NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Medical technology consultation:

GID-MT569 Memokath 051 Ureter stent for ureteric obstruction (guidance update)

Supporting documentation – Committee papers

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

1. **EAG assessment report** – an independent report produced by an external assessment centre who have reviewed and critiqued the available evidence.
2. **Assessment report overview (updated)** – an overview produced by the NICE technical lead which highlights the key issues and uncertainties in the company's submission and assessment report.
3. **Scope of evaluation** – the framework for assessing the technology, taking into account how it works, its comparator(s), the relevant patient population(s), and its effect on clinical and system outcomes. The scope is based on the sponsor's case for adoption.
4. **Expert questionnaires** – expert commentary gathered by the NICE team on the technology.
5. **EAC correspondence log** – a log of all correspondence between the external assessment centre (EAC) and the company and/or experts during the course of the development of the assessment report.
6. **Company information request** – updated information and new data provided by the company

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 technologies guidance update

GID-MT569 Memokath-051 stent for ureteric obstruction number and evaluation title (guidance update)

External Assessment Centre Assessment report update

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Number of attached appendices: [4]

Purpose of the assessment report update

The purpose of this External Assessment Centre (EAC) assessment report update is to review and critically evaluate evidence published since the original guidance was produced, as well as evidence and information submitted by the company during guidance review and guidance update. The report may also include additional analysis of the submitted evidence or new clinical and/or economic evidence. NICE has commissioned this work and provided the template for the report update. The report update forms part of the papers considered by the Medical Technologies Advisory Committee when it is making decisions about updating the guidance. It should be read alongside the original assessment report and guidance review decision.

Declared interests of the authors

Description of any declared interests with related companies, and the matter under consideration. See NICE's Policy on managing interests for board members and employees.

None.

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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
CI	Confidence interval
EAC	External Assessment Centre
IQR	Interquartile range
MAUDE	Manufacturer and User Facility Device Experience
MHRA	Medicines & Healthcare products Regulatory Agency
Mos.	Months
NHS	National Health Service
NICE	National Institute for Health and Care Excellence
NR	Not reported
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
RCT	Randomised controlled trial
SD	Standard deviation
SIE	Stent Insertion Episode
UK	United Kingdom
UTI	Urinary Tract Infection
Vs	Versus

Executive summary

The MTG35 guidance published in 2018 stated that the case for adopting Memokath-051 for treating ureteric obstruction is partially supported by the evidence. The evidence was limited but suggested that Memokath-051 is effective in patients with malignant ureteric obstruction and anticipated medium- or long-term survival after adjunctive therapy. Additionally, it was recommended in patients with benign ureteric obstruction who cannot or do not want reconstructive surgery and in patients with ureteric obstruction of any kind who cannot have or do not want a double-J stent, or for whom repeat procedures are associated with high risk. Memokath-051 was shown to be equivalent to the double-J stent in success rate and associated with better patient experience. The cost consequences for adopting Memokath-051 were deemed uncertain, but it was highlighted that when used in appropriate patients, by trained clinicians, Memokath-051 could be cost neutral or cost saving compared with standard treatment due to the fewer repeat procedures.

There has been no change to the technology, care pathway and cost of the technology since the original guidance was published. But a decision was made to update the guidance due to new evidence identified in the 2021 guidance review reporting on longer-term outcomes (mean follow-up of up to 5 years) for using Memokath-051. (Forster et al. 2021)

During the guidance review the company submitted 6 studies, however, only 1 of these studies (Forster et al. 2021) met the scope. The company did not submit any new evidence for this guidance update. The EAC included 7 studies (5 full texts and 2 conference abstracts) in total which met the scope. The included studies are mainly retrospective, non-comparative studies of a low-moderate sample size and varying follow-up periods. The studies were also all single-centre studies, only two full-text studies were conducted in a UK NHS setting, this limits the generalisability of the results. Similarly to the original guidance, the evidence was limited and the EAC believes the evidence base is of low-moderate quality.

Stent migration was the most common complication associated with Memokath-051 from the clinical evidence identified. Memokath-051 was associated with higher stent migration than its comparators. This is in line with the evidence identified for the original guidance. A study with longer follow-up of 5 years revealed that Memokath-051 was associated with a high overall complication rate (72%; Forster et al. 2021).

There was some variation amongst the studies for success rate and indwelling time of Memokath-051. Memokath-051 was associated with higher stent failure compared with Allium and Resonance (Khoo et al. 2021). But Memokath-051 was associated with higher success rate compared with UVENTA in a population of patients with chronic benign ureteral strictures with better durability for primary success in the second and third years (Choi et al. 2019). A study conducted in the UK with a low loss to follow-up (3%), reported a statistically significant higher stent indwelling time

in patients with malignant ureteral strictures compared with benign (Forster et al. 2021), these results are in line with the findings from the original guidance.

No new economic evidence was available in the literature for Memokath-051. The EAC updated the cost models with newer clinical parameters as reported in the clinical evidence review. Khoo et al. 2021 reported stent replacement for Memokath-051, but had a very high proportion of stent failure and short functional stent follow-up (5.5 months) but is a UK based study. The EAC noted the limitation and included Khoo et al. 2021 along with all new primary studies. The EAC conducted a sensitivity analysis to assess the robustness of the cost savings by excluding the Khoo et al. 2021 study, this did not change the cost saving conclusions. The EAC also conducted a sensitivity analysis to assess the assumption that double-J stent replacement occurs every 6 months with no unplanned replacement, the analysis showed that changes to this assumption does not change the cost saving conclusions. In the absence of UK specific evidence, the EAC updated the model with new evidence for UVENTA from a Korean study (Choi et al. 2019). The cost models suggest that under a conservative assumption of constant stent replacement over a 5-year period, Memokath-051 is cost saving compared to double-J stents, UVENTA, Allium and Resonance. It is cost incurring compared to reconstructive surgery. This suggest that Memokath-051 stents may be a plausible cost saving treatment option for ureteric obstruction in people who cannot have reconstructive surgery and need a ureteral stent.

The latest evidence continues to provide a basis for Memokath-051 as a potentially cost saving option for certain people with ureteric obstructions but highlights that clinicians should be aware of a potential increased risk of complications with Memokath-051, particularly stent migration.

1. Decision problem

The company did not propose any variation to the decision problem at guidance update.

Decision problem	Scope	EAC comment
Population	Adults with ureteric obstruction as a result of benign and ureteric obstruction	No variation
Intervention	Memokath-051	No variation
Comparator(s)	• Double-J stents • Nephrostomy • Reconstructive surgery • Metallic and alloy stents (including nitinol stents)	No variation
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,	No variation

	rates of stent migration, encrustation and infection, 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 perspective. The time horizon for the cost analysis will be sufficiently long to reflect any differences in costs and consequences between technologies compared. Sensitivity analysis will be undertaken to assess uncertainties in the model parameters.	No variation
Subgroups	• Patients unfit for surgery • Malignant or benign stricture • Antegrade or retrograde insertion (including the procedure	No variation

2. Overview of the technology

Memokath-051 is a thermo-expandable, nickel-titanium shape memory alloy ureteric stent (Kulkarni and Bellamy, 1999). It is intended as an alternative to conventional ureteric stents for people with malignant or benign ureteric obstruction, (PNN Medical, 2019). The benefits according to the manufacturer, include avoiding the side effects of major surgery and discomfort (PNN Medical, 2019). The company states that Memokath-051 stent is typically inserted in 30-45 minutes under general or spinal anaesthesia and can be inserted either antegrade (direction of the kidney to the bladder) or retrograde (from the direction of bladder to the kidney) (PNN Medical). The thermo-expandable alloy of Memokath-051, is designed to allow the stent to be inserted more easily and anchored in position (Maan et al. 2010). Moreover, its spiral coil aims to prevent endothelial ingrowth of the tumour or stricture into the stent so that it can be easily removed.

Memokath-051 stent is 1 of 4 types of urological stent offered by the company (Memokath-051, Memokath-028, Memokath-044 and Memokath-045), the other three versions are outside of the scope of this assessment because they are used for indications other than ureteric obstruction. The company states that, Memokath-051 stent is available in 6 lengths (30, 60,100,150, 200, and 250mm) for the single cone design and in 4 lengths (60, 80,100, and 120mm) for the double cone design (PNN Medical, 2019).

The CE mark has been updated in 2021 but the device class remained the same.

3. Clinical context

The ureter is a narrow muscular tube that flows through the kidney to the bladder. Ureteric stricture is characterised by the narrowing of the ureter, this can be due to malignant or benign causes. Obstruction of the ureter results in a disruption of normal flow of urine from the kidneys to the bladder which can result in complications such as urinary tract infections, kidney damage and stone formation due to urinary stasis. Relieving the obstruction in the ureter is vital, regardless of the reason for obstruction so the patient population requiring treatment will be heterogeneous.

Options for relieving obstruction includes reconstructive surgery, nephrostomy, plastic stents (double-J stents), metallic and alloy stents (Resonance, Allium and UVENTA) in addition to inserting thermos-

expandable metallic stents such as Memokath-051. The decision is influenced by the nature of the underlying disease process.

The MTG35 guidance recommended Memokath-051 as an option in patients with:

- Malignant ureteric obstruction and anticipated medium- or long-term survival after adjunctive therapy
- Benign ureteric obstruction who cannot have or do not want reconstructive surgery or
- Ureteric obstruction of any kind who cannot have or do not want a double-J stent, or for whom repeat procedures are a particularly high risk.

Experts noted that there has been no significant changes in the clinical pathway since the previous MTG53 guidance. One expert noted that they have begun inserting Memokath-051 stents in patients who were previously dependent on double-J. The experts did not note any new guidance affecting the treatment of patients with ureteric obstruction since the MTG53 guidance. This information is presented in the EAC correspondence log.

The following NICE guidance is relevant for the clinical management of patients with ureteric strictures due to various causes:

NICE guidance on acute kidney injury (CG169) states that people with upper urinary tract obstruction should be referred to a urologist and recommends that nephrostomy or stenting should be done as soon as possible (at least within 12 hours of diagnosis).

NICE guidance on prostate cancer (CG175) recommends decompression of the upper respiratory tract by nephrostomy or inserting a J-stent.

NICE guidance on bladder cancer (NG2) recommends nephrostomy or retrograde stenting (if feasible) for people with locally advanced or metastatic bladder cancer.

Special considerations, including issues related to equality

The considerations identified from the original guidance are included below.

Some ureteric obstruction is caused by malignancy, all people with cancer are protected under the Equality Act from the point of diagnosis. The previous guidance highlighted that people who use Memokath-051 as an alternative to double-J-stent, may be associated with reduced number of replacement

procedures and reduced adverse events which could improve the quality of life. It also noted that Memokath-051 could provide an alternative treatment for people with ureteric strictures who cannot tolerate or who would have failed conventional stents who would otherwise be nephrostomy-dependent and likely to be classed as disabled under the Equality Act.

The company did not provide any further information on equality issues associated with the technology at guidance update. The EAC did not identify any new considerations and further equality issues since the original guidance.

4. Clinical evidence selection

4.1 Evidence search strategy and study selection

This search was designed to identify any new potentially relevant evidence for this guidance update (GID-MT569) that had been published since the search conducted in 2017 for the original guidance.

The EAC repeated the search methods and strategies from the original evaluation on 8 April 2022. The search included 34 sources (details in Appendix A), including bibliographic databases (MEDLINE, Embase, CENTRAL, International HTA Database, CDSR, PubMed, and SCIE), conference proceedings, clinical trial registries, and subject-specific organisational websites. Where possible and available, a limitation to English language was applied.

Three sources were not searched for this update. Two of them (Database of Abstracts of Reviews of Effect (DARE) and Health Technology Assessment Database (HTA Database)) have not been updated since 2015 and the other one (EuroScan) was no longer available. The EAC replaced them with International HTA Database. In the original evaluation, British Association of Paediatric Urologists was reported twice as a unique search source (A.29 and A.30), the EAC removed the duplication. Because of changes in Google's search features, KiTEC changed the Google site search strategy moving 'Memokath' to the beginning of the search strategy for all the relevant sources.

Search results (910 records) were imported into EndNote 19 and after de-duplication of 334 records, 576 records were screened by 2 reviewers based on the eligibility criteria in ‘Decision problem’ section of this report. If any record met the healthcare condition and mentioned the device in title or abstract, EAC kept them for further assessment during the full-text screening by 2 reviewers.

Search strategies and PRISMA flow diagram are reported in Appendix A – Clinical literature search.

4.2 Included and excluded studies

After screening on title and abstract, the EAC included 7 studies (Bier et al. 2017, Choi et al. 2019, Forster et al. 2021, Khoo et al. 2021, Diaz Romero et al. 2018, Elbaroni et al. 2020 and Khoo et al. 2018) of a total 12 full-text studies. Five studies were excluded due to the following reasons: included in previous guidance (n=2), conference abstracts (full-text publication included) (n=2), MAUDE alert for Resonance from Khoo et al. 2021 (n=1). Reasons for exclusion are also reported in Appendix A – Clinical literature search

Five of the 7 included studies (Bier et al. 2017, Choi et al. 2019, Forster et al. 2021, Khoo et al. 2018 and Khoo et al. 2021) were also identified in the guidance review, the remaining two additional studies, reported as conference abstracts, were not included in the guidance review but the EAC considered them relevant to the decision problem (Diaz Romero et al. 2018 and Elbaroni et al. 2020).

See Table 1 for data from the included studies (n=7). The colour classifications indicate whether the study matches the scope fully (green), partially (amber), or not at all (red).

The company identified 6 studies in the guidance review (July 2021). The EAC included 1 of the 6 studies (Forster et al. 2021) and excluded the remaining 5 studies at guidance review (see Table 2). The company did not submit any further evidence for consideration in this guidance update.

Table 1: Studies selected by the EAC as the evidence base

Study name and location	Design and intervention(s)	Participants and setting	Outcomes	EAC comments
Bier et al. 2017 Germany	Retrospective single-arm, single-centre Memokath-051 ● **Green**	125 patients (malignant and benign) with stent implantation Setting, NR ● **Green**	**Median (range) indwelling time** 355 days (7 – 2125). Benign: 455 days; Malignant: 190 days, p = 0.006 **Stent removal reasons** Dislocation (n= 37, 42%) Occlusion (n=35, 40%) Prior to reconstructive surgery (n=8, 9%) Unknown reason (n=8, 9%) Infection (n=3, 3%) ● **Green**	Not UK based so less applicable to a UK NHS setting No comparator, retrospective Medium sample size Stent removal in all 91 patients (34 patients lost to follow-up)
Choi et al. 2019 South Korea	Retrospective comparative, single-centre Memokath-051 (n=21 stents, thermos-	36 patients with 46 ureter units (benign only) Hospital setting ● **Green**	**Mean (SD) follow-up, mos.** Memokath-051 (thermos-expandable stent): 34.4 (16.5) UVENTA (mesh stent): 41.4 (23.1); p=0.25	Not UK based so less applicable to UK NHS setting There is some discrepancies in the p

	expandable stent) vs. UVENTA (n=25 stents, mesh stent) ● **Green**		**Primary success** (maintaining patency after first stenting without additional procedures) at 1st year: Memokath-05, 14 (70.4%); UVENTA, 13 (54.9%); p=0.204 3rd year: Memokath-05, 4 (30.6%); UVENTA, 4 (16.9 %) **Over the entire observation period:** Memokath-051, 28.6%, UVENTA, 12.0% **Overall success** (maintaining patency after further salvage procedures during the observed period) 1st year: Memokath-05, 15 (75.4%); UVENTA, 18 (78.7%); p=0.586	values reported in the abstract and the body of text – p values used for 1st year primary success and overall success are used for the entire observation period in the body of text. Small sample size Long follow-up (3 yrs.)

			3rd year: Memokath-05, 7 (56.5%); UVENTA, 9 (49.1%) **Over the entire observation period:** Memokath-051, 57.1%; UVENTA, 40.0% **Complication events** Memokath-05, 15; UVENTA, 31; p=0.08 **Severe complications** Memokath-05, 10; UVENTA, 12; p=0.96 **Median (95%CI) time to 50% failure, mos. – primary** Memokath-051, 30.9 (15.2-39.9); UVENTA, 15.6 (9.3-21.5); p=0.204	

			Median (95%CI) time to 50% failure, mos. – overall Memokath-051, 54.3 (20.6 – 54.3); UVENTA, 29.0 (21.5 – 65.8); p=0.586 🟡 **Amber**	
Forster et al. 2021 UK	Retrospective single-arm, single-centre Memokath-051 🟢 **Green**	100 patients with 162 stents [malignant (n=59) and benign (n=41)] Hospital setting 🟢 **Green**	**Overall complication (Clavien-Dindo classification) rate** 72%: stent migration (36%), followed by failed ipsilateral upper tract drainage (27%: blockage 14%, encrustation 11%, lost renal function 2%) **Benign cohort complications** 85.4%. Most common, stent migration (53.7%) **Malignant cohort complications** 62.7%. Most common, failed renal	UK based study in an NHS hospital so potential more applicable to a UK NHS setting. Long follow-up (5 yrs.) No comparator Medium sized sample size Change incidence is mentioned in the abstract but not reported in results.

			drainage (30.5%); stent encrustation (10.2%) **Complication rate, malignant vs. benign** 62.7% vs. 85.4%, p=0.04 **Mean indwelling time, malignant vs. benign** 14.5 mos. vs. 13.4 mos., p=0.02 **Median time to first complication:** 12.5 mos. **Stent free after Memokath-051 removal-dislodgement, benign vs. malignant** 24.4% vs. 6.8%, p=0.03 **Memokath-051 salvage placement following complication:** 43% **Complication-free original memokath-051**	

			25% (25/100) 97 patients had follow-up data, survival plot showed median lifespan of stent: 14.5 mos. **Deaths** 21/100; 20/21 (95%) in malignant obstruction patients **Mean follow-up** 62 mos. (5 yrs.) ● **Green**	
Khoo et al. 2021 UK	Retrospective comparative, single-centre Memokath-051 (n=31) vs. Allium (n=16) vs. Resonance (n=29) ● **Green**	76 patients with 129 stent insertion episodes(SIE) for malignant and benign Hospital setting ● **Green**	**Median (IQR) stent survival per SIE (functional stent follow-up), mos.** Allium: 11.4 (2.6 – 31.6) Memokath-051**:** 5.5 (2.1 – 12.9) Resonance: 11.7 (7.8 – 13.1) **Intraoperative placement success** Allium: 95.7% (22/23)	UK based study in an NHS hospital so potential more applicable to a UK NHS setting. Medium sample size Shorter follow-up Comparative but retrospective

			Memokath-051**:** 100% Resonance: 100% **Stent failure (ureteric obstruction requiring premature stent removal/replacement, or nephrostomy insertion)** Allium: 47.8% (11/23) Memokath-051: 64.6% (31/48) Resonance: 19% (11/58) **Creatinine levels (in first 12 mos.)** Allium: 21.3% - 46.7% Memokath-051: -7.8% - 8.9% Resonance: - 9.4% - 27.3% ● **Green**	
Diaz Romero et al. 2018 Spain	Retrospective single-arm, single-centre Memokath-051 ● **Green**	23 patients (benign and malignant) Hospital setting ● **Green**	**Mean follow-up:** 15.95 mos. **Success rate:** 70.96% (permeability of the ureter, maintaining adequate renal	Conference abstract - minimal information reported. Small sample size

			function and absence of lower back pain) **Complications:** migration of the stent (35.48%); urinary tract infection (32.25%); obstruction of the stent (25.08%) 🟡 **Amber**	Retrospective, no comparator
Elbaroni et al. 2020 UK	Retrospective single-arm, single-centre Memokath-051 🟢 **Green**	95 patients (113 stents) with benign and malignant Hospital setting 🟢 **Green**	**Follow-up**: 4 mos. – 12 yrs. **Mean post-operative stay:** 1.7 days **Complications:** early UTI, 11%; migration, 26%; obstruction, 22% **Good long-term outcome (not defined):** 52% 🟡 **Amber**	Conference abstract - minimal information reported. Moderate sample size No comparator Large range for follow-up period “Good long-term outcome” is not defined

Khoo et al. 2018	Systematic review and meta-analysis (22 studies) Resonance (n=10) UVENTA (n=6) Memokath (n=5) Alium (n=1) ● **Green**	Malignant obstruction only ● **Green**	**Migration rate** Resonance (8 studies): 1% (0 – 3%); I^2 = 0% UVENTA (6 studies): 3% (0 – 8%); I^2=55% Memokath-051 (5 studies): 20% (11 – 30%); I^2=23.07 Allium (1 study): 12% (2 – 9%) **Obstruction rate** Resonance (8 studies): 17% (5 – 34%); I^2 = 88% UVENTA (6 studies): 6% (1 – 15%); I^2 = 75.87% Memokath-051 (5 studies): 11% (2 – 23%); I^2 = 70.16% Allium (1 study): 0% (0 – 10%) **Success rate** (no obstruction, improved renal function and no further intervention required for duration of follow-up) Resonance (7 studies): 79% (64 – 91%); I^2=78.28%	Majority of included studies were small, single-arm case series without comparator; high heterogeneity for migration rate, obstruction rate and success rate.

			UVENTA (5 studies): 81% (48 – 100%); I^2=95.71% Memokath-051 (5 studies): 65% (44%– 84%); I^2 =82.55% Allium (1 study): 88% (73 – 95%) ● **Green**	

Table 2: Studies included by company at guidance review and excluded by the EAC

Study name and location	Design and intervention(s)	Participants	Outcomes	EAC comments
Turner et al. 2018	NICE guidance	People with ureteric obstruction due to benign or malignant strictures	• 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	Excluded – publication of original NICE guidance for Memokath-051

			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	
Sampogna et al. 2018	Systematic review	People with ureteroileal stricture	•Safety •Efficacy	Excluded - literature review with no new information
Corrales et al. 2021	Systematic review	People with benign or malignant ureteral obstruction	•Stent duration •Stent failure •Complications	Excluded – literature review with no new information
Kang et al. 2020	Systematic review	People with malignant ureteral obstruction	•Success rate •Patency •Complications	Excluded – literature review with no new information
Miernik et al. 2018	Retrospective cohort	People with ureteroileal anastomotic stricture	•Mean stent indwelling time •Complications	Excluded – patient population (people with ureteroileal anastomotic stricture)

5. Clinical evidence review

5.1 Overview of the evidence presented in the original guidance

A total of 16 studies were used as key clinical evidence to inform the original guidance recommendations by the EAC.
The 16 studies identified by the EAC literature search and included as evidence base for the original guidance were:

- 10 single arm, observational case series studies, published as full papers that investigated 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). These ten studies ranged in size from 4 patients (Boyvat et al, 2005) to 73 patients (Papatsoris and Buchholz, 2010).
- 6 Comparative, retrospective observational studies:
    - 2 studies were available as full published papers (Kim et al, 2014 and Maan et al, 2010).
    - 3 studies were available as conference abstracts (Akbarov et al, 2017, Bolton et al, 2015, and Nam et al,2015).
    - 1 study available as clinical trial record and abstract (NCT00166361, 2014, Granberg et al, 2010)

The 6 comparative studies ranged in size from 9 patients (Bolton et al, 2015) to 27 patients (Akbarov et al, 2017) in each treatment arm.
10 of the 16 studies included as evidence base are studies from the United Kingdom while the remaining 2 studies (Boyvat et al, 2005 and Klarskov et al, 2005) were from Turkey and Denmark respectively.

The common outcomes reported in all the studies were clinical success, length of time stent remains in situ, stent removal/replacement and complications. Three studies reported theatre time and hospital stay time (Nam et al, 2015, Papatsoris et al, 2010 and Zaman et al, 2011) while two studies reported health related quality of life (Maan et al, 2010 and Nam et al, 2015).
Clinical success rates were 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). The clinical success rates ranged from 43% in (Kim et al., 2014) to 100% in (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) 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).However, the definition of clinical success was not consistent in all studies and it included one or more of the following, stent patency, functioning , successful tract decompression, improved renal function and lack of obstruction.

The length of time stent remained in situ was only reported in two studies that showed 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). The most common reasons for stent removal and/or replacement was either migration or encrustation. In the comparative studies, stent migrations 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).

The comparative studies reported that encrustation rates were higher in Memokath-051 compared to Allium (19% vs 0%) (Bolton et al., 2015) and double-J stents in 1 study (29% vs 0) (NCT00166361, 2014). There was no evidence in the comparative studies for stent removal and replacement. However, in the single arm studies, 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.

Subgroup analysis data reporting was limited for benign and malignant populations. Clinical success rates for Memokath-051 were 50% and 64% for benign populations in small sample sizes of 8 (Arya et al. 2001) and 11 in (Kim et al. 2014). However, Kim et al. 2014 is a mixed population study. The clinical success rate in malignant population was 82% (Nam et al. 2015) or 100% (Granberg et al. 2010, Zaman et al. 2011).

The EAC at original guidance, recognised the lack of quality RCT evidence and the fact that the review was informed mainly by small, poorly reported, observational studies and therefore the material uncertainty around these data. Although the observational nature of these studies may be more reflective of real life, due to the heterogeneity across them it is difficult to draw reliable conclusions. Hence the results and conclusions could change in light of further studies.

5.2 Overview of methodologies of all included studies

The EAC included 7 studies; 5 studies were reported as full text publications:

- 1 systematic review and meta-analyses (Khoo et al. 2018),
- 2 retrospective non-randomised comparative studies (Choi et al 2019 and Khoo et al. 2021),
- 2 retrospective single-arm studies (Bier et al 2017 and Forster et al 2021).

The remaining two studies were abstracts: Elbaroni et al. 2020 and Diaz Romero et al. 2018, which are both retrospective, single arm and single centre studies.

All of the studies included as new evidence were observational in design with the exception of one systematic review and meta-analysis (Khoo et al. 2018).

Four of the five full publications reported a total of 337 patients while the fifth was a systematic literature review. The two abstracts reported a total of 118 patients in their studies. Details of patient's demographics were reported in all the included studies except the systematic literature review. The mean age ranged from 57 years to 70 years in Forster et al. 2021 and Khoo et al. 2021, respectively. Three of the full publications and two abstracts reported benign and malignant ureteric obstruction together while Choi et al. 2019 reported only on benign ureteric obstruction. The systematic review Khoo et al. 2018, had a mix of benign and malignant ureteric strictures reported in some papers while others reported only benign or only malignant ureteric obstruction. All but 2 of the studies (Choi et al. 2019 and Khoo et al. 2021) included lacked direct comparators. Most of the studies are non-UK based studies; only two full publications and one abstract are UK based studies, Forster et al. 2021, Khoo et al. 2021 and Elbaroni et al. 2020, respectively. Common outcomes reported across all the studies include: clinical success rate, complications (e.g. migration, obstruction) and stent indwelling time.

Forster et al. 2021 and Khoo et al. 2021 are both low-moderate quality studies; they are UK based studies, have no or minimal loss to follow-up, and moderate sample size (see appendix B). However, Forster et al. 2021 has a longer follow-up period of 5 years with no comparator, while Khoo et al. 2021 has a shorter follow-up period of 5.5 months for Memokath-051 but does include three comparators, Resonance, UVENTA and Allium stents. The remaining studies are classed as medium to low quality. Khoo et al. 2018 included 21 studies in their systematic review and meta-analyses with 5 studies reporting data on Memokath-051; all 5 of these studies were included in the original guidance. The EAC included this study as the authors also

conducted a meta-analysis on success rate, migration rate and obstruction rate comparing 4 stents relevant to the scope (Allium, Memokath-051, Resonance, and UVENTA).

All of the five full publications reported no conflict of interest, however, Choi et al. 2019 and Khoo et al. 2018 declared receiving funding from the Ministry of Science and ICT in South Korea and a range of different pharmaceutical industries respectively.

5.3 Critical appraisal of studies and review of company's critical appraisal

A summary of the critical appraisal conducted by the EAC for all studies identified is presented in Appendix B. The EAC used the Cochrane's risk of bias tool for comparative studies, assessed the strengths and weaknesses for single-arm studies and used the AMSTAR-2 tool to assess the risk of bias associated with the systematic review identified.

In total, 6 studies had a retrospective study design (Forster et al. 2021, Choi et al. 2019, Elbaroni et al. 2019, Diaz Romero et al. 2018, Bier et al. 2017, Khoo et al. 2021) which is associated with selection bias. The retrospective data collection also means that it is possible that some data was missed or, for example, patients presented with adverse events at a different site so the adverse events could have been underestimated or stent survival overestimated. Two of the retrospective studies were comparative, due to the retrospective aspect of these studies, therefore it is not clear why patients might have received one stent over another. In addition, no blinding or randomisation was conducted which means there is a risk of performance and selection bias. One study, conducted in South Korea, reported that patients had sufficient discussion on the choice of treatment policies and included patients who did not want reconstructive surgery (Choi et al. 2019). Whilst the other study, conducted in the UK, reported that the choice of stent was at the surgeon's discretion (Khoo et al. 2021), this means the selection of the stent type was influenced by the preferences of the surgeon, for example, a surgeon may feel more comfortable inserting one stent over another.

Two studies had between-group differences at baseline. Bier et al. 2017 had statistically significant ($p<0.05$) differences for the presence of renal failure and causation (benign/malignant) of ureteral strictures. Moreover, concomitant urinary diseases (such as stones or prostate enlargement) were not recorded. Choi et al. 2019 had between-group differences for baseline stricture length and prior radiation therapy that were statistically significant ($p<0.05$). One expert noted that benign strictures generally perform better compared with malignant strictures due to less disease progression and

longer life expectancy, suggesting that the difference in causation could have an effect on stent outcomes. They highlighted that kidney stone disease should be a contraindication to using Memokath-051 due to a possible increased risk of encrustation. Another expert did not think the between-group differences were likely to affect the stent outcomes. This information is presented in the EAC correspondence log.

The 2 studies reported as conference abstracts reported minimal information and did not add much to the decision problem (Elbaroni et al. 2020 and Diaz Romero et al. 2018). However, Elbaroni et al. 2020 did report a large range for follow-up period (4 months – 12 years), therefore published results from this study beyond the 5-year study duration from Forster et al. 2021 will be of interest.

A high loss to follow-up was only associated with one single-arm study (Bier et al. 2017) conducted in Germany, reporting a 27% loss to follow-up. The reasons for patient withdrawal were not documented and an intention to treat analysis was not conducted (Bier et al. 2017), this means there is poor confidence in the long-term outcomes reported. Moreover, the reason for stent removal was examined retrospectively, adding to the uncertainty of the data recorded.

Khoo et al. 2021, a comparative study conducted in the UK was associated with a short follow-up period for the Memokath-051 group (5.5 months) and the follow-up period varied across the groups (Allium 11.4 months and Resonance with 11.7 months). The short follow-up period means that it is difficult to predict the long-term effect of the Memokath-051 stent on outcomes of interest outlined in the scope. The authors noted that due to the retrospective design of the study, there could be an overestimation of stent survival rate if failures and adverse events in patients presenting in other hospitals are not captured in the data.

The systematic review and meta-analysis (Khoo et al. 2018) included 21 studies of which the majority were small, single-arm case series studies. The study was associated with high heterogeneity and the authors reported that it was not possible to separate the data of patients with malignant stricture from those with benign aetiology.

One of the included studies did not report the source of funding (Bier et al. 2017). The remaining included studies were not funded by the company.

5.4 Results from the evidence base

The results from the evidence base are summarised in Table 3 and the EAC's interpretation of these outcomes are in section 8.

Table 3: summary of main outcomes from the evidence base

Study (Name and type)	**Number of patients, stent insertion and mean follow up time**	**Stent Indwelling time**	**Stent removal/replacement rate**	**Stent success rate**	**Complications**	**Other**
Forster et al. 2021 Retrospective, single centre study. UK.	Patients: N=100 Stents: N=162 (malignant, n=59, benign=41) Memokath-051 : 162	**Mean indwelling time:** Malignant vs benign: (mos.) 14.5 vs 13.4 p=0.02	**Stent free after Memokath-051 removal-dislodgement:** Malignant vs benign: 6.8% vs 24.4% p=0.03 **Memokath-051 salvage placement following complication:**	**Complication free original Memokath-051:** 25% (25/100). 97 patients had follow up data. Survival plot showed median lifespan of stent: 14.5 mos.	**Overall complications (Based on Clavien-Dindo classification) rate:** 72% (Stent migration, 36%, Ipsilateral upper tract drainage, 27%, Blockage, 14%, encrustation, 11% and lost renal function, 2%)	**Deaths:** Total, 21/100 20/21 (95%) in malignant obstruction patients.

