NICE advice

Rezum for treating benign prostatic hyperplasia

Medtech innovation briefing
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Summary

- The **technology** described in this briefing is Rezum, which uses steam to ablate prostate tissue with the aim of improving lower urinary tract symptoms secondary to benign prostatic hyperplasia.
- The **innovative aspects** are that the company claims that it is quicker to do than existing treatments and can be done as a day case.
- The intended **place in therapy** would be as an alternative to current standard care in people with lower urinary tract symptoms presumed to be secondary to benign prostatic hyperplasia.
- The **main points from the evidence** summarised in this briefing are from 4 studies (blinded control trial, 1 single-arm pilot study and 2 retrospective observational studies) including 522 adults in health centres in the US, Dominican Republic, Czech Republic, and Sweden. They show that Rezum is effective at improving prostate symptom scores.
- **Key uncertainties** around the evidence or technology are that Rezum has not been compared directly with either transurethral resection of the prostate or alternatives in current NHS practice.
- The **cost** of Rezum is £14,500 for a portable generator and £900 per disposable delivery device (excluding VAT). The **resource impact** would be additional to current practices, with potential cost savings if its use allows people to be treated more quickly in a day-case setting, or with a reduced rate of adverse events.

The technology

Rezum (NxThera Inc) is used for treating lower urinary tract symptoms (LUTS) presumed to be secondary to benign prostatic hyperplasia (BPH). The technology uses the heat from radiofrequency-generated water vapour to ablate excess prostate tissue with the aim of relieving symptoms.

The technology consists of a portable generator and a single-use disposable delivery device. The delivery device is introduced into the body through the urethra and is guided to the prostate using a telescopic lens, which can be placed within the delivery device. Radiofrequency energy is produced by the generator and applied to an induction coil in the delivery device. This heats up a controlled amount of water outside of the body to generate vapour or steam. The steam is then delivered to the prostate, where it is used to ablate obstructive prostate tissue. The procedure lasts up to 20 minutes and can be done as day-case surgery.

Rezum is indicated for treating prostates with a median lobe or elevated central zone tissue, and prostate volumes greater than 30 cm^3.

Innovations

Rezum differs from other prostate ablation techniques because it uses water vapour thermal energy. It does not use a laser and is designed to be used to treat both the median lobe and an enlarged central zone.

Current care pathway

Current management for BPH is outlined in NICE's guideline on lower urinary tract symptoms in men and in the NICE Pathway on lower urinary tract symptoms in men. Surgical options recommended by NICE include:

- monopolar or bipolar transurethral resection of the prostate (TURP; see NICE medical technologies guidance on the TURis system for transurethral resection of the prostate)
- transurethral vaporisation of the prostate (TUVP)
- holmium laser enucleation of the prostate (HoLEP)
- transurethral incision of the prostate (TUIP; only in prostates smaller than 30 ml)
- open prostatectomy (only in prostates larger than 80 ml).

Minimally invasive treatments such as transurethral needle ablation (TUNA), transurethral microwave thermotherapy (TUMT), high-intensity focused ultrasound (HIFU), transurethral ethanol ablation of the prostate (TEAP) and laser coagulation are not recommended by NICE.

NICE medical technologies guidance recommends:

- The UroLift prostatic urethral lift system as an alternative day-case treatment option for LUTS caused by BPH in men aged 50 years and older, who have a prostate of less than 100 ml without an obstructing middle lobe.
- The GreenLight XPS for treating benign prostatic hyperplasia in high-risk patients, defined as those with an increased risk of bleeding, or prostates larger than 100 ml, or with urinary retention.

NICE has published interventional procedures guidance on transurethral water vapour ablation for lower urinary tract symptoms caused by benign prostatic hyperplasia, which recommends that the procedure may be used with standard arrangements for clinical governance, consent and audit.

Population, setting and intended user

The technology is indicated for men with a prostate volume of 30 cm^3 or greater. It would be used in day-case settings and patients would usually be discharged on the same day as the procedure. The technology would be used by consultant urological surgeons.

Costs

Technology costs

The portable generator costs £14,500, and has an estimated lifespan of 5 to 7 years. Each disposable delivery device costs £900.

Costs of standard care

Standard care is currently TURP with increasing use of alternatives that do not affect sexual function or can be done as day cases. In the NICE medical technologies guidance on GreenLight XPS for BPH, the cost of consumables for TURP is estimated to be £190.50.

Resource consequences

Rezum would be an additional cost compared with TURP. There is potential for the use of Rezum to lead to cost savings, if the procedure allows for faster treatment as a day case and if the rate of adverse effects is lower.

