

# Rezum for treating lower urinary tract symptoms secondary to benign prostatic hyperplasia

Medical technologies guidance

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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.

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This guidance replaces MIB158.

# 1 Recommendations

- 1.1 Evidence supports the case for adopting Rezum for treating lower urinary tract symptoms (LUTS) caused by benign prostatic hyperplasia (BPH) in the NHS. Rezum relieves LUTS and improves quality of life.
- 1.2 Rezum is a minimally invasive procedure. It should be considered as a treatment option for people with:
  - moderate to severe LUTS (International Prostate Symptoms Score [IPSS] typically 13 or over) and
  - a moderately enlarged prostate (typically between 30 cm<sup>3</sup> and 80 cm<sup>3</sup>).
- 1.3 Cost modelling estimates that Rezum is cost saving compared with standard treatments such as transurethral resection of the prostate (TURP) and holmium laser enucleation of the prostate (HoLEP) by more than £550 per person over 4 years. Savings compared with UroLift are uncertain. This is because of uncertainty about some of the assumptions in the cost modelling for that comparison.

## Why the committee made these recommendations

Rezum is a minimally invasive procedure that involves injecting steam to destroy excess prostate tissue. Clinical evidence shows that using the Rezum procedure relieves LUTS caused by BPH in men with moderate to severe symptoms who have a moderately enlarged prostate. Evidence also shows that using Rezum is associated with improved quality of life and a low risk of sexual dysfunction. Cost analyses suggest that when Rezum is used as an alternative to standard treatment, such as TURP or HoLEP, it is likely to lead to cost savings because it is done as day surgery with reduced operating and recovery costs.

## 2 The technology

### Technology

- 2.1 Rezum is water vapour (steam) therapy for treating lower urinary tract symptoms (LUTS) associated with benign prostatic hyperplasia (BPH). The technology uses water vapour to destroy excess prostate tissue with the aim of relieving symptoms.

The water vapour is injected into the prostate through a single-use device attached to a urological endoscope. The process is intended to disrupt cell membranes, leading to cell death and shrinking the prostate. The intention is to relieve obstructive symptoms without interfering with surrounding tissues that might impair sexual function.

The vapour is injected for 9 seconds during treatment. The number of times this has to be done in each lobe of the prostate depends on the length of the prostatic urethra. It can be customised to the configuration of the gland. A maximum number of 15 full injections can be done with each delivery device although fewer injections are needed for most treatments. The procedure is usually done in the NHS under general anaesthesia or local anaesthesia with sedation, and lasts up to 20 minutes.

### Innovative aspects

- 2.2 Rezum differs from other prostate treatments because it uses water vapour thermal energy. It does not use a laser and can be used to treat the median or middle lobe.

### Intended use

- 2.3 Rezum is intended for the treatment of prostates with volumes greater than 30 cm<sup>3</sup> (equivalent to 30 g).
- 2.4 The instructions for use state that Rezum is contraindicated for patients:

- with a urinary sphincter implant
- who have a penile prosthesis.

## Costs

- 2.5 The typical cost of consumables for the Rezum procedure is estimated at £1,348 (excluding VAT) per treatment. The company supplies the generator, which is loaned free of charge. The company also provides servicing including maintenance and other services (such as software updates) free of charge.

For more details, see the [website for Rezum](#).

## 3 Evidence

### Clinical evidence

#### Relevant evidence comes from 4 studies presented in 10 publications, including 1 randomised controlled trial

3.1 Four studies were relevant to the decision problem in the scope:

- 1 randomised controlled trial (5 publications: McVary et al. 2019, McVary and Roehrborn 2018, Roehrborn et al. 2017, McVary et al. 2016a, McVary et al. 2016b)
- 1 prospective observational study (3 publications: Mynderse et al. 2015; Dixon et al. 2015, Dixon et al. 2016)
- 2 retrospective observational studies (Mollengarden et al. 2018, Darson et al. 2017).

The randomised controlled trial was in 197 people with an International Prostate Symptom Score (IPSS) of 13 or more and an estimated prostate volume between 30 cm<sup>3</sup> and 80 cm<sup>3</sup>, who did not have urinary retention and who had no previous surgical interventions for their prostate. The observational studies included people with prostate sizes from 20 cm<sup>3</sup> to 110 cm<sup>3</sup> who had the Rezum procedure. All are non-UK studies.