Study (Name and type)	Number of patients, stent insertion and mean follow up time	Stent Indwelling time	Stent removal/replacement rate	Stent success rate	Complications	Other
	Mean follow up time: 62 mos. (5 yrs.)		43%		**Benign cohort complications:** 85.4% (most common, stent migration, 53.7%) **Malignant cohort complications:** 62.7% (most common, failed renal drainage, 30.5% and stent encrustation, 10.2%). **Complication rate, malignant vs benign:**	

Study (Name and type)	Number of patients, stent insertion and mean follow up time	Stent Indwelling time	Stent removal/replacement rate	Stent success rate	Complications	Other
					62.7 vs 85.4%, p=0.04 **Median time to first complication:** 12.5 mos.	
Bier et al. 2017 Retrospective single arm, single centre. Germany.	Patients: N=125 Stents: N=125 (total) Memokath-051: n=125 (only 91 analysed, 34 lost to follow up)	**Median (range) indwelling time**: 355 days (7-2125). Benign: 455 days Malignant: 190 days P=0.006	**Stent removal reasons:** Dislocation (n= 37, 42%) Occlusion (n=35, 40%) Prior to reconstructive surgery (n=8, 9%) Unknown reason (n=8, 9%) Infection (n=3, 3%)	NR	NR	NR

Study (Name and type)	Number of patients, stent insertion and mean follow up time	Stent Indwelling time	Stent removal/replacement rate	Stent success rate	Complications	Other
Choi et al. 2019 Retrospective comparative study. South Korea.	Patients: N=36 Stents: N=46 (total) Memokath-051: n=21 UVENTA: n=25 **Mean (SD) follow up (mos.):** Memokath-051 34.4 ±16.5	NR	**Median (95% CI) time to primary failure (mos.):** Memokath-051: 30.9% (15.2-39.9) UVENTA: 15.6 (9.3-21.5) p=0.204 **Median (95%CI) time to overall failure (mos.):** Memokath-051: 54.3 (20.6-54.3) UVENTA: 29.0(21.5-65.8) p=0.586	**Primary success:** (maintaining patency after 1st stenting without additional procedures) at 1st year: Memokath-051: 14 (70.4%) UVENTA: 13 (54.9%) p=0.204 3rd Year:	**Complications events:** Memokath-051: 15 UVENTA: 31 p= 0.08 **Severe complications:** Memokath-051: 10 UVENTA: 12 p= 0.96	NR

Study (Name and type)	Number of patients, stent insertion and mean follow up time	Stent Indwelling time	Stent removal/replacement rate	Stent success rate	Complications	Other
	UVENTA (mesh stent): 41.4 ± 23.1			Memokath-051: 4 (30.6%) UVENTA: 4 (16.9%) **Over the entire observation period:** Memokath-051: 28.6% UVENTA: 12.0% **Overall success** (maintaining patency after further salvage		

Study (Name and type)	Number of patients, stent insertion and mean follow up time	Stent Indwelling time	Stent removal/replacement rate	Stent success rate	Complications	Other
				procedures during the observed period). 1st year: Memokath-051: 15 (75.4% UVENTA: 18 (78.7%) P=0.586 3rd year: Memokath-051: 7 (56.5%) UVENTA: 9 (49.1%)		

Study (Name and type)	Number of patients, stent insertion and mean follow up time	Stent Indwelling time	Stent removal/replacement rate	Stent success rate	Complications	Other
				Memokath-051: 57.1% UVENTA: 40.0%		
Diaz Romero et al. 2018 Retrospective single centre study. Abstract. Spain	Patients: N=23 Stents: N=31 Memokath-051 :31 **Mean follow up:** 15.9 mos.	NR	NR	Permeability of the ureter, maintaining adequate renal function and absence of lower back pain: 70.96%	Migration of stent: 35.48% Urinary tract infection: 32.25% Obstruction of the stent: 25.08%	NR

Study (Name and type)	Number of patients, stent insertion and mean follow up time	Stent Indwelling time	Stent removal/replacement rate	Stent success rate	Complications	Other
Elbaroni et al (2020) Retrospective single centre study. Abstract. UK	Patients: N=95 Stents: N=113 Memokath-051: 113 **Follow up:** 4 mos. to 12 yrs.	NR	NR	Had a good long-term outcome (not defined well): 52%	Early UTI: 11% Migration: 26% Obstruction: 22%	NR
Khoo et al. 2021 Retrospective comparative study.	Patients: N=76 Stents: N= 129(total)	NR	**Stent failure (ureteric obstruction requiring premature stent removal/replacement or nephrostomy):**	**Interoperative placement success rate:** Allium: 95.7% (22/23)	NR	**Creatinine levels (in first 12 mos.):**

Study (Name and type)	Number of patients, stent insertion and mean follow up time	Stent Indwelling time	Stent removal/replacement rate	Stent success rate	Complications	Other
UK.	Memokath-051: n=48 Allium: n=23 Resonance: n=58 **Median (IQR) stent survival per SIE (functional stent follow up)** Allium: 11.4 (2.6-31.6) mos. Memokath-051: 5.5 (2.1-12.9) mos.		Allium: 47.8% (11/23) Memokath-051: 64.6% (31/48) Resonance: 19% (11/58)	Memokath-051: 100% Resonance: 100%		Allium: 21.3% - 46.7% Memokath-051: 7.8% - 8.9% Resonance: 9.4% - 27.3%

Study (Name and type)	Number of patients, stent insertion and mean follow up time	Stent Indwelling time	Stent removal/replacement rate	Stent success rate	Complications	Other
	Resonance: 11.7 (7.8-13.1) mos.					
Khoo et al. 2018 Systematic literature review with meta-analysis. Setting: NR	Studies included: N=21 Stents: Memokath-051 compared with Resonance, UVENTA, Allium.	NR	NR	**No obstruction, improved renal function and no further intervention required for duration of follow up** Resonance (based on 7 studies): 79% (64-91%); I^2 =78.28% UVENTA (based on 5	**Migration rate:** Resonance (based on 8 studies): 1% (0-3%); I^2 =0% UVENTA (based on 6 studies): 3% (0-8%); I^2 =55% Memokath-051 (based on 5 studies); 20% (11-30%); I^2 =23.07% Allium (based on 1 study) : 12% (2-9%)	NR

Study (Name and type)	Number of patients, stent insertion and mean follow up time	Stent Indwelling time	Stent removal/replacement rate	Stent success rate	Complications	Other
				studies): 81% (48-100%); I^2 =95.71% Memokath-051 (based on 5 studies):65%(44%-84%); I^2 =82.55% Allium (based on 1 study): 88% (73%-95%)	**Obstruction rate:** Resonance (based on 8 studies): 17% (5 -34%); I^2 =88% UVENTA (based on 6 studies): 6% (1-15%); I^2 = 75.87% Memokath-051 (based on 5 studies): 11%(2-23%); I^2 =70.16% Allium (based on 1 study): 0% (0-10%).	

6. Adverse events

A summary of the adverse events reported in the evidence base are included in Table 4.

Experts noted that the long-term complications associated with Memokath-051 are not yet collated in a registry. Four experts noted that they had observed stent migration as being a main complication. One expert stated that they had also observed obstruction above the stent, encrustation, and sepsis associated with Memokath-051 usage. Another expert noted that one patient continued to experience bladder symptoms despite using Memokath-051. Experts highlighted that obstruction development can also be a result of disease progression. This information can be found in the EAC correspondence log.

The EAC searched the FDA Manufacturer and User Facility Device Experience (MAUDE) and MHRA for adverse events for Memokath-051 on the 7th April 2022, one record was identified from MAUDE however this was for Resonance stent for an adverse event included in Khoo et al. 2021. There were no records identified for Memokath-051.

Table 4: Summary of adverse events reported in included studies

Bier (2017)	Choi (2019)	Diaz Romero (2018)	Elbaroni (2020)	Forster (2021)	Khoo (2018)	Khoo (2021)
Dislocation (42%) Occlusion (40%) Infection (3%)	Stent migration (14.3%) Encrustation (33.3%) UTI (9.5%) Lower urinary tract symptoms (4.8%) Persistent pain (4.8%) Persistent haematuria (4.8%)	Stent migration (35.48%) UTI (32.25%) Obstruction (25.08%)	Stent migration (26%) Early UTI (11%) Obstruction (22%)	Stent migration (36%) Failed ipsilateral upper tract drainage (27%) Obstruction (14%) Encrustation (11%) Lost renal function (2%)	Stent migration (20%) Obstruction (11%)	Stent migration (16.7%) Obstruction (43.8%)

7. Evidence synthesis and meta-analysis

The company did not perform a meta-analysis or evidence synthesis. The EAC also did not conduct a meta-analysis as the number of new studies identified was small. There was also heterogeneity in the outcome definitions and the duration of follow-up across these studies.

8. Interpretation of the clinical evidence

Evidence from the original guidance

The previous guidance was informed by mainly small, poorly reported observational studies. There was high heterogeneity across the observational studies. Only two comparative studies were judged to have acceptable internal and external validity. The comparative evidence available for Memokath-051 compared to double-J stents, reconstructive surgery, other metallic and alloy stents (UVENTA, Allium and Resonance) was limited. Overall, the body of evidence was of low quality but suggested that Memokath-051 has similar success rates compared to double-J stents and Resonance stents. The most commonly reported adverse event associated with Memokath-051 was stent migration which occurred more frequently in Memokath-051 than in the other comparators assessed.

Evidence from the guidance update

Three studies (Forster et al. 2021, Khoo et al. 2021 and Elbaroni et al. 2020) reported as 2 full-text publications and 1 conference abstract were conducted in the UK and are most generalisable to the NHS population. Two studies were retrospective, and one study had a single-arm study design. The 3 studies had a moderate sample size of patients with malignant and benign ureteral obstruction. However, it should be noted that these studies were single-centre studies, this means they lack some rigor and external validity. The remaining studies were conducted in Europe and Asia, the results are less generalisable to a UK NHS setting.

Technical success

One study reported on technical success, defined as intraoperative placement success (Khoo et al. 2021); Memokath-051 was associated with 100% intraoperative placement success.

Clinical success

Three studies reported on clinical success rate (Choi et al. 2019, Diaz Romero et al. 2018 and Khoo et al. 2018). Similar to the studies included in

the original guidance, the clinical success rate was not consistently defined in the studies, making it difficult to determine the external validity of the outcomes and the relevance to clinical decision making. However, the studies did consistently include maintaining patency in their definition of clinical success, definitions also included maintaining adequate renal function and absence of lower back pain. One comparative retrospective study, Choi et al. 2019, with a small sample size (n=36) and limited to patient with chronic benign ureteral strictures reported 30.9 (15.2–39.9) months for Memokath-051 and 15.6 (9.3-21.5) months for UVENTA for the median time to primary failure. The median time to overall failure was 54.3 (20.6–54.3) months for Memokath-051 and 29.0 (21.5-65.8) months for UVENTA (Choi et al. 2019). The differences between the 2 stents were not statistically significant. Primary success (maintaining patency without procedures) was achieved for 28.6% of Memokath-051 stents and 12.0% for UVENTA. The overall success rates were 57.1% for Memokath-051 and 40.0% for UVENTA. Although the primary and overall success rates were not statistically significant between the 2 groups, Memokath-051 had better durability for primary success than the UVENTA stent in benign ureteric strictures, especially in the second and third years. This is in line with the original guidance which showed Memokath-051 to have similar clinical success rates to UVENTA in the population with benign aetiology but statistically significantly inferior success rates in the population with malignant aetiology. A summary of the evidence for this outcome is presented below in Table 5.

Length of time in situ, stent life span and stent failure

The previous guidance reported limited data in relation to the length of time the stent remained in situ, this does not seem to have changed since the MTG35 guidance.

Stent failure was defined by one comparative study (n=76) as ureteric obstruction requiring premature stent removal/replacement, or nephrostomy insertion (Khoo et al. 2021). Memokath-051 was associated with higher stent failure (64.6%) at 5.5 months follow-up compared with Allium (47.8%) at 11.4 months follow-up and Resonance (19%) at 11.7 months follow-up (Khoo et al. 2021). The time in-situ for Memokath-051 reported by Khoo et al. 2021 is considerably less than that reported by 2 studies included in the previous guidance which reported 14 months and 17 months indwelling time (Kim et al. 2014 and NCT00166361). However, Khoo et al. 2021 limited the actual stent follow-up to not only stent failure but also patient death/end of study period. The proportion of stent insertions episodes leading to death was comparable between the 3 stent types (Allium: 21.7% (5/23); Memokath-051: 22.9% (11/48); Resonance 22.4% (13/58), from Khoo et al. 2021).

For single-arm studies assessing Memokath-051 indwelling time, Bier et al. 2017 reported a median indwelling time of 11.8 months (range 1 week–70.8 months). Patients with benign ureteral strictures had higher indwelling time compared with strictures of malignant origin; 455 days vs.190 days, p=0.006 (Bier et al. 2017). However, Forster et al. 2021 (n=100) reported a statistically significant higher median stent life span in people with malignant ureter obstruction compared to people with benign ureter obstruction; 14.5 months vs.13.4 months (p=0.02). These results are more in line with the findings from the previous guidance than with Bier et al. 2017. Bier et al. 2017 was associated with a higher loss to follow-up than Forster et al. 2021, 27% vs. 3% and was not conducted in a UK NHS setting, so the results may be less reliable. Experts had varying experiences of Memokath-051 stent lifespan and stated it was difficult to predict the longevity without adequate prospective data collection. Generally there was agreement that Memokath-051 stent had a lifespan of at least 1 year. One expert reported experience of seeing patients with 2-year follow-up with Memokath-051. Another expert thought Memokath-051 stent could last up to 5 years. This information from the experts is presented in the EAC correspondence log.

Table 5: Results on clinical success from EAC's included studies

Study	Follow-up	Success as defined by publication	Result
Choi (2019) Retrospective comparative	Memokath-051: 34.4 (16.5) months UVENTA: 41.4 (23.1) months	**Primary success** - maintaining patency after first stenting without additional procedures **Overall success** - maintaining patency after further salvage procedures during the observed period	**Primary success** Memokath-051: 28.6%; UVENTA: 12.0% **Overall success** Memokath-051: 57.1%; UVENTA: 40.0%
Diaz Romero (2018) Retrospective single-arm study	15.95 months	Permeability of the ureter, maintaining adequate renal function and absence of lower back pain	70.96%

Khoo (2018) Systematic review	Varied	No obstruction, improved renal function and no further intervention required for duration of follow-up period	Resonance (7 studies): 79% (64 – 91%); I^2=78.28% UVENTA (5 studies): 81% (48 – 100%); I^2=95.71% Memokath-051 (5 studies): 65% (44%– 84%); I^2 =82.55% Allium (1 study): 88% (73 – 95%)

Complications

Overall, the most common complication was stent migration. Six (Diaz Romero et al. 2018, Elbaroni et al. 2020, Forster et al. 2021, Khoo et al. 2018 and Khoo et al. 2021) of the seven included studies (Bier et al. 2017, Choi et al. 2019, Diaz Romero et al. 2018, Elbaroni et al. 2020, Forster et al. 2021, Khoo et al. 2018 and Khoo et al. 2021) reported on stent migration with a range of 14.3% - 35.48% and obstruction/occlusion with a range of 11% - 43.8%. This is in line with findings from the assessment report for the original guidance which identified the most common adverse event associated with Memokath-051 to be stent migration. The evidence base underpinning the previous guidance showed “encrustation” to be another common complication rather than obstruction. The new evidence base identified only one study reporting encrustation (Choi et al. 2019). Experts commented that the most commonly seen complications were stent migration and encrustation. However, 1 expert noted that stent migration did not always result in the need for stent replacement. This information from the experts is presented in the EAC correspondence log. Section 6.0 outlines the common adverse events reported for Memokath-051 from the new evidence.

One comparative study (n=76) with a short follow-up period for Memokath-051 (5.5 months) reported that Resonance had lower migration, obstruction and infection rates than Allium and Memokath-051 in both patients with benign and malignant aetiology (Khoo et al. 2021).

Forster et al. 2021 used the Clavien-Dindo classification rate, the overall complication rate was 72%, the most common being stent migration (36%). The most common complication in the benign cohort was stent migration (53.7%) whilst the most common complication in the malignant cohort was failed renal drainage (30.5%) followed by stent encrustation (10.2%). There

was a statistically significant difference in complication rate between malignant and benign aetiology, 62.7% vs. 85.4%, p=0.04.

8.1 Integration into the NHS

Two studies identified were conducted in the UK NHS setting (Forster et al. 2021 and Khoo et al. 2021). In Khoo et al. 2021, patients with chronic ureteric obstruction were selected from operating theatre records from Charing Cross Hospital based in London. Forster et al. 2021 recruited patients from a UK NHS referral centre part of Bart's Health NHS trust in London. Patients were reviewed and selected from all electronic patient, operating room, radiologic, microbiology, pharmacy and urology department records on Memokath-051 stented patients. Both studies provide data in a UK NHS setting, however, both collected data from national tertiary referral centres in large London hospitals. This may reduce the generalisability of the results to hospitals outside of London and to district general hospitals. In general, experts noted that due to the different patient selection criteria and retrospective nature of these studies, the results are less generalisable to their practice. However, 1 expert, involved in 1 of the studies (Forster et al. 2021) thought that there was no issue with generalisability of these results. The information from the experts is presented in the EAC correspondence log.

Experts noted that Memokath-051 is currently only used in specialist centres in the UK following adequate training. Eight of the 9 experts thought Memokath-051 would not replace current standard care, however they noted that Memokath-051 has the potential to be used in addition to standard care in select individuals such as those with double-J stent dependent ureteral obstruction and those with malignant ureteric obstruction. Experts highlighted that in addition to improving the quality of life in patients, Memokath-051 could also prevent prolonged hospital stay and repeated attendance to hospital. Experts noted that it could reduce the number of surgeries therefore reducing NHS backlog and waiting lists. This information was given by experts through the NICE questionnaires.

8.2 Ongoing studies

The company provided information on a study that is in the protocol development stage for Memokath-051 double cone stent. The study group is working on including quality of life as a primary end point. They noted that 2 NHS centres have agreed to participate with potentially the addition of another 2 NHS centres. The study group is currently seeking ethical approval. The company did not identify further ongoing studies. The EAC did not identify further ongoing studies relevant to the scope.

9. Economic evidence

9.1 Published economic evidence

Search strategy and selection

Since the clinical search was not limited to specific clinical study designs, it also covered the economic evidence search.

KiTEC repeated the search methods and strategies from the original evaluation on 8 April 2022. This search was designed to identify any new potentially relevant evidence for this guidance update (GID-MT569) that had been published since the search conducted in 2017 for the original guidance. Search results were imported into EndNote 19 and after de-duplication, they were screened by 2 reviewers. If any record met the healthcare condition and mentioned the device in title or abstract, EAC kept them for further assessment during the full-text screening by 2 reviewers.

NHS Economic Evaluation Database (NHS EED) was not searched because it has not been updated since 2015.

Search strategies and PRISMA flow diagram were reported in Appendix A – Clinical literature search.

No new published economic evidence was found, but 4 of the studies (Forster et al. 2021, Khoo et al. 2021, Bier et al. 2017 and Choi et al. 2019) are deemed useful in updating the risk of unplanned stent replacement in the economic model.

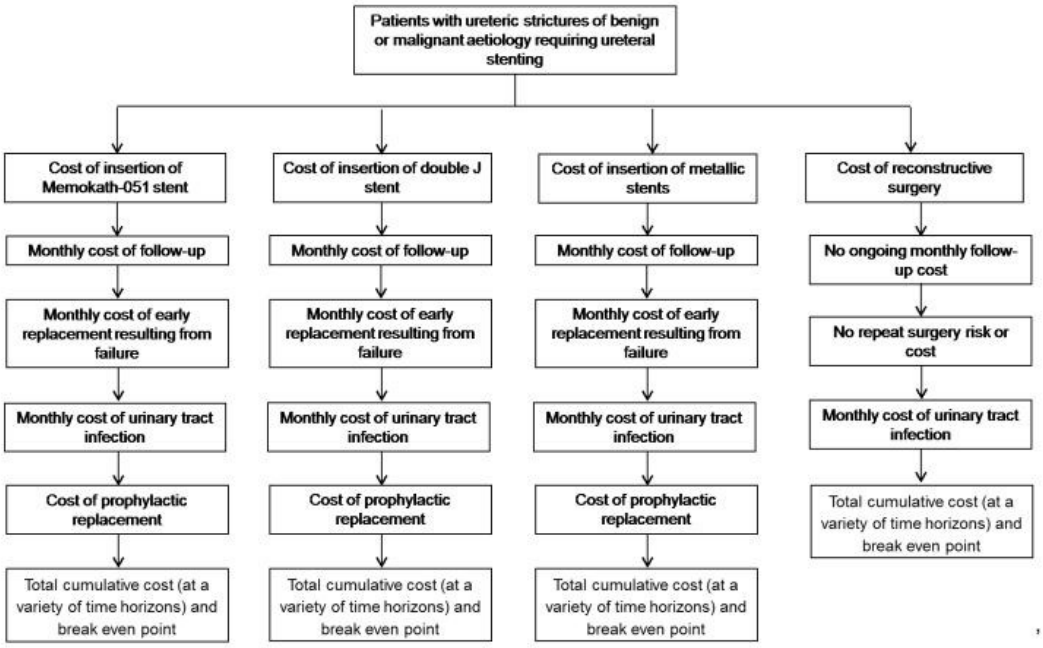
9.2 Company de novo cost analysis

Economic model structure

In the original model submitted by the company, a a cost-benefit approach based on an unpublished analysis comparing Memokath-051 with double-J stents was used. The model had a time horizon of 2.5 years, and did not include other metallic stents and reconstructive surgery. For the original guidance, the EAC extended the time horizon from 2.5 to 5 years (to reflect the indwelling duration for Memokath-051 after which planned replacement is required); included reconstructive surgery and other metallic stents as comparators; and included an ability to report a break-even time point between Memokath-051 and the comparators; and included the risk of urinary tract infections. The EAC cost model also included planned replacement of double-J stents after 6 months and no planned replacement of Memokath-051 over the 5-year time horizon, and a monthly risk of unplanned replacement for

both technologies based on clinical data. Complications were encapsulated within a risk factor for an unplanned stent exchange. There were 4 scenarios in respect to unplanned replacement; constant replacement over 5 year time horizon, replacement in the first 2 years with 0% thereafter, reduced replacement after 2 years (risk halved) and constant unplanned replacements over a 2 year time horizon. For the original guidance, 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. A diagrammatic representation of the EAC model structure is provided in Figure 1.

Fig 1. EAC model structure.



For this guidance update, the EAC thinks that the model structure, time horizon and key assumptions are valid. However, there is new clinical data available for Memokath-051 for longer follow-up periods. The EAC thinks that this evidence should be used to update the parameters in the model. The cost parameters have already been updated during the guidance review process.

Economic model parameters

Clinical parameters and variables

The key clinical parameters used in the model were length of time in situ in months, stent removal and replacement and urinary tract infections (UTI).

In the original guidance, 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 et al., 2014) for Memokath-051. The EAC considered the new clinical evidence and included the Bier et al 2017, Khoo et al 2021, Forster et al 2021 papers in addition to the previous nine studies. The Khoo et al. 2018 systematic review was excluded because of the high heterogeneity in the studies included.

- Bier et al. 2017 specified the most common reasons for stent explanation were dislocation (n=37, 42%) and occlusion (n=35, 40%). These were assumed to result in stent replacement and added together.

- Khoo et al. 2021 reported stent failure (ureteric obstruction requiring stent removal/replace) for Memokath to be 64.6% (31 out of the 48 procedures). This is a very high proportion and the follow-up is short (only 5.5 months) but is a UK based study. The EAC also notes the limitation that stent replacements are not reported patient wise but by number of procedures, for instance, a patient might have had more than one replacement. The EAC noted the limitation and included Khoo et al. 2021 along with all new primary studies

- The Forster et al. 2021 is a UK based study with longer follow-up of 62 months and reports a 43% salvage placement following complications.

In the original guidance, the total number of stent replacements were divided by the total number of patient months from the nine studies to derive a monthly probability of 1.4% per month, which was determined for use in the model's base case. The EAC included the three studies (Bier et al. 2017, Khoo et al. 2021 and Forster et al. 2021) along with the nine studies and estimated a monthly probability of 1.8% for Memokath-051. Two NICE experts (see EAC correspondence log) agreed that these were reasonable estimates. If the Khoo et al 2021 is excluded for its limitations, the estimated monthly probability is 1.54%. The EAC has explored these in the sensitivity analysis.

As there is no new evidence for double-J stents, the assumption from the original guidance, i.e. double-J stents have a planned replacement every 6 months and there was no risk of an unplanned stent exchange is still valid.

This was 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, clinical experts (see EAC correspondence log) opined that though double-J stents have lower unplanned stent replacement than Memokath-051, it is variable. The EAC tested this assumption by varying this parameter on sensitivity analysis.
In the original guidance, data for the comparator UVENTA came from a Korean comparative study was used to inform the rate of stent removal and replacement (Kim et al. 2014). A monthly probability of 4.41% was estimated for Memokath-051 and for UVENTA a probability of 0.49% was estimated by the assessing EAC. New Korean evidence (Choi et al. 2019) was available from the clinical review and the EAC decided to use this evidence in the absence of any UK based studies from head-to-head comparison of Memokath-051 with UVENTA. The monthly probability was estimated to be 3.57% for Memokath-051 and 4.99% for UVENTA. The estimated results are different from the Kim et al. 2014 paper, and this variation was explored in sensitivity analysis by the EAC.

In the original guidance, as there was no evidence available for Allium and Resonance, the rate of stent replacement for Allium was considered equal to UVENTA (0.49%) based on clinical experts opinion. For resonance stent, the rate of stent replacement was considered equal to Memokath-051 given the lack of evidence. From this guidance update, Khoo et al 2021 report stent replacement for Allium (5.54%) and Resonance (1.78%). The EAC used this estimated monthly probability in its model. Given that reconstructive surgery corrects the ureteric stricture, no further planned reconstructive surgery is included in the EAC's model, and same as in the original guidance.

The indwelling time for Memokath, double-J-stent, UVENTA, Allium and Resonance stents was same as in the original guidance, since no clinical evidence was available to indicate otherwise. This parameter was tested in the sensitivity analysis.

Similar to the original guidance a monthly probability of 0.4% (Papatsoris and Buchholz, 2010) for UTI for Memokath-051 and each stent comparator (double-J stents, UVENTA, Allium and Resonance) was used. For reconstructive surgery, a monthly probability of 1.25% and 0.17% (Akbarov et al. 2017) for Memokath-051 and reconstructive surgery respectively was used.

The updated clinical parameters are presented in Table 6.

Table 6: Clinical parameters used in the original model and any changes made by the EAC at guidance update

	Original value		Source/EAC comment	EAC update value		Source/EAC comment
Memokath-051 v. double-J stents	**Memokath-051**	**Double-J stents**		**Memokath-051**	**Double-J stents**	
Length of time in situ in months (no complications) (months)	60	6	Original Guidance	60	6	Original Guidance
Stent removal and replacement (to 24 months)	1.4%	0.0%	Memokath: Nine studies (see above section for references) used in the original guidance to estimate monthly risk Double-J Stents: Assumptions based on clinical experts, Maan et al. 2010	1.8%	0.00%	Memokath: Bier et al 2017, Khoo et al 2021, Forster et al 2021 included with the 9 studies (see above section for references) used in the original guidance to estimate monthly risk Double-J Stents: Assumptions based on clinical experts
Stent removal and replacement (to 24-60 months)	1.4%	0.0%		1.8%	0.0%	

Urinary tract infection (UTI)	0.42%	0.42%	Papatsoris and Buchholz, 2010	0.42%	0.42%	Papatsoris and Buchholz, 2010
Memokath-051 v. UVENTA	**Memokath-051**	**UVENTA**		**Memokath-051**	**UVENTA**	
Length of time in situ in months (no complications) (months)	60	18	Original guidance	60	18	Original guidance
Stent removal and replacement (to 24 months)	4.41%	0.49%	Kim et al. 2014	3.57%	4.99%	Choi et al 2019
Stent removal and replacement (to 24-60 months)	4.4%	0.5%		3.57%	4.99%	
Urinary tract infection (UTI)	0.42%	0.42%	Papatsoris and Buchholz, 2010	0.42%	0.42%	Papatsoris and Buchholz, 2010
Memokath-051 v. Allium	**Memokath-051**	**Allium**		**Memokath-051**	**Allium**	
Length of time in situ in months (no complications) (months)	60	36	Original guidance	60	36	Original guidance
Stent removal and replacement (to 24 months)	1.40%	0.49%	Memokath: Nine studies (see above section for references) used in the original guidance to	1.8%	5.54%	Memokath: Bier et al 2017, Khoo et al 2021, Forster et al 2021 included with the 9 studies (see

Stent removal and replacement (to 24-60 months)	1.4%	0.5%	estimate monthly risk Allium: Considered equivalent to Uventa, assumptions based on clinical experts	1.8%	5.54%	above section for references) used in the original guidance to estimate monthly risk Allium : Khoo et al 2021
Urinary tract infection (UTI)	0.42%	0.42%	Papatsoris and Buchholz, 2010	0.42%	0.42%	Papatsoris and Buchholz, 2010
Memokath-051 v. Resonance	**Memokath-051**	**Resonance**		**Memokath-051**	**Resonance**	
Length of time in situ in months (no complications) (months)	60	12	Original guidance	60	12	Original guidance
Stent removal and replacement (to 24 months)	1.40%	1.40%	Memokath: Nine studies (see above section for references) used in the original guidance to estimate monthly risk Resonance: Considered	1.8%	1.78%	Memokath: Bier et al 2017, Khoo et al 2021, Forster et al 2021 included with the 9 studies (see above section for references) used in the original guidance to
Stent removal and replacement (to 24-60 months)	1.4%	1.4%				

			equivalent to Memokath, assumptions based on clinical experts	1.8%	1.78%	estimate monthly risk Resonance : Khoo et al 2021
Urinary tract infection (UTI)	0.42%	0.42%	Papatsoris and Buchholz, 2010	0.42%	0.42%	Papatsoris and Buchholz, 2010
Memokath-051 v. Reconstructive Surgery	**Memokath-051**	**Surgery**		**Memokath-051**	**Surgery**	
Length of time in situ in months (no complications) (months)	60	120	Original guidance	60	120	Original guidance
Stent removal and replacement (to 24 months)	1.40%	0.0%	Memokath: Nine studies (see above section for references) used in the original guidance to estimate monthly risk	1.8%	0.0%	Memokath: Bier et al 2017, Khoo et al 2021, Forster et al 2021 included with the 9 studies (see above section for references) used in the original guidance to estimate monthly risk
Stent removal and replacement (to 24-60 months)	1.4%	0.0%		1.8%	0.0%	
Urinary tract infection (UTI)	1.25%	0.17%	Akbarov et al. 2017	1.25%	0.17%	Akbarov et al. 2017

Resource identification, measurement and valuation

As part of the guidance review decision which led to this guidance update, a cost update was carried out in August 2021. There were a few changes in assumptions used for the cost update compared to the original guidance. For staff costs, information on cost per hour was updated from Personal Social Services Research Unit (PSSRU) 2016 to 2020. Specifically, the cost information of Band 2 hospital-based nurses is unavailable in PSSRU 2020, hence this cost was inflated using the Personal Social Services (PSS) pay and prices index. Similarly, information on theatre cost, which was originally taken from Information Services Division (ISD) Scottish Tariff Theatre Services website, was inflated to 2020 values using NHS cost inflation index (NHSCII) due to information unavailability. Other cost parameters sourced from NHS Reference Costs 15/16 and BNF 2017 prices have been updated in line with the NHS Reference Costs 19/20 and BNF 2020 information. Information on price of Norfloxacin was originally sourced from BNF Legacy. However, current BNF website only lists norfloxacin as an ingredient in certain drugs instead of a standalone medication. As there is no NHS indicative price available on the BNF for this drug and is not routinely prescribed in practice as per clinical experts (see correspondence log), we replaced it with an alternatively used drug Co Amoxiclav 625mgs. On cost of hospital stay, costs of day case and inpatient is the weighted average of the non-elective excess bed day for Ureteric or Bladder Disorders in NHS Reference Costs 15/16. As NHS Reference Costs 19/20 does not contain unit cost information on cases of non-elective excess bed day, this cost has also been inflated to 2020 values using the NHSCII.

Cost of the Memokath-051, technology and related consumables did not change since the original MTG35 guidance according to the company. Costs of double-J stent, UVENTA, and Resonance have changed according to NHS Supply Chain and are incorporated in the updated report. For Allium, the costs was assumed to be same as in the original guidance, since prices could not be sourced from the NHS supply chain. The consumable costs are also assumed to stay the same as in the original guidance.

The updated costs are presented in Table 7.

