NICE National Institute for Health and Care Excellence

NICE guidance

Optilume for treating recurrent bulbar urethral strictures

Medical technologies guidance
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Your responsibility

This guidance represents the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, healthcare professionals are expected to take this guidance fully into account, and specifically any special arrangements relating to the introduction of new interventional procedures. The guidance does not override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

All problems (adverse events) related to a medicine or medical device used for treatment or in a procedure should be reported to the Medicines and Healthcare products Regulatory Agency using the Yellow Card Scheme.

Commissioners and/or providers have a responsibility to implement the guidance, in their local context, in light of their duties to have due regard to the need to eliminate unlawful discrimination, advance equality of opportunity, and foster good relations. Nothing in this guidance should be interpreted in a way that would be inconsistent with compliance with those duties. Providers should ensure that governance structures are in place to review, authorise and monitor the introduction of new devices and procedures.

Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should assess and reduce the environmental impact of implementing NICE recommendations wherever possible.

Contents

1 Recommendations

1.1 Optilume is recommended as an option to treat recurrent bulbar urethral strictures in adults only if comparative data is collected on:

- patient-reported outcome measures
- reintervention rates.

1.2 Find out details of required outcomes in the section on further research.

Why the committee made these recommendations

Optilume done in an outpatient setting could reduce the waiting times for treatment of recurrent bulbar urethral strictures. The comparative clinical evidence shows that Optilume is effective in the short term (up to 2 years). But how effective and safe it is in the long term (up to 5 years) compared with standard endoscopic management is uncertain. So, more long-term data collection is needed on retreatment rates and patient-reported outcomes.

The cost analysis shows that Optilume is cost saving at 5 years compared with standard care (urethral dilatation, urethrotomy and urethroplasty). The uncertainty about the likelihood of recurrence in the long term limits the reliability of the longer-term cost savings.

2 The technology

Technology

2.1 Optilume is a urethral balloon coated with paclitaxel (3.5 microgram/ mm^2). It is indicated for managing urethral stricture disease in 'adult males'. It is designed to be used as a drug-coated dilation balloon for a urethral stricture that is 3 cm or less in length.

2.2 Optilume is available in 6 sizes (3 cm and 5 cm length versions, both in 3 different diameters). It is passed over a guidewire under direct vision with or without fluoroscopy, and positioned along the length of the stricture. The balloon is then inflated with a provided pressure inflation device, using saline or water. The inflated device is kept in place for a minimum of 5 minutes, at the recommended pressure, to dilate the urethral stricture and allow uptake of paclitaxel. The pressure is measured in atmospheres, as per instructions for use.

2.3 Optilume urethral drug-coated balloon received a CE mark in September 2020 as a class 3 medical device.

Care pathway

2.4 Current treatment options for recurrent bulbar urethral strictures include endoscopic procedures, urethral dilatation, direct visual internal urethrotomy and urethroplasty. The choice of treatment is considered by a multidisciplinary team and is dependent on patient and clinician choice, and clinician expertise. People having urethroplasty in the UK have often had several previous endoscopic procedures.

2.5 Optilume is intended to be an additional option for treating recurrent strictures that could delay or prevent the need for the more invasive urethroplasty surgery.

Innovative aspects

2.6 Optilume combines balloon dilation of the urethra to widen the stricture with paclitaxel delivered to the tissue of the stricture. The aim of the paclitaxel is to prevent new tissue growth and reduce scar formation.

Intended use

2.7 Optilume is intended as a second-line treatment for urethral strictures in people who have had at least 1 previous endoscopic procedure that has failed. The technology is used by trained consultants in urology, urology trainees and urology nurse specialists. It can be done using local anaesthesia as a day case or in an outpatient setting.

Costs

2.8 Optilume is a single use device and costs £1,350 per unit (excluding VAT).

More details about Optilume are available on the company's website.

3 Evidence

NICE commissioned an external assessment centre (EAC) to review the evidence submitted by the company. This section summarises that review. Full details of all the evidence are in the project documents on the NICE website.