#### The evidence suggests that Rezum is clinically effective

3.2 The Rezum II study showed that Rezum was associated with statistically significant improvements in lower urinary tract symptoms (LUTS) compared with sham at the 3-month follow up. These improvements were maintained throughout 4 years of follow up. The treatment benefits of Rezum in relieving LUTS were also seen consistently in the observational studies. The incidence of sexual dysfunction after treatment with Rezum was low, with a few people reporting a decrease in ejaculatory function but little change in erectile function. Overall, the evidence base shows that Rezum is an effective treatment for LUTS in people with benign prostatic hyperplasia (BPH). Rezum also improved quality of life (McVary et al. 2019, Darson et al. 2017; Dixon et al. 2015 and 2016).

## **There is no evidence that directly compares Rezum with other interventions for BPH**

- 3.3 None of the included studies compared Rezum with other commonly used treatments for BPH. Clinical experts suggested that more invasive treatments such as transurethral resection of the prostate (TURP) were likely to be associated with a more substantial relief of urinary symptoms than Rezum. But there is currently no direct evidence to support this. Similarly, there are no direct comparisons of Rezum with UroLift, holmium laser enucleation of the prostate (HoLEP), or GreenLight laser. Expert opinion indicated that recruiting participants to clinical trials that directly compare different minimally invasive and invasive treatments is challenging because people often say they prefer to avoid more invasive treatment.

## **An indirect comparison suggests that Rezum is as effective as UroLift**

- 3.4 In the absence of direct comparative evidence, the company did an indirect comparison of Rezum and UroLift to relieve LUTS. This was based on the results of the Rezum II study and the Luminal Improvement Following prostatic Tissue (LIFT) study (Roehrborn et al. 2017b). Both technologies are minimally invasive procedures to treat LUTS, and the trial designs and study populations were similar. The main exception was that the Rezum II study included people with median lobe obstruction (31.1% of study participants) while the LIFT study did not. Results from the 2 trials indicated that the therapeutic effects of Rezum and UroLift in relieving LUTS were similar. Retreatment rates were different in the 2 trials: 4.4% for Rezum at year 4 and 13.6% for UroLift at year 5.

## **The clinical experts consider Rezum to be a safe procedure**

- 3.5 The Rezum II study reported 3 procedure-related serious adverse events in the 3-month follow up, including extended urinary retention, and nausea and vomiting, which were considered to be because of the sedative medication. An additional 3 procedure-related serious adverse events were reported with Rezum during the 3- to 12-month follow-up period, including bladder contracture, bladder stone and urosepsis after cystoscopy. The clinical experts did not identify any specific safety concerns with Rezum.

## Cost evidence

### The company suggests that using Rezum is cost saving compared with other treatments for BPH

3.6 The company developed a decision analytic model with a time horizon of 4 years. The model compared Rezum with 4 comparators: TURP, HoLEP, UroLift, and GreenLight laser. The model assumed that all the technologies had equal efficacy in alleviating LUTS associated with BPH. The model incorporated a cohort Markov structure. Erectile dysfunction and urinary incontinence were included as permanent adverse events that inform long-term health states. The need for surgical retreatment for recurrence of LUTS was also considered. The results of the company model indicated that Rezum was cost saving by £737, £758, £532, and £25 per person when compared with TURP, HoLEP, UroLift, and GreenLight respectively over 4 years.

### The external assessment centre's changes to the assumptions in the cost model reflect empirical evidence and expert opinion

3.7 The main parameters in the model were the technology costs, theatre time, hospital length of stay, adverse events and the need for another operation. The external assessment centre (EAC) adjusted some of the model's parameters, including the surgical retreatment rates and the adverse event rates, to reflect published empirical data and expert opinion.

### The model estimates that Rezum is cost saving compared with TURP, HoLEP and UroLift but cost neutral compared with GreenLight

3.8 The EAC base-case results showed that Rezum was cost saving by £569, £651 and £497 per person compared with TURP, HoLEP, and UroLift respectively over 4 years. Rezum remains cost saving when all parameters are subjected to a one-way deterministic sensitivity analysis. In the base case, Rezum is cost incurring by £62 per person over 4 years compared with GreenLight laser. The model assumed that GreenLight, like Rezum, was used as a day case. If, in practice, this is not the case, then Rezum is anticipated to be cost saving. Overall, the EAC considered Rezum, therefore, to be approximately cost neutral compared with GreenLight over the course of 4 years.