Table 7: Cost parameters used in the original model and changes made by the EAC at guidance update

Costs	Code, description	Original cost estimate	EAC Updated	Source & EAC comment

			cost estimate	
Costs of insertion				
Memokath-051	Device	£1,690	£1,690	Company information
Double-J stent	Device	£60	[redacted]	NHS Supply Chain
UVENTA	Device	£1,500	[redacted]	NHS Supply Chain
Allium	Device	£1,700	£1,700	Company information
Resonance	Device	£912	[redacted]	NHS Supply Chain
Other consumables for Memokath-051/UVENTA/Allium/Resonance		£243.12	£243.12	Company information
Other consumables for Double-J stent		£49.44	£49.44	Company information
Anaesthetist	Consultant: surgical, cost per working hour.	£105	£114	PSSRU 2020, Curtis, L. & Burns, A. (2020)
Surgeon	Consultant: surgical, cost per working hour.	£105	£114	PSSRU 2020, Curtis, L. & Burns, A. (2020)
Band 6 scrub	Band 6 hospital-based nurse, cost per working hour	£44	£50	PSSRU 2020, Curtis, L. & Burns, A. (2020)
Band 5 scrub	Band 5 hospital-based nurse, cost per working hour	£35	£40	PSSRU 2020, Curtis, L. & Burns, A. (2020)
Band 5 anaesthetist	Band 5 hospital-based nurse, cost per working hour	£35	£40	PSSRU 2020, Curtis, L. & Burns, A. (2020)
Band 2 circulating	Band 2 hospital-based nurse, cost per working hour	£23	£26.5	Inflated using PSS pay & prices index
Band 2 portering	Band 2 hospital-based nurse, cost per working hour	£23	£26.5	Inflated using PSS pay & prices index
Theatre cost	ISD Scottish Tariff Theatre allocated costs and total theatre hours used in years	£299	£325	Inflated using NHSCII

Diagnostic test before procedure	RD20A, Computerised Tomography Scan of one area, without contrast, 19 years and over, outpatient, and RD21A, Computerised Tomography Scan of one area, with post contrast only, 19 years and over, outpatient	£96.18	£77.99	NHS Reference costs 19/20
Diagnostic test during procedure	RD33Z, Contrast Fluoroscopy, Mobile or Intraoperative Procedures, with duration of less than 20 minutes	£92	£93	NHS Reference costs 19/20
Medication during procedure	Gentamicin	£15.54	£47.25	BNF 2020
Post-op medication	Co Amoxiclav 625mgs instead of Norfloxacin	£8.57	£4.80	No NHS indicative price available on the BNF for Norfloxacin, so an alternative drug used in practice Co Amoxiclav 625mgs which costs £9.60 for a pack of 21, and around £4.80 for 10 tablets
Follow-up visit after insertion				
Memokath-051/UVENTA/Allium/Resonance	RN25A, Renogram, 19 years and over	£255	£280	NHS Reference costs 19/20
Double-J stents	Urology, Outpatient Attendance	£105.19	£110	NHS Reference costs 19/20
Costs of hospital stay				
Day case	LB19C, Ureteric or Bladder Disorders, with Interventions, with CC Score 4+	£51	£59	Inflated using NHSCII

	LB19D, Ureteric or Bladder Disorders, with Interventions, with CC Score 0-3			
Inpatient	LB19C, Ureteric or Bladder Disorders, with Interventions, with CC Score 4+ LB19D, Ureteric or Bladder Disorders, with Interventions, with CC Score 0-3	£305	£351	Inflated using NHSCII
Total cost of hospital stay for Memokath-051/double-J stents/UVENTA/Allium/Resonance	Weighted average cost of hospital stay	£107.83	£116	Calculated from the sum product of costs of day case, inpatient, and current inpatient, and the proportion of patients in each case
Follow-up for day case				
Band 5 recovery	Band 5 hospital-based nurse, cost per working hour	£35	£40	PSSRU 2020, Curtis, L. & Burns, A. (2020)
Band 6 recovery	Band 6 hospital-based nurse, cost per working hour	£44	£50	PSSRU 2020, Curtis, L. & Burns, A. (2020)
Cost of Reconstructive surgery	Weighted average of LB60C, Complex, Open or Laparoscopic, Kidney or Ureter Procedures, with CC Score 7+, and LB62D, Complex, Open or Laparoscopic, Kidney or Ureter Procedures, with CC Score 4-6	£6,290	£6,846	NHS Reference costs 19/20
Cost of follow-up and medication after reconstructive surgery	Sum of YL12Z, Percutaneous, Attention to or Removal of, Ureteric Stent or Nephrostomy, and	£1,124	£1,120.5	NHS Reference costs 19/20

	RN25A, Renogram, 19 years and over			
Follow-up costs				
Follow-up costs for Memokath-051/UVENTA/Allium/Resonance	RN25A, Renogram	£255	£280	NHS Reference Costs 19/20
Costs of replacement				
Memokath-051	Device	£1,690	£1,690	Company information
Double-J stent	Device	£60	[redacted]	NHS Supply Chain
UVENTA	Device	£1,500	[redacted]	NHS Supply Chain
Allium	Device	£1,700	£1,700	Company information
Resonance	Device	£912	[redacted]	NHS Supply Chain
Other consumables for Memokath-051/UVENTA/Allium/Resonance		£243.12	£243.12	Company information
Other consumables for double-J stent		£49.44	£49.44	Company information
Anaesthetist	Consultant: surgical, cost per working hour.	£105	£114	PSSRU 2020, Curtis, L. & Burns, A. (2020)
Surgeon	Consultant: surgical, cost per working hour.	£105	£114	PSSRU 2020, Curtis, L. & Burns, A. (2020)
Band 6 scrub	Band 6 hospital-based nurse, cost per working hour	£44	£50	PSSRU 2020, Curtis, L. & Burns, A. (2020)
Band 5 scrub	Band 5 hospital-based nurse, cost per working hour	£35	£40	PSSRU 2020, Curtis, L. & Burns, A. (2020)
Band 5 anaesthetist	Band 5 hospital-based nurse, cost per working hour	£35	£40	PSSRU 2020, Curtis, L. & Burns, A. (2020)
Band 2 circulating	Band 2 hospital-based nurse, cost per working hour	£23	£26.5	Inflated using PSS pay & prices index
Band 2 portering	Band 2 hospital-based nurse, cost per working hour	£23	£26.5	Inflated using PSS pay & prices index

Theatre cost	ISD Scottish Tariff Theatre allocated costs and total theatre hours used in years	£299	£325	Inflated using NHSCII
Diagnostic test during procedure	RD33Z, Contrast Fluoroscopy, Mobile or Intraoperative Procedures, with duration of less than 20 minutes	£92	£93	NHS Reference costs 19/20
Medication during procedure	Gentamicin	£15.54	£47.25	BNF 2020
Post-op medication	Co Amoxiclav 625mgs instead of Norfloxacin	£8.57	£4.80	No NHS indicative price available on the BNF for Norfloxacin, so an alternative drug used in practice Co Amoxiclav 625mgs which costs £9.60 for a pack of 21, and around £4.80 for 10 tablets
Follow-up visit after insertion				
Memokath-051/UVENTA/Allium/Resonance	RN25A, Renogram, 19 years and over	£255	£280	NHS Reference costs 19/20
Double-J stents	Urology, Outpatient Attendance	£105.19	£110	NHS Reference costs 19/20
Costs of hospital stay				
Day case	LB19C, Ureteric or Bladder Disorders, with Interventions, with CC Score 4+ LB19D, Ureteric or Bladder Disorders, with Interventions, with CC Score 0-3	£51	£59	Inflated using NHSCII
Inpatient	LB19C, Ureteric or Bladder Disorders, with Interventions, with CC Score 4+	£305	£351	Inflated using NHSCII

	LB19D, Ureteric or Bladder Disorders, with Interventions, with CC Score 0-3			
Total cost of hospital stay for Memokath-051/UVENTA/Allium/Resonance	Weighted average cost of hospital stay	£207.19	£229.87	Calculated from the sum product of costs of day case, inpatient, and current inpatient, and the proportion of patients in each case
Total cost of hospital stay for Double-J stents	Weighted average cost of hospital stay	£107.83	£115.50	Calculated from the sum product of costs of day case, inpatient, and current inpatient, and the proportion of patients in each case
Follow-up for day case				
Band 5 recovery	Band 5 hospital-based nurse, cost per working hour	£35	£40	PSSRU 2020, Curtis, L. & Burns, A. (2020)
Band 6 recovery	Band 6 hospital-based nurse, cost per working hour	£44	£50	PSSRU 2020, Curtis, L. & Burns, A. (2020)
Urinary tract infection				
Antibiotics	Sum average of treatment for UTI including: trimethoprim, nitrofurantoin, or amoxicillin	£6.32	£5.66	BNF 2020
GP appointment	Cost per surgery consultation without qualification costs, including direct care staff cost	£31	£33	PSSRU 2020, Curtis, L. & Burns, A. (2020)

Sensitivity analysis

The EAC updated all the sensitivity analysis conducted in the original guidance. The ranges used were same as the original guidance, except for

the clinical parameters (monthly risk of unplanned stent replacement) that were updated as a result of the clinical review (Table 8). For Memokath-051, the range includes the estimate (1.54%) excluding the Khoo et al 2021 study. Since the updated base case replacement cost for UVENTA was higher than the high value, the EAC applied a 15% increment to base case estimate to get a high value. The price of Double-J stent was variable due to the range of prices and brands available. The EAC applied a 10%, 25% and 50% discount to the price to check how it affected the cost savings.

Table 8: Sensitivity analysis range for monthly risk of unplanned stent replacement

	Low value	High value	Source/EAC comment
Memokath-051	0.6%	4.4%	As reported in the clinical studies
Double-J stent	0.0%	4.4%	Same as highest value reported for Memokath-051 (Kim et al. 2014)
Uventa	0.0%	6.5%	Assumption of 25% increment from Choi et al 2019
Allium	0.0%	7%	Assumption of 25% increment from Khoo et al 2021
Resonance	0.0%	4.4%	Same as highest value reported for Memokath-051 (Kim et al. 2014)

9.3 Results from the updated economic modelling

Base case results

The base case reports for a time horizon of 5 years with constant replacement, being the most conservative assumption scenario. The other scenarios; replacement in the first 2 years with 0% thereafter, reduced replacement after 2 years (risk halved) and constant unplanned replacements over a 2-year time horizon are presented in the additional results section. The summary of results compared to Double-J stent, Uventa, Allium, Resonance and Reconstructive surgery are presented in Tables 9.1 to 9.5.

Table 9.1: Base case costing savings of Memokath-051 compared to Double-J Stents

	Original model results	EAC updated model results

	Memokath-051	Double-J stents	Cost saving per patient	Memokath-051	Double-J stents	Cost saving per patient
Total insertion cost	£3,010	£786	£2,224	£3,217	£929	£2,288
Follow-up cost	£2,346	£0	£2,346	£2,576	£0	£2,576
Unplanned replacement cost	£2,503	£0	£2,503	£3,472	£0	£3,472
Planned replacement cost	£0	£8,692	-£8,692	£0	£10,326	-£10,326
Adverse event cost	£9	£9	£0	£9	£9	£0
Total	£7,868	£9,487	-£1,619	£9,274	£11,264	-£1,990
Break even months	30			30		

Memokath-051 is cost saving compared to Double-J stent in the 5 year time horizon (Table 9.1). The difference in cost saving between the original and updated guidance is mainly attributed to the updated costs parameters.

Table 9.2: Base case costing savings of Memokath-051 compared to UVENTA

	Original model results			EAC updated model results		
	Memokath-051	Uventa	Cost saving per patient	Memokath-051	Uventa	Cost saving per patient
Total insertion cost	£3,010	£2,736	£274	£3,217	£3,235	-£18
Follow-up cost	£2,346	£2,346	£0	£2,576	£2,576	£0
Unplanned replacement cost	£7,672	£835	£6,837	£6,770	£9,620	-£2,851
Planned replacement cost	£0	£8,039	-£8,039	£0	£7,631	-£7,631
Adverse event cost	£9	£9	£0	£9	£9	£0
Total	£13,037	£13,965	-£928	£12,572	£23,072	-£10,500
Break even months	18			0		

The cost savings (Table 9.2) of UVENTA has increased significantly compared to the original guidance attributed to the fact that the monthly risk of unplanned replacement has increased from 0.49% (original guidance) to

4.99%. This has impacted the stent replacement cost and hence the cost savings.

Table 9.3: Base case costing savings of Memokath-051 compared to Allium

	Original model results			EAC updated model results		
	Memokath-051	**Allium**	**Cost saving per patient**	**Memokath-051**	**Allium**	**Cost saving per patient**
Total insertion cost	£3,010	£2,936	£74	£3,217	£3,135	£82
Follow-up cost	£2,346	£2,346	£0	£2,576	£2,576	£0
Unplanned replacement cost	£2,503	£888	£1,615	£3,472	£10,341	-£6,870
Planned replacement cost	£0	£2,835	-£2,835	£0	£2,577	-£2,577
Adverse event cost	£9	£9	£0	£9	£9	£0
Total	£7,868	£9,014	-£1,146	£9,274	£18,639	-£9,365
Break even months	36			1		

The cost savings (Table 9.3) of Allium has increased significantly compared to the original guidance attributed to the fact that the monthly risk of unplanned replacement has increased from 0.49% (original guidance) to 5.54%. This has impacted the stent replacement cost and hence the cost savings.

Table 9.4: Base case costing savings of Memokath-051 compared to Resonance

	Original model results			EAC updated model results		
	Memokath-051	**Resonance**	**Cost saving per patient**	**Memokath-051**	**Resonance**	**Cost saving per patient**
Total insertion cost	£3,010	£2,148	£862	£3,217	£2,335	£882
Follow-up cost	£2,346	£1,173	£1,173	£2,576	£1,288	£1,288
Unplanned replacement cost	£2,503	£1,921	£582	£3,472	£2,685	£787
Planned replacement cost	£0	£9,169	-£9,169	£0	£10,041	-£10,041
Adverse event cost	£9	£9	£0	£9	£9	£0

Total	£7,868	£14,420	-£6,552	£9,274	£16,357	-£7,084
Break even months	12			12		

Memokath-051 is cost saving compared to Resonance in the 5 year time horizon (Table 9.4). The difference in cost saving between the original and updated guidance is mainly attributed to the updated costs parameters.

Table 9.5: Base case costing savings of Memokath-051 compared to Reconstructive surgery

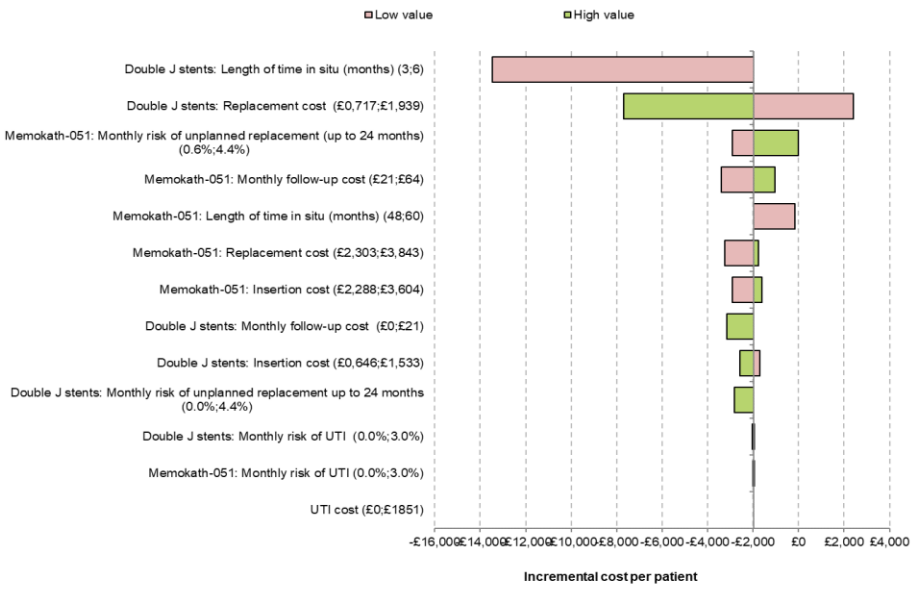
	Original model results			**EAC updated model results**		
	Memokath-051	**Surgery**	**Cost saving per patient**	**Memokath-051**	**Surgery**	**Cost saving per patient**
Total insertion cost	£3,010	£7,414	-£4,404	£3,217	£7,967	-£4,750
Follow-up cost	£2,346	£0	£2,346	£2,576	£0	£2,576
Unplanned replacement cost	£2,503	£0	£2,503	£3,472	£0	£3,472
Planned replacement cost	£0	£0	£0	£0	£0	£0
Adverse event cost	£26	£4	£22	£27	£4	£23
Total	£7,885	£7,417	£467	£9,291	£7,970	£1,321
Break even months	0			0		

As in the original guidance Memokath-051 is cost incurring compared to Reconstructive surgery in the 5 year time horizon (Table 9.5). The difference in cost saving between the original and updated guidance is mainly attributed to the updated costs parameters, and change in monthly risk of stent replacement for Memokath-051.

Sensitivity analysis results

<u>Memokath-051 vs Double-J stent</u>

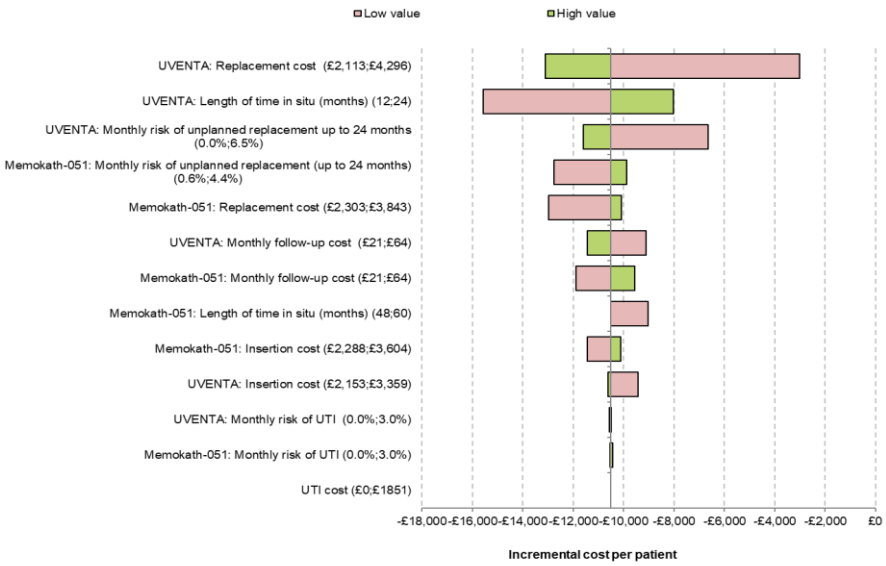
Figure 2.1: Tornado diagram based on EAC Sensitivity analysis (vs Double-J stent)



Length of time in situ for Double-J stents, replacement cost for double-J stents, Memokath-051 monthly risk of unplanned replacement and Memokath-051 monthly follow-up cost were the main cost drivers. Memokath-051 was cost saving with all the scenarios, except when the replacement cost of Double-J stents dropped to the lower value (£717). The threshold at which the replacement cost of Double-J stent is cost neutral is £1008. The threshold value of monthly risk of unplanned replacement of Memokath-051 at which the technology is no longer cost saving compared to Double-J stent is 4.42%. At a 10% discount on the price of Double-J stent, the cost savings was £1,952, at 20% was £1,914 and at 50% was £1,799.

Memokath-051 vs UVENTA

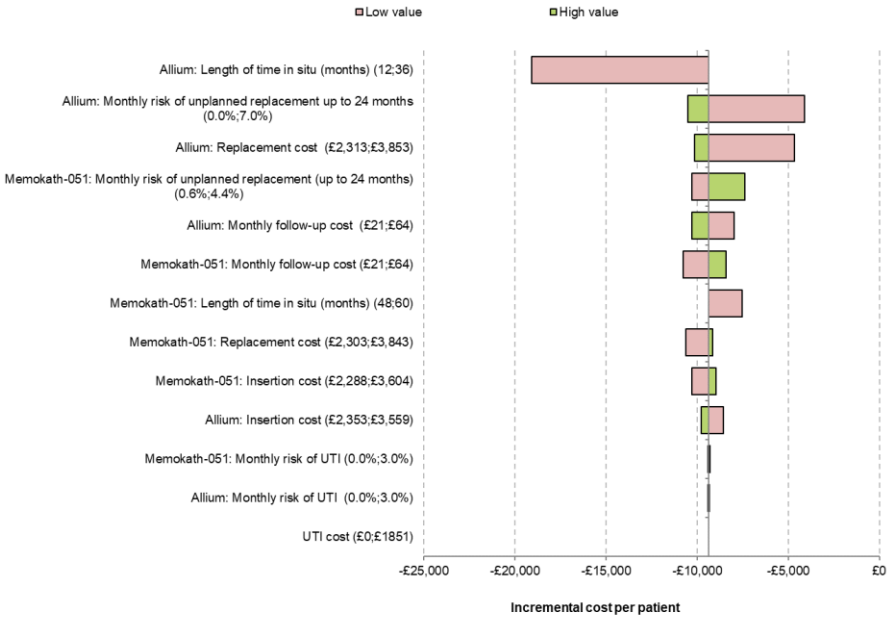
Figure 2.2: Tornado diagram based on EAC Sensitivity analysis (vs UVENTA)



Memokath-051 was cost saving in all scenarios, and the parameters that had the highest impact on the cost savings were replacement cost for UVENTA, length of time in situ-UVENTA, UVENTA monthly risk of unplanned replacement, Memokath-051 monthly risk of unplanned replacement and replacement costs.

Memokath-051 vs Allium

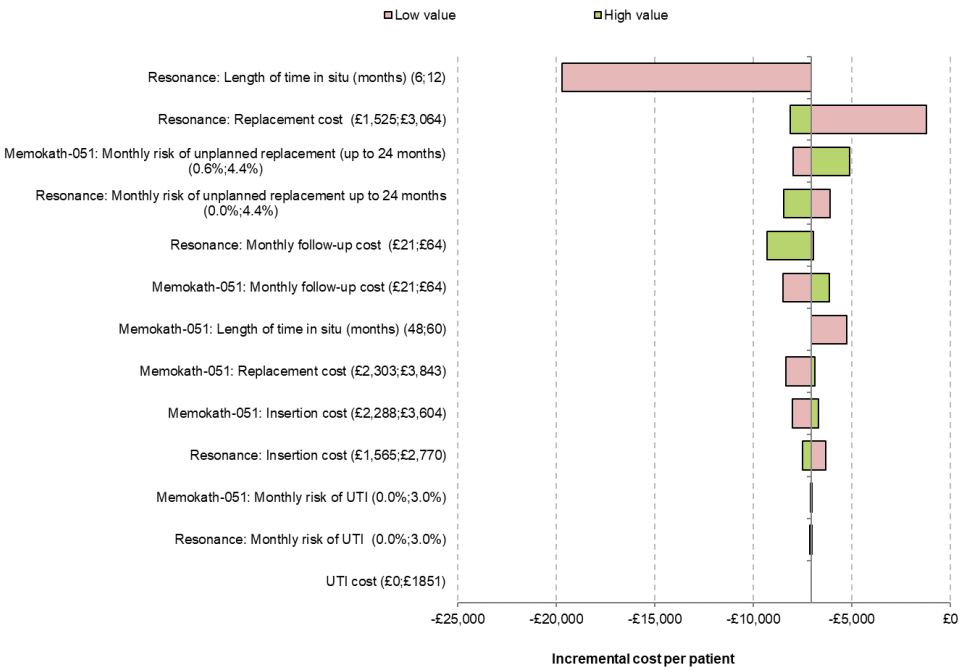
Figure 2.3: Tornado diagram based on EAC Sensitivity analysis (vs Allium)



Memokath-051 was cost saving in all scenarios, and the parameters that had the highest impact on the cost savings were Allium – Length of time in situ, monthly risk of unplanned replacement, replacement cost and Memokath-051 monthly risk of unplanned replacement.

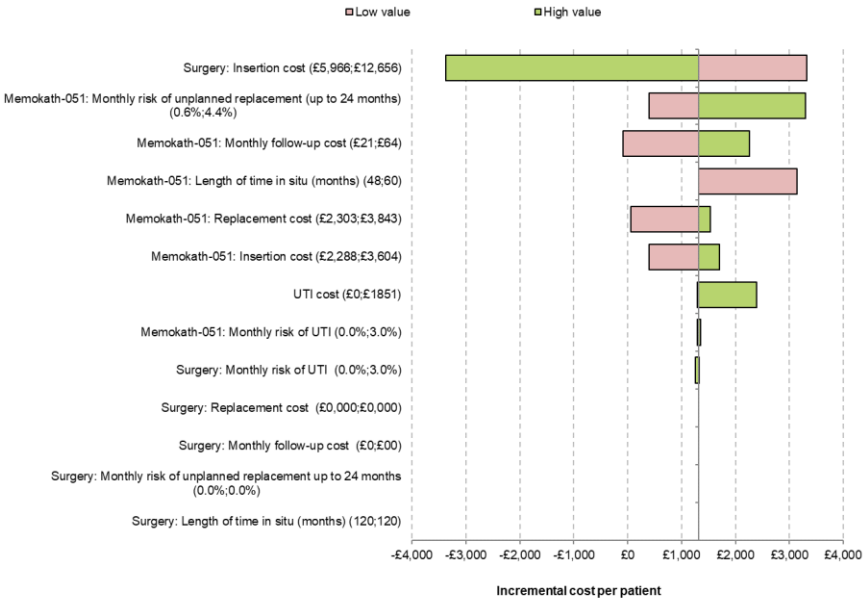
Memokath-051 vs Resonance

Figure 2.4: Tornado diagram based on EAC Sensitivity analysis (vs Resonance)



Memokath-051 was cost saving in all scenarios, and the parameters that had the highest impact on the cost savings were Resonance – length of time in situ, replacement costs, monthly risk of unplanned replacement and Memokath-051 monthly risk of unplanned replacement.

Memokath-051 vs Reconstructive Surgery **Figure 2.5: Tornado diagram based on EAC Sensitivity analysis (vs Reconstructive Surgery)**



Surgery insertion cost, Memokath-051 monthly risk of unplanned replacement, Memokath-051 length of time in situ, Memokath-051 monthly follow up costs were the main cost drivers. Memokath-051 was cost incurring with all the scenarios, except when the surgery cost was at the higher value (£12,656) and the Memokath-051 monthly follow-up cost was at the lower value (£21 i.e 1 visit per year). The threshold at which Surgery insertion cost made Memokath-051 cost neutral was £9,287.

Additional results

The full results of the three scenarios; where replacement in the first 2 years with 0% thereafter and reduced replacement after 2 years (risk halved), and constant unplanned replacements over a 2 year time horizon are provided in Appendix D – Full results of scenario analysis.

Memokath-051 compared to Double-J stent is cost incurring in a scenario of constant replacements over a 2 year time horizon, making the results uncertain.

Memokath-051 is cost saving compared to UVENTA under the scenarios where replacement in the first 2 years with 0% thereafter and reduced replacement after 2 years (risk halved), and constant unplanned replacements over a 2 year time horizon, giving more confidence in the results. However, this is attributed to higher stent replacement rate used (Choi et al 2019) with UVENTA compared to the original guidance. Moreover, the evidence is from Korea due to the non-availability of UK studies and this adds uncertainty of generalisability of results to the UK NHS setting.

Memokath-051 is cost saving compared to Allium under the scenarios where replacement in the first 2 years with 0% thereafter and reduced replacement after 2 years (risk halved), and constant unplanned replacements over a 2 year time horizon, giving more confidence to the results. Moreover, the stent replacement rates of Allium were considered equivalent to UVENTA in the original guidance on the basis of assumptions based on clinical experts. In this guidance, the replacement rates were taken from a UK based study (Khoo et al 2021). Hence, the results are more valid than the original guidance.

Memokath-051 is cost saving compared to Resonance under the scenarios where replacement in the first 2 years with 0% thereafter and reduced replacement after 2 years (risk halved) , and constant unplanned replacements over a 2 year time horizon, giving more confidence in the results. Moreover, in terms of stent replacement rates, Resonance was considered equivalent to Memokath-051 in the original guidance on the basis of assumptions based on clinical experts. In this guidance, the replacement rates were taken from a UK based study (Khoo et al 2021). Hence, the results are more valid than the original guidance

Memokath-051 is cost saving compared to Reconstructive surgery under the scenarios where replacement in the first 2 years with 0% thereafter and constant unplanned replacements over a 2-year time horizon but is cost incurring in the scenario of reduced replacement after 2 years (risk halved). This makes the results highly uncertain, because in the base case results with constant replacement over a 5-year period, Memokath-051 was cost incurring.

9.4 The EAC's interpretation of the economic evidence

. The main revision to the original model includes the change in monthly risk of unplanned stent replacement based on the new evidence found in the clinical review. Further the cost parameters were updated with more recent costs.

After updating the model, Memokath-051 was cost saving compared to Double-J Stent, UVENTA, Allium and Resonance for a conservative scenario of constant replacement over a 5-year time horizon. In the sensitivity analysis, Memokath was cost saving compared to Double-J stent in most scenarios expect when the replacement cost of Double-J stent reduced beyond 20% and when the monthly risk of unplanned replacement for Memokath was above 4.42%. In relation to UVENTA, Memokath-051 was cost saving in all scenarios. Length of time in situ which influenced the planned replacements, and monthly risk of unplanned replacement for UVENTA and Memokath-051

were the key cost drivers in the UVENTA model. The UVENTA model has limitations because it is based on a non-UK study (Korea). In terms of Allium and Resonance, Memokath-051 was cost saving in all scenarios, and length of time in situ which influenced planned replacements and monthly risk of unplanned replacement for had the highest influence on cost savings. With reconstructive surgery, Memokath-051 was cost incurring, expect if surgery costs increased by more than 16%.

Memokath-051 is cost saving compared to Double-J stent under the scenarios where replacement in the first 2 years with 0% thereafter and reduced replacement after 2 years (risk halved) , but is cost incurring in a scenario of constant unplanned replacements over a 2 year time horizon, making the results uncertain. Memokath-051 is cost saving in all scenarios when compared to UVENTA, Allium and Resonance. There is more confidence in the Allium and Resonance results, because the monthly risk of unplanned replacement is taken from a UK based study, and less confidence in the UVENTA results since it is based on a Korean study. In terms of comparison with reconstructive surgery, the cost savings results are mixed, and makes the case very uncertain.

In the original guidance, the cost models had uncertainty. Though Memokath-051 is cost saving compared to Double-J Stent, UVENTA, Allium and Resonance in a 5-year time horizon, and the cost savings conclusions remain same in this updated guidance, there is uncertainty. Particularly Double-J stent, which shows that it is cost incurring in a scenario of constant unplanned replacements over a 2-year time horizon. Moreover, there is uncertainty surrounding the main assumption that Double-J stent has a planned replacement every 6 months and there was no risk of an unplanned stent exchange, but experts seem to think it is variable. We tested this assumption in the sensitivity analysis, and changing the parameters does not seem to make Memokath-051 cost incurring against Double-J Stent. There is more confidence in terms of comparison with Allium and Resonance, as the monthly risk of unplanned replacement is based on a UK study rather than on assumptions. Length of time in situ, which impacts the planned replacement is a key cost driver when compared to Double-J stent, UVENTA, Allium and Resonance. Compared to Reconstructive surgery the plausible cost savings depends on the extrapolation of unplanned replacements but under a conservative assumption of constant replacement over a 5 year period, Memokath-051 is cost incurring.

10. Conclusions

10.1 Conclusions from the clinical evidence

The evidence available is of low-moderate quality and does present some biases which makes it difficult to make solid conclusions. The included studies are mainly retrospective, non-comparative studies of a low-moderate sample size and varying follow-up periods. The studies were also all single-centre studies, only two full-text studies were conducted in a UK NHS setting, this limits the generalisability of the results. Two experts thought that even with the UK-based studies there was a limit in the generalisability to practice across sites in the UK due to the variability in patient selection and retrospective nature of the studies.

The included studies were focused on reporting of complications, some reported on success rate and indwelling time of the stent. Only one study, presented as a conference abstract, reported on hospital stay (Elbaroni et al. 2020). There was no reported data on outcomes such as quality of life, frequency of follow-up visits and pain scores.

Stent migration was the most common complication associated with Memokath-051 from the clinical evidence identified. Memokath-051 was associated with higher stent migration than its comparators. This is in line with the evidence identified for the original guidance. A study with longer follow-up of 5 years revealed that Memokath-051 was associated with a high overall complication rate (72%; Forster et al. 2021). Forster et al. 2021 reported higher stent migration and encrustation compared with the pooled evidence underpinning the original guidance; 36% vs. 17.7% (13 pooled studies) and 11% vs. 6.3% (8 pooled studies) respectively.

There was some variation amongst the studies for success rate and indwelling time of Memokath-051. Memokath-051 was associated with higher stent failure compared with Allium and Resonance (Khoo et al. 2021). But Memokath-051 was associated with higher success rate compared with UVENTA in a population of patients with chronic benign ureteral strictures with better durability for primary success in the second and third years (Choi et al. 2019).

One study with a high loss to follow-up (27%) conducted in Germany showed a statistically significant higher stent indwelling time in patients with benign ureteral strictures compared with malignant ureteral strictures (Bier et al. 2017). Whilst another study, conducted in the UK with a low loss to follow-up (3%), reported a statistically significant higher stent indwelling time in patients with malignant ureteral strictures compared with benign (Forster et al. 2021), these results are more in line with the findings from the previous guidance.

Experts seem to agree that Memokath-051 stents last longer than 1 year and are generally changed less often than double-J stents. One expert noted that Memokath-051 could last up to 5 years. Another expert noted that they are a good option in long-term obstruction groups. Please see the EAC correspondence log for this expert input.

The EAC's opinion is that the latest evidence continues to provide a basis for Memokath-051 as an option for certain people with ureteric obstructions but highlights that clinicians should be aware of a potential increased risk of complications with Memokath-051, particularly stent migration.

10.2 Conclusions from the economic evidence

No new economic evidence was available in the literature for Memokath-051. The cost models were updated with newer clinical parameters as reported in the clinical evidence review. The cost models suggest that under a conservative assumption of constant stent replacement over a 5-year period, Memokath-051 is cost saving compared to Double-J stents, UVENTA, Allium and Resonance. It is cost incurring compared to reconstructive surgery. This suggest that Memokath-051 stents may be a plausible cost-saving treatment option for ureteric obstruction in people who cannot have reconstructive surgery and need a ureteral stent. There was new clinical evidence available for Allium and Resonance from a UK study, and this adds confidence to the results. Though Double-J stent has an assumption of planned stent replacement every 6 months and no need for any unplanned replacement, sensitivity analysis report that changing this assumption does not change the cost savings conclusions. In terms of comparison with UVENTA, new evidence was available from Korea and has been used in the updated model. The EAC acknowledges this limitation of using a non-UK study, in the absence of UK specific evidence. Khoo et al 2021 reports stents replacement for Memokath-051, but has a very high proportion and the follow-up is short (only 5.5 months) but is a UK based study. The EAC noted the limitation and included Khoo et al 2021 along with all new primary studies. The robustness of the cost savings was checked by excluding the Khoo et al 2021 study, and using the rate as included in the range for sensitivity analysis, and it did not change the cost savings conclusions. Though Forster et al 2021 reported various clinical outcomes according to whether they were malignant vs benign, the study does not segregate the risk of unplanned stent replacement. Hence it could not be applied to the cost model. The EAC believes that the sensitivity analysis would address this variation.

11. Summary of the combined clinical and economic sections

The EAC's opinion is that the latest evidence continues to provide a basis for Memokath-051 as an option for certain people with ureteric obstructions but highlights that clinicians should be aware of a potential increased risk of complications with Memokath-051, particularly stent migration.

The cost models suggest that under a conservative assumption of constant stent replacement over a 5-year period, Memokath-051 is cost saving compared to Double-J stents, UVENTA, Allium and Resonance. It is cost incurring compared to reconstructive surgery. This suggest that Memokath-051 stents may be a plausible cost-saving treatment option for ureteric obstruction in people who cannot have reconstructive surgery and need a ureteral stent.

12. Implications for research

In an ideal scenario, a UK multi-centre prospective RCT which assesses stent functionality, complication rate and patient reported outcomes is preferred. But randomisation would raise serious ethical concern and it would be difficult to implement due to the variation in indication. Please see the EAC correspondence log for expert input.

A large-scale prospective comparative cohort study could be conducted to assess long-term stent patency rates, complication rates, and patient reported outcomes. Institutions using Memokath-051 could contribute to prospective data collection that feeds into a centralised registry so that long-term outcomes can be assessed. Experts consulted for this guidance highlighted the importance of having a central registry to capture long-term outcomes.

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14. Appendices

Appendix A – Clinical literature search

Clinical data search strategy.