Clinical evidence

The main clinical evidence comprises the 3 ROBUST studies, 1 of which is a randomised controlled trial

3.1 The EAC included 4 publications, 1 unpublished trial report and 10 abstracts as evidence. All publications and abstracts related to 3 studies (ROBUST 1, ROBUST 2 and ROBUST 3). ROBUST 3 is an ongoing randomised controlled trial comparing Optilume with standard endoscopic management (direct visual internal urethrotomy or dilatation). ROBUST 1 and ROBUST 2 were single-arm non-comparative open-label studies. The ROBUST studies have included a total of 196 people, of which 148 have had Optilume. Fourteen studies identified by the company were excluded by the EAC because they did not include Optilume. For full details of the clinical evidence, see section 4 of the assessment report in the supporting documentation.

ROBUST 3 is most relevant to the decision problem

3.2 ROBUST 3 (n=127; 79 randomised to Optilume and 48 to standard endoscopic management) was most relevant to the decision problem. It is an ongoing multicentre single-blind randomised controlled trial being done in the US and Canada. It becomes open label 6 months after randomisation. Then, people are given the choice to cross over to the Optilume group if they have confirmed stricture recurrence. The study includes adult men with anterior strictures 3 cm or less in length and who have had 2 or more previous endoscopic treatments. People in the intervention group had predilatation before having Optilume.

The other studies are non-comparative and at high risk of bias

3.3 ROBUST 1 (n=53) and ROBUST 2 (n=16) included Optilume but had no comparator. ROBUST 1 was done in 4 Latin American centres and ROBUST 2 was done in 5 US centres. They both included adult men with anterior urethral strictures 3 cm or less in length. People in ROBUST 1 had to have had up to 4 previous endoscopic treatments. People in ROBUST 2 had to have had 2 or more previous endoscopic treatments. The EAC concluded that, for both studies, methodological issues reduced the reliability of the findings and recruitment created the potential for selection bias. There were also inconsistencies in defining the primary outcome for follow up in ROBUST 1.

The ROBUST studies report that Optilume reduces objective outcomes related to stricture recurrence

3.4 In ROBUST 3, compared with standard care, Optilume significantly improved anatomical success at 6 months (74.6% compared with 26.8%) and the stricture-free outcome without repeat interventions at 1 year (83.0% compared with 22.0%; $p<0.0001$). Also, maximum flow rate and postvoid residual both improved after Optilume compared with baseline. These results were supported by findings from ROBUST 1 and 2, with similar rates reported in the 4-year follow-up data from ROBUST 1.

The ROBUST studies report that Optilume improves quality-of-life outcomes

3.5 Using the international prostate symptom score (IPSS) in ROBUST 3:

- with Optilume, there were large and sustained improvements in quality-of-life and IPSS responder-rate outcomes from baseline to 1 year
- in the control group, there was an initial large improvement at 3 months, but this started to deteriorate to near baseline levels by 1 year.

  ROBUST 1 and 2 reported a similar improvement with Optilume. This was sustained over 4 years in ROBUST 1. All ROBUST studies found a slight (but not statistically significant) improvement in the overall satisfaction domain of the

international index of erectile function with Optilume up to 1-year follow up. The Urethral Stricture Surgery-Patient Reported Outcome Measure was only reported in ROBUST 1 and 2, and decreased at 1-year follow up compared with baseline in both. This indicated an improvement in voiding symptoms and quality of life.

Optilume is safe to use

3.6 Adverse events were reported in all 3 ROBUST studies. ROBUST 1 and 3 also assessed the safety of Optilume. Urinary tract infection and acute urinary retention were the most reported adverse events. Pharmacokinetic studies found systemic exposure to paclitaxel was minimal. Clinical experts using Optilume acknowledged that there is still limited data on paclitaxel use in the urinary tract for preventing stricture recurrence. Nevertheless, they advised the device was very well tolerated with minimum side effects. Five out of 6 experts said that adverse events happening later than 30 days after the procedure would be unlikely with Optilume. The EAC acknowledged the Medicines and Healthcare products Regulatory Agency safety concerns about the ongoing use of paclitaxel-coated balloons and implantable drug-eluting stents in peripheral artery disease. The systemic paclitaxel concentration after Optilume is low and paclitaxel is primarily localised to the urethra. The EAC concluded that, based on the available evidence, Optilume causes very few adverse events and does not raise safety concerns. For full details of the adverse events, see sections 5.2 and 6 of the assessment report in the supporting documentation.

There is a lack of long-term comparative studies to confirm the long-term benefits of Optilume

3.7 The 2-year evidence showed that Optilume improved clinical and patient-reported outcomes, and is an effective treatment for recurrent bulbar urethral strictures. The results of ROBUST 1 suggested long-term efficacy at a 4-year follow up but it only included 53 people and was non-comparative. So, there is a lack of long-term comparative data. However, ROBUST 3 is ongoing and will collect 5-year follow-up data until December 2025.