## **Additional analysis suggests uncertainties in the cost saving when Rezum is compared with UroLift**

- 3.9 In response to consultation comments on the draft recommendations, the EAC ran additional scenario analyses. These included different parameters relating to the current use of UroLift. The EAC also added the cost of catheter removal to the analysis to reflect that this is needed after Rezum but not after UroLift. The results showed that Rezum remains cost saving compared with UroLift when individual parameters are varied. But when all parameters are combined Rezum is cost incurring compared with UroLift. The probabilistic sensitivity analysis results indicate that there is uncertainty about whether Rezum is cost saving compared with UroLift.

## 4 Committee discussion

### Clinical-effectiveness overview

#### Rezum is an effective minimally invasive procedure with clinical benefits

- 4.1 The committee concluded that the evidence from the Rezum II study demonstrated the effectiveness of Rezum in relieving lower urinary tract symptoms (LUTS) associated with benign prostatic hyperplasia (BPH) with a sustained benefit up to 4 years after the procedure. The committee noted that this is supported by the results of the observational studies. The committee noted that there are no studies that directly compare Rezum with other treatments in relieving symptoms in people with BPH, but considered an indirect comparison between Rezum and UroLift, which was drawn from analogous trial data. This suggests that Rezum is at least as effective as UroLift over 4 years. The clinical experts explained that these 2 minimally invasive procedures are used in similar cohorts of populations in clinical practice and that, in their experience, both procedures provide a similar degree of symptom relief. They also noted that Rezum is versatile in treating different shapes of prostate.

#### Rezum should be used for men with moderate to severe LUTS with an estimated prostate volume of 30 cm<sup>3</sup> to 80 cm<sup>3</sup>

- 4.2 The committee noted that there is 1 pivotal study that provides the evidence for the efficacy of Rezum. The clinical experts explained that Rezum II was a US study and designed to meet US Food and Drug Administration eligibility criteria. Its major inclusion criteria were: men aged 50 or over who have symptomatic BPH with an International Prostate Symptoms Score (IPSS) of 13 or greater, and with a prostate volume, measured by transrectal ultrasound, of 30 cm<sup>3</sup> to 80 cm<sup>3</sup>. The committee concluded that there is limited evidence on the efficacy of Rezum in men outside this cohort. The clinical experts confirmed that, in their clinical practice, this cohort of patients corresponds closely to those that they treat with Rezum and that this encompasses approximately 75% to 85% of the overall population that need treatment to relieve LUTS. The clinical experts also

explained that, for people with mild LUTS (IPSS less than 8), first-line treatment is medication or lifestyle change. For people with an estimated prostate volume 120 cm<sup>3</sup> and greater, more invasive surgical interventions are recommended.

## **Rezum is unlikely to damage surrounding tissue and nerves, and the risk of sexual dysfunction is low**

- 4.3 The clinical experts explained that loss of sexual function is an important concern for people undergoing invasive treatment for LUTS because the invasive procedure is likely to damage nerves on the external surface of the prostate. They also explained that Rezum involves injecting steam into carefully directed and localised areas of the prostate from the inner, urethral surface of the prostate, and this may avoid possible damage to surrounding nerves. The committee considered that the published evidence suggests that sexual function is retained after treatment with the Rezum procedure. It did note, however, a high incidence of sexual inactivity in people included in the Rezum II study and that overall sexual function showed a tendency to decline during study follow up. The experts explained that there are different types of sexual dysfunction. They said that after treatment with Rezum erectile dysfunction is rare, but ejaculatory dysfunction has been reported. Overall, the committee concluded that the risk to sexual function is low with Rezum, and that this may be particularly important to people who are sexually active at the time of treatment. The committee was uncertain, however, about the impact of Rezum on longer-term sexual function because no data are available for longer than 4 years.

## **Quality of life is an important outcome when considering patient benefit**

- 4.4 The evidence from the Rezum II study and observational studies indicated that treatment with Rezum with significant relief of LUTS is associated with a significant improvement in quality of life, which persists for up to 4 years of follow up. The clinical experts confirmed that, in their experience, people who underwent Rezum express a high level of satisfaction after the procedure.