Number of results per source

1	Ovid MEDLINE(R) ALL <1946 to April 07, 2022>	161
2	Embase via Ovid SP <1974 to 2022 April 07>	257
3	Cochrane Central Register of Controlled Trials (CENTRAL) in the Cochrane Library (Issue 3 of 12; 2022)	15
4	International HTA Database	0
5	Cochrane Database of Systematic Reviews (CDSR) in the Cochrane Library	4
6	PubMed	71
7	Science Citation Index Expanded (SCIE) (1900 - Present)	199
8	Conference Proceedings Citation Index-Science (CPCI-S) (1900 - Present)	43
9	ClinicalTrials.gov	76
10	WHO International Clinical Trials Registry Portal (ICTRP Search Portal)	25
11	ISRCTN Registry	20
12	Action on Bladder Cancer	0
13	Bladder and Bowel Foundation	0
14	British Kidney Patient Association	0
15	Fight Bladder Cancer	0
16	Jo’s Trust	0
17	Kidney Cancer UK (KCUK)	0
18	Kidney Research UK	0
19	Ovacome	0
20	Ovarian Cancer Action	0
21	Pelvic Pain Support Network	0
22	Prostate Cancer UK	1
23	Target Ovarian Cancer	0
24	British Uro-oncology Group (BUG)	0
25	British Association of Urological Surgeons	11

26	British Association of Urological Nurses (BAUN)	0
27	British Association of Pediatric Urologists	0
28	PNN Medical	1
29	American Urological Association Annual Meeting (AUA)	0
30	European Association of Urology (EAU) Congress	0
31	Société Internationale d'Urologie (SIU) Annual Congress	7
32	British Association of Urological Surgeons (BAUS)	2
33	British Uro-oncology Group (BUG) Annual Meeting	1
34	World Congress of Endourology & SWL Annual Meeting	16

Search strategies

A1 Ovid MEDLINE(R) ALL <1946 to April 07, 2022>

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. (142)

2 (stents/ or self expandable metallic stents/) and (temperature/ or hot temperature/) (110)

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. (208)

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. (80)

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. (48)

6 or/2-5 (386)

7 (stents/ or self expandable metallic stents/) and ((nickel/ and titanium/) or alloys/) (1621)

8 ((niti or nitinol or (nickel and titanium)) and stent$).ti,ab,kf. (2278)

9 ((long-term or longterm or long-lasting or longlasting or permanent$ or semipermanent$) adj5 stent$).ti,ab,kf. (3591)

10 ((self-expand$ or selfexpand$) and stent$).ti,ab,kf. (7000)

11 or/7-10 (11986)

12 Ureter/ or exp Ureteral Diseases/ or Hydronephrosis/ (53651)

13 (ureter$ or pelviuret$).ti,ab,kf. (62924)

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. (48084)

15 (hydronephros$ or hydroureter$ or megaureter$ or ((kidney$ or renal) adj5 (disten$ or dilat$))).ti,ab,kf. (16855)

16 or/12-15 (123538)

17 11 and 16 (368)

18 1 or 6 or 17 (814)

19 exp animals/ not humans/ (4986736)

20 (news or comment or editorial or letter or case reports).pt. or case report.ti. (4323134)

21 18 not (19 or 20) (602)

22 limit 21 to english language (532)

23 limit 22 to ed=20170425-20221231 (126)

24 limit 22 to dt=20170425-20221231 (149)

25 23 or 24 (161)

A2 Embase <1974 to 2022 April 07>

1 (memokath$ or MK051 or MK-051 or memo-kath$ or memocath$ or memo-cath$).ti,ab,kw,dv. (244)

2 (pnn medical$ or (engineers adj2 doctors$)).ti,ab,kw,dm. (183)

3 1 or 2 (341)

4 (stent/ or exp self expanding stent/ or ureter stent/) and (temperature/ or high temperature/ or heat sensitivity/) (183)

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. (273)

6 ((thermoexpan$ or thermo-expan$ or thermoactiv$ or thermo-activ$ or thermoformable or thermo-formable or thermosensitiv$ or thermosensitiv$ or thermoresponsiv$ or thermo-responsiv$ or thermoreactiv$ or thermo-reactiv$) and stent$).ti,ab,kw. (153)

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. (59)

8 or/4-7 (616)

9 exp nitinol stent/ (2831)

10 (stent/ or exp self expanding stent/ or ureter stent/) and ((nickel/ and titanium/) or alloy/ or nitinol/) (2460)

11 ((niti or nitinol or (nickel and titanium)) and stent$).ti,ab,kw. (3840)

12 ((long-term or longterm or long-lasting or longlasting or permanent$ or semipermanent$) adj5 stent$).ti,ab,kw. (6027)

13 ((self-expand$ or selfexpand$) and stent$).ti,ab,kw. (12052)

14 or/9-13 (21800)

15 Ureter/ or exp Ureter disease/ (52452)

16 hydronephrosis/ (25059)

17 (ureter$ or pelviuret$).ti,ab,kw. (81617)

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. (67873)

19 (hydronephros$ or hydroureter$ or megaureter$ or ((kidney$ or renal) adj5 (disten$ or dilat$))).ti,ab,kw. (23340)

20 or/15-19 (165167)

21 14 and 20 (706)

22 3 or 8 or 21 (1453)

23 (animal/ or animal experiment/ or animal model/ or animal tissue/ or nonhuman/) not exp human/ (6436928)

24 (editorial or letter or note).pt. or case report/ (5258445)

25 22 not (23 or 24) (1126)

26 limit 25 to english language (1022)

27 limit 26 to dc=20170425-20220408 (257)

A3 CENTRAL

Date Run: 08/04/2022 22:37:38

#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*) 12

#2 [mh ^stents] or [mh ^"self expandable metallic stents"] 3189

#3 [mh ^temperature] or [mh ^"hot temperature"] 3284

#4 #2 and #3 1

#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* 5

#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* 5

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

#8 #4 or #5 or #6 or #7 14

#9 [mh ^stents] or [mh ^"self expandable metallic stents"] 3189

#10 [mh ^nickel] and [mh ^titanium] 196

#11 [mh ^alloys] 176

#12 #9 and (#10 or #11) 60

#13 (niti or nitinol or (nickel and titanium)) and stent* 327

#14 ("long-term" or longterm or "long-lasting" or longlasting or permanent* or semipermanent*) near/5 stent* 606

#15 (self next expand* or selfexpand*) and stent* 794

#16 #12 or #13 or #14 or #15 1541

#17 [mh ^ureter] or [mh "ureteral diseases"] or [mh ^hydronephrosis] 779

#18 ureter* or pelviuret* 3753

#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*) 8295

#20 hydronephros* or hydroureter* or megaureter* or ((kidney* or renal) near/5 (disten* or dilat*)) 641

#21 #17 or #18 or #19 or #20 11481

#22 #16 and #21 27

#23 #1 or #8 or #22 46

#24 #23 with Cochrane Library publication date from Apr 2017 to present, in Trials 15

A4 International HTA Database

Memokat* OR Memocat* OR PNN OR (Engineers AND Doctors) 0

A5 CDSR

Date Run: 08/04/2022 22:45:13

#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*) 12

#2 [mh ^stents] or [mh ^"self expandable metallic stents"] 3189

#3 [mh ^temperature] or [mh ^"hot temperature"] 3284

#4 #2 and #3 1

#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* 5

#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* 5

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

#8 #4 or #5 or #6 or #7 14

#9 [mh ^stents] or [mh ^"self expandable metallic stents"] 3189

#10 [mh ^nickel] and [mh ^titanium] 196

#11 [mh ^alloys] 176

#12 #9 and (#10 or #11) 60

#13 (niti or nitinol or (nickel and titanium)) and stent* 327

#14 ("long-term" or longterm or "long-lasting" or longlasting or permanent* or semipermanent*) near/5 stent* 606

#15 (self next expand* or selfexpand*) and stent* 794

#16 #12 or #13 or #14 or #15 1541

#17 [mh ^ureter] or [mh "ureteral diseases"] or [mh ^hydronephrosis] 779

#18 ureter* or pelviuret* 3753

#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*) 8295

#20 hydronephros* or hydroureter* or megaureter* or ((kidney* or renal) near/5 (disten* or dilat*)) 641

#21 #17 or #18 or #19 or #20 11481

#22 #16 and #21 27

#23 #1 or #8 or #22 46

#24 #23 with Cochrane Library publication date from Apr 2017 to present, in Cochrane Reviews, Cochrane Protocols 4

A6 PubMed

((((kidney*[tiab] OR renal[tiab]) AND (disten*[tiab] OR dilat*[tiab])) OR hydronephros*[tiab] OR hydroureter*[tiab] OR megaureter*[tiab] OR ((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])) OR ureter*[tiab] OR pelviuret*[tiab] OR "Ureter"[Mesh:NoExp] OR "Ureteral Diseases"[Mesh] OR "Hydronephrosis"[Mesh:NoExp]) AND (((self-expand*[tiab] OR selfexpand*[tiab]) AND stent*[tiab]) OR ((long-term[tiab] OR longterm[tiab] OR long-lasting[tiab] OR longlasting[tiab] OR permanent*[tiab] OR semipermanent*[tiab]) AND stent*[tiab]) OR ((niti[tiab] OR nitinol[tiab] OR (nickel[tiab] AND titanium[tiab])) AND stent*[tiab]) OR (("Stents"[Mesh:NoExp] OR "Self Expandable Metallic Stents"[Mesh:NoExp]) AND "Alloys"[Mesh:NoExp]) OR (("Stents"[Mesh:NoExp] OR "Self Expandable Metallic Stents"[Mesh:NoExp]) AND "Nickel"[Mesh:NoExp] AND "Titanium"[Mesh:NoExp]))) OR (((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*) OR ((thermoexpan*[tiab] OR thermo-expan*[tiab] OR thermoactiv*[tiab] OR thermo-activ*[tiab] OR thermoformable[tiab] OR thermo-formable[tiab] OR thermosensitiv*[tiab] OR thermosensitiv*[tiab] OR thermoresponsiv*[tiab] OR thermo-responsiv*[tiab] OR thermoreactiv*[tiab] OR thermo-reactiv*[tiab]) AND stent*[tiab]) OR ((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]) OR (("Stents"[Mesh:NoExp] OR "Self Expandable Metallic Stents"[Mesh:NoExp]) AND ("Temperature"[Mesh:NoExp] OR "Hot Temperature"[Mesh:NoExp]))) OR (memokath*[tiab] OR MK051[tiab] OR MK-051[tiab] OR memokath*[tiab] OR memocath*[tiab] OR memo-cath*[tiab] OR (pnn[tiab] AND medical*[tiab]) OR

memokath*[ad] OR MK051[ad] OR MK-051[ad] OR memokath*[ad] OR memocath*[ad] OR memo-cath*[ad] OR (pnn[ad] AND medical*[ad]) OR (engineers[ad] AND doctors[ad])) NOT (news[pt] OR comment[pt] OR editorial[pt] OR letter[pt] OR case reports[pt] OR case report[ti] OR (animals[mh] NOT humans[mh:noexp]) OR medline[sb]) AND English[LA] AND (2017/4/25:3000/12/12[pdat]) 71

A7 SCIE

Science Citation Index Expanded (SCI-EXPANDED)--1900-present

21 #4 OR #8 OR #17 and Notes or Letters or Editorial Materials or News Items (Exclude – Document Types) and English (Languages) and 2017 or 2018 or 2019 or 2020 or 2021 or 2022 (Publication Years) 199

20 #4 OR #8 OR #17 and Notes or Letters or Editorial Materials or News Items (Exclude – Document Types) and English (Languages) 710

19 #4 OR #8 OR #17 and Notes or Letters or Editorial Materials or News Items (Exclude – Document Types) 754

18 #4 OR #8 OR #17 783

17 #12 AND #16 385

16 #13 OR #14 OR #15 92,362

15 TS=(hydronephros* OR hydroureter* OR megaureter* OR ((kidney* OR “renal”) NEAR/5 (disten* OR dilat*))) 12,536

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*)) 39,405

13 TS=(ureter* OR pelviuret*) 52,215

12 #9 OR #10 OR #11 13,832

11 TS=((self-expand* OR selfexpand*) AND stent*) 7,203

10 TS=((“long-term” OR “longterm” OR “long-lasting” OR “longlasting” OR permanent* OR semipermanent*) NEAR/5 stent*) 4,562

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*) 3,731

8 #5 OR #6 OR #7 289

7 TS=(((thermal* OR temperature* OR “heat”) NEAR/5 (expand* OR expansion* OR activat* OR reactiv* OR sensitiv* OR responsiv* OR “formable”)) AND stent*) 84

6 TS=((thermoexpan* OR thermo-expan* OR thermoactiv* OR thermoactiv* OR “thermoformable” OR “thermo-formable” OR thermosensitiv* OR thermo-sensitiv* OR thermoresponsiv* OR thermo-responsiv* OR thermoreactiv* OR thermo-reactiv*) AND stent*) 111

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*) 120

4 #3 OR #2 OR #1 185

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

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

1 TS=(memokath* OR “MK051” OR “MK-051” OR memo-kath* OR memocath* OR memo-cath* OR “pnn medical*” OR ("engineers" NEAR/2 doctors*)) 185

A8 CPCI-S

20 #17 OR #8 OR #4 and English (Languages) and 2017 or 2018 or 2019 or 2020 or 2021 (Publication Years) 43

19 #17 OR #8 OR #4 and English (Languages) 157

18 #17 OR #8 OR #4 158

17 #16 AND #12 33

16 #13 OR #14 OR #15 7,214

15 TS=(hydronephros* OR hydroureter* OR megaureter* OR ((kidney* OR “renal”) NEAR/5 (disten* OR dilat*))) 708

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*)) 3,015

13 TS=(ureter* OR pelviuret*) 4,131

12 #9 OR #10 OR #11 2,265

11 TS=((self-expand* OR selfexpand*) AND stent*) 1,083

10 TS=((“long-term” OR “longterm” OR “long-lasting” OR “longlasting” OR permanent* OR semipermanent*) NEAR/5 stent*) 833

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*) 578

8 #5 OR #6 OR #7 63

7 TS=(((thermal* OR temperature* OR “heat”) NEAR/5 (expand* OR expansion* OR activat* OR reactiv* OR sensitiv* OR responsiv* OR “formable”)) AND stent*) 17

6 TS=((thermoexpan* OR thermo-expan* OR thermoactiv* OR thermoactiv* OR “thermoformable” OR “thermo-formable” OR thermosensitiv* OR thermo-sensitiv* OR thermoresponsiv* OR thermo-responsiv* OR thermoreactiv* OR thermo-reactiv*) AND stent*) 17

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*) 32

4 #1 OR #2 OR #3 74

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

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

1 TS=(memokath* OR “MK051” OR “MK-051” OR memo-kath* OR memocath* OR memo-cath* OR “pnn medical*” OR ("engineers" NEAR/2 doctors*)) 74

A9 ClinicalTrials.gov

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) 15 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) 21 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 “selfexpanding”) 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) 30 results

A10 WHO ICTRP

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* 1 result

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* 8 results

5 niti AND stent* AND ureter* 0 result

6 nitinol AND stent* AND ureter* 1 result

7 nickel AND titanium AND stent* 0 result

8 long-term AND stent* AND ureter* 6 results

9 longterm AND stent* AND ureter* 1 result

10 long-lasting AND stent* AND ureter* 0 result

11 longlasting AND stent* AND ureter* 0 result

12 permanent* AND stent* AND ureter* 1 result

13 semipermanent* AND stent* AND ureter* 0 result

14 selfexpand* AND stent* AND ureter* 0 result

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

A11 ISRCTN Registry

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) 6 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 "selfexpanding") 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) 13 results

A12: Action on Bladder Cancer

Retrieved records: 0

Site wide search: Memokath

Search Google using site limit: Memokath
site:http://actionbladdercanceruk.org/

A13: Bladder and Bowel Foundation

Retrieved records: 0

Site wide search: Memokath

Search Google using site limit: Memokath
site:https://www.bladderandbowelfoundation.org/

A14: British Kidney Patient Association

Retrieved records: 0

Site wide search: Memokath

Search Google using site limit: Memokath site:http://www.britishkidney-pa.co.uk/

A15: Fight Bladder Cancer

Retrieved records: 0

Site wide search: Memokath

Search Google using site limit: Memokath site:http://fightbladdercancer.co.uk/

A16: Jo's Trust

Retrieved records: 0

Site wide search: Memokath

Search Google using site limit: memokath site:https://www.jostrust.org.uk/

A17: Kidney Cancer UK (KCUK)

Retrieved records: 0

Site wide search: Memokath

Search Google using site limit: Memokath site:https://www.kcuk.org.uk/

A18: Kidney Research UK

Retrieved records: 0

Interface / URL: http://www.kidneyresearchuk.org/

Site wide search: Memokath

Search Google using site limit: Memokath
site:http://www.kidneyresearchuk.org/

A19: Ovacome

Retrieved records: 0

Site wide search: Memokath

Search Google using site limit: Memokath site:http://www.ovacome.org.uk/

A20: Ovarian Cancer Action

Retrieved records: 0

No site wide search option

Search Google using site limit: memokath site:http://ovarian.org.uk/

A21: Pelvic Pain Support Network

Retrieved records: 0

Site wide search: Memokath

Search Google using site limit: Memokath site:http://www.pelvicpain.org.uk/

A22: Prostate Cancer UK

Retrieved records: 1

Site wide search: Memokath

Search Google using site limit: Memokath site:https://prostatecanceruk.org/

A23: Target Ovarian Cancer

Retrieved records: 0

Site wide search: Memokath

Search Google using site limit: Memokath
site:http://www.targetovariancancer.org.uk/

A24: British Uro-oncology Group (BUG)

Retrieved records: 0

No site wide search option

Search Google using site limit: Memokath site:http://www.bug.uk.com/

A25: British Association of Urological Surgeons (BAUS)

Interface / URL: http://www.baus.org.uk/

Retrieved records: 11

Site wide search: Memokath

Search Google using site limit: Memokath site:http://www.baus.org.uk/

A26: British Association of Urological Nurses (BAUN)

Retrieved records: 0

No site wide search option

Search Google using site limit: Memokath site:http://www.baun.co.uk/

A27: British Association of Pediatric Urologists

Retrieved records: 0

Site wide search: Memokath

Search Google using site limit: Memokath site:http://www.bapu.org.uk/

A28: PNN Medical

Retrieved records: 1

Browsed “Memokath” section of the webpage

A29: American Urological Association Annual Meeting (AUA)

Retrieved records: 0

Years 2018, 2019, 2020, 2021 were indexed in Embase – covered by database searches – handsearches not required.

Proceedings from 2022 (May 13-16 New Orlean) searchable via the conference webpages:
https://www.auajournals.org/toc/juro/207/Supplement+5

Boolean search not supported – single terms or phrases only. Can search only on device name: Memokath between Jan 2022 – Dec 2022

A30: European Association of Urology (EAU) Congress

Retrieved records: 0

2018, 2019, 2020, 2021 indexed in Embase – covered by database searches – handsearches not required. The congress for 2022 is in the future.

A31: Société Internationale d'Urologie (SIU) Annual Congress

Retrieved records: 7

2017: https://link.springer.com/content/pdf/10.1007/s00345-017-2090-9.pdf

2018: https://link.springer.com/content/pdf/10.1007/s00345-019-02955-9.pdf

2019: https://link.springer.com/content/pdf/10.1007/s00345-019-02955-9.pdf

2020 and 2021: https://academy.siu-urology.org/siu/#!*search=memokath*browseby=8*listing=0*sortby=1

Annual Congress for 2022 is in the future.

A32: British Association of Urological Surgeons (BAUS)

Retrieved records: 2

Annual Scientific Meeting

2017: https://journals.sagepub.com/doi/pdf/10.1177/2051415817707638

2018: https://www.baus.org.uk/_userfiles/pages/files/AGM/BAUS2018-Abstracts.pdf

2019: https://www.baus.org.uk/_userfiles/pages/files/agm/BAUS%202019%20Abstracts.pdf

2020: https://www.baus.org.uk/_userfiles/pages/files/agm/BAUS2020%20Abstracts.pdf

2021: https://www.baus.org.uk/_userfiles/pages/files/agm/BAUS%202021%20Absracts.pdf

Search this issues for memokath as single terms

A33: British Uro-oncology Group (BUG) Annual Meeting

Retrieved records: 1

All years are getting published in Clinical Oncology. Unclear which issue/supplement the abstracts are found in – therefore the term “memokath” was searched for across all journal content.

A34: World Congress of Endourology & SWL Annual Meeting

Retrieved records: 16

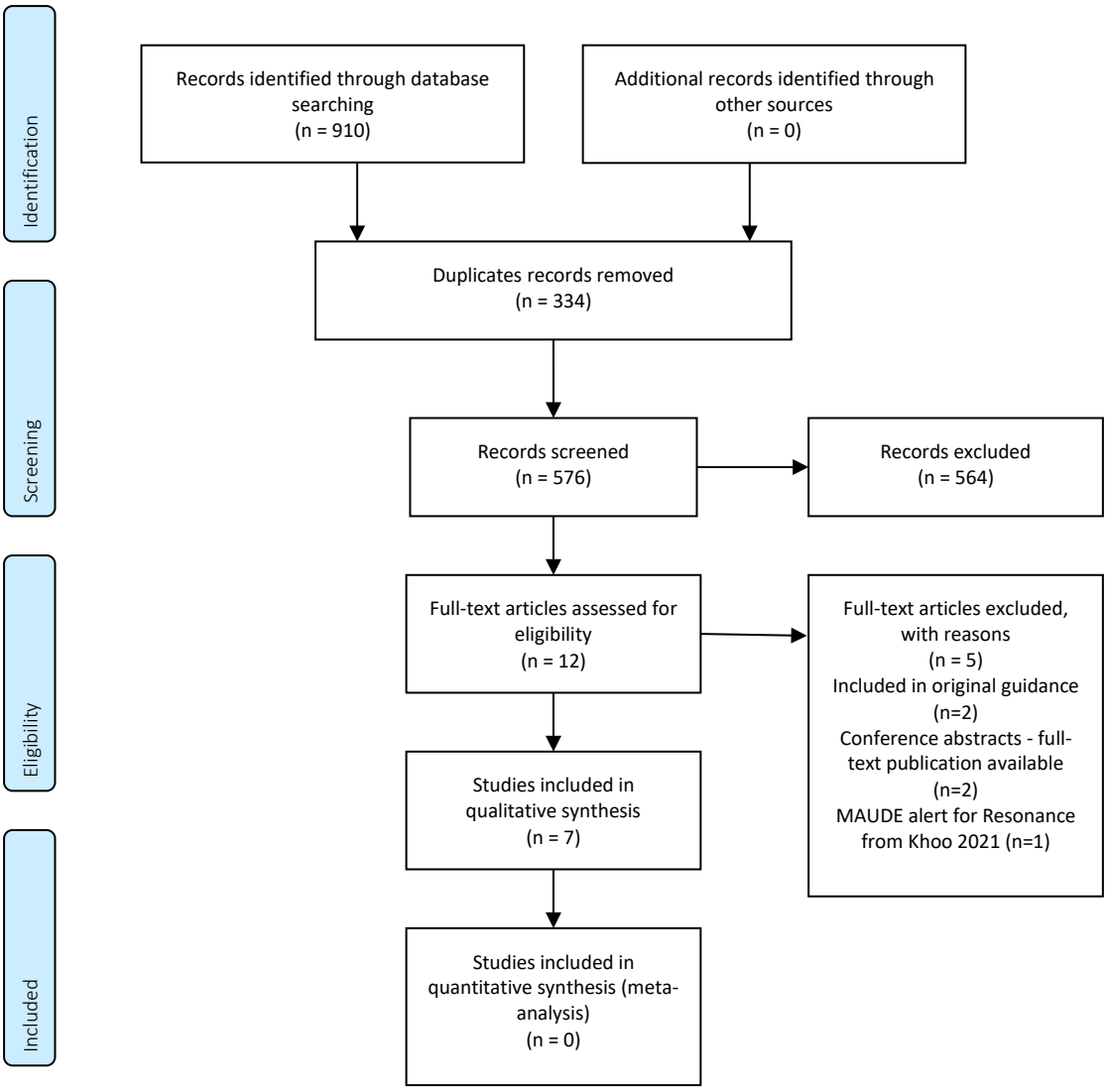
The conference abstract are being published in the Journal of Endourology.

Searched Memokath as single term between 2016 and 2022 in Journal of Endourology

Critique of company strategy.

Not applicable.

PRISMA diagram.



List of excluded studies.

Study ID	Reason for exclusion
Akbarov et al. (2017) European Urology, Supplements 16(3): e802	Included inoriginal guidance
Ho et al. 2021. British Journal of Surgery 108(SUPPL 6): vi283-vi4	Conference abstract – full text already included
Kallidonis P et al (2017). Arab Journal of Urology 15(4): 280-8	Review with studies included in original guidance

Khoo C et al (2017) Journal of Endourology 35(SUPPL 1): A217	Conference abstract – full text already included
MAUDE Adverse Event Report: COOK IRELAND LTD RESONANCE STENT SET FAD STENT, URETERAL. 2021	MAUDE alert for Resonance.

Appendix B – Critical appraisal of clinical evidence

Summary of the strengths and weaknesses of the trial incorporating internal and external validity

Bier et al. 2017

	Strengths	Weaknesses
Study design	Medium sample size Most of the data was generated at stent placement	Retrospective study design. Single-arm study design so it's difficult to know how results compare to current practice. The reason for stent removal was examined retrospectively
Patient selection	Included patients with causes of ureteral strictures that were benign or malignant. Appears to reflect eligible population.	Conducted in Germany so might not reflect UK population Statistically significant ($p<0.05$) differences in presence of renal failure and causation (benign/malignant) of ureteral strictures. Concotimant urinary diseases (such as stones or prostate enlargement) were not recorded.
Randomisation	Randomisation not applicable.	Randomisation not performed, single-arm retrospective study.
Blinding	No blinding	Not feasible to blind patients or treating/assessing clinicians. Moderate to high risk of performance bias.
Patient attrition	Reasons for patient withdrawal documented.	High proportion of patients lost to follow-up (27%) so poor confidence in longer term results and risk of bias in results

		High risk of attrition bias.
Reporting of outcomes	Reported on primary outcomes pre-specified in protocol.	Lacked a standardised protocol for follow-up.
Statistical analysis	Not applicable	Details of statistical analysis not reported.
Study company	The authors declared no conflict of interest.	Study funding not reported.

Diaz Romero et al. 2018

	Strengths	Weaknesses
Study design	Length of stenosis was reported	Retrospective study design. Single-arm study design so it's difficult to know how results compare to current practice. Small sample size
Patient selection	Included patients with causes of ureteral strictures that were benign or malignant.	Conducted in Spain so might not represent the UK population.
Randomisation	Randomisation not applicable	No randomisation
Blinding	NA - no blinding	No blinding – not feasible to blind treating/assessing clinicians.
Patient attrition	Not reported – conference abstract, lack of information reported.	Not reported – conference abstract, lack of information reported.
Reporting of outcomes	Reported on success rate and complication rate	Lacked information of standardised protocol.
Statistical analysis	Not reported – conference abstract, lack of information reported.	Not reported – conference abstract, lack of information reported.
Study company	Not reported – conference abstract, lack of information reported.	Not reported – conference abstract, lack of information reported.

Elbaroni et al. 2020

	Strengths	Weaknesses
Study design	Moderate sample size	Retrospective study design
Patient selection	Included patients with causes of ureteral strictures that were benign or malignant. Conducted in the UK.	Conference abstract – lack of information reported on patient selection.
Randomisation	Randomisation not applicable	No randomisation
Blinding	NA – no blinding	No blinding
Patient attrition	Not reported – conference abstract, lack of information reported.	Not reported – conference abstract, lack of information reported.
Reporting of outcomes	Included long follow-up	Large range in follow-up period (4 mos. – 12 yrs.)
Statistical analysis	Not reported – conference abstract, lack of information reported.	Not reported – conference abstract, lack of information reported.
Study company	Not reported – conference abstract, lack of information reported.	Not reported – conference abstract, lack of information reported.

Choi et al. 2019

Study identification: Choi 2019					
Guideline topic:	**Review question no:**				
Checklist completed by:					
Circle or highlight one option for each question:					
A. Selection bias (systematic differences between the comparison groups)					
A1	The method of allocation to treatment groups was unrelated to potential confounding factors	~~Yes~~	~~No~~	Unclear	Retrospective study. It is not know why patients received one stent over another. But the authors report that patients included in this study had sufficient discussion on the choice of treatment policies and included patients who did not want reconstructive surgery.
A2	Attempts were made within the design or analysis to balance the comparison groups for potential confounders	~~Yes~~	~~No~~	Unclear	
A3	The groups were comparable at baseline, including all major confounding and prognostic factors	~~Yes~~	No	~~Unclear~~	There were between-group differences for baseline stricture length and prior radiation therapy.
Based on your answers to the above, in your opinion was selection bias present? If so, what is the likely direction of its effect?					
~~Low risk of bias~~	Unclear~~/~~unknown risk	~~High risk of bias~~			
Likely direction of effect: not known.					
B. Performance bias (systematic differences between groups in the care provided, apart from the intervention under investigation)					
B1	The comparison groups received the same care apart from the intervention(s) studied	~~Yes~~	~~No~~	Unclear	NA
B2	Participants receiving care were kept 'blind' to treatment allocation	~~Yes~~	No	~~Unclear~~	NA

B3	Individuals administering care were kept 'blind' to treatment allocation	~~Yes~~	No	~~Unclear~~	NA
Based on your answers to the above, in your opinion was performance bias present? If so, what is the likely direction of its effect? Paper does not report this detail.					
~~Low risk of bias~~	Unclear/unknown risk		~~High risk of bias~~		
Likely direction of effect: not known.					
C. Attrition bias (systematic differences between the comparison groups with respect to loss of participants)					
C1	All groups were followed up for an equal length of time (or analysis was adjusted to allow for differences in length of follow up)	~~Yes~~	No	~~Unclear~~	Follow-up was slightly less for the Memokath-051 group (34.4 months) compared with the UVENTA group (41.4 months).
C2	a. **How many participants did not complete treatment in each group?**				
	b. The groups were comparable for treatment completion	~~Yes~~	~~No~~	Unclear	NA
C3	a. For how many participants in each group were no outcome data available?				
	b. The groups were comparable with respect to the availability of outcome data	Yes	~~No~~	~~Unclear~~	
Based on your answers to the above, in your opinion was attrition bias present? If so, what is the likely direction of its effect?					
~~Low risk of bias~~	Unclear/unknown risk		~~High risk of bias~~		
Likely direction of effect: not known.					
D. Detection bias (bias in how outcomes are ascertained, diagnosed or verified)					
D1	The study had an appropriate length of follow up	Yes	~~No~~	~~Unclear~~	
D2	The study used a precise definition of outcome	Yes	~~No~~	~~Unclear~~	

D3	A valid and reliable method was used to determine the outcome	Yes	~~No~~	~~Unclear~~	
D4	Investigators were kept 'blind' to participants' exposure to the intervention	~~Yes~~	No	~~Unclear~~	NA
D5	Investigators were kept 'blind' to other important confounding and prognostic factors	~~Yes~~	No	~~Unclear~~	NA
Based on your answers to the above, in your opinion was detection bias present? If so, what is the likely direction of its effect?					
~~Low risk of bias~~	Unclear/unknown risk	~~High risk of bias~~			
Likely direction of effect: not known					

Forster et al. 2021

	Strengths	Weaknesses
Study design	Moderate sample size Long follow-up (5 years)	Retrospective study design Single-arm, no comparator so difficult to know how results compare to current practice.
Patient selection	Appears to reflect the eligible population. UK based study, generalisable to the UK NHS setting.	Concotimant urinary diseases and other comorbidities not reported.
Randomisation	Randomisation not applicable, single-arm study	Randomisation not performed, single-arm retrospective study
Blinding	No blinding	Not feasible to blind patients or treating/assessing clinicians. Moderate to high risk of performance bias.
Patient attrition	Low loss to follow-up (3%) ITT analysis conducted Low attrition bias	Reasons for loss to follow-up in three patients not reported.
Reporting of outcomes	Primary outcome analysis reported	Some discrepancies among complication rates reported in the abstract, results and figure 1.
Statistical analysis	ITT analysis used	No power calculations, sample size requirement not clear.
Study company	The authors declared no conflicts of interest. No funding received. All researchers were new and independent of the original research team.	Not applicable

Khoo et al. 2021

Study identification: Khoo et al. 2021					
Guideline topic:	**Review question no:**				
Checklist completed by:					
		Circle or highlight one option for each question:			
A. Selection bias (systematic differences between the comparison groups)					
A1	The method of allocation to treatment groups was unrelated to potential confounding factors	~~Yes~~	~~No~~	Unclear	Retrospective study, not clear why a particular stent was chosen. Authors note that the stent choice was the surgeon's discretion.
A2	Attempts were made within the design or analysis to balance the comparison groups for potential confounders	~~Yes~~	~~No~~	Unclear	NA
A3	The groups were comparable at baseline, including all major confounding and prognostic factors	Yes	~~No~~	~~Unclear~~	NA
Based on your answers to the above, in your opinion was selection bias present? If so, what is the likely direction of its effect?					
~~Low risk of bias~~	Unclear/unknown risk	~~High risk of bias~~			
Likely direction of effect: not known.					
B. Performance bias (systematic differences between groups in the care provided, apart from the intervention under investigation)					
B1	The comparison groups received the same care apart from the intervention(s) studied	Yes	~~No~~	~~Unclear~~	Authors outline the care given to all groups suggesting the care was the same.
B2	Participants receiving care were kept 'blind' to treatment allocation	~~Yes~~	No	~~Unclear~~	
B3	Individuals administering care were kept 'blind' to treatment allocation	~~Yes~~	No	~~Unclear~~	

Based on your answers to the above, in your opinion was performance bias present? If so, what is the likely direction of its effect? Paper does not report this detail.						
~~Low risk of bias~~	Unclear/unknown risk			~~High risk of bias~~		
Likely direction of effect: not known.						
C. Attrition bias (systematic differences between the comparison groups with respect to loss of participants)						
C1	All groups were followed up for an equal length of time (or analysis was adjusted to allow for differences in length of follow up)		Yes	No	Unclear	
C2	a. **How many participants did not complete treatment in each group?**					
	b. The groups were comparable for treatment completion	Yes		~~No~~	~~Unclear~~	There were no patients lost to follow-up.
C3	a. For how many participants in each group were no outcome data available?					
	b. The groups were comparable with respect to the availability of outcome data		~~Yes~~	~~No~~	Unclear	Not clear. Aalthough Mercaptoacetyltriglycine (MAG3) renograms were performed at the first clinical follow-up, they were seldom performed subsequently, and baseline imaging for comparison was often lacking
Based on your answers to the above, in your opinion was attrition bias present? If so, what is the likely direction of its effect?						
Low risk of bias	~~Unclear/unknown risk~~			~~High risk of bias~~		
Likely direction of effect: not known.						
D. Detection bias (bias in how outcomes are ascertained, diagnosed or verified)						
D1	The study had an appropriate length of follow up	~~Yes~~		No	~~Unclear~~	Follow-up varied between the three groups.
D2	The study used a precise definition of outcome	Yes		~~No~~	~~Unclear~~	NA

D3	A valid and reliable method was used to determine the outcome	~~Yes~~	~~No~~	Unclear	Ffunctional stent survival might have been overestimated if failures or adverse events have been missed (for example, if patients presented elsewhere).
D4	Investigators were kept 'blind' to participants' exposure to the intervention	~~Yes~~	No	~~Unclear~~	NA
D5	Investigators were kept 'blind' to other important confounding and prognostic factors	~~Yes~~	No	~~Unclear~~	NA
Based on your answers to the above, in your opinion was detection bias present? If so, what is the likely direction of its effect?					
~~Low risk of bias~~	Unclear/unknown risk	~~High risk of bias~~			
Likely direction of effect: not known.					

