malignant ureteric obstruction and anticipated medium- or long-term survival after adjunctive therapy or · benign ureteric obstruction who cannot have reconstructive surgery or · ureteric obstruction of any kind who cannot have a double-J stent or other stent or who need to avoid repeated procedures. for second point, benign ureteric obstruction: what about long term benign patients (like retroperitoneal fibrosis) who desire a better quality of life and less cost and less hospitalization and anesthesia. I believe they also have the right to have a better chance with MK051	Thank you for your comment. Please see response to comment number 5b.

Resolution of stricture

Com. no.	Consultee number and organisation	Sec. no.	Comments	Response
7b	4 Private Sector Professional	3.4	Nowhere has been taken into account that there is a 13-18% spontaneous resolution rate with Memokath. These are strictures where stent migration occurs after some time due to an opening of the strictures. No more stenting is then required. It is thought that temporary inert scaffolding allows some strictures to heal. This is not migration but treatment success!	Thank you for your comment. With Memokath, the reported resolution risk is wide (likely from around 0% to 19%) from the studies considered in the evaluation. The EAC advised that any improvement in resolution risk with Memokath is not supported by the current evidence base. The clinical experts advised that the term 'resolution of a stricture' may be confusing because the stricture does not disappear as a result of the stent. The committee decided to re-word the consideration in section 4.6.of the guidance to avoid this term.
14c	5 Healthcare industry (other)	3.4	For migration rate, the calculation ignored the complete resolve of the stricture in most of studies related to MK51. This represents 13%-18% of cases. When this calculation is adapted, the migration rates of MK51 is the best	Thank you for your comment. Please see response to comment number 7b.
3a	2 Manufacturer	-	Through my work at pnn medical, it was also great to find in some patients that the ureter was 100% stricture resolved after inserting Memokath and that they didn't require any further treatment.	Thank you for your comment.
4a	3 Healthcare Other	-	It improves the quality of Life in addition it is cost-effective as the patient avoids stent replacement every 6 months. In 13-18% of cases, a complete resolve of the stricture occurred.	Thank you for your comment. Please see response to comment number 7b.

Clinician experience

Com. no.	Consultee number and organisation	Sec. no.	Comments	Response
16	5 Healthcare industry (other)	4.6	the decision of insertion of MK051 may need an experienced clinician but we have to differentiate between the decision and actual procedure. in most of NHS hospitals now, the insertion itself as a procedure can be done by any surgeon as it very easy. but the decision is different	Thank you for your comment. The committee makes recommendations after considering all of the relevant evidence including expert advice about NHS practice. The committee concluded that a multidisciplinary team should make the decision to use Memokath-051 (see section 4.8) and that the clinician inserting it should be trained in its use (see section 4.9). The committee decided to amend the potential members of the multidisciplinary team.
9	4 Private Sector Professional	4.8	The crucial step to success with MK is the right indication. However, as long as the indication is right (i.e. under consultation with an endourology expert), after some training any urologist can insert a MK which is easy.	Thank you for your comment.
4b	3 Healthcare Other	-	Memokath-051 stent is a Minimally Invasive Reversible technique so its a safe, simple and reliable ureteric stent.	Thank you for your comment.

Advantages against reconstruction surgery

Com. no.	Consultee number and organisation	Sec. no.	Comments	Response
11b	5 Healthcare industry (other)	1.2	also I totally think, shared with many other opinions, that MK051 must be the first option before constructive surgery as it is much less invasive and needs less skills for insertion. then if it is failed, then comes the constructive surgery	Thank you for your comment. Section 4.3 outlines the rationale for patient selection. Section 1.2 has been amended to reflect some patients may prefer to decline surgery.
6	4 Private Sector Professional	2.3	MK is a minimally invasive treatment compared to reconstructive surgery. It can be regarded as a first line approach, with reconstructive surgery remaining always a follow up option.	Thank you for your comment. Section 2.3 reflects the company's claimed benefits. Reconstructive surgery was identified as a valid comparator in the scope.
12a	5 Healthcare industry (other)	2.3	there are also some more advantages to be considered: it is a minimal invasive technique compared with classic reconstruction	Thank you for your comment. The claimed benefits are made by the company and are outlined at the notification stage. Claimed benefits cannot be amended at this stage. The committee considered the impact of surgery on patients and amended the guidance to reflect the possibility that some patients may decline surgery.

Ease of stent removal

Com. no.	Consultee number and organisation	Sec. no.	Comments	Response
12b	5 Healthcare industry (other)	2.3	there are also some more advantages to be considered: other metal stents and it is reversible and this is a very important point for patient safety	Thank you for your comment. The company and the EAC did not identify any comparative evidence outlining the ease of stent removal. Clinical expert advice to the committee was that Memokath-051 is not always easier to remove than JJ stents.
7c	4 Private Sector Professional	3.4	In my experience, polyurethane coated metal scaffold stents, such as Allium, work well in the distal ureter, especially to occlude uretero-vaginal fistulas. The polyurethane layer decays after that and that makes stent removal quite messy.	Thank you for your comment.
14d	5 Healthcare industry (other)	3.4	Reversibility was also ignored in comparison and again to the best of our knowledge, there is no proof for other stents to be easily removed after more than one year indwelling time	Thank you for your comment. Please see response to comment 12b.
3b	2 Manufacturer	-	Patients either malignant or benign cases who had Memokath stents had a better quality of life especially that the procedure is simple and most important reversible knowing that its removal at any time is very easy unlike other stents.	Thank you for your comment. Please see response to comment 12b.
18	6 Other	-	I have used the memokath 051 ureteric stent since 2009 in selected patients. As stated in the report patient selection is the key to success. At Rigshospitalet in Copenhagen the memokath 051 has been used in both malignant and also in several benign cases. Stent insertion demands a well demarked stricture for the stent to "cling" to, and of cause you must be able to accomplish dilatation to the neccessary 14F. If this can be acchieved then the patient will generally be pleased to find him(herself) without the usual drawbacks of a JJ stent (urgency, dysuria, pollakisuria etc). When the memokath becomes obstructed either due to incrustrations or if further stenosis develops - then the memokath is easily removed and can be replaced with a longer one if needed. I have inserted more than 70 memokath stents - and must say that the stent in general does a very good job.	Thank you for your comment.