Cost evidence

The company's cost modelling finds Optilume to be cost saving compared with endoscopic management

3.8 The company submitted a new analysis because none of the economic studies identified included Optilume as a comparator. A Markov model compared Optilume with endoscopic management for treating recurrent anterior urethral strictures 3 cm or less in length over a 5-year time horizon. The model was based on data from ROBUST 3. Additional clinical and cost data was taken from the OPEN trial, a randomised controlled trial comparing urethrotomy with urethroplasty with a 2-year follow up (Pickard et al. 2020). The company's base case showed a cost saving of £2,502 per person using Optilume. For full details of the cost evidence, see section 9 of the assessment report in the supporting documentation.

The company's cost model is appropriate and the EAC only made minor changes to costs of training and readmission to hospital

3.9 The EAC accepted the company's model structure, comparators, time horizon, and most of the assumptions and parameters. The EAC's initial base case was amended to 100% of day-case procedures. The clinical experts confirmed that Optilume is also being used in an outpatient setting. The EAC's base case was amended to 50% of day cases and 50% of outpatient procedures. The EAC made minor changes to the costs of training with Optilume and readmission to hospital. These changes had a small effect on the incremental cost saving. The cost saving in the EAC's base case increased to £2,510 per person using Optilume.

Stricture recurrence rate is the key cost driver

3.10 The key cost driver in the model was the probability of recurrence, and therefore the expected cost of retreatment. Cost savings were dependent on the savings from reduced repeat interventions being greater than the additional cost of treatment with Optilume when

compared with standard endoscopic procedures. The probabilistic sensitivity analysis for the EAC's base case found that 94% of the 1,000 iterations resulted in cost saving.

The EAC noted that there is some uncertainty around clinical evidence in relation to recurrence rates

3.11 The EAC noted that the clinical evidence showed that Optilume improved clinical outcomes in the shorter term. However, there was some uncertainty around the extent and duration of the improvement in the longer term and how this translated to recurrence in the model. This was related to several factors including:

- There is only 1 comparative study available for Optilume (ROBUST 3), which is ongoing.
- The study is limited to 2-year follow up, although ROBUST 1 had follow up to 4 years.
- There is not an agreed single outcome measure that defines recurrence.
- Standard endoscopic methods encompass several different procedures.

Optilume remains cost saving at 5 years when using different clinical data inputs for the probability of recurrence

3.12 The clinical experts agreed that there is not a single outcome measure for recurrence that is used consistently. Several additional scenarios using different clinical inputs for the probability of recurrence were provided. The company's and EAC's base cases used the IPSS score to indicate recurrence rates. The company included 2 additional scenarios: 1 using anatomical success from ROBUST 3 and 1 using patient-reported outcome measures from the OPEN trial. When using the EAC's base case, both scenarios decreased the cost saving from £2,510 to £1,127 and £995 respectively. The EAC included an additional scenario that explored using retreatment rates from ROBUST 3. This increased the cost saving from £2,510 to £3,340. All scenarios reported treatment with Optilume to be cost saving at 5 years.

Optilume in an outpatient setting increases cost savings

3.13 The company stated that Optilume can be done as a day case and in an outpatient setting. Its base case assumed that 50% of the procedures would be done as a day case and 50% in an outpatient setting. Based on expert advice, the EAC accepted this assumption, which resulted in a cost saving of £2,510. The EAC analysed the effect of varying the proportion of Optilume procedures done as a day case and in an outpatient setting. Results showed that increasing the proportion of day-case procedures decreased cost savings (100%, £1,877), while increasing the proportion of outpatient procedures increased cost savings (100%, £3,142).

Using endoscopic methods to retreat recurrent strictures moderately decreases cost savings

3.14 The company's model assumed people initially having Optilume or endoscopic methods would have retreatment using the same method. In practice, it is likely that people who do not have urethroplasty have a mix of sequential endoscopic treatments, including Optilume. This will depend on patient and clinician choice, and availability of resources. The EAC included an additional scenario allowing for a mix of Optilume and endoscopic procedures for retreatment. The results showed that increasing the proportion having retreatment using a standard endoscopic treatment resulted in a moderate decrease in total cost savings.