Khoo et al. 2018

Critical appraisal for systematic review using AMSTAR 2 checklist

Did the research questions and inclusion criteria for the review include the components of PICO?	Yes
Did the report of the review contain an explicit statement that the review methods were established prior to conduct of the review and did the report justify any significant deviations from the protocol?	Yes

Did the review authors explain their selection of the study designs for inclusion in the review?	No
Did the review authors use a comprehensive literature search strategy?	Partially yes
Did the review authors perform study selection in duplicate?	Yes
Did the review authors perform data extraction in duplicate?	Not reported
Did the review authors provide a list of excluded studies and justify the exclusions?	No
Did the review authors describe the included studies in adequate detail?	Yes
Did the review authors use a satisfactory technique for assessing the risk of bias (RoB) in individual studies that were included in the review?	Yes
Did the review authors report on the sources of funding for the studies included in the review?	Yes
If meta-analysis was performed did the review authors use appropriate methods for statistical combination of results?	Yes

For non-randomized studies of intervention, did the authors do the following: (1) Justify combining data in a meta-analysis (2) Use an appropriate weighted technique to combine study results, adjusting for heterogeneity if present (3) Statistically combined effect estimates from NRSI that were adjusted for confounding, rather than combining raw data, or justified combining raw data when adjusted effect estimates were not available (4) Report separate summary estimates for RCTs and NRSI separately when both were included in the review	Yes
If meta-analysis was performed, did the review authors assess the potential impact of RoB in individual studies on the results of the meta-analysis or other evidence synthesis?	Yes
Did the review authors account for RoB in individual studies when interpreting/ discussing the results of the review?	Yes
Did the review authors provide a satisfactory explanation for, and discussion of, any heterogeneity observed in the results of the review?	Partially yes – reported heterogeneity but did not expand on potential reasons for heterogeneity. The authors included studies included studies with mixed benign and malignant aetiologies to make a conclusion on malignant aetiology without running a sensitivity analysis

If they performed quantitative synthesis did the review authors carry out an adequate investigation of publication bias (small study bias) and discuss its likely impact on the results of the review?	No
Did the review authors report any potential sources of conflict of interest, including any funding they received for conducting the review?	Financial interest: the authors reported that they had no relevant financial interest to declare.

Appendix C – Economic literature search

Economic data search strategy.

Number of results per source

Since the clinical search was not limited to specific clinical study designs, it also covered the economic evidence search. So, the sources listed for clinical search can also be listed for economic search. In addition to the above sources, KiTEC repeated the searches from the original evaluation for all the relevant sources:

1	EconLit via ProQuest <1886 to 4 April 2022>	3
2	CEA Registry	0

E1 EconLit

ti(memokath* OR MK051 OR MK-051 OR memo-kath* OR memocath* OR memo-cath* OR pnn medical* OR (engineers NEAR/2 doctors*) OR ((thermal memory OR shape memory OR smart metal* OR memory metal* OR memory alloy* OR muscle wire* OR smart alloy*) AND stent*) OR ((thermoexpan* OR thermo-expan* OR thermoactiv* OR thermo-activ* OR thermoformable OR thermo-formable OR thermosensitiv* OR thermosensitiv* OR thermoresponsiv* OR thermo-responsiv* OR thermoreactiv* OR thermo-reactiv*) AND stent*) OR (((thermal* OR temperature* OR heat) NEAR/5 (expand* OR expansion* OR activat* OR reactiv* OR sensitiv* OR responsiv* OR formable)) AND stent*) OR ((niti OR nitinol OR (nickel AND titanium)) AND stent*) OR ((long-term OR longterm OR long-lasting OR longlasting OR permanent* OR semipermanent*) NEAR/5 stent*) OR ((self-expand* OR selfexpand*) AND stent*)) OR ab(memokath* OR MK051 OR MK-051 OR memo-kath* OR memocath* OR memo-cath* OR pnn medical* OR (engineers NEAR/2 doctors*) OR ((thermal memory OR shape memory OR smart metal* OR memory metal* OR memory alloy* OR muscle wire* OR smart alloy*) AND stent*) OR ((thermoexpan* OR thermo-expan* OR thermoactiv* OR thermo-activ* OR thermoformable OR thermo-formable OR thermosensitiv* OR thermosensitiv* OR thermoresponsiv* OR thermo-responsiv* OR thermoreactiv* OR thermo-reactiv*) AND stent*) OR (((thermal* OR temperature* OR heat) NEAR/5 (expand* OR expansion* OR activat* OR reactiv* OR sensitiv* OR responsiv* OR formable)) AND stent*) OR ((niti OR nitinol OR (nickel AND

titanium)) AND stent*) OR ((long-term OR longterm OR long-lasting OR longlasting OR permanent* OR semipermanent*) NEAR/5 stent*) OR ((self-expand* OR selfexpand*) AND stent*)) 3

E2 CEA Registry

Memokath in Methods 0

Memocath in Methods 0

Memokath in Ratios 0

Memocath in Ratios 0

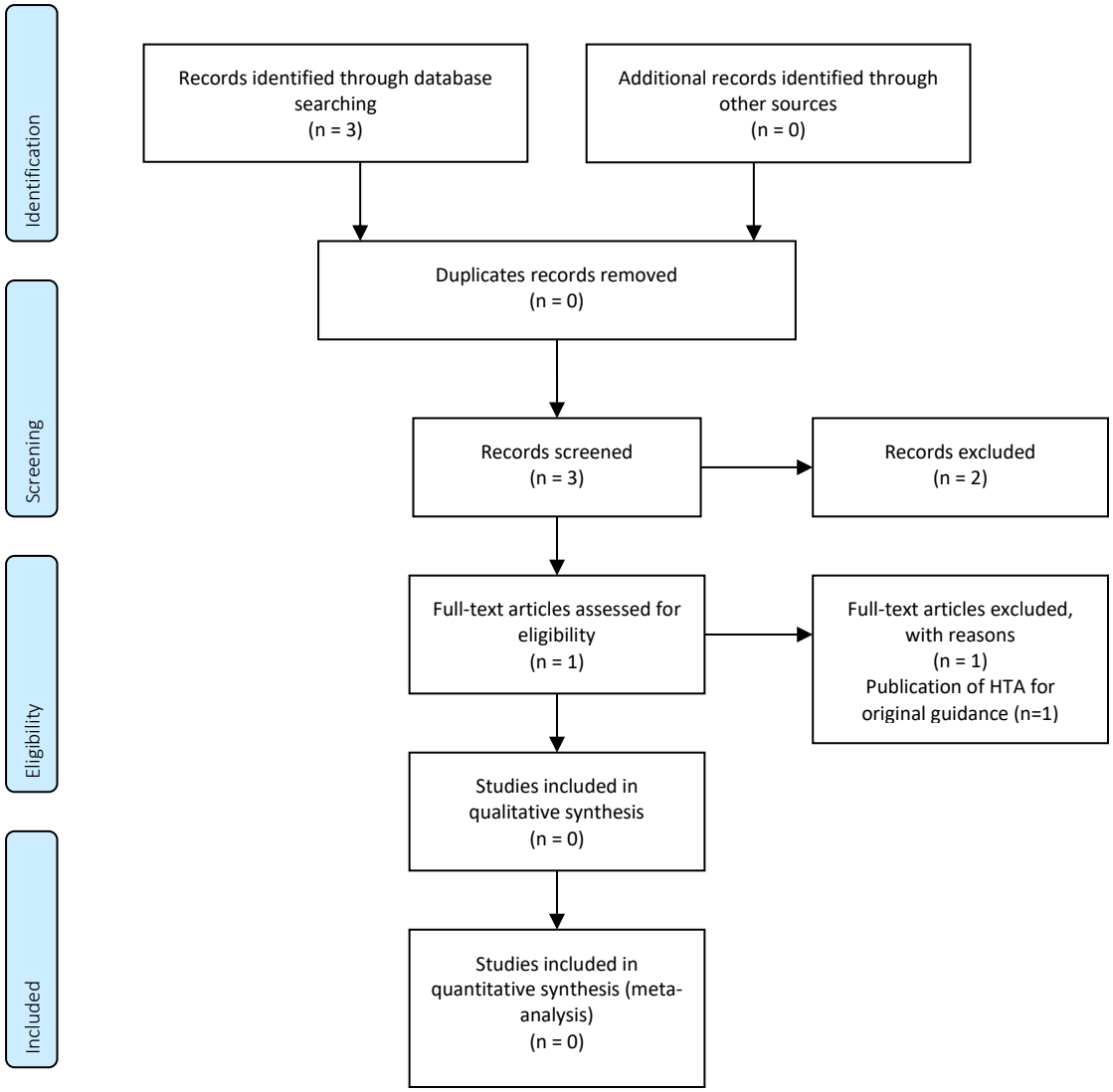
Memokath in Utility Weights 0

Memocath in Utility Weights 0

Critique of company strategy.

Not applicable.

PRISMA diagram.


Identification
Screening
Eligibility
Included
Records identified through database searching (n = 3)
Additional records identified through other sources (n = 0)
Duplicates records removed (n = 0)
Records screened (n = 3)
Records excluded (n = 2)
Full-text articles assessed for eligibility (n = 1)
Full-text articles excluded, with reasons (n = 1) Publication of HTA for original guidance (n=1)
Studies included in qualitative synthesis (n = 0)
Studies included in quantitative synthesis (meta-analysis) (n = 0)

Appendix D – Full results of scenario analysis

Scenario analysis - Memokath-051 compared to double-J Stents (replacement in the first 2 years with 0% thereafter)

	Original model results			EAC updated model results		
	Memokath-051	**double-J stents**	**Cost saving per patient**	**Memokath-051**	**double-J stents**	**Cost saving per patient**
Total insertion cost	£3,010	£786	£2,224	£3,217	£929	£2,288
Follow-up cost	£2,346	£0	£2,346	£2,576	£0	£2,576
Unplanned replacement cost	£1,027	£0	£1,027	£1,424	£0	£1,424
Planned replacement cost	£0	£8,692	-£8,692	£0	£10,326	-£10,326
Adverse event cost	£9	£9	£0	£9	£9	£0
Total	£6,391	£9,487	-£3,095	£7,226	£11,264	-£4,038

Scenario analysis - Memokath-051 compared to double-J Stents (reduced replacement after 2 years (risk halved))

	Original model results			EAC updated model results		
	Memokath-051	**double-J stents**	**Cost saving per patient**	**Memokath-051**	**double-J stents**	**Cost saving per patient**
Total insertion cost	£3,010	£786	£2,224	£3,217	£929	£2,288
Follow-up cost	£2,346	£0	£2,346	£2,576	£0	£2,576
Unplanned replacement cost	£1,770	£0	£1,770	£2,457	£0	£2,457
Planned replacement cost	£0	£8,692	-£8,692	£0	£10,326	-£10,326
Adverse event cost	£9	£9	£0	£9	£9	£0
Total	£7,134	£9,487	-£2,352	£8,259	£11,264	-£3,005

Scenario analysis - Memokath-051 compared to double-J Stents (constant unplanned replacements over a 2 year time horizon)

	Original model results	EAC updated model results

	Memokath-051	double-J stents	Cost saving per patient	Memokath-051	double-J stents	Cost saving per patient
Total insertion cost	£3,010	£786	£2,224	£3,217	£929	£2,288
Follow-up cost	£987	£0	£987	£1,084	£0	£1,084
Unplanned replacement cost	£1,027	£0	£1,027	£1,424	£0	£1,424
Planned replacement cost	£0	£3,048	-£3,048	£0	£3,621	-£3,621
Adverse event cost	£4	£4	£0	£4	£4	£0
Total	£5,027	£3,837	£1,190	£5,729	£4,554	£1,175

Scenario analysis - Memokath-051 compared to Uventa (replacement in the first 2 years with 0% thereafter)

	Original model results			EAC updated model results		
	Memokath-051	Uventa	Cost saving	Memokath-051	Uventa	Cost saving per patient

			per patient			
Total insertion cost	£3,010	£2,736	£274	£3,217	£3,235	-£18
Follow-up cost	£2,346	£2,346	£0	£2,576	£2,576	£0
Unplanned replacement cost	£3,150	£342	£2,807	£2,779	£3,950	-£1,171
Planned replacement cost	£0	£8,345	-£8,345	£0	£8,474	-£8,474
Adverse event cost	£9	£9	£0	£9	£9	£0
Total	£8,514	£13,778	-£5,264	£8,581	£18,244	-£9,664

Scenario analysis - Memokath-051 compared to Uventa (reduced replacement after 2 years (risk halved))

	Original model results			EAC updated model results		
	Memokath-051	**Uventa**	**Cost saving**	**Memokath-051**	**Uventa**	**Cost saving per patient**

			per patient			
Total insertion cost	£3,010	£2,736	£274	£3,217	£3,235	-£18
Follow-up cost	£2,346	£2,346	£0	£2,576	£2,576	£0
Unplanned replacement cost	£5,458	£589	£4,869	£4,808	£6,852	-£2,044
Planned replacement cost	£0	£8,187	-£8,187	£0	£7,933	-£7,933
Adverse event cost	£9	£9	£0	£9	£9	£0
Total	£10,823	£13,867	-£3,044	£10,610	£20,605	-£9995

Scenario analysis - Memokath-051 compared to Uventa (constant unplanned replacements over a 2 year time horizon)

	Original model results			**EAC updated model results**		
	Memokath-051	**Uventa**	**Cost saving**	**Memokath-051**	**Uventa**	**Cost saving per patient**

			per patient			
Total insertion cost	£3,010	£2,736	£274	£3,217	£3,235	-£18
Follow-up cost	£987	£987	£0	£1,084	£1,084	£0
Unplanned replacement cost	£3,150	£342	£2,807	£2,779	£3,950	-£1,171
Planned replacement cost	£0	£2,802	-£2,802	£0	£2,036	-£2,036
Adverse event cost	£4	£4	£0	£4	£4	£0
Total	£7,150	£6,872	£278	£7,083	£10,308	-£3,225

Scenario analysis - Memokath-051 compared to Allium (replacement in the first 2 years with 0% thereafter)

	Original model results			**EAC updated model results**		
	Memokath-051	**Allium**	**Cost saving per patient**	**Memokath-051**	**Allium**	**Cost saving per patient**
Total insertion cost	£3,010	£2,936	£74	£3,217	£3,135	£82
Follow-up cost	£2,346	£2,346	£0	£2,576	£2,576	£0
Unplanned replacement cost	£1,027	£364	£663	£1,424	£4,246	-£2,822
Planned replacement cost	£0	£3,003	-£3,003	£0	£3,039	-£3,039

Adverse event cost	£9	£9	£0	£9	£9	£0
Total	£6,391	£8,658	-£2,266	£7,226	£13,006	-£5,780

Scenario analysis - Memokath-051 compared to Allium (reduced replacement after 2 years (risk halved))

	Original model results			**EAC updated model results**		
	Memokath-051	**Allium**	**Cost saving per patient**	**Memokath-051**	**Allium**	**Cost saving per patient**
Total insertion cost	£3,010	£2,936	£74	£3,217	£3,135	£82
Follow-up cost	£2,346	£2,346	£0	£2,576	£2,576	£0
Unplanned replacement cost	£1,770	£627	£1,143	£2,457	£7,374	-£4,917
Planned replacement cost	£0	£2,918	-£2,918	£0	£2,769	-£2,769
Adverse event cost	£9	£9	£0	£9	£9	£0
Total	£7,134	£8,835	-£1,701	£8,259	£15,863	-£7,604

Scenario analysis - Memokath-051 compared to Allium (constant unplanned replacements over a 2 year time horizon)

	Original model results			EAC updated model results		
	Memokath-051	**Allium**	**Cost saving per patient**	**Memokath-051**	**Allium**	**Cost saving per patient**
Total insertion cost	£3,010	£2,936	£74	£3,217	£3,135	£82
Follow-up cost	£987	£987	£0	£1,084	£1,084	£0
Unplanned replacement cost	£1,027	£364	£663	£1,424	£4,246	-£2,822
Planned replacement cost	£0	£0	£0	£0	£0	£0
Adverse event cost	£4	£4	£0	£4	£4	£0
Total	£5,027	£4,291	£736	£5,729	£8,469	-£2,740

Scenario analysis - Memokath-051 compared to Resonance (replacement in the first 2 years with 0% thereafter)

	Original model results			EAC updated model results		
	Memokath-051	**Resonance**	**Cost saving per patient**	**Memokath-051**	**Resonance**	**Cost saving per patient**
Total insertion cost	£3,010	£2,148	£862	£3,217	£2,335	£882
Follow-up cost	£2,346	£1,173	£1,173	£2,576	£1,288	£1,288

Unplanned replacement cost	£1,027	£788	£239	£1,424	£1,101	£323
Planned replacement cost	£0	£9,303	-£9,303	£0	£10,217	-£10,217
Adverse event cost	£9	£9	£0	£9	£9	£0
Total	£6,391	£13,421	-£7,029	£7,226	£14,950	-£7,724

Scenario analysis - Memokath-051 compared to Resonance (reduced replacement after 2 years (risk halved))

	Original model results			**EAC updated model results**		
	Memokath-051	**Resonance**	**Cost saving per patient**	**Memokath-051**	**Resonance**	**Cost saving per patient**
Total insertion cost	£3,010	£2,148	£862	£3,217	£2,335	£882
Follow-up cost	£2,346	£1,173	£1,173	£2,576	£1,288	£1,288
Unplanned replacement cost	£1,770	£1,358	£412	£2,457	£1,900	£557
Planned replacement cost	£0	£9,233	-£9,233	£0	£10,124	-£10,124
Adverse event cost	£9	£9	£0	£9	£9	£0
Total	£7,134	£13,921	-£6,787	£8,259	£15,656	-£7,397

Scenario analysis - Memokath-051 compared to Resonance (constant unplanned replacements over a 2 year time horizon)

	Original model results			EAC updated model results		
	Memokath-051	**Resonance**	**Cost saving per patient**	**Memokath-051**	**Resonance**	**Cost saving per patient**
Total insertion cost	£3,010	£2,148	£862	£3,217	£2,335	£882
Follow-up cost	£987	£494	£494	£1,084	£542	£542
Unplanned replacement cost	£1,027	£788	£239	£1,424	£1,101	£323
Planned replacement cost	£0	£2,412	-£2,412	£0	£2,640	-£2,640
Adverse event cost	£4	£4	£0	£4	£4	£0
Total	£5,027	£5,846	-£818	£5,729	£6,622	-£893

Scenario analysis - Memokath-051 compared to Reconstructive surgery (replacement in the first 2 years with 0% thereafter)

	Original model results			EAC updated model results		
	Memokath-051	**Surgery**	**Cost saving per patient**	**Memokath-051**	**Surgery**	**Cost saving per patient**
Total insertion cost	£3,010	£7,414	-£4,404	£3,217	£7,967	-£4,750
Follow-up cost	£2,346	£0	£2,346	£2,576	£0	£2,576
Unplanned replacement cost	£1,027	£0	£1,027	£1,424	£0	£1,424
Planned replacement cost	£0	£0	£0	£0	£0	£0
Adverse event cost	£26	£4	£22	£27	£4	£23
Total	£6,408	£7,417	-£1,009	£7,244	£7,970	-£726

Scenario analysis - Memokath-051 compared to Reconstructive surgery (reduced replacement after 2 years (risk halved))

	Original model results			EAC updated model results		
	Memokath-051	**Surgery**	**Cost saving per patient**	**Memokath-051**	**Surgery**	**Cost saving per patient**
Total insertion cost	£3,010	£7,414	-£4,404	£3,217	£7,967	-£4,750
Follow-up cost	£2,346	£0	£2,346	£2,576	£0	£2,576
Unplanned replacement cost	£1,770	£0	£1,770	£2,457	£0	£2,457
Planned replacement cost	£0	£0	£0	£0	£0	£0
Adverse event cost	£26	£4	£22	£27	£4	£23
Total	£7,151	£7,417	-£266	£8,276	£7,970	£306

Scenario analysis - Memokath-051 compared to Reconstructive surgery (constant unplanned replacements over a 2 year time horizon)

	Original model results			EAC updated model results		
	Memokath-051	**Surgery**	**Cost saving per patient**	**Memokath-051**	**Surgery**	**Cost saving per patient**
Total insertion cost	£3,010	£7,414	-£4,404	£3,217	£7,967	-£4,750
Follow-up cost	£987	£0	£987	£1,084	£0	£1,084
Unplanned replacement cost	£1,027	£0	£1,027	£1,424	£0	£1,424
Planned replacement cost	£0	£0	£0	£0	£0	£0
Adverse event cost	£11	£1	£9	£11	£2	£10
Total	£5,034	£7,415	-£2,381	£5,736	£7,968	-£2,232

Addendum to the EAC report

Scenario 1: Base case analysis excluding VAT from stent prices

The EAC assessment report base case was based on NHS Supply Chain (NHSSC) stent prices which include a VAT rate of 20%. The base case analyses have been re-run in a scenario analysis using the prices excluding VAT as presented in table 1. The base case reports for a time horizon of 5 years with constant replacement, being the most conservative assumption scenario. The other scenarios; replacement in the first 2 years with 0% thereafter, reduced replacement after 2 years (risk halved) and constant unplanned replacements over a 2-year time horizon are presented in the Appendix.

Table 1: NHS Supply Chain prices for comparator used in base case and excluding VAT

Comparator name	NHSSC NPC code(s)	Supplier	Brand (as listed on NHSSC)	NHSSC price used in the model (including VAT)	**Price excluding VAT**
Double-J stent	FAL18848 - FAL18863	COLOPLAST LIMITED	Biosoft Duo	[redacted]	[redacted]
Resonance	FAL5763	COOK (UK) LTD	Resonance (Cook UK Medical)	[redacted]	[redacted]
Uventa	FUQ2229	AQUILANT INTERVENTIONAL	UVENTA (Taewoong)	[redacted]	[redacted]

Table 2.1: Base case costing savings of Memokath-051 compared to Double-J Stents

	Original model results			**EAC updated model results**		
	Memokath-051	**Double-J stents**	**Cost saving per patient**	**Memokath-051**	**Double-J stents**	**Cost saving per patient**
Total insertion cost	£3,010	£786	£2,224	£3,217	£922	£2,295

Follow-up cost	£2,346	£0	£2,346	£2,576	£0	£2,576
Unplanned replacement cost	£2,503	£0	£2,503	£3,472	£0	£3,472
Planned replacement cost	£0	£8,692	-£8,692	£0	£10,269	-£10,269
Adverse event cost	£9	£9	£0	£9	£9	£0
Total	£7,868	£9,487	-£1,619	£9,274	£11,200	-£1,926
Break even months	30			30		

Table 2.2: Base case costing savings of Memokath-051 compared to UVENTA

	Original model results			**EAC updated model results**		
	Memokath-051	**Uventa**	**Cost saving per patient**	**Memokath-051**	**Uventa**	**Cost saving per patient**
Total insertion cost	£3,010	£2,736	£274	£3,217	£2,935	£282
Follow-up cost	£2,346	£2,346	£0	£2,576	£2,576	£0
Unplanned replacement cost	£7,672	£835	£6,837	£6,770	£8,847	-£2,077
Planned replacement cost	£0	£8,039	-£8,039	£0	£7,018	-£7,018
Adverse event cost	£9	£9	£0	£9	£9	£0
Total	£13,037	£13,965	-£928	£12,572	£21,384	-£8,813
Break even months	18			0		

Table 2.3: Base case costing savings of Memokath-051 compared to Resonance

	Original model results			**EAC updated model results**		
	Memokath-051	**Resonance**	**Cost saving**	**Memokath-051**	**Resonance**	**Cost saving per patient**

			per patient			
Total insertion cost	£3,010	£2,148	£862	£3,217	£2,185	£1,032
Follow-up cost	£2,346	£1,173	£1,173	£2,576	£1,288	£1,288
Unplanned replacement cost	£2,503	£1,921	£582	£3,472	£2,542	£929
Planned replacement cost	£0	£9,169	-£9,169	£0	£9,509	-£9,509
Adverse event cost	£9	£9	£0	£9	£9	£0
Total	£7,868	£14,420	-£6,552	£9,274	£15,533	-£6,260
Break even months	12			12		

Scenario 2: Double J-Stents-Lowest and highest per unit price

There are a number of brands of Double-J stents available with varying NHS Supply Chain prices associated with them. Scenario analyses have been run to assess the impact on base case results if the lowest or highest per unit price (excluding VAT) is used (table 3). The unit of issue of products on NHS Supply Chain also varies, with some products available as individual items and others in multipack boxes (table 4), and these prices have also been re-run.

Table 3. NHS Supply Chain per unit prices for Double-J stent items sold individually

	NHSSC NPC code	Supplier	Brand (as listed on NHSSC)	Price on NHSSC (including VAT)	**Price excluding VAT**
Lowest per unit price	FUQ3613	BIOSPECTRUM LTD	Standard Double-J (Marflow)	[redacted]	[redacted]
Highest per unit price	FRM13152	COOK (UK) LTD	Black Silicone Filiform Double Pigtail Ureteral Stent Set (Cook)	[redacted]	[redacted]

Table 3.1: Base case costing savings of Memokath-051 compared to Double-J Stents (lowest unit price-Individual)

	Original model results			EAC updated model results		
	Memokath-051	**Double-J stents**	**Cost saving per patient**	**Memokath-051**	**Double-J stents**	**Cost saving per patient**
Total insertion cost	£3,010	£786	£2,224	£3,217	£896	£2,321
Follow-up cost	£2,346	£0	£2,346	£2,576	£0	£2,576
Unplanned replacement cost	£2,503	£0	£2,503	£3,472	£0	£3,472
Planned replacement cost	£0	£8,692	-£8,692	£0	£10,057	-£10,057
Adverse event cost	£9	£9	£0	£9	£9	£0
Total	£7,868	£9,487	-£1,619	£9,274	£10,962	-£1,688
Break even months	30			30		

Table 3.2: Base case costing savings of Memokath-051 compared to Double-J Stents (highest unit price-Individual)

	Original model results			EAC updated model results		
	Memokath-051	**Double-J stents**	**Cost saving per patient**	**Memokath-051**	**Double-J stents**	**Cost saving per patient**
Total insertion cost	£3,010	£786	£2,224	£3,217	£1,092	£2,125
Follow-up cost	£2,346	£0	£2,346	£2,576	£0	£2,576
Unplanned replacement cost	£2,503	£0	£2,503	£3,472	£0	£3,472
Planned replacement cost	£0	£8,692	-£8,692	£0	£11,679	-£11,679
Adverse event cost	£9	£9	£0	£9	£9	£0

Total	£7,868	£9,487	-£1,619	£9,274	£12,780	-£3,506
Break even months	30			30		

Table 4 NHS Supply Chain per unit prices for Double-J items sold in multipacks

	NHSSC NPC code	Supplier (as listed on NHSSC)	Brand (as listed on NHSSC)	Price on NHSSC (including VAT)	**Price excluding VAT**
Lowest per unit price	FRM11705	COLOPLAST LIMITED	Imajin Hydro	[redacted]	[redacted]
Highest per unit price	FUQ2185	GBUK HEALTHCARE	Urotech Magnetic Black Star	[redacted]	[redacted]

Table 4.1: Base case costing savings of Memokath-051 compared to Double-J Stents (lowest unit price-Multipack)

	Original model results			**EAC updated model results**		
	Memokath-051	**Double-J stents**	**Cost saving per patient**	**Memokath-051**	**Double-J stents**	**Cost saving per patient**
Total insertion cost	£3,010	£786	£2,224	£3,217	£897	£2,320
Follow-up cost	£2,346	£0	£2,346	£2,576	£0	£2,576
Unplanned replacement cost	£2,503	£0	£2,503	£3,472	£0	£3,472
Planned replacement cost	£0	£8,692	-£8,692	£0	£10,064	-£10,064
Adverse event cost	£9	£9	£0	£9	£9	£0
Total	£7,868	£9,487	-£1,619	£9,274	£10,970	-£1,697
Break even months	30			30		

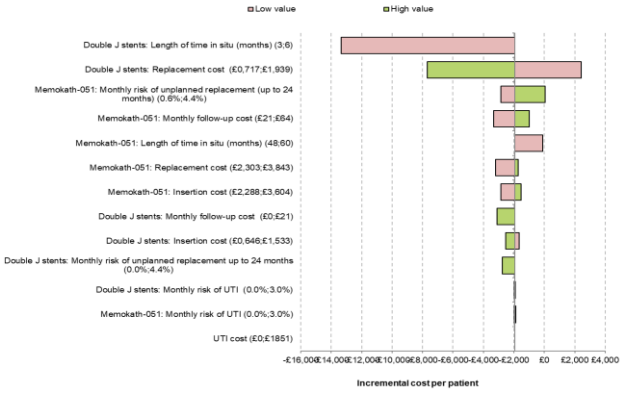
Table 4.2: Base case costing savings of Memokath-051 compared to Double-J Stents (highest unit price-Multipack)

	Original model results			EAC updated model results		
	Memokath-051	**Double-J stents**	**Cost saving per patient**	**Memokath-051**	**Double-J stents**	**Cost saving per patient**
Total insertion cost	£3,010	£786	£2,224	£3,217	£1,021	£2,196
Follow-up cost	£2,346	£0	£2,346	£2,576	£0	£2,576
Unplanned replacement cost	£2,503	£0	£2,503	£3,472	£0	£3,472
Planned replacement cost	£0	£8,692	-£8,692	£0	£11,092	-£11,092
Adverse event cost	£9	£9	£0	£9	£9	£0
Total	£7,868	£9,487	-£1,619	£9,274	£12,122	-£2,848
Break even months	30			30		

Sensitivity analysis results

Memokath-051 vs Double-J stent

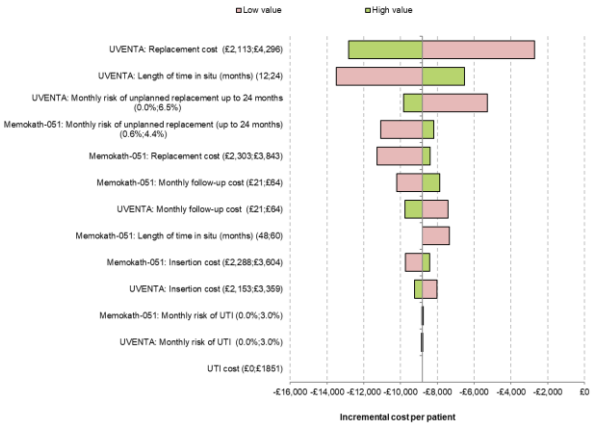
Figure 1.1: Tornado diagram based on EAC Sensitivity analysis (vs Double-J stent) with updated prices excluding VAT



The updated tornado diagram with prices excluding VAT showed similar results as with prices including VAT. Length of time in situ for Double-J stents, replacement cost for double-J stents, Memokath-051 monthly risk of unplanned replacement and Memokath-051 monthly follow-up cost were the main cost drivers. Memokath-051 was cost saving with all the scenarios, except when the replacement cost of Double-J stents dropped to the lower value (£717). The threshold at which the replacement cost of Double-J stent is cost neutral is £1009. The threshold value of monthly risk of unplanned replacement of Memokath-051 at which the technology is no longer cost saving compared to Double-J stent is 2.81%.

Memokath-051 vs UVENTA

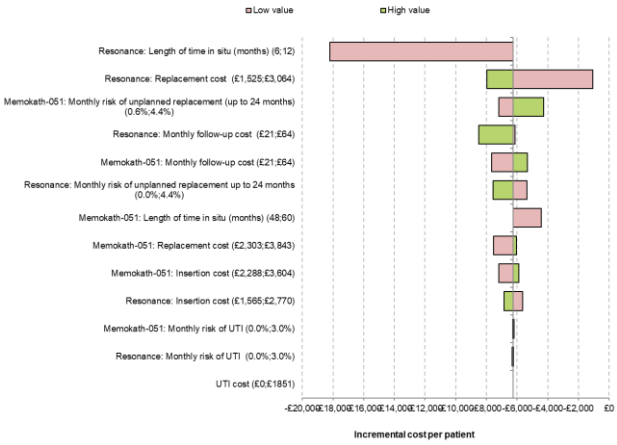
Figure 1.2: Tornado diagram based on EAC Sensitivity analysis (vs UVENTA) with updated prices excluding VAT



With prices excluding VAT, Memokath-051 was cost saving in all scenarios, and the parameters that had the highest impact on the cost savings were replacement cost for UVENTA, length of time in situ-UVENTA, UVENTA monthly risk of unplanned replacement, Memokath-051 monthly risk of unplanned replacement and replacement costs. This is similar to the results with prices including VAT

Memokath-051 vs Resonance

Figure 1.3: Tornado diagram based on EAC Sensitivity analysis (vs Resonance) with updated prices excluding VAT



Similar to the model with prices including VAT, the updated prices excluding VAT model showed that Memokath-051 was cost saving in all scenarios, and the parameters that had the highest impact on the cost savings were Resonance – length of time in situ, replacement costs, monthly risk of unplanned replacement and Memokath-051 monthly risk of unplanned replacement.