Com. no.	Consultee number and organisation	Sec. no.	Comments	Response
			The overall impression is that the patients clearly prefer the memokath over a JJ stent(but one of our selection criterias is JJ side-effects). I have encountered a couple of stricture resolvement due to the long-term dilatation. I can recommend the 051 memokath for use in ureteric strictures.	

Cost model

Com. no.	Consultee number and organisation	Sec. no.	Comments	Response
15	5 Healthcare industry (other)	3.8	JJ stents is calculated for 6 month indwelling time! this is not correct by any means and I believe that NHS can get the actual average of stay forJJ from the records of any related hospital and from my experience the average never exceeds 4 moths. this can totally change the calculation in the favor of MK051 All the data calculated for other metal stents are derived from companies and not from studies as the situation for MK51. This means that all the calculation made for competitors are according to their best interest Despite of the above, all results from the external report are in the favour of MK51 regarding QOL, Cost effectiveness and reversibility	Thank you for your comment. The 6 month indwelling time for double J stents reflects the company's basecase model. The company did not provide any analysis against other comparators. Thank you for your comment. The committee noted that the company's basecase model assumed a 6 month in-dwelling time for double J stents. The EAC used the available data to compare MemoKath -051 with the other metallic stents. The committee was aware of the uncertainties in the model because of the limited data available.

General

Com. no.	Consultee number and organisation	Sec. no.	Comments	Response
1	1 Private Sector Professional	-	I have been using this with my patients for more than 8 years now and I want to stress the simplicity and effectiveness of the procedure, I also have very positive feedback from my patients regarding tolerability and cost effectiveness.	Thank you for your comment
2	1 Private Sector Professional	-	Another point is the continuous support of the Pnn Medical team here in Egypt in training and assisting the urologists on the Memokath051 procedure.	Thank you for your comment
3c	2 Manufacturer	-	I have been working at Pnn Medical for 10 years and throughout the 10 years i have seen how Memokath has changed the Quality of Life of patients all around the world. Patients had to visit the hospital every 6 months for stent exchange and follow up which meant having to go into theatres every 6 months which affected the Quality of Life of the patient and was not cost effective. Not having the necessity to return back to theatres after 6 months guaranteed a happy life for the patient and the cost effectiveness for both patient and hospital. Satisfaction of the patient was and will always be pnn medical's aim.	Thank you for your comment

Register

Com. no.	Consultee number and organisation	Sec. no.	Comments	Response
19	Professional society	-1	Please see the response from BAUS in appendix 1	Thank you for your comment. The committee considered that data collection is still needed to better understand the benefits of Memokath-051 (see section 4.7). The committee decided to remove a specific recommendation in section 1 about the type of data collection, to allow further appropriate discussions to take place (see section 4.7 of the guidance).

"Comments received in the course of consultations carried out by NICE are published in the interests of openness and transparency, and to promote understanding of how recommendations are developed. The comments are published as a record of the submissions that NICE has received, and are not endorsed by NICE, its officers or advisory committees."

Appendix 1

THE BRITISH ASSOCIATION OF UROLOGICAL SURGEONS

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07 November 2017

Peter Groves
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Dear Peter

Re; NICE Evaluation Memokath -501

Thanks for taking the opportunity to chat with me last Friday.

As a charity, BAUS currently spends £150,000 per year on data and audit and collects information on eight different areas of urological surgery. With respect to implantable devices, the association currently collects information on mesh implantation for urinary stress incontinence and penile prosthesis insertion for erectile dysfunction. These activities are largely funded through the charity and place a significant financial burden on the organisation.

If the final report from NICE on Memokath- 501 endorses the view that a registry should be established, BAUS would welcome the opportunity to work with NICE through one of its External Assessment Centres. However, we estimate that the cost of setting up a registry is approximately £7,000 excluding professional input and data analysis and BAUS would not be a financial position to support this registry to the exclusion of others. Across the NHS, there are concerns about a number of implanted devices (breast, buttock and calf implants, mesh for pelvic organ prolapse and urinary stress incontinence etc). For these reasons, we believe that it would be useful for NICE to take a lead in setting up a summit on registries for implanted devices, so we can look at funding models and learn lessons from those which are already established and maybe from those which are perceived to have failed; such a summit should include NHSE, NHS Digital and MHRA.

I look forward to seeing the final draft of the Memokath-051 consultation.

Yours sincerely,

Kieran O'Flynn
President, BAUS

Cc Patricia Hagan (BAUS Deputy CEO)