An exploratory analysis that extended the time horizon to 20 years suggests that Optilume remains cost saving

3.15 The company's base-case time horizon was 5 years. This was because there was a lack of long-term data and because the effect of Optilume would be greater in the initial years of using it. The company included an additional scenario using a 10-year time horizon and the EAC investigated the effect of a longer time horizon of 20 years. Increasing the time horizon to 20 years had a small effect on the EAC's base case, increasing the cost saving from £2,510 to £3,175. The EAC noted that, because of the lack of longer-term comparative data, the results were

uncertain.

4 Committee discussion

Clinical-effectiveness overview

The evidence shows that Optilume is effective in the short term, but the long-term benefits are uncertain

4.1 The committee noted that the clinical evidence showed Optilume to be effective in improving clinically relevant outcomes including anatomical success, peak flow rate and international prostate symptom score (IPSS) at 2 years. The single-arm study data suggested that Optilume remains effective at 4 years (unpublished data from ROBUST 1). The committee considered that the studies of Optilume seemed to be well conducted and that the results were plausible. It concluded that the results to date are promising, although long-term comparative evidence was needed to see if the short-term benefits would be sustained at 5 years.

The evidence is broadly generalisable to NHS practice

4.2 The committee had some concerns about the generalisability of the evidence to clinical practice in the NHS. None of the ROBUST studies included any centres in the UK. Optilume is proposed for second-line treatment after stricture recurrence, but people in ROBUST 3 had more than 2 endoscopic treatments before having Optilume. The clinical experts noted that this reflects NHS practice. In ROBUST 3, strictures were predilatated in the entire Optilume group and in 58% of the control group. The clinical experts confirmed that this is not standard practice for either procedure in the NHS but that using a guidewire could dilate the stricture slightly. The company stated that, from the available evidence, predilatation does not appear to have affected Optilume's effectiveness. The clinical experts also agreed that predilatation is unlikely to affect Optilume's drug delivery and the overall results of ROBUST 3. The committee concluded that the evidence is broadly generalisable to NHS practice.

Side effects and adverse events

Evidence suggests that Optilume is safe and 5-year safety data will be collected in ROBUST 3

4.3 The most common adverse events reported in the literature were urinary tract infection and acute urinary retention. Biological, haematological and serological studies in ROBUST 1 and 3 identified no significant effects on health. The external assessment centre (EAC) considered Optilume to be safe based on the evidence and expert feedback. The company stated that paclitaxel is locally delivered and washed out with urine. There is very little systemic exposure, and paclitaxel is mostly cleared within a day and cannot be detected. The company also noted that it is in the process of collecting safety data for up to 5-year follow up in ROBUST 3. The committee concluded that the data provided reasonable assurance that Optilume is safe to use and understood that longer-term safety data will be collected in ROBUST 3.

A postmarket study is planned to assess the effect of Optilume on semen characteristics

4.4 The committee acknowledged that the presence of paclitaxel in semen may potentially affect semen quality, testicular function and fertility. It queried how the clinical experts counsel people about fertility. The clinical experts advised that they tell people that there is a theoretical risk of altered semen characteristics. They explained that it is up to the person having Optilume whether to continue with the treatment. The clinical experts advise them to abstain from sexual activity for 2 weeks and use barrier contraception for 3 months. They noted that so far, this has not affected the decision making of the people who have had treatment with Optilume. A postmarket study (STREAM PMS) to assess semen characteristics after treatment with Optilume in men younger than 55 is currently enrolling participants.

Outcome measures

There is more than 1 outcome measure for recurrence, but none is used consistently

4.5 The clinical experts agreed that there is no single outcome measure for recurrence that is used consistently. ROBUST 3 is collecting both objective (anatomical success, freedom from repeat intervention, postvoid residual and maximum flow rate) and subjective outcomes for recurrence (IPSS and IPSS quality of life). The clinical experts noted that subjective symptom outcomes are the easiest way to assess whether there is a stricture. The objective outcomes need more invasive assessments. They are not measured until someone presents with symptoms. IPSS, maximum flow rates and postvoid residual outcomes can be used because they are indicators that there is reasonable bladder emptying. The clinical experts noted that IPSS is not a disease-specific patient-reported outcome for strictures but that it has relevance because strictures also affect flow rates. It assesses how bothered people are about their symptoms. The committee concluded that all the outcomes in ROBUST 3 are clinically relevant. It also concluded that the results from the ROBUST studies are in line with what the clinical experts have seen in clinical practice.