APPENDIX

Scenario analysis - Memokath-051 compared to double-J Stents (replacement in the first 2 years with 0% thereafter)

	Original model results			EAC updated model results		
	Memokath-051	**double-J stents**	**Cost saving per patient**	**Memokath-051**	**double-J stents**	**Cost saving per patient**
Total insertion cost	£3,010	£786	£2,224	£3,217	£922	£2,295
Follow-up cost	£2,346	£0	£2,346	£2,576	£0	£2,576
Unplanned replacement cost	£1,027	£0	£1,027	£1,424	£0	£1,424
Planned replacement cost	£0	£8,692	-£8,692	£0	£10,269	-£10,269
Adverse event cost	£9	£9	£0	£9	£9	£0
Total	£6,391	£9,487	-£3,095	£7,226	£11,200	-£3,974

Scenario analysis - Memokath-051 compared to double-J Stents (reduced replacement after 2 years (risk halved))

	Original model results			EAC updated model results		
	Memokath-051	**double-J stents**	**Cost saving per patient**	**Memokath-051**	**double-J stents**	**Cost saving per patient**
Total insertion cost	£3,010	£786	£2,224	£3,217	£922	£2,295
Follow-up cost	£2,346	£0	£2,346	£2,576	£0	£2,576
Unplanned replacement cost	£1,770	£0	£1,770	£2,457	£0	£2,457
Planned replacement cost	£0	£8,692	-£8,692	£0	£10,269	-£10,269
Adverse event cost	£9	£9	£0	£9	£9	£0
Total	£7,134	£9,487	-£2,352	£8,259	£11,200	-£2,941

Scenario analysis - Memokath-051 compared to double-J Stents (constant unplanned replacements over a 2 year time horizon)

	Original model results			EAC updated model results		
	Memokath-051	**double-J stents**	**Cost saving per patient**	**Memokath-051**	**double-J stents**	**Cost saving per patient**
Total insertion cost	£3,010	£786	£2,224	£3,217	£922	£2,295
Follow-up cost	£987	£0	£987	£1,084	£0	£1,084
Unplanned replacement cost	£1,027	£0	£1,027	£1,424	£0	£1,424
Planned replacement cost	£0	£3,048	-£3,048	£0	£3,601	-£3,601
Adverse event cost	£4	£4	£0	£4	£4	£0
Total	£5,027	£3,837	£1,190	£5,729	£4,527	£1,202

Scenario analysis - Memokath-051 compared to Uventa (replacement in the first 2 years with 0% thereafter)

	Original model results			EAC updated model results		
	Memokath-051	**Uventa**	**Cost saving per patient**	**Memokath-051**	**Uventa**	**Cost saving per patient**
Total insertion cost	£3,010	£2,736	£274	£3,217	£2,935	£282
Follow-up cost	£2,346	£2,346	£0	£2,576	£2,576	£0
Unplanned replacement cost	£3,150	£342	£2,807	£2,779	£3,632	-£854
Planned replacement cost	£0	£8,345	-£8,345	£0	£7,793	-£7,793
Adverse event cost	£9	£9	£0	£9	£9	£0
Total	£8,514	£13,778	-£5,264	£8,581	£16,945	-£8,365

Scenario analysis - Memokath-051 compared to Uventa (reduced replacement after 2 years (risk halved))

	Original model results			EAC updated model results		
	Memokath-051	**Uventa**	**Cost saving per patient**	**Memokath-051**	**Uventa**	**Cost saving per patient**
Total insertion cost	£3,010	£2,736	£274	£3,217	£2,935	£282
Follow-up cost	£2,346	£2,346	£0	£2,576	£2,576	£0
Unplanned replacement cost	£5,458	£589	£4,869	£4,808	£6,301	-£1,493
Planned replacement cost	£0	£8,187	-£8,187	£0	£7,295	-£7,295
Adverse event cost	£9	£9	£0	£9	£9	£0
Total	£10,823	£13,867	-£3,044	£10,610	£19,116	-£8,506

Scenario analysis - Memokath-051 compared to Uventa (constant unplanned replacements over a 2 year time horizon)

	Original model results			EAC updated model results		
	Memokath-051	**Uventa**	**Cost saving per patient**	**Memokath-051**	**Uventa**	**Cost saving per patient**
Total insertion cost	£3,010	£2,736	£274	£3,217	£2,935	£282
Follow-up cost	£987	£987	£0	£1,084	£1,084	£0
Unplanned replacement cost	£3,150	£342	£2,807	£2,779	£3,632	-£854
Planned replacement cost	£0	£2,802	-£2,802	£0	£1,872	-£1,872
Adverse event cost	£4	£4	£0	£4	£4	£0
Total	£7,150	£6,872	£278	£7,083	£9,527	-£2,444

Scenario analysis - Memokath-051 compared to Resonance (replacement in the first 2 years with 0% thereafter)

	Original model results			EAC updated model results		
	Memokath-051	**Resonance**	**Cost saving per patient**	**Memokath-051**	**Resonance**	**Cost saving per patient**
Total insertion cost	£3,010	£2,148	£862	£3,217	£2,185	£1,032
Follow-up cost	£2,346	£1,173	£1,173	£2,576	£1,288	£1,288
Unplanned replacement cost	£1,027	£788	£239	£1,424	£1,043	£381
Planned replacement cost	£0	£9,303	-£9,303	£0	£9,675	-£9,675
Adverse event cost	£9	£9	£0	£9	£9	£0
Total	£6,391	£13,421	-£7,029	£7,226	£14,200	-£6,974

Scenario analysis - Memokath-051 compared to Resonance (reduced replacement after 2 years (risk halved))

	Original model results			EAC updated model results		
	Memokath-051	**Resonance**	**Cost saving per patient**	**Memokath-051**	**Resonance**	**Cost saving per patient**
Total insertion cost	£3,010	£2,148	£862	£3,217	£2,185	£1,032
Follow-up cost	£2,346	£1,173	£1,173	£2,576	£1,288	£1,288
Unplanned replacement cost	£1,770	£1,358	£412	£2,457	£1,799	£658
Planned replacement cost	£0	£9,233	-£9,233	£0	£9,588	-£9,588
Adverse event cost	£9	£9	£0	£9	£9	£0
Total	£7,134	£13,921	-£6,787	£8,259	£14,869	-£6,610

Scenario analysis - Memokath-051 compared to Resonance (constant unplanned replacements over a 2 year time horizon)

	Original model results			EAC updated model results		
	Memokath-051	**Resonance**	**Cost saving per patient**	**Memokath-051**	**Resonance**	**Cost saving per patient**
Total insertion cost	£3,010	£2,148	£862	£3,217	£2,185	£1032
Follow-up cost	£987	£494	£494	£1,084	£542	£542
Unplanned replacement cost	£1,027	£788	£239	£1,424	£1,043	£381
Planned replacement cost	£0	£2,412	-£2,412	£0	£2,500	-£2,500
Adverse event cost	£4	£4	£0	£4	£4	£0
Total	£5,027	£5,846	-£818	£5,729	£6,273	-£545

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Medical technology guidance

Final SCOPE

GID-MT569 Memokath 051 Ureter stent for ureteric obstruction

1 Technology

1.1 Description of the technology

Memokath 051 is a thermo-expandable, nickel-titanium alloy ureteric stent. It is intended as an alternative to conventional ureteric stents for people with benign or malignant ureteric obstruction. Stents are used to allow the free flow of urine from the kidneys to the bladder. 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 can be used to treat obstructions elsewhere in the urinary tract, but this is outside the scope of this evaluation.

1.2 Relevant diseases and conditions

Memokath 051 is intended for use in ureteric obstruction, specifically as a result of malignant or benign strictures.

The number of people who require a long-term ureteric stent as a result of malignant or benign ureteric strictures is hard to estimate, particularly because the most recently available figures are lower than in previous years, possibly due to system restraints during the COVID-19 pandemic. In the NHS in England, between 2020 and 2021, there were 3,272 retrograde insertions and 1,210 retrograde removals of ureteric stents (7,674 and 2,733 respectively

between 2014 and 2015; NHS Digital, Hospital Admitted Patient Care Activity: Procedures and interventions), 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 reliable estimates currently available. There were 51 percutaneous insertions and 23 replacements of ureteric metallic stents between 2020 and 2021 (80 and 22 respectively between 2014 and 2015; NHS Digital, Hospital Admitted Patient Care Activity: Procedures and interventions).

1.3 Current management

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 all people with upper urinary tract obstruction should be referred to a urologist. If appropriate, nephrostomy or stenting should be done as soon as possible (within 12 hours of diagnosis).

NICE has produced specific guidance for malignant 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.

1.4 Regulatory status

The Memokath 051 received a CE mark as a class IIb device in October 1997 for malignant or benign ureteric strictures. Its CE mark was updated in May 2021.

1.5 Claimed benefits

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 051 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.

2 Decision problem

Population	Adults with ureteric obstruction as a result of malignant or benign strictures.
Intervention	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, rates of stent migration, encrustation and infection, 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 parameters.
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	Memokath 051 is contraindicated in children. 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

related to equality	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	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
Any other special considerations	Not applicable	

3 Related NICE guidance

Published

- Bladder cancer: diagnosis and management (2015) NICE guideline NG2.
- Prostate cancer: diagnosis and management (2019, updated 2021) NICE guideline NG131
- Acute kidney injury: prevention, detection and management (2019) NICE guideline NG148
- Improving outcomes in urological cancers (2002) NICE cancer service guideline CSG2

Under development

None.

4 External organisations

4.1 Professional organisations

The following organisations were asked to comment on the draft scope:

- British Uro-oncology Group (BUG)

- British Association of Day Surgery
- British Association of Urological Surgeons (BAUS)
- British Association of Urological Nurses (BAUN)
- British Association of Paediatric Urology
- British Society of Interventional Radiologists (BSIR)
- UK Kidney Association (previously named The Renal Association)
- Royal College of Physicians
- Royal College of Physicians, Edinburgh
- Royal College of Radiologists
- Royal College of Surgeons
- Royal College of Nursing

4.2 Patient organisations

NICE's Public Involvement Programme contacted the following organisations for patient commentary and asked them to comment on the draft scope:

- Action on Bladder Cancer
- Bladder and Bowel Foundation
- British Kidney Patient Association
- 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
- Prostate Cancer UK (formerly prostate cancer charity)

- Rarer Cancers Foundation
- Sue Ryder
- Target Ovarian Cancer

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Medical technology guidance

Guidance update assessment report overview

Memokath 051 ureter stent for ureteric obstruction

An update of MTG35

This assessment report update overview has been prepared by the Medical Technologies Evaluation Programme team to highlight the significant findings of the External Assessment Centre (EAC) report. It summarises additional clinical and economic evidence along with any other relevant changes since the guidance was developed. It should be read along with the original assessment report and the assessment report update. The assessment report update overview forms part of the information received by the Medical Technologies Advisory Committee when it updates 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 overview also contains:

- Appendix A: Sources of evidence
- Appendix B: Comments from professional bodies
- Appendix C: Comments from patient organisations
- Appendix D: Company claimed benefits
- Appendix E: Decision problem from the scope

1 Current guidance

Medical technologies guidance on Memokath 051 for ureteric obstruction (MTG35) was issued in February 2018. The recommendations of the original guidance were as follows:

2.1 The case for adopting Memokath-051 for treating ureteric obstruction is partially supported by the evidence. The evidence is limited but suggests that in selected cases, Memokath-051 is effective at relieving ureteric obstruction and improving quality of life. When inserted by trained clinicians (see section 4.8) and in appropriate patients (see section 1.2), Memokath-051 is associated with equivalent success rates and a better patient experience compared with double-J stents. Using Memokath-051 may also reduce the number of stent replacements needed compared with using double-J stents.

2.2 Memokath-051 stents should be considered as an option in patients with:

- *malignant ureteric obstruction and anticipated medium- or long-term survival after adjunctive therapy*
- *benign ureteric obstruction who cannot have or do not want reconstructive surgery or*
- *ureteric obstruction of any kind who cannot have or do not want a double-J stent, or for whom repeat procedures are a particularly high risk.*

2.3 The cost consequences of adopting Memokath-051 are uncertain. However, when used in appropriate patients and by clinicians trained in its use, it may be cost neutral or cost saving compared with standard treatment. Potential cost savings mainly come from fewer repeat procedures with Memokath-051.

2 Changes since publication of guidance

2.1 The technology

Memokath 051 is a thermo-expandable, nickel-titanium alloy ureteric stent. It is intended as an alternative to conventional ureteric stents for people with benign or malignant 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. The device is CE marked as a Class IIb device.

The technology is still available in the UK. The Company has confirmed that there have been no changes to the technology since MTG35 was issued. There are no new indications or applications not covered by the original guidance and no changes to the pricing of Memokath 051 stents.

2.2 Current management

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 all people with upper urinary tract obstruction should be referred to a urologist. If appropriate, nephrostomy or stenting should be done as soon as possible (within 12 hours of diagnosis).

NICE has produced specific guidance for treating malignant 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.

Current care pathway: There have been no substantial changes to the clinical pathway since MTG35 was issued. NICE's guideline on bladder cancer (NG2) has not been updated. NICE guidelines on acute kidney injury (NG148) and prostate cancer (NG131) were both updated in 2019. None of the guideline updates impact the original recommendations for Memokath 051.

3 Company claimed benefits and the decision problem

The company claimed benefits and the decision problem can be found in Appendix D and E of this overview. The company and EAC did not propose any variations to the decision problem.

4 The evidence

4.1 Summary of evidence of clinical benefit

Original guidance (2018): 16 studies were used as the clinical evidence base in the original guidance. Six were comparative observational studies (2 full text publications, 3 conference abstracts and 1 clinical trial record and abstract). The other 10 were single-arm observational studies published as full texts. At original guidance, the EAC concluded that the evidence came mainly from small, poorly reported observational studies. The Committee however concluded that there was sufficient evidence to partially support the claimed patient benefits of Memokath-051 compared with double-J stents but that the claimed patient benefits compared with other metallic stents were not fully substantiated by the limited evidence available. The Committee concluded that when inserted by trained clinicians and in appropriate patients, Memokath-051 is more effective and most likely to be cost neutral or cost saving compared with double-J stents.

Guidance update: The company submitted 6 studies at guidance review (2022). No further studies were submitted by the company at guidance

update. The EAC agreed with the inclusion of one of the studies (Forster et al. 2021) but excluded the remaining 5. Details of the excluded studies and the rationale for exclusion are presented in table 2 of the EAC's assessment report update and table 1 of this document.

The EAC reran the searches from the original guidance and identified a further 6 studies as being relevant to the scope. In total, the EAC included 7 studies in their evidence review for this guidance update (5 full text publications and 2 conference abstracts). They comprised of the following:

- 1 systematic review and meta-analyses (Khoo et al. 2018)
- 2 retrospective non-randomised comparative studies (Choi et al 2019 and Khoo et al. 2021)
- 4 retrospective single-arm, single-centre studies; 2 presented as full text publications (Bier et al 2017 and Forster et al 2021) and 2 conference abstracts (Elbaroni et al. 2020 and Diaz Romero et al. 2018)

Table 1. Summary of included and excluded studies

Studies included by both EAC and company (n=1)	
Publication and study design	• 1 retrospective single-arm, single-centre study (Forster et al. 2021)
Studies submitted by the company at guidance review but excluded by the EAC (n=5)	
Publication, study design and reasons for exclusion	• Summary of NICE guidance (Eaton Turner et al. 2018) – publication summarising original Memokath 051 guidance • 3 systematic reviews (Sampogna et al. 2018, Kang et al. 2020, Corrales et al. 2021) – literature reviews with no new information • Retrospective cohort (Miernik et al. 2018) – patient population deemed out of scope
Additional studies included by the EAC	
Publication and study design	• 1 systematic review and meta-analyses (Khoo et al. 2018) • 2 retrospective non-randomised comparative studies (Choi et al 2019 and Khoo et al. 2021)

	• 3 retrospective single-arm, single-centre studies; 1 presented as full text publication (Bier et al 2017) and 2 conference abstracts (Elbaroni et al. 2020 and Diaz Romero et al. 2018)
***Abbreviations**: EAC external assessment centre*	

The new primary evidence reported as full text publications was retrospective and observational in design and included a total of 337 people. The EAC stated that 2 studies presented as conference abstracts (including 118 people) reported minimal information, but noted that Elbaroni et al. (2020) has a large range of follow-up (4 months to 12 years) and results from this study beyond the 5-year study duration may be of interest once published.

Two of the full text studies were comparative (Choi et al. 2019 and Khoo et al. 2021), both of which compared Memokath 051 to other metallic ureteric stents (Allium URS, Resonance and UVENTA). Two studies were done in the UK (Forster et al. 2021 and Khoo et al. 2021). One study included people with benign ureteric obstruction only (Choi et al. 2019), while the remaining studies included people with either benign or malignant ureteric obstruction. Most of the Memokath 051 studies included in the systematic review (Khoo et al. 2018) had a mixed population of benign and malignant ureteric strictures, with one study reporting on malignant ureteric obstruction only.

The included studies were mainly focused on reporting complications. Stent migration was the most common complication associated with Memokath 051 (migration rate ranging from 14.3% to 36%), and this was higher than other metallic ureteric stents (Khoo et al. 2021). Longer-term 5-year follow-up data also reported a 72% complication rate with Memokath 051 (Forster et al. 2021). Success rate and indwelling time varied across studies. Stent failure was higher for Memokath 051 compared to Allium URS and Resonance (Khoo et al. 2021). Memokath 051 was associated with a higher success rate compared with UVENTA in people with benign ureteral strictures (Choi et al. 2019). Two studies compared indwelling times in people with benign and malignant ureteral strictures. Forster et al. (2021) reported a statistically significant higher stent indwelling time in patients with malignant ureteral strictures compared with benign, in line with findings from the original guidance, whilst Bier et al. (2017) reported the opposite. The EAC noted that Bier et al. (2017) was a study done in Germany and had a high loss to follow-up (27%). Only one study presented as a conference abstract reported on hospital stays. There was no reported data on outcomes such as quality of life, frequency of follow-up visits and pain scores. A summary of the included studies and results can be found in table 2 below. Full results and the EAC's

interpretation of the results can be found in tables 1 and 3, and section 8 of the EAC's assessment report update.

The EAC did not do a meta-analysis because the number of number studies was small and there was heterogeneity in terms of the outcome definitions and duration of follow-up across the studies.

4.2 EAC conclusions from new clinical evidence

Overall, the EAC concluded that the new evidence available is of low to moderate quality with some bias. The EAC's opinion is that the latest evidence continues to provide a basis for Memokath 051 as an option for certain people with ureteric obstructions but that clinicians should be aware of a potential increased risk of complications with Memokath 051, particularly stent migration. The EAC's full critical appraisal of the new evidence base can be found in section 5.3 and appendix A of the EAC's assessment report update.

Table 2. Summary of included studies and results

Study name, design and funding	Participants/ population	Intervention and comparator	Outcomes and results	EAC comments
Systematic reviews and meta-analyses (n=1)				
Khoo et al. (2018) Systematic literature review with meta-analysis.	Included 21 studies describing the use of metallic stents for malignant ureteral obstruction.	Intervention: Memokath 051 (n=5 studies) Comparators: Allium URS (n=1 study); Resonance (n=10 studies); UVENTA (n=6 studies)	Migration rate Resonance (8 studies): 1% (0 – 3%); I^2 = 0% UVENTA (6 studies): 3% (0 – 8%); I^2=55% Memokath 051 (5 studies): 20% (11 – 30%); I^2=23.07 Allium (1 study): 12% (2 – 9%) Obstruction rate Resonance (8 studies): 17% (5 – 34%); I^2 = 88% UVENTA (6 studies): 6% (1 – 15%); I^2 = 75.87% Memokath 051 (5 studies): 11% (2 – 23%); I^2 = 70.16% Allium (1 study): 0% (0 – 10%) Success rate (no obstruction, improved renal function and no further intervention required for duration of follow-up) Resonance (7 studies): 79% (64 – 91%); I^2=78.28% UVENTA (5 studies): 81% (48 – 100%); I^2=95.71% Memokath 051 (5 studies): 65% (44%– 84%). I^2 =82.55% Allium (1 study): 88% (73 – 95%)	Majority of included studies were small, single-arm case series without comparator; high heterogeneity for migration rate, obstruction rate and success rate.

Comparative studies (n=2)				
Choi et al. (2019) Retrospective comparative study done in South Korea. Study funded by the Ministry of Science and ICT.	36 patients with 46 ureter units (benign ureteral strictures only).	Intervention: Memokath 051 (n=21 stents) Comparator: UVENTA (n=25 stents)	Mean (SD) follow-up, mos. Memokath 051 (thermos-expandable stent): 34.4 (16.5) UVENTA (mesh stent): 41.4 (23.1); p=0.25 Primary success (maintaining patency after first stenting without additional procedures) 1st year: Memokath 051, 14 (70.4%); UVENTA, 13 (54.9%); p=0.204; 3rd year: Memokath 051, 4 (30.6%); UVENTA, 4 (16.9 %) Over the entire observation period: Memokath 051, 28.6%, UVENTA, 12.0% Overall success (maintaining patency after further salvage procedures during the observed period) 1st year: Memokath 051, 15 (75.4%); UVENTA, 18 (78.7%); p=0.586 3rd year: Memokath 051, 7 (56.5%); UVENTA, 9 (49.1%) Over the entire observation period: Memokath 051, 57.1%; UVENTA, 40.0% Complication events	Not UK based so less applicable to UK NHS setting There are some discrepancies in the p values reported in the abstract and the body of text – p values used for 1st year primary success and overall success are used for the entire observation period in the body of text. Small sample size. Long follow-up (3 yrs.)

			Memokath 051, 15; UVENTA, 31; p=0.08 Severe complications Memokath 051, 10; UVENTA, 12; p=0.96 Median (95%CI) time to 50% failure, mos. – primary Memokath 051, 30.9 (15.2-39.9). UVENTA, 15.6 (9.3-21.5); p=0.204 Median (95%CI) time to 50% failure, mos. – overall Memokath 051, 54.3 (20.6 – 54.3); UVENTA, 29.0 (21.5 – 65.8); p=0.586	
Khoo et al. (2021) Retrospective comparative, single centre study done in the UK. No funding was received.	76 patients with 129 stent insertion episodes for chronic ureteral obstruction (benign or malignant).	Intervention: Memokath 051 (n=31) Comparators: Allium URS (n=16); Resonance (n=29)	Median (IQR) stent survival per SIE (functional stent follow-up), mos. Allium: 11.4 (2.6 – 31.6) Memokath 051: 5.5 (2.1 – 12.9) Resonance: 11.7 (7.8 – 13.1) Intraoperative placement success Allium: 95.7% (22/23) Memokath 051: 100% Resonance: 100% Stent failure (ureteric obstruction requiring premature stent removal/replacement, or nephrostomy insertion) Allium: 47.8% (11/23) Memokath 051: 64.6% (31/48) Resonance: 19% (11/58)	UK based study in an NHS hospital so potential more applicable to a UK NHS setting. Medium sample size. Shorter follow-up. Comparative but retrospective.

			Creatinine levels (in first 12 mos.) Allium: 21.3% to 46.7% Memokath 051: -7.8% to 8.9% Resonance: - 9.4% to 27.3%	
Single arm studies (n=2)				
Bier et al. (2017) Retrospective single arm, single centre done in Germany. Study funding not reported.	125 patients with malignant or benign ureteral strictures who underwent implantation of Memokath 051.	Intervention: Memokath 051 No comparator	Median (range) indwelling time 355 days (7 – 2125). Benign: 455 days; Malignant: 190 days, p = 0.006 Reasons for stent removal Dislocation (n= 37, 42%) Occlusion (n=35, 40%) Prior to reconstructive surgery (n=8, 9%) Unknown reason (n=8, 9%) Infection (n=3, 3%)	Not UK based so less applicable to a UK NHS setting. No comparator, retrospective. Medium sample size. Stent removal in all 91 patients (34 patients lost to follow-up).
Forster et al. (2021) Retrospective, single centre .study done in the UK.	100 patients with 162 stents [malignant (n=59) and benign (n=41)].	Intervention: Memokath 051 No comparator	Overall complication rate 72%: stent migration (36%), failed ipsilateral upper tract drainage (27%: blockage 14%, encrustation 11%, lost renal function 2%) Benign cohort complication rate 85.4%. Most common, stent migration (53.7%)	UK based study in an NHS hospital so potentially more applicable to a UK NHS setting. Long follow-up (5 yrs.) No comparator.

No funding received.			Malignant cohort complication rate 62.7%. Most common, failed renal drainage (30.5%); stent encrustation (10.2%) Complication rate, malignant vs. benign 62.7% vs. 85.4%, p=0.04 Mean indwelling time, malignant vs. benign 14.5 mos. vs. 13.4 mos., p=0.02 Median time to first complication 12.5 mos. Stent free after Memokath 051 removal-dislodgement, benign vs. malignant 24.4% vs. 6.8%, p=0.03 Memokath 051 salvage placement following complication 43% Complication-free original Memokath 051 25% (25/100). 97 patients had follow-up data; survival plot showed median lifespan of stent: 14.5 mos. Deaths 21/100 ; 20/21 (95%) in malignant obstruction patients Mean follow-up 62 mos. (5 yrs.)	Medium sized sample size. Change incidence is mentioned in the abstract but not reported in results.

Conference abstracts				
Diaz Romero et al. (2018) (abstract) Retrospective single-arm, single-centre done in Spain.	Intervention: Memokath 051 No comparator	23 patients; ureteral stenosis (benign and malignant)	Mean follow-up 15.95 mos. Success rate 70.96% (permeability of the ureter, maintaining adequate renal function and absence of lower back pain) Complications Migration of the stent (35.48%); urinary tract infection (32.25%); obstruction of the stent (25.08%)	Conference abstract - minimal information reported. Small sample size. Retrospective, no comparator.
Elbaroni et al. (2020) (abstract) Retrospective single-arm, single-centre done in UK.	Intervention: Memokath 051. No comparator	95 patients (113 stents) with benign and malignant ureteral strictures	Follow-up 4 mos. – 12 yrs. Mean post-operative stay 1.7 days Complications Early UTI, 11%; migration, 26%; obstruction, 22% Good long-term outcome (not defined) 52%	Conference abstract - minimal information reported. Moderate sample size. No comparator. Large range for follow-up period. “Good long-term outcome” is not defined.

4.3 Summary of economic evidence

No new published economic studies were identified by either the company or the EAC.

De novo analysis

The EAC reviewed and updated the EAC cost model used to inform the Committee recommendations during development of the original guidance. This was a simple costing model that compared the cost consequences of Memokath 051 compared with Double- J stents, other metallic stents (Resonance, UVENTA and Allium URS) and reconstructive surgery. The model captured the cost of inserting stents or reconstructive surgery. It also captured the monthly costs of follow-up, early replacement resulting from stent failure, urinary tract infection and prophylactic stent replacement associated with each treatment option. The population modelled were people with ureteric strictures of benign or malignant aetiology requiring ureteric stenting. The model had a time horizon of 5 years. The model structure is presented in Figure 1 of the EAC assessment report update. During guidance update, the EAC reviewed the model and stated that model structure, time horizon and key assumptions of the original cost model remain valid.

Model clinical parameters

The key clinical parameters used in the model were length of time in situ in months, stent removal and replacement and urinary tract infections (UTI).

The EAC updated stent removal and replacement parameters based on data available from the new clinical evidence. In the original guidance, a monthly probability for Memokath 051 stent replacement of 1.4% per month was used. This value was estimated using data from 9 studies reporting on the probability of stent replacement. At guidance update, the EAC included data from 3 new studies (Bier et al. 2017, Khoo et al. 2021 and Forster et al. 2021) in addition to the original 9 studies and estimated a new monthly probability for stent replacement of 1.8% for Memokath 051.

New comparative clinical evidence was available for Memokath 051 versus UVENTA (Choi et al. 2019). For this cost comparison, the EAC used data from Choi et al. 2019 to update the monthly probability of stent replacement from 4.41% to 3.57% for Memokath 051 and 0.49% to 4.99% for UVENTA.

At original guidance, no comparative data was available on this parameter for Memokath 051 versus Allium URS or Resonance. The monthly probability of stent replacement for Allium URS was considered equal to UVENTA based on clinical expert opinion and Resonance was considered equal to Memokath 051. At guidance update the EAC used data from Khoo et al. 2021 and updated the monthly probabilities of stent replacement from 0.49% to 5.54% for Allium URS and from 1.4% to 1.78% for Resonance. The monthly probability of stent replacement used for Memokath 051 in these 2 cost comparisons was 1.8%.

The EAC did not update parameters for length of time in situ or urinary tract infection because there was no new clinical evidence to inform these.

The parameters that were considered in the original EAC model and the EAC's adjustments during guidance update are summarised in table 6 of the EAC assessment report update.

Costs and resource use

Staff costs were updated to Personal Social Services Research Unit (PSSRU) 2020 values. Costs for Band 2 nurses were inflated using Personal Social Services (PSS) pay and prices index because the costs per hour were not included in PSSRU 2020. Cost parameters sourced from NHS Reference Costs 15/16 and BNF 2017 prices in the original guidance were updated in line with the NHS Reference Costs 19/20 and BNF 2020 information. Theatre costs, costs of hospital stay, and cost of day case and inpatient were inflated to 2020 values using NHS cost inflation index (NHSCII).

The price of Memokath 051 and related consumables remained the same as the original guidance based on company information. Comparator prices for

Double-J stents, Resonance and UVENTA were updated based on prices available on NHS supply chain. For Allium, the price was assumed to be same as in the original guidance since prices could not be sourced from the NHS supply chain. Consumable costs were assumed the same as in the original guidance.

The cost parameters that were considered in the original EAC model and the EAC's adjustments during guidance update are summarised in table 7 of the EAC assessment report update and also in the EAC assessment report update addendum.

Base-case results

The original and updated base case results are shown in table 3 below.

Table 3. Summary of original and updated base case results (constant risk of replacement over full 5-year time horizon)

	Cost estimates per patient for Memokath 051 versus comparator				
	Double J	UVENTA	Allium URS	Resonance	Reconstructive surgery
Base case from original guidance	-£1,619	-£928	-£1,146	-£6,552	£467
Base Case Updated 2022	-£1,926	-£8,813	-£9,365	-£6,260	£1,321

The updated cost modelling suggests that under a conservative assumption of constant stent replacement over a 5-year period, Memokath 051 remains cost saving compared to Double-J stents, UVENTA, Allium URS and Resonance. It remains cost incurring compared to reconstructive surgery.

A full breakdown of cost saving estimates for Memokath 051 compared to the Double-J stents, UVENTA and Resonance are presented in tables 2.1 to 2.4 of the EAC assessment report update addendum. Results for that comparison to Allium URS are presented in table 9. 3 of the EAC's assessment report update.

Sensitivity analysis

The EAC reran the univariate deterministic sensitivity analyses to assess the impact of parameter uncertainty on the results of the model.

Compared with Double J stents, results were most sensitive to the length of time in situ for Double-J stents, replacement costs for Double-J stents and unplanned replacement and follow-up costs for Memokath 051. Memokath 051 became cost incurring when the replacement costs of Double-J stent reduced beyond 20% and when the monthly risk of unplanned replacement for Memokath 051 was above 4.42%.

Compared with the other metallic stents (UVENTA, Allium URS and resonance), results were most sensitive to the length of time in situ,

replacement costs and unplanned replacement of the comparators, as well as unplanned replacement for Memokath 051. Memokath 051 was cost saving in all scenarios.

Compared with reconstructive surgery, results were most sensitive to the cost of reconstructive surgery, as well as the length of time in situ, follow-up costs and unplanned replacement for Memokath 051. The threshold at which the cost of reconstructive surgery made Memokath 051 cost neutral was £9,287.

Full results of the EAC's deterministic sensitivity analysis presented as tornado diagrams can be found in figures 2.1 to 2.5 of the EAC's assessment report update.

Scenario analysis

The EAC repeated the scenario analyses done at original guidance which modelled the risk of unplanned replacement of Memokath 051 stents in 3 alternative scenarios:

- replacement in the first 2 years with 0% thereafter
- reduced replacement after 2 years (risk halved)
- constant unplanned replacements over a 2-year time horizon

Compared with Double-J stents, Memokath 051 was cost-incurring in the scenario of constant replacements over a 2-year time horizon but cost saving in the other 2 scenarios. Compared with other metallic stents (UVENTA, Allium URS and Resonance), Memokath 051 was cost saving in all 3 scenarios. Compared with reconstructive surgery, Memokath 051 was cost incurring in the scenario of reduced replacement after 2 years (risk halved) but cost saving in the other 2 scenarios.

Full results of the scenario analyses for Double-J stent, UVENTA and Resonance can be found in Appendix D of the EAC assessment report update addendum. For Allium URS and reconstructive surgery please see section 9.3 and appendix D of the EAC's assessment report update.

Additional scenario analysis – variation in Double-J stent prices

A variation of prices for Double-J stents were available on NHS Supply Chain. The EAC ran scenario analyses to assess the impact on cost saving estimates when the lowest and highest available prices for Double-J stents were used. Memokath 051 remained cost saving compared with Double-J stents in all scenarios. Please see the EAC's addendum to the assessment report update for full details.

5 Ongoing research

The EAC did not identify any ongoing study relevant to the scope after searching ClinicalTrials.Gov, WHO International Clinical Trials Registry Platform (ICTRP), and ISRCTN.org. The company stated that a UK study is in the protocol development stages. This is a multicentre study evaluating the Memokath 051 double cone stent and it plans to include quality of life as a primary end point.

6 Issues for consideration by the Committee

Clinical evidence

- Similar to that at original guidance, the new evidence base is deemed to be of low to moderate quality. New comparative data comparing Memokath 051 to other metallic stents corroborates the higher rates of migration associated with Memokath 051. Longer-term 5-year data show high rates of complications (72%) with Memokath 051. Clinical success outcomes varied among studies and were not consistently defined. There is still limited data in relation to the length of time the stent remained in situ. No new data comparing Memokath 051 to Double-J stents or nephrostomy was identified.

Cost evidence

- The updated cost models suggest that under a conservative assumption of constant stent replacement over a 5-year period,

Memokath 051 remains cost saving compared with Double-J stents, UVENTA, Allium and Resonance. It remains cost incurring compared to reconstructive surgery.

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NICE Medical Technologies Evaluation Programme

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Appendix A: Sources of evidence considered in the preparation of the overview

Guidance update report:

Manounah L, Isaaq A, Shokraneh F at al. MT569 Memokath 051 stent for ureteric obstruction, June 2022

Submission for the guidance review from the following sponsor:

PNN medical (note, no additional submission for the guidance update)

Current guidance:

Memokath 051 stent for ureteric obstruction. NICE medical technologies guidance [MTG35] (2018) Available from https://www.nice.org.uk/guidance/mtg35

Related NICE guidance:

- Bladder cancer: diagnosis and management. NICE guideline [NG2] (2015) Available from https://www.nice.org.uk/guidance/NG2
- Prostate cancer: diagnosis and management. NICE guideline [NG131] (2019, updated 2021) Available from https://www.nice.org.uk/guidance/ng131
- Acute kidney injury: prevention, detection and management. NICE guideline [NG148] (2019) Available from https://www.nice.org.uk/guidance/ng148

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Appendix B: Comments from professional bodies

Expert advice for the update 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 Ranan Dasgupta

Consultant Urological Surgeon, Imperial College Healthcare NHS Trust

Mr Deepak Batura

Consultant Urological Surgeon, London North West University Healthcare NHS Trust

Stuart Graham,

Director of Endourology, Stone & Laser Surgeon, Barts Health NHS Trust

Matthew Shaw

Consultant Urological Surgeon, Newcastle upon Tyne NHS Foundation Trust

Chandrasekharan Badrakumar

Consultant Urologist, South Tees Hospitals NHS Foundation Trust

Chandra Shekhar Biyani

Consultant Urologist, St James's University Hospital

Mr Andreas Bourdoumis

Consultant Urological Surgeon, Rochdale Infirmary Northern Care Alliance NHS Trust

Tamer El-Husseiny

Consultant Urological Surgeon, Imperial College Healthcare NHS Trust

Priyadarshi Kumar

Consultant Urological Surgeon, University Hospital Coventry & Warwickshire

Please see the expert adviser questionnaire (EAQ) responses included in the Committee pack for full details

Appendix C: Comments from patient organisations

The following patient and carer organisations were contacted for comment during the update:

- Action on Bladder Cancer
- Bladder and Bowel Foundation
- British Kidney Patient Association
- 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
- Prostate Cancer UK (formerly prostate cancer charity)
- Rarer Cancers Foundation
- Sue Ryder
- Target Ovarian Cancer

A response was received from Fight Bladder Cancer. Please see the response in the Committee pack for full details.

