NICE advice

Optilume for anterior urethral strictures

Medtech innovation briefing
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Summary

- The **technology** described in this briefing is Optilume. It is used to treat anterior urethral strictures that need treating again because they have re-occurred after first-line endoscopic treatment.
- The **innovative aspects** are that it incorporates balloon dilation with an anti-proliferative drug called paclitaxel, which is delivered around the inside surface of the urethra during the procedure.
- The intended **place in therapy** would be as an alternative to standard care for urethral strictures.
- The **main points from the evidence** summarised in this briefing are from 1 single-arm prospective study including a total of 53 men. It shows that Optilume is safe for treating urethral strictures, and early 2-year efficacy results are encouraging.
- **Key uncertainties** around the evidence or technology are that there are no comparative studies, the evidence has limited applicability to the NHS, and longer-term evidence is needed for Optilume, including the effect of paclitaxel on the tissues.

- The **cost** of Optilume is £1,350 per unit (excluding VAT). The **resource impact** would be more than urethrotomy or dilation (£937) but less than urethroplasty (£4,300).

The technology

Optilume (Urotronic) is a drug-coated balloon indicated for treating anterior urethral strictures. The technology combines balloon dilation, to expand or widen the strictured area, with delivering an anti-proliferative drug (paclitaxel) to reduce stricture recurrence. Optilume is inserted under direct endoscopic vision (with or without fluoroscopy) and inflated under pressure. It stays inflated in position for up to 10 minutes. The balloon's inflation can be measured with a manometer, using radiography and inflation media, or with direct visualisation using cystoscopy. After the treatment has been delivered, the balloon is deflated, removed and safely disposed of.

Innovations

The company claims that Optilume is a novel treatment for urethral strictures because, as well as dilating the urethra, it directly treats the strictured urethra with paclitaxel. Paclitaxel limits the hyperactive cell proliferation and formation of fibrotic scar tissue that causes strictures to recur. The company claims that Optilume can reduce the rate of stricture recurrence and the need for retreatment (compared with standard balloon dilation or urethrotomy procedures) and reduce the need for urethroplasty, a more invasive procedure. The company also claims that Optilume is a minimally invasive procedure that may reduce operating and recovery time and is likely to have lower risks compared with more invasive treatments.

Current care pathway

Urethral stricture is a narrowing of the urethra, which restricts urine flow rate and can cause inflammation or infection. Treatment options depend on the site and length of stricture, age and general wellbeing. Treatment options include:

- Urethral dilation (widening) of the stricture using metal or plastic dilators. This is done endoscopically under local or general anaesthesia. A stricture can narrow again gradually after dilation, requiring repeat dilation.
- Urethrotomy. This is done endoscopically under general anaesthesia. About 50% of people have a successful widening of their urethral stricture after this procedure. The stricture can reform, leading to repeat procedures.

- Urethroplasty. This is offered if dilation or urethrotomy does not work. Urethroplasty is open surgery done under general anaesthesia and has a higher success rate in resolving urethral strictures, with no further treatment needed compared with existing standard endoscopic treatments.

A long course of antibiotics may be advised to prevent urine infections until a stricture has been widened.

The NICE guideline on lower urinary tract symptoms in men has been identified as relevant to this care pathway.

Population, setting and intended user

Optilume is used for treating anterior urethral strictures in adult men. The technology is intended for use in urethral strictures that need treating again after they have recurred after first-line endoscopic treatment.

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.

The company says that balloon dilation of the urethra without a drug coating is common practice in the NHS. But it offers additional training so that healthcare practitioners are fully compliant and audited for the Optilume procedure. Training is provided by the company free of charge.

Costs

Technology costs

Optilume is intended for single, one-off use and costs £1,350 per unit.

Costs of standard care

- Urethrotomy or dilation: £937 per treatment.
- Urethroplasty: £4,300 per treatment (National Schedule of Reference Costs 2017/18).

Resource consequences

The technology is not yet used in the NHS. The company says that it is talking to NHS trusts and consultant urologists about adopting Optilume as part of their standard urethral stricture

procedure.

The company says that adopting the technology will require minimal additional training and can be used in existing endoscopy settings. It claims that using Optilume could reduce the need for retreatments because urethral stricture is less likely to recur. It also claims that using the technology could be resource releasing in the NHS because of reduced bed days, operating theatre time, use of general anaesthesia, clinic appointments and ongoing treatments.

Regulatory information

Optilume is a CE marked class III medical device.

The MHRA has made recommendations on the ongoing use of paclitaxel drug coated balloons and implantable drug eluting stents in peripheral artery disease because of safety concerns.

Equality considerations

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others.

Optilume is intended for men with urethral strictures. Some people may not identify as men but have a penis. Urethral strictures become more common in people over 55. Sex, physical disability, gender reassignment and age are protected characteristics under the Equality Act (2010).