Table 1 Breakdown of procedure costs per patient from company

	Rezum
Staff and hospital costs	£263.33
Capital costs	£20.70
Consumables cost	£900.00
Total	**£1,184.03**

The technology is currently in use in 5 NHS hospitals in England, and is due to be implemented in a further 15.

Regulatory information

Rezum is a CE-marked class IIb medical device

Equality considerations

NICE is committed to promoting equality, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. In producing guidance and advice, NICE aims to comply fully with all legal obligations to: promote race and disability equality and equality of opportunity between men and women, eliminate unlawful discrimination on grounds of race, disability, age, sex, gender reassignment, marriage and civil partnership, pregnancy and maternity (including women post-delivery), sexual orientation, and religion or belief (these are protected characteristics under the Equality Act 2010).

No equality issues were identified.

Clinical and technical evidence

A literature search was carried out for this briefing in accordance with the 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

Four studies are summarised in this briefing: 1 blinded control trial, 1 single-arm pilot study, 2 retrospective observational studies, involving a total of 522 men with LUTS presumed secondary to BPH.

Table 2 summarises the clinical evidence as well as its strengths and limitations.

Overall assessment of the evidence

The evidence includes 1 blinded controlled trial involving multiple centres in the US (Rezum II trial). This trial intends to follow up patients for 5 years, and the most recent published findings at 3 years, McVary et al. (2018), are summarised in table 2. This study showed that, compared with a sham device or control procedure, Rezum showed significantly better symptom control 3 months after treatment and that the improvements over baseline are maintained at 3 years. One observational study (Dixon et al. [2015]) found no impairment of sexual function after Rezum treatment.

Table 2 Summary of selected studies

McVary et al. (2018)	
Study size, design and location	197 men aged 50 and over with IPSS≥13, a prostate volume of 30cc to 80cc, Qmax≤15 ml/s, and a measured PVR urine<250 ml; prospective multicentre blinded control trial, US.
Intervention and comparator(s)	Intervention: Rezum. Control: Sham or control procedure with rigid cystoscopy.

Key outcomes	Primary outcome: IPSS reduction at 3 months, −11.3 +/−7.6 Rezum compared to −4.3 +/−6.9 control, p<0.0001. Statistically significant (p<0.0001) improvements in IPSS compared to control were further seen at 6, 12, 24 and 36 months' follow-up compared to baseline. There was a statistically significant improvement (p<0.0001) in QoL scores (IPSS QoL, BPHII, ICS IS, and OAB HQoL), as well as Qmax, at 3 months for Rezum compared to the control group, and at 6, 12, 24 and 36 months compared to baseline. No significant difference was seen in measures of ejaculatory function and erectile function between Rezum, with the exception of ejaculatory function at 36 months, p=0.0033.
Strengths and limitations	The study reports a large number of outcomes to 3 years' follow-up from a trial that intends to follow patients for up for 5 years. However it is powered for the primary outcome at 3 months. Control patients were unblinded at 3 months, and if they elected to continue were crossed over into the intervention arm. The study is funded by the company, and one of the authors declared a financial interest in the company.
Dixon et al. (2015)	
Study size, design and location	65 men aged 45 and over with IPSS ≥15, a prostate volume of 20 ml to 120 ml, Qmax ≤15 ml/s, and a measured PVR urine<300 ml; multicentre (Dominican Republic, Czech Republic, and Sweden) single-arm pilot studies.
Intervention and comparator(s)	Intervention: Rezum. No control.
Key outcomes	Statistically significant (p<0.001) clinical improvements over baseline at 1, 3, 6, and 12 months were reported for IPSS (decreased by 6.8, 13.4, 13.1, and 12.5 points respectively) and Qmax (increased by 2.0, 4.7, 4.3, and 4.6 ml/sec respectively) equating to a 56% improvement in IPSS and an 87% improvement in Qmax. QoL also improved (p<0.001) at collection points over 12 months. There were no significant changes in sexual function measures, meaning sexual function was maintained. 125 adverse events were recorded in 45 patients, most of which were minor (Clavien Dindo grade 1), of short duration and related to endoscopic instrumentation.