Appendix D: Company claimed benefits

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 051 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

Appendix E: Decision problem from scope

Population	Adults with ureteric obstruction as a result of malignant or benign strictures.
Intervention	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, rates of stent migration, encrustation and infection, 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 parameters.
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,	Memokath 051 is contraindicated in children. Some ureteric obstructions are a result of malignancy - all people with cancer are

including those related to equality	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	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
Any other special considerations	Not applicable	

National Institute for Health and Care Excellence

Collated comments table

MTG Medtech Guidance:

Expert contact details and declarations of interest:

Expert #1	Ranan Dasgupta, Consultant Urological Surgeon, Imperial College Healthcare NHS Trust, [redacted]
	Nominated by:
	DOI: NONE
Expert #2	Deepak Batura. Consultant Urological Surgeon, London North West University Healthcare NHS Trust, [redacted]
	Nominated by:
	DOI: NONE
Expert #3	Stuart Graham, Director of Endourology, Stone & Laser Surgeon, Barts Health NHS Trust, [redacted]
	Nominated by : NICE
	DOI: None
Expert #4	Matthew Shaw, Consultant Urological Surgeon, Newcastle upon Tyne NHS Foundation Trust, [redacted]
	Nominated by: Company
	DOI: ***Direct - financial*** Provided a GP educational meeting for Astellas on use of mirabegron, **10/21**
Expert #5	Chandrasekharan Badrakumar, Consultant Urologist, South Tees Hospitals NHS Foundation Trust, [redacted]
	Nominated by: Company
	DOI: Non-financial professional and personal interests: Project Title: MK-051 DC IRAS Project ID: 309977 It is a multi centric UK national study involving other urology departments that are using Memokath 051.

	I am the chief investigator for this study. We are in the process of applying for ethics approval. South Tees Hospitals NHS foundation Trust is the sole sponsor for this study. The study is part funded by the manufacturing company (PNN). Company is not sponsoring the study. I am also applying for other grants such as NIHR to fund the study. I am employed full time by South Tees Hospitals NHS foundation Trust as consultant urologist. I am not paid for the research. I am not receiving any personal payment from the company for undertaking research. Interest arose 26/10/2021 - On-going
Expert #6	Chandra Shekhar Biyani, Consultant Urologist, St James's University Hospital, [redacted]
	Nominated by: NICE
	DOI: None
Expert #7	MR ANDREAS BOURDOUMIS, CONSULTANT UROLOGICAL SURGEON, ROCHDALE INFIRMARY NORTHERN CARE ALLIANCE NHS TRUST, [redacted]
	Nominated by: Company
	DOI: None
Expert #8	Tamer El-Husseiny, Consultant Urological Surgeon, Imperial College Healthcare NHS Trust, [redacted]
	Nominated by: Company
	DOI: None
Expert #9	Priyadarshi Kumar, Consultant Urological Surgeon, University Hospital Coventry & Warwickshire, [redacted]
	Nominated by: Company
	DOI: None

			Response
1	Please describe your level of experience with the procedure/technology, for example: Are you familiar with the procedure/technology? Have you used it or are you currently using it? Do you know how widely this procedure/technology is used in the NHS or what is the likely speed of uptake? Is this procedure/technology performed/used by clinicians in specialities other than your own? − If your specialty is involved in patient selection or referral to another specialty for this procedure/technology, please indicate your experience with it.	Expert 1 Yes, have used this technology for over 10 years intermittently, and based at a busy tertiary unit, with complex endourology, am well versed with its positive and negative aspects	
		Expert 2 Yes	
		Expert #3 I place these devices and have done for over 10 years, up to 20 per year	
		Expert #4 I have experience of using this procedure and also similar technologies. Procedure used across NHS, but in relatively small numbers. Memmokath implantations are almost always through Urologists I have extensive experience of using this technology and selecting appropriate patients.	

		Are you familiar with the procedure/technology? Yes. I perform this procedure regularly Have you used it or are you currently using it? I am using it since February 2020 Do you know how widely this procedure/technology is used in the NHS or what is the likely speed of uptake? It was introduced in 1995 in the UK. I am aware of the few centres that are using this stent. But unsure if it is not widely used. Is this procedure/technology performed/used by clinicians in specialities other than your own? Memokath 051 is specific for use in the ureter. It is used in many urology departments across the country. If your specialty is involved in patient selection or referral to another specialty for this procedure/technology, please indicate your experience with it. I include patients for this stent if they are dependent on JJ stent for management of unilateral or bilateral ureteric obstruction due to benign or malignant obstruction. There has to be a normal ureter below and above the level of obstruction as demonstrated by retrograde pyelogram or ureteroscopy (Pelvi-ureteric junction and vesico-ureteric junction should be normal). The stricture should not be suitable or patient unfit for reconstructive surgery, or patient choice. The patient should be fit to undergo retrograde Memokath insertion under GA or RA. I do not use this stent in patients aged less than 18, Nickel allergy, active stone former (stones	

		present in the kidney, Metabolic stone disease, forming stones within 2 years or disease that require ureteric instrumentation for treatment. I do not insert this stent as a primary stent in patients with ureteric obstruction that are not on JJ stent I do not do ante-grade insertion of this stent. I do not use it for renal transplant ureteric strictures and uretero-ileal anastomotic strictures.	
		Expert #6 I have used this before and currently using Allium stent. Long-term short stents (Memokath, Allium and Uventa) are used in a limited number of centres. In our hospital it is done by urologists and radiologists. I do get referral from oncology colleagues and from radiologists as well.	
		Expert #7 I have received training in all aspects of Endourological procedures as a post CCT trainee between 2012-2014 at Barts and the London NHS Trust, for which I hold relevant accreditation. My training included the Memokath stent range, with focus on MMK 051 (ureteric stent). I have participated both as trainee and faculty in dedicated training sessions regarding the MMK 051 during the same time period, for which I hold relevant accrediatation.	

		Following the initial training, I have attended a refresher course in 2018 at Imperial College London under Mr Tamer El-Husseiny in order to be able to start providing the service at my Trust. I have started introducing MMK 051 stents in my Trust on February 2019 and have been doing so ever since. I am aware the technology has been used in the UK since before 2001. To my knowledge, only Urological surgeons with relevant training introduce the MMK 051 stent, there is a possibility for the select few Interventional Radiologists, although I am not certain.	
		Expert #8 Yes. High volume centre for Memokath stents Yes. Regular user Not widely used across the NHS, usually done in specialist centres after adequate training. No This procedure is mainly done by urologists	

		Expert #9 I perform this procedure currently and have been trained in this in my Endourology fellowship. It is performed in a small variety of centres.	
2	− Please indicate your research experience relating to this procedure (please choose one or more if relevant):	Expert #1	
		Expert #2	
		I have done bibliographic research on this procedure. I have done research on this procedure in laboratory settings (e.g. device-related research). I have done clinical research on this procedure involving patients or healthy volunteers. I have published this research. - Journal of EndourologyVol. 35, No. 2Experimental EndourologyFree Access The Fate of Ureteral Memokath Stent(s) in a High-Volume Referral Center: An Independent Long-Term Outcomes Review Luke R. Forster, Laura Watson, Charles E. Breeze, Antonina Di Benedetto, Stuart Graham, Prasad Patki, and Anup Patel Published Online:15 Feb 2021https://doi.org/10.1089/end.2020.0542	

		I have had no involvement in research on this procedure. Other (please comment)	
		Expert #4 I have had no involvement in research on this procedure.	
		Expert #5 I have written a protocol to conduct clinical research on this stent. I am in preparation for ethics approval. The protocol is currently being peer-reviewed and reviewed by patients & public. I audit my experience with this stent regularly. Our abstract has been accepted for presentation at BAUS annual meeting in June 2022.	
		Expert #6 I have done bibliographic research on this procedure. I have done research on this procedure in laboratory settings (e.g. device-related research). I have done clinical research on this procedure involving patients or healthy volunteers. X I have published this research. I have had no involvement in research on this procedure.	

		Expert #7 I have done bibliographic research on this procedure. I am currently involved in designing and participating in a clinical trial on this procedure involving patients or healthy volunteers. I have published research work in this field.	
		Expert #8 I have done bibliographic research on this procedure I have done clinical research on this procedure involving patients or healthy volunteers. No, but currently setting up a UK multicentre longitudinal trial on the use of the double cone Memokath stents I have published this research.	
		Expert #9 I have had no involvement in research on this procedure.	

Current management

3	How innovative is this procedure/technology, compared to the current standard of care? Is it a minor variation or a novel approach/concept/design? Which of the following best describes the procedure (please choose one):	Expert #1 Yes – we use this technology at our centre, and referred cases from other hospitals We have just had accepted our centre's experience of this technology and its comparison with other metallic stents; article In Press; I am the senior author for this study Khoo et a Single-Centre Experience with Three Metallic Ureteric Stents (Allium® URS, Memokath™-051 and Resonance®) for Chronic Ureteric Obstruction J Endourol (In Press)	
		Expert #2 b and c No	
		Expert #3 Established practice and no longer new. yes	
		Expert #4 There are numerous other technologies that also perform the same role. This technology is innovative, however there are other (newer) technologies that are more innovative.	

		Established practice and no longer new.	
		Expert #5 Established practice and no longer new. This stent is in use from 1996 in UK. Few stent design modifications have happened to reduce stent migration	
		Expert #6 One issue I noticed with this product is hyperplasia of urothelium through the wire. Allium stent has a polymer coating prevents tissue growth in the lumen. Established practice and no longer new. xx A minor variation on an existing procedure, which is unlikely to alter the procedure's safety and efficacy. Definitely novel and of uncertain safety and efficacy. The first in a new class of procedure.	

		Expert #7 The first results in the UK were published By Mr Kulkarni around 2001. To my knowledge, the technique and indications of inserting the stent have developed since, albeit remain the same on principle. A minor variation on an existing procedure, which is unlikely to alter the procedure's safety and efficacy.	
		Expert #8 The concept is certainly innovative, It is a long term metallic ureteric stent for management of chronic ureteric obstruction. Does not require regular change as compared to the standard of care which is a 6 monthly change of the polymer JJ stents. Stent itself is not new, has been on the market for many years. Established practice and no longer new.	
		Expert #9 It is a wholly different concept to classical plastic stents with its self retaining and thermoexpandable properties	

		Established practice and no longer new.	
4	Does this procedure/technology have the potential to replace current standard care or would it be used as an addition to existing standard care?	Expert 1 Sadly not. Yes streamlining the management of the obstructed upper tract would definitely help patients in the longer term. Maybe reducing unnecessary repeated JJ stenting would assist in the upcoming NHS backlog by insertion of a semi-permanent stent, but then need to ensure adequate f./up in place. Ideal to set up such a prospective RCT (for efficacy and clinical effectiveness) or at least a registry (akin to insertion of prostheses).	
		Expert 2 No	
		Expert #3 Addition to care in selected individuals	
		Expert #4 No	
		Expert #5 Memokath has a potential to replace standard care in many patients. Patient selection is important.	
		Expert #6 Yes	

		Expert #7 This procedure/technology has the potential to be used as an addition to existing standard of care.	
		Expert #8 Will be used as an addition to the existing practice for suitable patients with ureteric strictures requiring long term ureteric stents	
		Expert #9 It would be used as an additional treatment in a specific subset of patients	

Potential patient benefits

5	Please describe the current standard of care that is used in the NHS.	Expert #1	
		Expert #2	
		Expert #3 1) Palliative care Benign strictures not amenable to other techniques, after full discussion of options, including reconstruction	
		Expert #4 JJ stent	

		Expert #5 The standard care for patients with ureteric obstruction, who are not suitable for major reconstructive surgery, is the insertion of a JJ stent by an endoscope via the urethra under anaesthesia. These stents need to be changed every 3, 6 or 12 months under anaesthesia, for the rest of their life. These patients have varying degrees of stent-related symptoms requiring several hospital visits resulting in poor quality of life.	
		Expert #6 Log-term stent or extra-anatomic stent.	
		Expert #7 Percutaneous nephrostomy placement or JJ ureteric stent insertion.	
		Expert #8 The current standard of care is regular 6 monthly change of polymer JJ stent. Risks of repeated procedures under GA is one of the problems to the current practice.	
		Expert #9 Double J stents	
6	Are you aware of any other competing or alternative procedure/technology available to the NHS which have a similar function/mode of action to this? If so, how do these differ from the procedure/technology described in the briefing?	Expert 1 Yes, we use this, though since the advent of Allium since the last MMK guidance, this alternative technology has replaced some of the MMK cases	
		Expert 2 Yes No Prefer using another brand of metallic stent. Not trained in use of this stent	

		Expert #3 Allium stents, urolume stents Similar devices	
		Expert #4 Allium stent are similar, but have a watertight construction allowing for a wider range of treatments. These stents are a nitinol metal scaffold around which is a silicon polymer. They are deployed using a technique similar to vascular stent deployment.	
		Expert #5 1. Reconstructive surgery is a major operation. Patient should be suitable to undergo this procedure and they should accept the risks of major abdominal surgery. Successful patients are stent free for rest of their life. 2. Allium stents need to be changed after 3 years. 3. UVENTA I am not aware if it is used in UK Resonance stent needs change every year	
		Expert #6 Allium Uventa stents	
		Expert #7 As far as anatomical and intraluminal stents are concerned, other ureteric metal stents include the Resonance stent, the Allium stent and the Uventa stent. There is also the use of extraanatomical stent called the Detour stent. Other than technical specifications of insertion, the location and duration of stent insertion differ significantly compared to the MMK 051 stent. In brief, the majority of the stents mentioned above can	

		be introduced in the distal ureter only, may last only up to 12 months and then need exchanging and in the case of the Detour stent involve an open procedure instead of a minimally invasive endoscopic procedure.	
		Expert #8 Other novel metallic stents such as the Resonance stent or the Allium stent Main differences are mainly in the stents design, mode of insertion and longevity of their indwelling time	
		Expert #9 Allium metal stent Nitinol covered with polymer	
7	What do you consider to be the potential benefits to patients from using this procedure/technology?	Expert 1 The same technology has been applied to prostatic stenting, with less success from personal communication, and there are several alternatives for the prostate which are better. In the ureter, typically the technology is applied retrogradely by urologists rather than antegradfely by radiology. Pertinent question at last MTAC was by the interventional radiologist on the panel as to why we cannot offer primary metal stenting antegradely rather than nephrostomy only. No clear pathway for acute obstruction that is common across the UK	
		Expert 2 Yes, in secondary care and only for ureteral strcitures Ureteric strictures not suitable for surgical correction and requiring frequent polyurethane stent exchanges	
		Expert #3	

		Single placement leads to not needing to come to theatre for repeated stenting	
		Expert #4 Reduced number of anaesthetics for stent changes.	
		Expert #5 Improved quality of life Reduce hospital visits for JJ stent-related complications Reduced or no stent symptoms Reduce stent changes and in some patients, avoid stent change completely. Reduce the need for complex pre-assessment and anaesthesia	
		Expert #6 • No regular general anaesthetic for stent replacement • No ureteric stent-induced bladder symptoms • Reduced hospital admission and attendance	
		Expert #7 Improves QoL, preserves renal function and precludes regular visits to the Hospital and need for regular exchange of ureteric stent.	
		Expert #8 Longer indwelling time and therefore reduce the need for repeated change of stents and reduced exposure and risk of the repeated GA's	
		Expert #9 Longer duration, less anaesthetics for stent changes, less stent symptoms, work in malignant ureteric obstruction when double J stents may not	

Potential system impact

8	Are there any groups of patients who would particularly benefit from using this procedure/technology?	Expert 1 Differences in the single vs dual cone; differences in length. Alternative technology (ie not thermoexpandable Allium) is now increasingly used.	
		Expert 2 Yes	
		Expert #3 Palliative care patients, cancer patients, appropriately counselled benign patients	
		Expert #4 Patients with malignant ureteric obstruction may particularly benefit	
		Expert #5 Patients with intractable ureteric obstruction due to benign or malignant conditions and who are dependent on JJ stent would benefit from Memokath. My view is a normal segment of ureter below and above the level of obstruction is important.	
		Expert #6 Patients with malignancy and ureteric obstruction	

		Expert #7 Cancer patients on a palliative pathway with ureteric obstruction, excluded if history of renal stone formation.	
		Expert #8 Stent dependant ureteric strictures	
		Expert #9 Malignant ureteric obstruction, patients having side effects due to double J stents	
9	Does this procedure/technology have the potential to change the current pathway or clinical outcomes to benefit the healthcare system? Could it lead, for example, to improved outcomes, fewer hospital visits or less invasive treatment?	Expert #1 Uventa (common in Korea and the Far East) and Allium (introduced in our practice). As with all of these devices, infection/colonisation/migration and difficulty with extraction remains a question One of the deficiencies highlighted at MTAC was the series of small single centre experiences – with no validated outcome measures. A helpful re-assessment of some of the original datasets by reviewing long-term outcomes is published in J Endourol 2021 Feb;35(2):180-186. doi: 10.1089/end.2020.0542. Epub 2020 Sep 23. The Fate of Ureteral Memkokath stent(s) in a high-volume referral center: an independent long-term outcomes review. Forster LR et al Other clinical studies are mainly single centre experiences, along lines of Khoo et al, relevant for British data.	
		Expert #2	

		Yes None since 2014 Kulkarni R. Metallic stents in the management of ureteric strictures. Indian J Urol. 2014;30(1):65-72.	
		Expert #3 yes	
		Expert #4 It may lead to reduced number of operating surgeries in some patients. The number is likely to be small.	
		Expert #5 Yes. As mentioned in the answer to question 7 Frees up theatre time for other operations and helps reduce waiting list. Potential for reducing administrative work load.	
		Expert #6 • Yes It can improve patients quality of life	
		Expert #7 There is substantial evidence to support the MMK 051 improves QoL and prevents prolonged stay and repeated attendances to hospital.	
		Expert #8 Yes	

		By reducing the need for repeated procedures	
		Expert #9 Yes Less stent changes and anaesthetics, less visits for stent symptoms	
10	Considering the care pathway as a whole, including initial capital and possible future costs avoided, is the procedure/technology likely to cost more or less than current standard care, or about the same? (in terms of staff, equipment, care setting etc)	Expert 1 No – clearly needed is a register to ensure safe monitoring of long-term outcome. After training of individual centres, little universal audit of national practice	
		Expert 2 Image intensifier, Memokath insertion system, access sheath, temperature controlled irrigation fluid for both insertion and retrieval, post insertion imaging.	
		Expert #3 The device is far more expensive, but the lack of repeated theatre visits far outweighs this cost	
		Expert #4 Good quality cost-effectiveness analysis is lacking. While there will be a reduction in the number of surgeries, there is also a surveillance requirement for all medium-term stent implantations.	
		Expert #5	

		We did a cost calculation for a JJ stent change in my institution. We compared it with the cost of insertion of the Memokath 051. It appears that if Memokath 051 can avoid 4 stent changes then it becomes cost neutral (approximately for 2 years assuming most patients have stent changes every 6 months). It the Memokath 051 lasts more than 2 year or avoids more than 4 stent change then it could be cost effective. We have not factored in cost of follow up, complications and failure of Memokath	
		Expert #6 Difficult to say. My understanding is the cost of 3 GA stent changes would be required to cover the cost. However, the indirect immediate benefit would be an increase in the theatre capacity following the insertion.	
		Expert #7 Overall, the procedure is likely to cost less than the current standard care in the long term.	
		Expert #8 The stent will initially cost more, but on the longer term and the longer it stays insitu this could provide cost savings	
		Expert #9 May cost less if duration is more than double J	
11	What do you consider to be the resource impact from adopting this procedure/technology (is it likely to cost more	Expert 1 Yes, typically during training or mentored introduction of the technique	

	or less than standard care, or about same-in terms of staff, equipment, and care setting)?	Expert 2 Yes	
		Expert #3 A lack on need to repeat theatre visits , and therefore the cost of this	
		Expert #4 It is important to remember that the patients will require follow up between stent changes.	
		Expert #5 Cost of Memokath 051 is several times more than JJ stent. This cost has to be recovered by preventing regular JJ stent changes which is the advantage of this stent.	
		Expert #6 Initially more than the standard care.	
		Expert #7 Overall, the procedure is likely to cost less than the current standard care in the long term.	
		Expert #8 The stent will initially cost more, but on the longer term and the longer it stays insitu this could provide cost savings	
		Expert #9 As isolated procedure will cost more but as noted above cost benefits lie in decrease number of stent changes	

12	What clinical facilities (or changes to existing facilities) are needed to do this procedure/technology safely?	Expert 1 Safe generally; reliability- as above, needs adequate outcome measures to comments on this aspect; maintenance – how long can they remain safely in-situ, again a question without a strong evidence base to answer this	
		Expert 2 Stent encrustations and stent migration/ dislodgement are frequent complications	
		Expert #3 Education in case selection 2) education in device fitting	
		Clinic for assessment Radiology assessment Operating department facility Clinic and radiology follow up	
		Expert #5 Patient selection is important. Multi-disciplinary approach to choose the right patients who will benefit from this stent is important.	
		Expert #6 Nothing specific. Endourological skills.	
		Expert #7 There is no need for additional changes and/or modifications required to adopt	

		the MMK 051 in any current practice within the NHS.	
		Expert #8 Staff training Operating theatres Intraoperative fluoroscopy	
		Expert #9 None	

General advice

13	Is any specific training needed in order to use the procedure/technology with respect to efficacy or safety?	Expert #1	
		Expert #2	
		Expert #3 yes	
		Expert #4 Yes	
		Expert #5 A department aspiring to introduce this procedure requires training for the urologist and theatre staff to insert Memokath. Workshops and mentoring is available.	

		Expert #6 A short training session would be useful.	
		Expert #7 All interested parties wishing to develop the service should attend a relevant workshop and obtain certification and are also encouraged to perform the first procedures under supervision (mentorship).	
		Expert #8 Yes. Staff training is required	
		Expert #9 Yes	

Other considerations

14	What are the potential harms of the procedure/technology? Please list any adverse events and potential risks (even if uncommon) and, if possible, estimate their incidence: Adverse events reported in the literature (if possible, please cite literature) Anecdotal adverse events (known from experience) Theoretical adverse events	Expert #1	
		Expert #2	
		Expert #3 Migration, device failure V rarely, fistulation – I have seen 2 vascular fistulae and one enteral fistula in 27 years practice	
		Expert #4 Stents can migrate	

		Stents can encrust and block	
		Expert #5 Immediate 1. Failure to insert Memokath 2. Sepsis / Uninary tract infection 3. Immediate ureteric obstruction by ureteric spasm, blood clot or inadequate stent length. Delayed 1. Migration 2. Ureteric obstruction above or below Memokath due to progressive disease 3. Encrustation Ureteric perforation	
		Expert #6 • Migration • Encrustation • Sepsis Malfunction of the device during deployment	
		Expert #7 The potential harms/risks are no different than the ones compared to existing practice of inserting JJ ureteric stent or percutaneous nephrostomy, namely risk of recurrent obstruction, infection and significant stent - related symptoms requiring stent exchange.	
		Expert #8 Risks include: Stent migration Stent obstruction UTI's Need for stent change	

		Expert #9 Migration, encrustation, failure	
15	Please list the key efficacy outcomes for this procedure/technology?	Expert #1	
		Expert #2	
		Expert #3 Renal function, a lack of hydronephrosis / pain	
		Expert #4 Migration rate Patency rate	
		Expert #5 1. Reduce hospital visits for JJ stent related complications 2. No stent symptoms 3. Improved quality of life 4. Reduce stent changes and in some cases avoid stent change completely. 5. Reduce the need for complex pre-assessment and anaesthesia 6. Frees up theatre time for other cases and helps reduce waiting list. Potential for reducing administrative work load.	
		Expert #6 • Improved drainage from the renal unit	

		Expert #7 Improves Qol, Reduces LoS, Reduces long term costs to health care, Preserves renal function, Introduced via minimally invasive endoscopic technique as a day case in the majority of cases.	
		Expert #8 Kidney drainage Preserve renal functions Reduce repeated GA's	
		Expert #9 Longer lasting and work inmalignant obstruction	
16	Please list any uncertainties or concerns about the efficacy and safety of this procedure/?	Expert 1 The previous MTAC review used the estimation of repeat stenting by JJ stenting as the comparator; nowadays other competing technology, eg Allium might be a more appropriate comparator	
		Expert #2 More expensive than polyurethane stents.Cost savings likely in cases where Memokath replacement is not needed.	
		Expert #3 Migration of the device has previously been an issue	
		Expert #4 Variable results published	
		Expert #5 Quality of life improvement Cost benefit	

		Expert #6	
		Expert #7 There is no concern regarding safety.	
		Expert #8 none	
		Expert #9	
17	Is there controversy, or important uncertainty, about any aspect of the procedure/technology?	Expert #1	
		Expert #2	
		Expert #3 No, not in carefully selected and conselled individuals	
		Expert #4 Variable migration and encrustation rates	
		Expert #5 Primary insertion of Memokath ureteric obstruction Suitability for uretero ileal anastamotic stricture Suitability for transplant uretero vesical anastamotic stricture	
		Expert #6	
		Expert #7 There is no controversy or uncertainty regarding the technology to the best of my knowledge.	

		Expert #8 Ensuring adequate case selection which is a key	
		Expert #9	
18	If it is safe and efficacious, in your opinion, will this procedure be carried out in (please choose one):	Expert #1	
		Expert #2	
		Expert #3 Most or all district general hospitals. A minority of hospitals, but at least 10 in the UK. YES Fewer than 10 specialist centres in the UK.	
		Expert #4 A minority of hospitals, but at least 10 in the UK.	
		Expert #5 Most or all district general hospitals.	
		Expert #6 Most or all district general hospitals. A minority of hospitals, but at least 10 in the UK. x Fewer than 10 specialist centres in the UK.	

		Cannot predict at present.	
		Expert #7 Most or all district general hospitals.	
		Expert #8 A minority of hospitals, but at least 10 in the UK.	
		Expert #9 Most or all district general hospitals. A minority of hospitals, but at least 10 in the UK. Fewer than 10 specialist centres in the UK. Cannot predict at present.	
19	Please list any abstracts or conference proceedings that you are aware of that have been recently presented / published on this procedure/technology (this can include your own work). Please note that NICE will do a comprehensive literature search; we are only asking you for any very recent abstracts or conference proceedings which might not be found using standard literature searches. You do not need to supply a comprehensive reference list but it will help us if you list any that you think are particularly important.	Expert #1 Oncology patients Long-term data now available – showing the controversy of outcome measurement and the need to ideally change these measurements going forward, so that future technology reviews/updates will have addressed these deficiencies in current data	
		Expert #2 As in No 16 above In the absence of any new devices or clinical evidence superseding what was known, an update does not seem warranted at this moment.	
		Expert #3 See above	

		Expert #4	
		Expert #5 My experience with Memokath 051 for the past 2 years has been prospectively reviewed. An abstract has been accepted for presentation in BAUS 2022 annual Meeting at Birmingham. My migration rate is 18% (6 out of 33 Memokath insertions). In these 6 patients 4 did not require re-insertion of Memokath and they have remained stent free.	
		Expert #6 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6028873/ https://pubmed.ncbi.nlm.nih.gov/34074131/ https://pubmed.ncbi.nlm.nih.gov/32762263/	
		Expert #7 **I**nsertion of thermoexpandable metallic ureteric stents can be aided by ureteric predilation. The Annals of The Royal College of Surgeons of England, 2016, 98(2), pp. 158–159 Bourdoumis A, Kachrilas S, Kapoor S et al. The use of a thermoexpandable metal alloy stent in the minimally invasive management of retroperitoneal fibrosis: a single center experience from the United Kingdom. J Endourol 2014; 28: 96–99. 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 Int. 2010; 84(3):286-91. (UHSM, Wythenshaw) Agrawal S1, Brown CT, Bellamy EA, Kulkarni R. The thermo-expandable metallic ureteric stent: an 11-year follow-up. BJU Int. 2009;103(3):372-6. Kulkarni R1, Bellamy E. Nickel-titanium shape memory alloy Memokath 051 ureteral stent for managing long-term ureteral obstruction: 4-year experience. J Urol. 2001;166(5):1750-4.	
		Expert #8 No recent abstracts up to my knowldege	
		Expert #9	
20	Are there any major trials or registries of this procedure/technology currently in progress? If so, please list.	Expert #1	
		Expert #2	
		Expert #3 NO	
		Expert #4	

		Expert #5 Project Title: MK-051 DC IRAS Project ID: 309977 I am the chief investigator for this study. The protocol is currently being peer reviewed. We are in the process of applying for ethics approval. The study is sponsored by South Tees Hospitals NHS foundation Trust (I am employed by this trust). The study is part funded by the manufacturing company (PNN)	
		Expert #6 No It would be worth doing a comparison with regular stent replacement.	
		Expert #7 I am not aware at this moment.	
		Expert #8 Yes. I am currently involved in setting up a longitudinal 2 years prospective multicentre trial to assess the dual cone Memokath stent in managing chronic ureteric obstruction	
		Expert #9	
21	Approximately how many people each year would be eligible for an intervention with this procedure/technology, (give either as an estimated number, or a proportion of the target population)?	Expert 1 Long-term safety and suitability of case selection often undertaken without recourse to an MDT approach as for cancer treatments. Reference to the Discussion of the Forster et al paper will highlight areas that could be improved	
		Expert 2 No	

		Expert #3 We have a population of 2.5 million, and we need about up to 20 a year	
		Expert #4 We would expect to implant 10-15 stents per year on a tertiary referral population of 1.5 million	
		Expert #5 10 to 20 per institution	
		Expert #6 We do around 15 procedures a year. There are a number of patients on regular stent replacement.	
		Expert #7 In my practice I estimate between 30-50 patients per year.	
		Expert #8 200-300	
		Expert #9 < 5%	

22	Are there any issues with the usability or practical aspects of the procedure/technology?	Expert 1 We use for ureteric strictures (typically malignant but also some benign)	
		Sparingly used. Main use are malignant and benign strictures, not amenable to surgery, specially in individuals who are unfit for regular polyurethane stent exchanges.	
		Expert#3 The ureter must be dilatable enough to place the device. I use a double ended device to prohibit upwards migration	
		Expert #4 Stent requires heating and cooling for the implantation and explantation process	
		Expert #5 None	
		Expert #6 No apart from above mentioned risk	
		Expert #7 No issues.	
		Expert #8 Careful case selection	
		Expert #9 No	
23	Are you aware of any issues which would prevent (or have prevented) this procedure/technology being adopted in your organisation or across the wider NHS?	Expert 1 Yes, excellent MTAC discussion last time	
		Expert 2 Yes	

		Expert#3 The can be difficult to place. I would favour centres such as ours fitting them	
		Expert #4	
		Expert #5 None to my knowledge	
		Expert #6 No, we are using a different stent as they are a bit cheap and has a polymer coating	
		Expert #7 No issues.	
		Expert #8 No	
		Expert #9 No	
24	Is there any research that you feel would be needed to address uncertainties in the evidence base?	Expert#1	
		Expert#2	
		Expert#3 no	
		Expert #4 A stent registry should be mandated.	
		Expert #5 Quality of life improvement Cost benifit	
		Expert #6	

		Expert #7 Prospective double blind trial	
		Expert #8 Yes – hopefully our prospective longitudinal study will help with more efficacy data	
		Expert #9 Useful to have registry to record all insertions as limited number done individually by surgeons	
25	Please suggest potential audit criteria for this procedure/technology. If known, please describe: − Beneficial outcome measures. These should include short- and long-term clinical outcomes, quality-of-life measures and patient-related outcomes. Please suggest the most appropriate method of measurement for each and the timescales over which these should be measured. − Adverse outcome measures. These should include early and late complications. Please state the post procedure timescales over which these should be measured	Expert#1	
		Expert#2	
		Expert#3 Beneficial outcome measures: Renal function, hydronephrosis, symptoms. Possible split renal function Adverse outcome measures: The opposite of the above	

		Expert #4 Beneficial outcome measures: Number of stent changes required per year Maintain GFR Pain score Adverse outcome measures: Stent migration Stent encrustation Stent fistulation	
		Expert #5 Beneficial outcome measures: • QOL improvement • Relief from stent related symptoms as assessed by USSQ • Renal function preservation • Cost-benefit • Longevity of Memokath In our study we planned to follow up recruited patients for 2 years from the time of insertion of Memokath. Because the Memokath becomes cost neutral in comparison to standard care if it avoids JJ stent change for 2 years.	

		Adverse outcome measures: Failure to insert, Sepsis, Migration, Encrustation, Obstruction, Ureteric perforation	
		Expert #6 Beneficial outcome measures: • No stent-related symptoms • No regular GA stent replacement • Better quality of life Adverse outcome measures: • Sepsis • Migration • Stone formation	
		Expert #7 Beneficial outcome measures: QoL, LoS, pre and post operative renal function as per renal function blood tests and functional renograms Adverse outcome measures:	

		Post operative comlications reporting as per Clavien-Dindo classification system.	
		Expert #8 Beneficial outcome measures: Kidney drainage Preservation of renal functions Quality of life improvement Adverse outcome measures: Side effects such as stent migration and stent encrustation	
		Expert #9 Beneficial outcome measures: QoL questionnaires Duration Adverse outcome measures: Migration Failure Encrustation	
26		Expert#1	

	Please add any further comments on your particular experiences or knowledge of the procedure/technology		
		Expert# 2	
		Expert#3 I've used a lot and in the correct patient after counselling, they are extremely valuable	
		Expert #4	
		Expert #5 In my experience with Memokath from February 2020 a good majority of the patients with migrated Memokath did not require re-insertion of Memokath. (Please refer to my response to question 19). This may or may not be the view shared by other users. So in the study that I am planning we have a special case report form to collect data on this aspect	
		Expert #6 One has to be a bit selective. Should be avoided in stone formers. We had a patient who formed stones in the kidney during the follow up	
		Expert #7	
		Expert #8	
		Expert #9	

NICE National Institute for Health and Care Excellence

External Assessment Centre correspondence log

GID MT569 Memokath Guidance Update

The purpose of this log is to show where the External Assessment Centre relied in their assessment of the topic on information or evidence not included in the company's original submission. This is normally where the External Assessment Centre:

a) become aware of additional relevant evidence not submitted by the company;
b) needs to check "real world" assumptions with NICE's expert advisers, or;
c) needs to ask the company for additional information or data not included in the original submission, or;
d) needs 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 captured. The table is shared with the NICE medical technologies advisory committee (MTAC) as part of the committee documentation, and is published on the NICE website at public consultation.