Clinical and technical evidence

A literature search was carried out for this briefing in accordance with NICE's interim process and methods statement. This briefing includes the most relevant or best available published evidence relating to the clinical effectiveness of the technology. Further information about how the evidence for this briefing was selected is available on request by contacting mibs@nice.org.uk.

Published evidence

One study including 53 men is summarised in this briefing. It was a multicentre, single-arm, prospective open-label study investigating the safety and efficacy of Optilume.

The clinical evidence and its strengths and limitations is summarised in the overall assessment of the evidence.

Overall assessment of the evidence

The evidence is limited and of low methodological quality. The study is small in terms of patient numbers and was done in the Dominican Republic and Panama. Furthermore, Optilume is intended to be used without predilation so this study has limited applicability to an NHS setting. The evidence shows that Optilume is safe for the treatment of urethral strictures and early efficacy results are encouraging. The evidence came from 1 non-comparative study. High-quality comparative research is needed to evaluate Optilume.

Mann et al. (2020)

Study size, design and location

Fifty-three adult men with recurrent bulbar strictures 2 cm or smaller with 1 to 4 prior endoscopic treatments in a multicentre, single-arm, prospective, open-label study in the Dominican Republic and Panama.

Intervention and comparator(s)

Intervention: Optilume.

Key outcomes

Forty-six men completed the 24-month follow up. The mean number of endoscopic treatments before the study was 1.7. Before Optilume treatment, predilation was done with an uncoated balloon in 59%, direct visual internal urethrotomy (DVIU) in 15%, or a combination of the 2 in 26%. There was 'functional treatment success' (defined as an improvement of at least 50% in International Prostate Symptom Score [IPSS] without retreatment) in 32 out of 46 men (70%) at 24 months. Baseline IPSS improved from a mean of 25.2 to 6.9 at 24 months ($p<0.0001$). Quality of life, flow rate, and post-void residual urine volumes improved significantly from baseline. There was no impact on erectile function. At 24 months, 39 out of 46 men (85%) had not needed a repeat intervention. There were no serious adverse events related to treatment at 2 years. There were 6 non-urinary serious adverse events but none were directly attributable to the device or procedure. In total, there were 71 adverse events, most commonly urinary tract infection (17%), fever (8%), dysuria (7%), acute urinary retention (6%) and headache (6%). Most were classified as mild (61%) or moderate (31%). Twenty-three per cent were categorised as 'possibly', 'probably', or 'definitely'

related to the procedure or device.

Strengths and limitations

This is the first study of using a paclitaxel-coated balloon for urethral strictures. Optilume is intended to be used without predilation. However in this study strictures were pretreated with uncoated balloon dilation, DVIU or both until the urethral lumen diameter increased by 50%. The funding for this study included support from Urotronic and 3 authors are consultants for Urotronic.

Sustainability

The company claims that using technology could mean fewer consumables being used than is needed in standard care (DVIU or urethroplasty, or both). There is no published evidence to support these claims.

Recent and ongoing studies

- ROBUST I pilot study. ClinicalTrials.gov identifier: NCT03014726. Status: active, not recruiting. Indication: urethral stricture. Device: Optilume. Expected completion date: December 2022. Countries: Dominican Republic and Panama.
- Re-establishing flow via drug coated balloon for the treatment of urethral stricture disease (ROBUST-II). ClinicalTrials.gov identifier: NCT03270384. Status: active, not recruiting. Indication: urethral stricture. Device: Optilume. Expected completion date: December 2022. Country: US.
- ROBUST III re-establishing flow via drug coated balloon for the treatment of urethral stricture disease (ROBUST-III). ClinicalTrials.gov identifier: NCT03499964. Status: active, not recruiting. Indication: urethral stricture. Devices: Optilume and control treatment. Expected completion date: June 2025. Countries: US and Canada.
- Re-establishing flow via drug coated balloon for the treatment of urethral stricture disease - registry study (ROBUST IV). ClinicalTrials.gov identifier: NCT03851952. Status: withdrawn (company decision). Indication: urethral stricture, urethral stricture anterior, lower urinary tract symptoms, anterior urethral stricture. Devices: Optilume. Expected completion date: December 2024. Country: Canada.

The company and experts were aware of a potential new study comparing urethrotomy with 2 control arms.

Expert comments

Comments on this technology were invited from clinical experts working in the field and relevant patient organisations. The comments received are individual opinions and do not represent NICE's view.

All experts were familiar with but none of them had used this technology before.

Level of innovation

Five experts agreed that Optilume is the first in a new class of procedures. Five experts also said that it is novel, and 4 said its safety and efficacy is not certain. One expert said the technology uses the same delivery method as endovascular drug-eluting balloons applied to the urethra. None of the experts were aware of any competing or alternative procedures available to the NHS. Two experts said that the novel aspect is the drug coating of the balloon, designed to inhibit fibrosis and reduce stricture recurrence. One noted that it falls between urethroplasty and urethrotomy. The experts were not aware of this technology being used in the NHS but 4 of them expected rapid uptake and use in the NHS.