## Side effects and adverse events

### Urinary tract infection is a common complication after Rezum

4.5 The clinical experts advised that complications after the Rezum procedure are similar to those after other procedures for LUTS because of BPH and include urinary tract infections (UTIs), bleeding, epididymitis and abscess. The clinical experts also explained that, after the Rezum procedure, a urinary catheter is left in place for 5 to 7 days to allow the dead prostate tissue to drain away. The need for catheterisation, combined with the presence of necrotic tissue, are considered by the clinical experts to be predisposing factors for developing UTIs and, more rarely, urosepsis. This risk is higher for Rezum than UroLift, which usually does not need a post-operative urinary catheter. The clinical experts estimated that the risk of UTIs associated with a urinary catheter is around 5% to 7%, so a short course of prophylactic antibiotics may be prescribed after the procedure. The committee heard that post-procedure UTI rates associated with Rezum may be difficult to record because patients may present to their GP for treatment. It also noted that antibiotic use was not reported in the Rezum II study. The committee concluded that UTI is a common complication after Rezum but the risk of UTI can be reduced using prophylactic antibiotics.

### The rate of surgical reintervention is low with Rezum

4.6 The committee noted that the Rezum II study reported a 4.4% rate of surgical retreatment after Rezum over 4 years of follow up. The LIFT study reported a 13.6% rate of surgical retreatment after UroLift over 5 years of follow up. The clinical experts suggested that the average retreatment rate in their experience is low after Rezum, and that retreatment is most likely in the first year after the procedure. The clinical experts explained that, because there is no direct view of the prostate cavity during the Rezum procedure, additional transurethral resection of the prostate (TURP) is sometimes needed to remove residual prostate tissue after Rezum. Overall, the committee concluded that the retreatment rate with Rezum is low and compares favourably with similar treatments like UroLift.

## Relevance to the NHS

### The evidence for Rezum is broadly generalisable to the NHS

- 4.7 The clinical experts explained that Rezum is currently done in some NHS trusts and that there has been an increased demand by people for this procedure in some centres. The committee noted that the published evidence for Rezum is from studies that were done outside the UK. Nonetheless, the clinical experts explained that the study population included in the Rezum II study is similar to the people that they treat with Rezum in their own practices in the NHS. The committee concluded that the evidence is generalisable to UK NHS practice.

## NHS considerations overview

### Rezum is a day surgery procedure that can be done under local anaesthetic with sedation but it may not be suitable for everyone

- 4.8 The clinical experts said there are currently 8 different treatments, including Rezum, available in the NHS for people with significant LUTS that have not responded to conservative therapy including medication and lifestyle changes. The clinical experts considered TURP to be the standard of care for LUTS secondary to BPH, but emphasised that treatments need to be offered to people on an individual basis guided by their individual circumstances. Key factors for consideration include: the availability of procedures in their local hospitals, age, prostate gland size and characteristics, and comorbidities. Rezum's advantages over some other technologies are that it is a minimally invasive procedure that can be done under local anaesthesia with sedation, and it takes only around 20 minutes. Despite this, the clinical experts estimated that around two thirds of procedures done in the NHS are under general anaesthetic. People usually do not need an overnight stay in hospital, however. The clinical experts said that Rezum should be avoided in people with prostatitis or confirmed prostate cancer, in people for whom day case treatment is impractical or unsafe, and if there's a risk of increased bleeding, for example if they're having anticoagulant treatment.

## Rezum is used to treat patients with benign prostate enlargement but there is no consensus on how to measure prostate size

- 4.9 The clinical experts said that an enlarged prostate that causes LUTS as a result of prostatic obstruction is caused by prostatic hyperplasia, which is a benign histopathological diagnosis. The clinical experts explained that there is currently no consensus on how prostate size should be estimated or measured in UK clinical practice. They considered that normally imaging would be used to estimate prostate size before surgically invasive treatment. The clinical experts said that imaging modalities could complement information from rectal digital examination of the prostate. Common imaging tools include transrectal ultrasound, cystoscopy and MRI. On the basis of these measurements, the committee heard that Rezum is usually offered to people with moderate prostatic enlargement with a prostate that is typically estimated to be 30 cm<sup>3</sup> to 80 cm<sup>3</sup>.

