Prostate: Water Vapor Thermotherapy for Benign Prostatic Hyperplasia
(All Lines of Business Except Medicare)

Effective Date: 10/1/2019

Medical Policy Committee Approved Date: 9/19

See Policy CPT/HCPCS CODE section below for any prior authorization requirements

SCOPE:

Providence Health Plan, Providence Health Assurance, Providence Plan Partners, and Ayin Health Solutions as applicable (referred to individually as “Company” and collectively as “Companies”).

APPLIES TO:

All Lines of Business Except Medicare

BENEFIT APPLICATION

Medicaid Members

Oregon: Services requested for Oregon Health Plan (OHP) members follow the OHP Prioritized List and Oregon Administrative Rules (OARs) as the primary resource for coverage determinations. Medical policy criteria below may be applied when there are no criteria available in the OARs and the OHP Prioritized List.

POLICY CRITERIA

Water vapor thermotherapy (i.e., Rezūm System) is considered investigational and is not covered for the treatment of any indication, including but not limited to, benign prostatic hyperplasia.

Link to Policy Summary
MEDICAL POLICY

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CPT/HCPCS CODES

<table>
<thead>
<tr>
<th>All Lines of Business Except Medicare</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not Covered</td>
</tr>
<tr>
<td>53854</td>
</tr>
<tr>
<td>Transurethral destruction of prostate tissue; by radiofrequency generated water vapor thermotherapy</td>
</tr>
<tr>
<td>Unlisted</td>
</tr>
<tr>
<td>All unlisted codes will be reviewed for medical necessity, correct coding, and pricing at the claim level. If an unlisted code is billed related to services addressed in this policy then it will be denied as not covered.</td>
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<tr>
<td>53899</td>
</tr>
<tr>
<td>Unlisted procedure, urinary system</td>
</tr>
</tbody>
</table>

DESCRIPTION

Benign Prostatic Hyperplasia

Benign prostatic hyperplasia (BPH) refers to the enlargement of the prostate gland, which effects approximately 8 million men in the U.S. BPH may cause urinary symptoms (e.g. restricted flow of urine out of the bladder, frequency, urgency, incomplete emptying), as well as bladder, urinary tract or kidney problems. Symptoms may lead to decreased quality of life and depression.¹

The Rezum System

According to Hayes:

“The Rezum System [i.e. Rezum] is a minimally invasive, transurethral treatment for BPH that utilizes convective radiofrequency water vapor energy to ablate the hyperplastic tissue. The Rezum System consists of a radiofrequency power generator and a disposable delivery device. The rigid shaft of the delivery device incorporates a standard lens so that the procedure may be performed under cystoscopic visualization. The delivery device also contains a needle, which injects wet thermal energy (i.e., steam) into diseased prostatic tissue. The steam immediately condenses to water thereby dispersing thermal energy and killing the surrounding cells. The dead cells are eventually absorbed, which reduces the volume of prostatic tissue and opens the urethra … Once the Rezum delivery device is within the prostate, the needle is deployed and a 9-second burst of 103°C water vapor is injected into the prostatic tissue creating a spherical lesion of 1.5 to 2 centimeters (cm). The total number of treatments in each lobe is based upon the length of the hyperplastic prostatic tissue and the length of the urethra, but typically 1 to 3 sites are treated per lobe. The goal is to create contiguous, overlapping lesions approximately 1 cm apart along the urethra.”¹
A review of the ECRI, Hayes, Cochrane, and PubMed databases was conducted regarding the use of the Rezum System (NxThera Inc.) as a treatment for benign prostatic hyperplasia. Below is a summary of the available evidence identified through 7/26/2019.

**Systematic Reviews**

- In 2019, Hayes conducted an evidence review evaluating the safety and efficacy of the Rezum System for the treatment of benign prostatic hyperplasia (BPH).\(^1\) Searching the literature through February, Hayes included 8 publications for review. The publications reported data from 4 clinical studies (1 randomized, sham-controlled study, and 3 pretest-post-test studies.) Sample sizes across studies ranged from 65 to 197. Primary outcomes of interest included urinary symptoms, health-related quality of life, sexual function, safety and treatment failure. Results across 4 studies suggested that, compared to the sham group, Rezum patients’ LUTS and quality of life significantly improved from baseline at 3-years’ follow-up (50% vs. 20%; p < 0.0001). Measures of clinically meaningful response ranged from 67% to 85% at 12-month follow-up. No significant effect on sexual function was reported across either Rezum or sham patients. Adverse events and failure rates were also minimal.

Hayes judged the overall quality of evidence to be of “very-low,” concluding that Rezum may relieve lower urinary tract symptoms (LUTS) associated with BPH and improve patients’ health-related quality of life at up to 3 years. Limitations across studies may undermine results’ validity, however. Individual studies suffered from small sample sizes, a lack of comparison groups, a lack of long-term follow-up, and substantial loss to follow-up. Hayes ultimately assigned a “D2” rating (insufficient evidence) for use of Rezum in men with LUTS secondary to BPH. Investigators stated that, in addition to unestablished patient selection criteria, “substantial uncertainty remains regarding [Rezum’s] comparative effectiveness and safety due to a lack of comparative studies, as well as limited long-term evidence regarding the durability and safety.”\(^1\)