Potential patient impact

The experts said that the procedure is less invasive than other treatments for the condition and that it can be done with local anaesthesia and does not require an overnight stay. One expert said that it can be done with local anaesthesia but it may be uncomfortable for patients. It can also reduce the number of procedures needed. Experts said that people with recurrent urethral strictures in the bulbar urethra up to 3 cm in length would particularly benefit from this procedure. One expert said that it is not suitable for longer strictures and that it has not been studied in the penile urethra in any detail. Two experts said it can be beneficial for people who do not want to undergo urethroplasty. One expert noted that there was anecdotal evidence from the US that this procedure could be used to treat urethral strictures at the level of the external urethral sphincter, which is not feasible with current treatment options.

Potential system impact

All experts agreed that this technology has the potential to change clinical outcomes. One expert said that in clinical practice people are usually offered repeat endoscopic dilation or urethrotomy. Benefits to the healthcare system include fewer invasive procedures and fewer hospital visits and follow-ups. One expert said that the operating time and recovery period can be shorter, which

could improve patient flow and so reduce NHS waiting times.

All experts agreed that this technology has the potential to be cost saving compared with current standard care. One predicted a modest cost saving only. Three experts said that the technology could reduce resource use in terms of staff, equipment, and care setting. One expert said that it would likely have a minimal impact on resources but another said that the upfront cost of the balloon may be significantly more than a simple balloon.

Three experts said that no changes were needed to clinical facilities. One noted that sometimes during balloon dilation the balloon is filled with contrast so it can be imaged to make sure the balloon is fully inflated. A radiographer and image intensifier are needed for this. Another expert said that it should be possible to do the procedure outside the operating theatre.

All experts agreed that some training will be needed for surgeons using this technology, to ensure the correct positioning of the balloon and adequate inflation. One added that it is not a difficult procedure to learn. Four experts said that the first few cases should be supervised by someone who has experience with using the technology.

Risks and adverse events include urethral bleeding, urethral rupture, urinary tract infection, dysuria and recurrent strictures. Two experts said that the risks and adverse events are similar to standard care. One said that urethral rupture can be prevented by using X-ray visualisation or endoscopic placement of a guidewire. Three experts expressed concerns about a theoretical risk of paclitaxel being released in the tissue. One noted that the amount of the drug on the balloon is not documented and there is no literature on the absorption of the drug into the blood. This expert also noted some concerns when paclitaxel has been used in angioplasty, in which it reduced the rate of stenosis but overall increased mortality. The expert expects a lower rate of absorption with this technology. The experts said the long-term effects of paclitaxel on human tissue need to be determined. One said that standard disposal protocols for biohazard products needs to be in place.

General comments

Five experts agreed that Optilume has the potential to replace current standard care. One said that it will be an additional treatment for short, recurrent strictures. Three experts noted it has the potential to replace urethroplasty for short strictures, and 2 said it could replace urethrotomy. One expert said that the lack of evidence on efficacy or safety may prevent the adoption of Optilume in the NHS.

Five experts said that this procedure will be carried out in most or all district general hospitals.

Only 1 said that it will be used in a minority of hospitals. The prevalence of urethral stricture in the UK has been estimated at between 10 in 100,000 in younger men and 100 in 100,000 in men over 65. Five experts said that a large proportion of these will be eligible for this procedure: about 4,000 to 5,000 per year.

Three experts raised issues with the usability of the technology, including the costs, restricting it to appropriate cases, and the need for X-ray control, pinhole ureteroscopes or rigid cystoscopes. One expert noted that urethral strictures can be divided into 2 categories: bulbar strictures and strictures secondary to lichen sclerosus. Strictures secondary to lichen sclerosus are less likely to be affected by the technology because of ongoing inflammatory processes.

All experts agreed that further research is needed to address the uncertainties in the evidence base. Research should include randomised controlled trials in the UK and address long-term efficacy and safety. Three experts noted that research is currently underway, and 1 expert said that decisions to adopt this technology should be made after these trails are completed.

Expert commentators

The following clinicians contributed to this briefing:

- Christopher Chapple, consultant urologist, Sheffield Teaching Hospitals NHS Foundation Trust. Did not declare any interests.
- Petros Tsafrakidis, consultant urologist, NHS Fife. Did not declare any interests.
- Wasim Mahmalji, consultant urologist, Wye Valley NHS Trust. Did not declare any interests.
- Peter Malone, consultant urological surgeon, Royal Berkshire NHS Foundation Trust. Did not declare any interests.
- Trevor J Dorkin, consultant urological surgeon, the Newcastle upon Tyne Hospitals NHS Foundation Trust. Did not declare any interests.
- Richard Hindley, consultant urologist, Hampshire Hospitals NHS Foundation Trust. Did not declare any interests.

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