NHS considerations overview

Optilume is not widely used in the NHS, but adoption is increasing

4.6 Optilume has been available in the UK since June 2021. The company stated that 10 NHS trusts have adopted Optilume and 82 procedures have been completed. It also stated that several NHS trusts have put in a business case for it, and more NHS trusts are looking to do so. The committee concluded that there is clinical interest in, and a rise in the adoption of, Optilume within the NHS.

Optilume can reduce waiting lists for urethroplasty and relieve

pressure on the NHS

4.7 The clinical experts stated that, before the COVID-19 pandemic, waiting times for routine urethroplasty were 7 to 8 months. Waiting times are now more than 2 years. Standard endoscopic treatments are typically done as day cases under general anaesthesia, but some may incorporate a short inpatient stay. Optilume can be done more routinely in an outpatient setting under local anaesthesia. After the procedure, people empty their bladder and can go home. The clinical experts confirmed that no changes are needed to the existing infrastructure because urology units would already be set up to do flexible cystoscopy and urethrograms. Using Optilume in an outpatient setting could reduce the waiting lists substantially. The committee recognised that the NHS is under severe pressure post the pandemic. It concluded that Optilume has the potential to reduce waiting lists, and that this may not be fully captured in the cost analysis.

Equality considerations

Optilume can be used in anyone with a stricture in their bulbar urethra

4.8 The clinical experts noted that trans women, with or without gender reassignment, have a bulbar urethra. If a bulbar stricture occurs, this is managed in the same way as for cisgender men. They considered that the evidence is generalisable to this group.

Cost-modelling overview

The cost model is robust and reflects NHS practice

4.9 The EAC accepted the model structure from the company but graphically redesigned the model diagram to provide a clearer presentation of the structure. The committee agreed that the model reflected NHS practice but noted that there should be a clearer distinction between what is an event compared with a health state. The health states labelled 'cured'

have been amended to 'asymptomatic' because strictures can recur and people then move into the 'symptomatic' health state. The committee concluded that the rationale for the model was sensible and that the model structure was now clearer.

The EAC's base case assumes that the proportion of day-case and outpatient procedures with Optilume is equal

4.10 The company's base case assumed that 50% of procedures would be done as a day case and 50% in an outpatient setting. The initial EAC's base case was amended to 100% of day-case procedures. The clinical experts confirmed that Optilume is also being used in an outpatient setting. The EAC's base case was amended to 50% of day-case and 50% of outpatient procedures. The clinical experts noted that this was a reasonable assumption and that there is a high likelihood of more procedures being done in an outpatient setting in the future. The committee accepted the EAC's base-case assumption and recognised this may be a conservative estimate with a trend toward increasing outpatient procedures.

Optilume is cost saving compared with standard endoscopic methods but the evidence on recurrence rate is uncertain

4.11 The EAC's base case showed that Optilume was cost saving compared with standard endoscopic methods. The key cost driver was the probability of recurrence. Using deterministic one-way sensitivity analysis, this was the only variable that could make the base-case cost incurring at 5 years. However, the probabilistic sensitivity analysis for the EAC's base case showed that 94% of the iterations were cost saving. Scenario analysis, including using different clinical outcomes for recurrence rates, also showed that Optilume was cost saving. The committee concluded that the results were robust and suggested that Optilume is likely to be cost saving. However, long-term comparative data on recurrence is needed to improve the certainty of the cost saving associated with Optilume at 5 years and beyond.

Further research

Further research to address the long-term uncertainty should include 5-year efficacy and patient-reported outcome data

4.12 One-year data from ROBUST 3 has been published but the trial is ongoing with a 5-year follow up. The committee understood that the planned follow up will include patient-reported outcomes. But the committee also considered it important to request further evidence to be collected in the NHS. It considered that real-world evidence and observational studies are important to assess clinical and operational effectiveness alongside ROBUST 3. The committee noted that outcomes should include:

- patient-reported outcome measures including IPSS and quality of life
- objective outcome measures indicating stricture-free success such as reintervention rates.

The clinical experts noted that a large European registry has been set up to collect objective outcomes for stricture recurrence prospectively for several technologies, including Optilume. This registry includes NHS trust hospitals and NHS patients.

5 Committee members and NICE project team

Committee members

This topic was considered by NICE's medical technologies advisory committee, which is a standing advisory committee of NICE.

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

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

NICE project team

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

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