- In 2016 (updated 2019), ECRI conducted an evidence review assessing the safety and efficacy of Rezum for the treatment of benign prostatic hyperplasia.\(^2\) Searching the literature through March 2019, ECRI reviewed the full texts of 1 RCT and 3 pre-post studies reporting outcomes for 522 patients. The RCT included for review is the evaluated below.\(^3\) The pre-post studies are the same as those evaluated in the Hayes review discussed above.\(^4\) ECRI concluded that the balance of evidence regarding Rezum’s efficacy is “somewhat favorable,” with statistically and clinically significant improvements in patients’ LUTS and quality of life across all studies. Investigators noted that study limitations may undermine results’ validity, noting the limited quantity of RCTs comparing Rezum to a sham procedure (n =1), and the absence of any RCTs comparing Rezum to any other BPH treatment. Sham procedures and pre-post studies were also vulnerable to placebo effects due to the lack of blinding. In the case of the sham procedure, LUTS may also decrease due to temporary urethral dilation caused by rigid cystoscopy, although the placebo
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effect is thought to dissipate within 6 months. The reviewed pre-post studies also included patients with prostate volumes smaller or larger than described in the FDA-labeled indication (30 to 80cm3), which may have generated results different from reported findings in the on-label population. ECRI concluded that additional studies comparing Rezum to alternative treatments were necessary (e.g. transurethral resection of the prostate, microwave ablation, prostatic urethral lift) so as to more definitively establish Rezum’s safety and efficacy.

**Randomized Controlled Trials**

In 2019, McVary and colleagues conducted a manufacturer-funded randomized controlled trial reporting lower urinary tract symptoms (LUTS) associated with BPH in patients receiving Rezum. In total, 188 patients with International Prostate Symptom Score ≥13, with a maximum flow rate (Qmax) ≤ 15mL/s and prostate volume 30 to 80cc were treated and followed for 4 years. A subset of 53 patients who initially received sham treatment “crossed over” to active treatment after unblinding at 3-months. This group was followed for 3 years. Results indicated significant improvement in both groups’ LUTS and quality of life within 3 months of treatment, sustained throughout 4 years (p < 0.0001). Results’ validity may be limited by the investigators’ financial conflicts of interest with Rezum’s manufacturer, the lack of treatment groups receiving an alternative BPH therapy, narrow inclusion criteria (e.g. all patients 50 years old, without history of urinary retention or UTI) and significant loss to follow-up (primary group: 32.8%, n = 44/134; cross-over group 45.3% n = 24/53). Investigators concluded that Rezum can provide effective symptom relief and improve quality of life for patients with BPH.

**CLINICAL PRACTICE GUIDELINES**

American Urological Association

In 2018, the American Urological Association (AUA) published an evidence-based clinical practice guideline evaluating surgical management of LUTS attributed to BPH. On the basis of grade “C” evidence (i.e. low-quality), the AUA issued a conditional recommendation for water vapor thermal therapy “to patients with LUTS/BPH provided prostate volume <80g.” The guideline noted, however, that “evidence of efficacy, including longer-term retreatment rates, remains limited.” Rezum is not named specifically in the guideline. Several investigators maintain financial conflicts of interest with device manufacturers, including Rezum’s manufacturer.

**POLICY SUMMARY**

Evidence is insufficient to support the use of Rezum for the treatment of BPH. While studies to date have reported positive results, only one manufacturer-funded RCT has been conducted that compares Rezum to sham treatment and no studies have been conducted comparing Rezum to either gold standard treatment for BPH (i.e. transurethral resection of the prostate) or minimally invasive alternative treatments. Only one clinical practice guideline addresses water vapor thermal therapy,
conditionally endorsing the treatment on the basis of low-quality evidence despite an acknowledged lack of demonstrated efficacy. Moreover, several authors of the guideline have financial conflicts of interest with Rezum’s manufacturer. The largest RCT conducted to date reported significant improvements in patients’ LUTS compared to baseline, but validity was limited by the study’s manufacturer-funding, and significant potential for attrition bias (primary group: 32.8%, n = 44/134; cross-over group 45.3% n = 24/53). Additional high-quality RCTs with longer term follow-up and broader inclusion criteria are required to establish patient selection criteria, as well as Rezum’s superiority relative to current treatment options.

**INSTRUCTIONS FOR USE**

Company Medical Policies serve as guidance for the administration of plan benefits. Medical policies do not constitute medical advice nor a guarantee of coverage. Company Medical Policies are reviewed annually and are based upon published, peer-reviewed scientific evidence and evidence-based clinical practice guidelines that are available as of the last policy update. The Companies reserve the right to determine the application of Medical Policies and make revisions to Medical Policies at any time. Providers will be given at least 60-days’ notice of policy changes that are restrictive in nature.

The scope and availability of all plan benefits are determined in accordance with the applicable coverage agreement. Any conflict or variance between the terms of the coverage agreement and Company Medical Policy will be resolved in favor of the coverage agreement.

**REGULATORY STATUS**

The Rezum System received 501(k) approval in 2015.5

<table>
<thead>
<tr>
<th>Indications for Use</th>
<th>Contraindications</th>
</tr>
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<tbody>
<tr>
<td>The Rezum™ System is intended to relieve symptoms, obstructions, and reduce prostate tissue associated with BPH. It is indicated for men ≥ 50 years of age with a prostate volume 30cm³ ≤ 80cm³. The Rezum System is also indicated for treatment of prostate with hyperplasia of the central zone and/or a median lobe.</td>
<td>The use of the Rezūm System is contraindicated for the following:</td>
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<tr>
<td></td>
<td>• Patients with a urinary sphincter implant</td>
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<td>• Patients who have a penile prosthesis</td>
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</table>

5. Reference or additional information.
Mental Health Parity Statement

Coverage decisions are made on the basis of individualized determinations of medical necessity and the experimental or investigational character of the treatment in the individual case.

REFERENCES