## The Rezum procedure is easy to learn

- 4.10 The clinical experts explained that urologists need specialist training to do the Rezum procedure. This training is provided by the company and includes lectures and simulation training. The clinical experts suggested that Rezum is relatively easy to learn and that the training requirement is minimal. The committee concluded that the amount of training needed to carry out the Rezum procedure is reasonable.

## Cost modelling overview

### Rezum is estimated to be cost saving compared with standard treatments for BPH but there are limitations in the cost model

- 4.11 The committee noted that the external assessment centre's (EAC) cost modelling results showed that Rezum is likely to be cost saving compared with TURP and holmium laser enucleation of the prostate (HoLEP) by £569 and £651 per patient respectively over 4 years. The committee noted, however, that there are some limitations in the model, including the assumption that all treatments are equally effective in relieving LUTS. Indirect comparative data from the trials suggest that the technologies may not all reduce the IPSS score to the same extent. The clinical experts confirmed that more invasive procedures such as

TURP, which removes prostate tissue, would be expected to have greater IPSS improvements. It's uncertain to what extent this impacts the need for retreatment. The committee identified other limitations in the cost model, including the fact that no consideration was given to the impact of urinary catheterisation and removal, or the need for antibiotics after Rezum. The EAC said that the key drivers of the cost savings for Rezum over standard treatments such as TURP and HoLEP are the length of hospital stay and procedure time. Adding the cost of catheter removal to the modelling for Rezum does not substantially affect its cost savings compared with standard treatments. The EAC also noted that prophylactic antibiotics are likely to be common to all treatments, as well as Rezum. The committee concluded that the costs of catheter and prophylactic antibiotic use were unlikely to substantially affect Rezum's cost savings.

## The comparative costs of using Rezum compared with UroLift are uncertain

- 4.12 The committee noted that the base-case results, which are based on published data sources, suggested that Rezum saves £497 per person compared with UroLift over 4 years. The committee also noted, however, the results of the EAC's additional analyses, which included parameters that may better reflect current use of UroLift. The committee noted that 1 of the parameter changes was to include the cost of catheter removal for Rezum but not for UroLift. Based on the expert advice received, the committee agreed with this parameter change. The committee also noted the uncertainty about the current cost of the UroLift technology and its impact on the cost modelling results. Overall, the committee concluded that there are currently too many uncertainties to be able to draw any firm conclusions about the costs of using Rezum compared with UroLift.

## Main cost drivers

### Doing Rezum as day surgery is the main driver for cost savings

- 4.13 The committee heard from the clinical experts that Rezum is commonly done as day surgery and people are not usually admitted to hospital after the procedure. The EAC considered that this was a key driver in the estimated cost savings when Rezum is compared with standard treatments such as TURP. The

company's model showed that the cost of consumables for Rezum such as a delivery device was estimated to be around £1,348 per person. The company provides the generator and servicing such as maintenance free of charge. The cost of consumables relative to competitor treatments also influenced the cost modelling results. The company representatives confirmed that they do not anticipate any changes to this cost model for the foreseeable future. The committee concluded that the main driver for cost savings in the model is that Rezum is done as day surgery and people do not stay overnight at hospital.

## Cost savings

### Rezum is cost saving compared with standard treatments for BPH

4.14 The EAC did deterministic sensitivity and probability sensitivity analyses that varied parameters in the cost models, and the results showed that Rezum remained cost saving compared with standard treatments such as TURP and HoLEP. The committee concluded that, based on the published evidence, cost modelling and expert opinion, using Rezum is likely to lead to a cost saving of £569 compared with TURP, and £651 compared with HoLEP, for every person treated over a 4-year time horizon.

## Further research

### The efficacy of Rezum compared with other treatments needs research

4.15 Further evidence to address the efficacy of Rezum when directly compared with other treatments such as TURP would be welcome, including their relative impact on symptom relief, quality of life, short and long-term sexual function, and their possible benefits in people with urinary retention and with large prostate glands. More information is also needed on the number of steam injections needed with Rezum in normal clinical practice, and whether more injections are harmful.

## 5 Committee members and NICE project team

### Committee members

This topic was considered by the [medical technology advisory committee](#) which is a standing advisory committee of NICE.

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

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

### NICE project team

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

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## Accreditation