#	Date	Who / Purpose	Question/request	Response received
X.	*XX/XX/XXXX*	*Who was contacted? (if an expert, include clinical area of expertise)* *Why were they contacted? (keep this brief)*	*Insert question here. If multiple questions, please break these down and enter them as new rows*	*Only include significant correspondence and attach additional documents/graphics/tables in Appendix 1, citing question number*
1.	01/04/2022	**Expert – Mr Ranan Dasgupta (Consultant Urological Surgeon)**	Have there been any changes to the clinical pathway for managing ureteric obstruction (in benign and malignant) since the original guidance for Memokath-051 stent was published in 2018?	Across the country, not really - some centres such as ours continue to offer high volume experience, but some centres also offer this at lower volume. No national registry yet.

2.			Are double-J stents still the most commonly used stent for ureteric obstruction in clinical practice, if not, which stents do you most commonly use? Does the choice of stent vary between benign and malignant ureteric obstruction?	Yes JJ stents are the commonest nationally and globally (Dasgupta et al SIU Journal 2021, can provide link to this as needed) I tend to avoid MMK in patients with stone disease if possible
3.			In your experience, does Memokath-051 stent raise any safety concerns in practice?	Long-term complications not recorded in any collated registry yet; important for any prosthesis, and similarly all hospitals have different systems for regular JJ stents also...
4.			Are there any common complications you have observed with Memokath-051 stent?	Not common complications, probably reflective of highly selective case selection in local practice
5.			If you have experience of treating patients who have had Memokath-051 stent, what has been the lifespan of the stent? Have you observed an increase or decrease in the need to replace the stent compared with other stents such as double J-stents?	Hard to answer objectively without adequate prospective data collection, aside from 'expert' subjective views, even in 2022. They can certainly last longer, but failure due to obstruction/migration can occur within months or at several years. Generally changed less often than JJ stents.
6.	01/04/2022	**Expert – Mr Priyadarshi Kumar (Consultant Urological Surgeon)**	Have there been any changes to the clinical pathway for managing ureteric obstruction (in benign and malignant) since the original guidance for Memokath-051 stent was published in 2018?	There have been no changes to the clinical pathway.

7.			In your experience, does Memokath-051 stent raise any safety concerns in practice?	No.
8.			Are there any common complications you have observed with Memokath-051 stent?	One patient had bladder symptoms despite Memokath being used instead of DJ stent for this indication.
9.			If you have experience of treating patients who have had Memokath-051 stent, what has been the lifespan of the stent? Have you observed an increase or decrease in the need to replace the stent compared with other stents such as double J-stents?	They have lasted longer than a year at least.
10.	01/04/2022	**Expert – Mr Stuart Graham, (Director of Endourology, Stone & Laser Surgeon)**	Have there been any changes to the clinical pathway for managing ureteric obstruction (in benign and malignant) since the original guidance for Memokath-051 stent was published in 2018?	Our paper demonstrated that patient selection was key to this, especially in benign obstructive disease. We also feel that a material risk discussion, including reconstructive options should happen in this group of patients.
11.			Are double-J stents still the most commonly used stent for ureteric obstruction in clinical practice, if not, which stents do you most commonly use? Does the choice of stent vary between benign and malignant ureteric obstruction?	Hydrodynamically, wall stents such as the Memokath are a better device but are costly. the abiding majority of stents are used in the short term, and a JJ stent, which is easy to put in and remove, and is cheap, is the device of choice. Often , I find obstructive length and the ability to dilate the ureter up to 14ch are the 2 main factors in long term obstructive groups (malignancy, RPF, etc) to choose Memokath.

12.			In your experience, does Memokath-051 stent raise any safety concerns in practice?	There are rare cases of fistulae - *but these are extremely rare!*
13.			Are there any common complications you have observed with Memokath-051 stent?	Migration is the main one. The double ended devices are better. poor patient selection by predecessors is another.
14.			If you have experience of treating patients who have had Memokath-051 stent, what has been the lifespan of the stent? Have you observed an increase or decrease in the need to replace the stent compared with other stents such as double J-stents?	A good 5 years or so. usually, the malignancy group need a single device, and that sees them out.
15.		**Expert – Mr Chandrasekharan Badrakumar (Consultant Urologist)**	Have there been any changes to the clinical pathway for managing ureteric obstruction (in benign and malignant) since the original guidance for Memokath-051 stent was published in 2018?	There have been changes in the clinical pathway in my department since 2018. I started inserting Memokath 051 in patients with ureteric obstruction who are dependent on JJ stent in February 2020
16.			Are double-J stents still the most commonly used stent for ureteric obstruction in clinical practice, if not, which stents do you most commonly use? Does the choice of stent vary between benign and malignant ureteric obstruction?	JJ stent is the common method of relieving the benign and malignant ureteric obstruction.
17.			In your experience, does Memokath-051 stent raise any safety concerns in practice?	No safety concerns to my knowledge. The urologist inserting these stents requires adequate training by an experienced urologist who performs these procedures regularly.

18.			Are there any common complications you have observed with Memokath-051 stent?	Migration of Memokath, Ureteric obstruction above the Memokath, Encrustation, and Sepsis.
19.			If you have experience of treating patients who have had Memokath-051 stent, what has been the lifespan of the stent? Have you observed an increase or decrease in the need to replace the stent compared with other stents such as double J-stents?	It is difficult to answer this question by a number. There is no fixed time limit for this stent. However some patients expel/migrate these stents, some develop obstruction above the stent due to disease progression. I had been inserting Memokath 051 from Feb 2020. I have inserted 36 Memokath-051s. 9 of my patients have completer 2 years follow up. Of this 9 patients 1 encrusted needing removal. one developed block above the Memokath in the ureter due to disease progression. Two of the Memokath migrated. These two did not require further memokath or JJ stent insertion. They have remained stent free for over 18 months. I am presenting my experience in BAUS 2020 at Birmingham in mid-June.
20.	01/04/2022	**Expert – Mr Chandra Shekhar Biyani (Consultant Urologist)**	Have there been any changes to the clinical pathway for managing ureteric obstruction (in benign and malignant) since the original guidance for Memokath-051 stent was published in 2018?	No significant change. I think there is more awareness.
21.			Are double-J stents still the most commonly used stent for ureteric obstruction in clinical practice, if not, which stents do you most commonly use? Does the choice of stent vary between benign and malignant ureteric obstruction?	Yes, double J stents are commonly used. Some units are using metal J stent for malignant stricture occasionally.

22.			In your experience, does Memokath-051 stent raise any safety concerns in practice?	I have not used it recently. Previously I have used it and there were 2 concerns - stone formation due to exposed wires and mucosal hyperplasia due to gaps in the stent.
23.			Are there any common complications you have observed with Memokath-051 stent?	as above including migration. This can happen with any stent.
24.			If you have experience of treating patients who have had Memokath-051 stent, what has been the lifespan of the stent? Have you observed an increase or decrease in the need to replace the stent compared with other stents such as double J-stents?	I have used a small number of patients. One case I remember required a j stent through the memokath. Mostly used in terminally ill patients and a change was not required. The cost was the limiting factor. More recently we have used an Allium stent appx 20 patients. We do more extra-anatomic stents for difficult cases.
25.	01/04/2022	**Expert – Mr Tamer El-Husseiny (Consultant Urological Surgeon)**	Have there been any changes to the clinical pathway for managing ureteric obstruction (in benign and malignant) since the original guidance for Memokath-051 stent was published in 2018?	No.
26.			Are double-J stents still the most commonly used stent for ureteric obstruction in clinical practice, if not, which stents do you most commonly use? Does the choice of stent vary between benign and malignant ureteric obstruction?	Yes. Double J stents remain the most widely used current method for dealing with ureteric obstructions.
27.			In your experience, does Memokath-051 stent raise any safety concerns in practice?	No.

28.			Are there any common complications you have observed with Memokath-051 stent?	Common complications (also as quoted in the published literature) include; stent migration, stent obstruction, encrustations, UTI's
29.			If you have experience of treating patients who have had Memokath-051 stent, what has been the lifespan of the stent? Have you observed an increase or decrease in the need to replace the stent compared with other stents such as double J-stents?	The lifespan differs mainly depending on the indication for insertion (benign Vs malignant) and also depends on the careful patient selection. Benign strictures tend to do better. If inserted in the correct indication they tend to stay much longer than the normal double J stent, meaning less need for repeated changes under general anaesthesia.
30.	22/04/2022	**Expert – Mr Chandra Shekhar Biyani (Consultant Urologist)**	In practice how are patients selected for Memokath-051 over another stent or surgery? Do you think there has been a change in patient selection since the original guidance was published?	There are various factors I look at. Patients' factors (preference, previous procedures, stones etc) and disease (prognosis, site of disease etc). I feel it would be difficult to follow a specific guidance specially in patients with cancer.
31.			Would the adoption of Memokath-051 require significant changes to the current care pathway?	Yes, cost implications and training. A normal stent can be done most trainees and urologists.
32.			Does Memokath-051 require specific training? What is your experience of training and insertion of Memokath-051?	Yes. Lately i have use more Allium stents. Training is almost similar.

33.			Do you think what was stated by the experts in terms of training, patient selection, care pathway and NHS considerations in the original guidance is still valid? Are there any other factors that you think need to be considered when integrating Memokath-051 into NHS clinical practice?	I do not think so.
34.	22/04/2022	**Expert – Mr Stuart Graham, (Director of Endourology, Stone & Laser Surgeon)**	In practice how are patients selected for Memokath-051 over another stent or surgery? Do you think there has been a change in patient selection since the original guidance was published?	By definition, they must face permanent stenting - there are patients who will need a stent for the rest of their life due to malignant compression or benign compression/ stricturing and would face 6 monthly stent changes forever. also the ureter has to be dilatable up to 14 French, (i.e. an external diameter of 14mm), so intraoperatively, there are a group selected out, as this may not be possible. I think the original guidance was mainly for malignancy, the scope has moved to include benign conditions who have the same needs as the malignant group.
35.			Would the adoption of Memokath-051 require significant changes to the current care pathway?	No - but see below
36.			Does Memokath-051 require specific training? What is your experience of training and insertion of Memokath-051?	Yes. I think there should be centres to put these in - for example I place them for most of north east London. I think surgeons should be carefully trained and I would include the company in this (they have a vested interest in these insertions succeeding) - I think that this aids case selection, counselling of material risk, and discussion of alternatives, and safe placement of a potentially one-off expensive device. the balance here is the

				lack of repeat stenting, freeing more time for other procedures and for the particular patient, a cost saving due to the lack of extra visits to theatre.
37.			Do you think what was stated by the experts in terms of training, patient selection, care pathway and NHS considerations in the original guidance is still valid? Are there any other factors that you think need to be considered when integrating Memokath-051 into NHS clinical practice?	There should be appropriate training & patient selection, with a set of alternatives, including reconstruction, discussed.
38.	22/04/2022	**Expert – Mr Chandrasekharan Badrakumar (Consultant Urologist)**	In practice how are patients selected for Memokath-051 over another stent or surgery? Do you think there has been a change in patient selection since the original guidance was published?	I use Memokath only for retrograde insertion. I have strict criteria for patient selection. All the cases are discussed in the department Endo Urology MDT before offering Memokath. There has not been any change since the original guidance
39.			Would the adoption of Memokath-051 require significant changes to the current care pathway?	Yes. Patient selection is important.
40.		**Expert – Mr Stuart Graham, (Director of Endourology, Stone & Laser Surgeon)**	Does Memokath-051 require specific training? What is your experience of training and insertion of Memokath-051?	Yes. I did the workshop. I visited the Mentors place to understand the setup. My mentor supervised me doing the cases for the first 5 in my hospital.

41.			Do you think what was stated by the experts in terms of training, patient selection, care pathway and NHS considerations in the original guidance is still valid? Are there any other factors that you think need to be considered when integrating Memokath-051 into NHS clinical practice?	It is pretty much the same as said in the original guidance.
42.	28/04/2022	**Expert – Mr Stuart Graham, (Director of Endourology, Stone & Laser Surgeon)**	The monthly risk of unplanned stent replacement for Memokath was estimated as 1.4% in the original guidance. We now have new evidence from Bier, Khoo and Forster and this results in an estimated monthly probability of unplanned stent replacement as 1.8%. Do you think this is a reasonable estimate?	Yes, that's a reasonable estimate, probably related to more benign work involved.
43.	28/04/2022	**Expert – Mr Chandrasekharan Badrakumar (Consultant Urologist)**	The monthly risk of unplanned stent replacement for Memokath was estimated as 1.4% in the original guidance. We now have new evidence from Bier, Khoo and Forster and this results in an estimated monthly probability of unplanned stent replacement as 1.8%. Do you think this is a reasonable estimate?	I have read these 3 articles (Bier 2017 Scandinavian Journal, Forster 2021 J. Endourol and Koo 2021 J. Endourol). They are retrospective studies. Forster's paper does not give any information about patient selection and it is not a planned data collection. There were 19 patients that had primary memokath insertion (No stent 16, Nephrostomy 3). More this paper is a 5 year follow up. Whereas Koo and Bier are Could you elaborate on how the monthly risk of unplanned stent replacement for Memokath was estimated in 2018 and now? It will help me answer your question.
44.	03/05/2022	**Expert – Mr Chandrasekharan Badrakumar (Consultant Urologist)**	Thanks for your response. To answer your question, in the original guidance, the total number of stent replacements were divided by the total number of patient months from the nine studies to derive a monthly probability of 1.4% per month,	

			which was determined for use in the model's base case. The EAC included the three studies (Bier 2017, Khoo 2021 and Forster 2021) along with the nine studies and estimated a monthly probability of 1.8% for Memokath.	
45.	28/04/2022	**Expert – Mr Chandra Shekhar Biyani (Consultant Urologist)**	The monthly risk of unplanned stent replacement for Memokath was estimated as 1.4% in the original guidance. We now have new evidence from Bier, Khoo and Forster and this results in an estimated monthly probability of unplanned stent replacement as 1.8%. Do you think this is a reasonable estimate?	I would say that should be OK.
46.	12/05/2022	**Company**	You mentioned that there is currently a study in the developmental stage for Memokath-051 double cone stent and that two centres have agreed to take part in the study. Do you know if this will be a UK based study? Are the centres NHS or private?	The under development study is based in UK and all the centers participating in the study to the best of our knowledge are NHS centers. We know that they are waiting now for the ethical committee approvals. We before have sent the name of the lead investigator and the center name to NICE. We expect the total number of centers will be between 2 and 4 centers, all NHS centers.
47.	12/05/2022	**Expert – Mr Chandrasekharan Badrakumar (Consultant Urologist)**	In the cost model, after stent insertion, Norfloxacin has been used as the post op medication. Is this still the case? We ask this because Norfloxacin is no longer listed in the BNF. Is it still available in the UK?	I do not use Norfloxacin in my practice. I use Co Amoxiclav 625mgs.

			If not what is the alternative post op drug used?	
48.			An assumption has been used in the original guidance that double-J stents have a planned replacement every 6 months and there was no risk of an unplanned stent exchange. Is this assumption still valid?	Not correct. Double J stent has lower risk of unplanned stent exchange compared to Memokath.
49.			Please see the information below regarding between group differences (highlighted in blue) in a couple of studies, NICE would like to know if you think these differences are likely to affect stent outcomes. Two studies had between-group differences at baseline. Bier et al. 2017 had statistically significant ($p<0.05$) differences for the presence of renal failure and causation (benign/malignant) of ureteral strictures. Moreover, concomitant urinary diseases (such as stones or prostate enlargement) were not recorded. Choi et al. 2019 had between-group differences for baseline stricture length and	Bier et al. 2017 – Retrospective study, 18 patients (14%), the length of the inserted stent was not documented. 34 (27%) were lost to follow-up. His data was on over all renal function based on EGFR < 60 Whereas Agarwal et al 2008, BJU had noted DMSA scan split renal function of <15% on the

			prior radiation therapy that were statistically significant (p<0.05).	affected side is associated with poor outcomes. But this has not been replicated in other UK series including my experience. Choie et al 2019 experience is retrospective and not replicated in UK studies.
50.			A couple of the studies were conducted outside of the UK: Germany (Bier et al. 2017) and South Korea (Choi et al. 2019) Do you think the results are likely to be less generalizable to a UK NHS setting?	Yes. Retrospective series have variable patient selection criteria.
51.			Do you think a multi-centre prospective RCT conducted in the UK which assesses stent functionality, complication rate and patient reported outcomes is viable and ethical in the patient population of interest?	Multi-centre prospective RCT is the gold standard but not feasible for the following reasons: Randomisation, ethical issues, unachievable sample size, variable background condition causing stricture that affect over all outcome of stent and patient quality of life.
52.			Do you know if the BAUS registry is still used and relevant for collecting data for Memokath?	There is no BAUS registry for long-term stents.

53.			Two included studies were conducted in the UK they were conducted in the following sites: 1. Royal London Bart's Health NHS Foundation Trust 2. Imperial Endourology, Imperial College Healthcare NHS Trust, Charing Cross Hospital In what way are practices likely to differ to these sites across the UK? Do you think the results from these sites would be generalisable to your current practice?	The definitions are not standardized. These studies are retrospective. Patient selection is variable. So these results are not generalizable.
54.			Below are the complication rates for Memokath-051 identified from the studies, is this what you have seen in practice and do they raise any concerns? See appendix 1 for table.	Stent migration is still the commonest complication. Next commonest complication is obstruction. The percentage of these complications is widely variable between the studies. This in itself indicates the unreliability of the retrospective nature of the study, poor/not standardised patient selection, variable definition of the complication and varied follow up duration. Hence these data are not generalizable.
55.	12/05/2022	**Expert – Mr Chandra Shekhar Biyani (Consultant Urologist)**	In the cost model, after stent insertion, Norfloxacin has been used as the post op medication. Is this still the case? We ask this because Norfloxacin is no longer listed in the BNF. Is it still available in the UK?	No, we do not use it routinely.

			If not what is the alternative post op drug used?	
56.			An assumption has been used in the original guidance that double-J stents have a planned replacement every 6 months and there was no risk of an unplanned stent exchange. Is this assumption still valid?	What do you mean by an unplanned stent exchange? We do have risk from the repeated anaesthesia as well.
57.	12/05/2022	**Expert – Mr Priyadarshi Kumar (Consultant Urological Surgeon)**	In the cost model, after stent insertion, Norfloxacin has been used as the post op medication. Is this still the case? We ask this because Norfloxacin is no longer listed in the BNF. Is it still available in the UK? If not what is the alternative post op drug used?	Norfloxacin is not routinely used post-operatively, we only tend to give prophylactic antibiotics a time of surgery just as for any other endoscopic procedure.
58.			An assumption has been used in the original guidance that double-J stents have a planned replacement every 6 months and there was no risk of an unplanned stent exchange. Is this assumption still valid?	The duration of conventional stent duration is quite variable as these cases will tend to be quite complex. There may be cases where stents may not last that long in some cases – perhaps even just a few months. Other cases stents may last longer upto 12 months however they may be a cohort having Memokath due to stent symptoms.

59.	12/05/2022	**Expert – Mr Tamer El-Husseiny (Consultant Urological Surgeon)**	Please see the information below regarding between group differences (highlighted in blue) in a couple of studies, NICE would like to know if you think these differences are likely to affect stent outcomes. Two studies had between-group differences at baseline. Bier et al. 2017 had statistically significant ($p<0.05$) differences for the presence of renal failure and causation (benign/malignant) of ureteral strictures. Moreover, concomitant urinary diseases (such as stones or prostate enlargement) were not recorded. Choi et al. 2019 had between-group differences for baseline stricture length and prior radiation therapy that were statistically significant ($p<0.05$).	Benign strictures generally perform better with those stents as compared to the malignant strictures (less disease progression, longer life expectancy). Active stone disease should be a contraindication to using the memokath stent (due to the increased risk of stent encrustation).
60.			A couple of the studies were conducted outside of the UK: Germany (Bier et al. 2017) and South Korea (Choi et al. 2019) Do you think the results are likely to be less generalizable to a UK NHS setting?	Don't see why the results could not be generalized to the UK population.
61.			Do you think a multi-centre prospective RCT conducted in the UK which assesses stent functionality, complication rate and patient	Of course that would be of great value, but such a RCT has been extremely difficult to design and perform given the significant heterogenicity of the patient group. In addition,

			reported outcomes is viable and ethical in the patient population of interest?	randomisation will be extremely difficult, as the indication could sometimes be different. So it will be very challenging to deliver such a trial. However, a prospective national stent registry might provide a lot of the required information.
62.			Do you know if the BAUS registry is still used and relevant for collecting data for Memokath?	Not in use and did not include the metallic stents.
63.			Two included studies were conducted in the UK they were conducted in the following sites: 3. Royal London Bart's Health NHS Foundation Trust 4. Imperial Endourology, Imperial College Healthcare NHS Trust, Charing Cross Hospital In what way are practices likely to differ to these sites across the UK? Do you think the results from these sites would be generalisable to your current practice?	The patient selection criteria from both units were different therefore the results might vary.
64.			Below are the complication rates for Memokath-051 identified from the studies, is this what you have seen in practice and do they raise any concerns?	These are real world data that do not raise any particular concern. Patient groups are extremely heterogenous and the patient selection criteria is different from one study to

			See appendix 1 for table.	another, and hence the differences in outcomes.
65.			In the cost model, after stent insertion, Norfloxacin has been used as the post op medication. Is this still the case? We ask this because Norfloxacin is no longer listed in the BNF. Is it still available in the UK? If not what is the alternative post op drug used?	Co-amoxicalv or Ciprofloxacin
66.			An assumption has been used in the original guidance that double-J stents have a planned replacement every 6 months and there was no risk of an unplanned stent exchange. Is this assumption still valid?	Not really, there is always a risk that the planned 6 monthly JJ stent change might have to be done ealier should the stent obstruct, or should the patient be experiencing complications such as recurrent UTI's.
67.	12/05/2022	**Expert – Mr Stuart Graham, (Director of Endourology, Stone & Laser Surgeon)**	Please see the information below regarding between group differences (highlighted in blue) in a couple of studies, NICE would like to know if you think these differences are likely to affect stent outcomes. Two studies had between-group differences at baseline. Bier et al. 2017 had statistically significant ($p<0.05$) differences for the	I doubt these will make a huge difference in outcomes.

			presence of renal failure and causation (benign/malignant) of ureteral strictures. Moreover, concomitant urinary diseases (such as stones or prostate enlargement) were not recorded. Choi et al. 2019 had between-group differences for baseline stricture length and prior radiation therapy that were statistically significant ($p<0.05$).	
68.			A couple of the studies were conducted outside of the UK: Germany (Bier et al. 2017) and South Korea (Choi et al. 2019) Do you think the results are likely to be less generalizable to a UK NHS setting?	However, it is often the indications that are different. If these are corrected for, the differences may be less of an issue.
69.			Do you think a multi-centre prospective RCT conducted in the UK which assesses stent functionality, complication rate and patient reported outcomes is viable and ethical in the patient population of interest?	I think this would be extremely difficult ethically.
70.			Do you know if the BAUS registry is still used and relevant for collecting data for Memokath?	Not relevant.

71.			Two included studies were conducted in the UK they were conducted in the following sites: 5. Royal London Bart's Health NHS Foundation Trust 6. Imperial Endourology, Imperial College Healthcare NHS Trust, Charing Cross Hospital In what way are practices likely to differ to these sites across the UK? Do you think the results from these sites would be generalisable to your current practice?	I think they are generalizable. I was involved in study 1 (Barts) – the indications discussions with patients over material risk and alternatives remain key, so they are relatively generalizable – bearing in mind these centres do a lot of memmokaths, and others may do very small numbers.
72.			Below are the complication rates for Memokath-051 identified from the studies, is this what you have seen in practice and do they raise any concerns? See appendix 1 for table.	Migration may have been mitigated by double ended devices. The other complications are minor (UTI) or less than a jj stent is likely to see (remember there is a different timeframe for encrustation, for example. So no.
73.			In the cost model, after stent insertion, Norfloxacin has been used as the post op medication. Is this still the case? We ask this because Norfloxacin is no longer listed in the BNF. Is it still available in the UK? If not what is the alternative post op drug used?	I give prophylactic antibiotics at the time of insertion - either gentamicin or amikacin, or I am guided by culture results. I do not think there is a place for Norfloxacin.

74.			An assumption has been used in the original guidance that double-J stents have a planned replacement every 6 months and there was no risk of an unplanned stent exchange. Is this assumption still valid?	There is never no risk of an unplanned stent exchange - sepsis, migration, dysfunction, and in some cases, stent symptoms, may all lead to an unplanned exchange of the JJ stent.

Insert more rows as necessary

Appendix 1.

During correspondence with the company and experts, additional information is sometimes included as file attachments, graphics and tables. Any questions that included additional information of this kind is added below in relation to the relevant question/answer:

File attachments/additional information from question 54:

Bier (2017)	Choi (2019)	Diaz Romero (2018)	Elbaroni (2020)	Forster (2021)	Khoo (2018)	Khoo (2021)
Dislocation (42%) Occlusion (40%) Infection (3%)	Stent migration (14.3%) Encrustation (33.3%) UTI (9.5%) Lower urinary tract symptoms (4.8%) Persistent pain (4.8%) Persistent haematuria (4.8%)	Stent migration (35.48%) UTI (32.25%) Obstruction (25.08%)	Stent migration (26%) Early UTI (11%) Obstruction (22%)	Stent migration (36%) Failed ipsilateral upper tract drainage (27%) Obstruction (14%) Encrustation (11%) Lost renal function (2%)	Stent migration (20%) Obstruction (11%)	Stent migration (16.7%) Obstruction (43.8%)

GID-MT569 Memokath Guidance Update Company Meeting – minutes – 22.04.2022

Introductions and roles:

KiTEC:

- Lina Manounah – Health Technology Assessor - project lead (apologies)
- Abdinasir Isaaq – Health Technology Assessor – project lead
- Murali Kartha – Senior Health Economist
- Mariusz Grzeda – Medical Statistician
- Babak Jamshidi – Medical Statistician
- Jo Boudour – Project Manager
- Anna Barnes – KiTEC Director

NICE:

- Amy Crossley – Technical Adviser
- Rebecca Brookfield – Technical Analyst

Company:

- Ossama Abuldahab – Medical Director, Pnn Medical

Questions for the company:

- **Can we double-check that there have been no changes to the technology since MTG35 was published in 2018?**
- OA – there has been no change to the technology since 2018.
- **Is Double J Stent still the main comparator?**
- OA – yes, the main comparator is still Double J stent.
- MK – should we do analysis on other stents as well?

- OA - there is also Allium and Resonance but Double J is the main competitor.
- MK – do you think the evidence has changed for Memokath?
- OA – no, nothing has changed in the market, its use or in the literature.
- MK – are you aware of the Forster et al, 2021 paper?
- AI – there is one new study - Forster et al, (2021) which talks about 5 year follow-up. This may lead to changes in the health economic section in terms of costing.
- OA - yes, I don't think this paper should affect the health economics of the MK051 because the study concludes that the functionality of the stent is of good value but the choice of the right patient is important.
- OA – in our literature, we state there is no need to remove Memokath unless there are complications. Our basic indication is not to remove the stent unless there is a complication, just arrange a follow-up and if there is a complication remove it, otherwise keep it in.
- OA – NICE decided to use three years as a guide, but there is no literature to support this.
- MK – the cost model shows replacements occurring from two years onwards.
- OA – replacements may happen after two years if there are complications.
- OA – there are records of patients successfully functioning up to eight years with Memokath. We recommend inserting the stent, do a follow-up every six months and if it's functioning, leave it alone.
- RB – the company had mentioned an ongoing or planned study in the UK. We will get in touch with the expert you have provided details of. Do you have any further information at this point?
- OA – Yes, the study for the Memokath double cone stent. The clinician working on this is including quality of life as a primary endpoint. We will be funding 16-20% of the study and the clinician is trying to find other funds for the rest. Two centres have agreed to participate and he is trying to convince others to join. They are currently seeking ethical approval.

Future correspondence and EAC correspondence log:

- RB – are you happy for us to pass on your contact details to the EAC if they have follow-up questions?
- OA – yes, this is fine.
- RB – all correspondence will be included in a correspondence log which will be published, same as the assessment report process.
- RB – please ensure you alert the EAC if any of the information is confidential, so it can be removed from the correspondence log.

Next steps and AOB:

- RB – the EAC will conduct their evaluation and put together the report. The final report will be sent to you by NICE on 19th May.
- RB – the guidance recommendations will either stay the same or there may be some amendments following the MTAC meeting.
- JB – could NICE send us the contact details for the expert advisers?
- RB – yes, we will send these onto you.

NICE National Institute for Health and Care Excellence

National Institute for Health and Care Excellence

Medical Technologies Evaluation Programme

Information request from the company

MTEP review of MTG35 Memokath-051 stent for ureteric obstruction

Review of MTG35 Memokath-051 stent for ureteric obstruction
The original guidance was issued February 2018
The review date for this guidance is April 2021

Company Update

1.	Changes in the technology: MTG35 was on Memokath-051 stents
a.	Is the technology still available to the NHS in the UK? Yes
b.	If the technology has changed, what it the latest current version and when was this model first marketed in the UK? Please provide technical specifications which show the differences. No new versions since the original guidance
c.	Does the new model perform the same function and use the same mode of action as the technology in MTG35 No new models

d.	Does the new model have a new CE mark? No new models	
e.	Has the cost of the technology changed since the original guidance? Please give details (this can be kept commercial-in-confidence). The cost of the technology did not change	
2	Is the company aware of any new clinical evidence on the use of Memokath-051 available since the original evaluation (i.e. after 26/04/2014) If new evidence is available, please give brief details, a reference for published evidence or a title and one line description for unpublished evidence – please complete a form in appendix 1 for each piece of unpublished evidence.	**1. The Memokath-051 Stent for the Treatment of Ureteric Obstruction: A NICE Medical Technology Guidance** Emily Eaton Turner [1], Michelle Jenks [2], Rachael McCool [2], Chris Marshall [2], Liesl Millar [3], Hannah Wood [2], Alison Peel [2], Joyce Craig [2], Andrew J Sims [4 5] https://pubmed.ncbi.nlm.nih.gov/29616460/ this is an article briefing the research which has been done by NICE and the results published on August 2018 **2. Expandable metallic ureteral stent: indications and results** Gianluca Sampogna 1, Angelica Grasso 1, Emanuele Montanari 2 https://pubmed.ncbi.nlm.nih.gov/29595037/ this is an article reviewing 20 studies made about the metal stents (MK051 included) and concluding the need for more clinical evaluations published in March 2018 **3. A systematic review of long-duration stents for ureteral stricture: which one to choose?** Mariela Corrales 1 2, Steeve Doizi 1 2, Yazeed Barghouthy 1 2, Hatem Kamkoum 1 2, Bhaskar Somani 3, Olivier Traxer 4 5 https://pubmed.ncbi.nlm.nih.gov/33386951/ This is a systematic review on 35 studies discussing the results of Memokath, Uventa, Resonance and Allium metal stents. They concluded that the metal stents are a suitable option for treatment of chronic benign and malignant obstruction of ureter compared to JJ Published on January 2021 **4. The Fate of Ureteral Memokath Stent(s) in a High-Volume Referral Center: An Independent Long-Term Outcomes Review** Luke R Forster 1, Laura Watson 2, Charles E Breeze 3, Antonina Di Benedetto 1, Stuart Graham 1, Prasad Patki 1, Anup Patel 1 https://pubmed.ncbi.nlm.nih.gov/32762263/ this is a review for results of 100 patient received 162 stents after 5 years. They concluded that MK051 stents had optimal utility in management on malignant ureteric obstruction and stressed on pateint selection is important to have good outcome and avoid comlications

		published on September 2020 **5. Application of metallic ureteral stents in gynecological malignancies: a literature review** Qianyu Kang 1, Fengze Jiang 2, Yang Yu 1, Bo Yang 1 https://pubmed.ncbi.nlm.nih.gov/30793634/ this is follow up of three types of metallic stents in treatment of ureteric obstruction due to gynaecological origin. They mentioned that relief of obstruction for MK051 is over 90% but migration is high (did not mention numbers) published on February 2020 **6. Impact of Thermo-Expandable Memokath Ureteral Stent on Renal Function in the Management of Ureteroileal Anastomotic Stricture** Arkadiusz Miernik 1, Rodrigo Suarez-Ibarrola 1, Andreas Bourdoumis 2, Noor Buchholz https://pubmed.ncbi.nlm.nih.gov/30196306/ they treated 6 pateints with MK051 and followed effect on GFR. They concluded that MK is safe and minimal invasive long term option to preserve GFR. Published on September 2018

3	Is the company aware of any adoption or usage data (such as audit) from the NHS or elsewhere? Please give details where possible, this can be kept commercial-in-confidence as required.	No adoptions

4	Does the company have a list of NHS users? If so, could you please append a list to this submission, this can be kept commercial-in-confidence as required	Yes attached.
5	Has the technology added new indications or is now used in new applications not covered by the original guidance? If so, please give details.	No new indications

Additional information

6	Any other relevant information supporting the use of the technology.	

Declaration

Company representative:	Dr. Ossama Abuldahab
Position:	Medical director
Date:	24/52021

Appendix 1

Unpublished study details	
Should this study be seen as: publicly available, academic-in-confidence, commercial-in-confidence? Is there a planned publication date?	
Study details [e.g. Trial code if registered as a clinical trial, authors, title, details of funding]	
Design [e.g. was it randomised, was there a control group or comparator technology, was it a post-marketing study]	
Assigned interventions [how was the technology used, how often]	
Participants [how many people were in the study, how were they selected, which indication did they have, which setting were they in e.g. hospital, GP etc]	
Follow-up period	
Primary outcome [what was the main symptom or parameter measuring the effect of the technology]	
Secondary outcome(s) [any other symptoms, parameters measured]	
Key results – efficacy	
Key results – safety [were there any side effects or adverse events]	
Information source [e.g. webpage or link to details of the study, if available]	
Any other comments	

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