Strengths and limitations	Treatment approach and dosimetry varied from the first patients at the first site (Dominican Republic) to the final patients in Sweden. This and the lack of a control make the results harder to interpret. The study was sponsored by the company, and all but 1 of the authors were paid consultants or study investigators funded by the company.
Darson et al. (2017)	
Study size, design and location	131 patients, multicentre, retrospective observational study of consecutive patients with moderate to severe (IPSS 8 to 35) LUTS at 2 large medical practices in US.
Intervention and comparator(s)	Intervention: Rezum. No comparator.
Key outcomes	There were significant improvements (reductions) in IPSS scores ($p<0.0001$) from baseline values at 1, 3, 6 and 12 months, in QoL (IPSS question 8) scores, and PVR volumes. These results were found for all patients and when split into moderate (IPSS 8 to 19) and severe (IPSS 20 to 35) subgroups. The differences from baseline for Qmax and voided volume were not statistically significant ($p>0.05$), except for Qmax 3 to 6 months, all patients and moderate LUTS.
Strengths and limitations	The study confirms the findings from randomised studies, but is limited by the lack of a control. Three of the authors, including the lead author, have acted as consultants for the company.
Mollengarden et al. (2017)	
Study size, design and location	129 patients, retrospective observational study involving a single surgeon and practice in Texas, US.
Intervention and comparator(s)	Intervention: Rezum. No comparator.

Key outcomes	There were statistically significant improvements ($p<0.001$) in IPSS and Qmax at 15 to 45 days, 46 to 90 days, and 91 to 180 days post-operation; and in PVR ($p<0.05$) over the same periods. These results were largely consistent across the sub groups evaluated: whether or not a median lobe was treated, whether the prostate was greater or less than 60 cc, whether preoperative PVR was greater or <200 ml, and whether preoperative LUTS were mild, moderate, or severe. The most common adverse even was urinary tract infection (17.1%), followed by urinary retention (14%).
Strengths and limitations	The study includes 25 patients who were also involved in the Rezum II trial, see McVary et al. (2015). The lack of a standardised follow-up, and the retrospective analysis design meant that there was a noticeable loss to follow-up and variation in collection rates for different outcomes.
Abbreviations: BPHII, Benign Prostatic Hyperplasia Impact Index; HQoL, health-related quality of life; ICS IS, International Incontinence Society Incontinence Scale; IPSS, International Prostate Symptom Score; LUTS, lower urinary tract symptoms; OAB, overactive bladder; PVR, post-void residual; Qmax, peak urinary flow; QoL, quality of life.	

Recent and ongoing studies

- Rezum FIM Optimization. Clinical trials identifier: NCT02940392. Status: Active, not recruiting, no results posted. Indication: individuals with BPH symptoms, 15 enrolled. Devices: Rezum system, estimated completion date: June 2018.
- Rezum I Pilot Study for BPH. Clinical trials identifier: NCT02943070. Status: Active, not recruiting, no results posted. Indication: individuals with BPH symptoms, 50 enrolled. Devices: Rezum system, estimated completion date: December 2018.

Specialist commentator comments

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

Four specialists were familiar with or had used this technology before.

Level of innovation

Two of the experts considered the technology to be novel in its design or concept. The aspect that the experts considered novel, was the use of steam, as opposed to conductive heating, to ablate prostate tissue. The remaining experts considered it a minor variation on medical technologies recently evaluated by NICE, adding to currently recommended options that enable surgery to be carried out in a day-case outpatient setting but using a different form of energy to reduce prostate volume.

Potential patient impact

Less time spent in hospital and surgery, avoiding the need for general anaesthetic, minimal or reduced risk to sexual function and the avoidance of implants were identified as potential patient benefits. People wishing to preserve sexual function, those with an enlarged median lobe, and those too unfit for general anaesthetic were identified as groups who could particularly benefit from this technology.

Potential system impact

Less time spent by patients in surgery and hospital, allowing for greater throughput, lower waiting times, and possible cost savings were identified as potential system benefits. One expert considered that it would just add to current treatment options and not replace them. Two experts, based on figures provided by the company or their expectations considered that the technology could save money, 2 were uncertain. Three experts specified that further research was needed to determine any cost savings, with consideration given to time to return to work, and greater follow-up to capture post-operative healthcare encounters.

General comments

The experts agreed that there would be no need for changes to infrastructure to adopt this technology, with training requirements mostly considered minimal. No safety concerns were raised. The eligible population was estimated to be 7,000 to 10,000 per annum in England. Direct comparative evidence with current treatment options and cost-effectiveness studies were identified as research needed to address current uncertainties.

Specialist commentators

The following clinicians contributed to this briefing:

- Ian Pearce, consultant urological surgeon, Manchester Royal Infirmary, did not declare any interests.
- Amr Emara, consultant urologist, Hampshire Hospitals Foundation Trust, has received proctoring fees from the company, was part of a team who first introduced the technology into the UK.
- Richard Hindley, consultant urological surgeon, Hampshire Hospitals NHS Foundation Trust, has received occasional fees for training and teaching from the company and its distributor.
- John McGrath, consultant urological surgeon, Royal Devon and Exeter NHS Trust, did not declare any interests.

Development of this briefing

This briefing was developed by NICE. The interim process and methods statement sets out the process NICE uses to select topics, and how the briefings are developed, quality-assured and approved for publication.

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