

Transurethral Water Vapor Thermal Therapy of the Prostate

Effective: May 1, 2021

Next Review: December 2021

Last Review: March 2021

IMPORTANT REMINDER

Medical Policies are developed to provide guidance for members and providers regarding coverage in accordance with contract terms. Benefit determinations are based in all cases on the applicable contract language. To the extent there may be any conflict between the Medical Policy and contract language, the contract language takes precedence.

PLEASE NOTE: Contracts exclude from coverage, among other things, services or procedures that are considered investigational or cosmetic. Providers may bill members for services or procedures that are considered investigational or cosmetic. Providers are encouraged to inform members before rendering such services that the members are likely to be financially responsible for the cost of these services.

DESCRIPTION

Transurethral water vapor thermal therapy is a minimally invasive surgical therapy for the treatment of benign prostatic hypertrophy.

MEDICAL POLICY CRITERIA

- I. Transurethral water vapor thermal therapy may be considered **medically necessary** for the treatment of benign prostatic hyperplasia (BPH) when all of the following criteria are met (A. – D.):
 - A. Moderate to severe symptomatic BPH; and
 - B. Patient is at least 50 years of age; and
 - C. Prostate volume is 30 cc to 80 cc by ultrasound or other radiologic assessment; and
 - D. A trial of conservative medical therapy (defined as one month of an alpha blocker, 3 months of a 5-alpha reductase inhibitor, or 3 months of an anticholinergic) for BPH has been unsuccessful, is contraindicated, or is not tolerated.

- II. Transurethral water vapor thermal therapy of the prostate is considered **investigational** when the above criteria are not met.

NOTE: A summary of the supporting rationale for the policy criteria is at the end of the policy.

POLICY GUIDELINES

BENIGN PROSTATIC HYPERPLASIA SEVERITY

The American Urological Association Symptom Index (AUA-SI) is a validated clinical tool for measuring severity of benign prostatic hyperplasia (BPH).^[1] BPH severity is reported as mild (AUA-SI score of 0 to 7), moderate (8 to 19), and severe (20 to 35). The IPSS is the same as the AUA-SI but includes an additional question regarding impact of symptoms on quality of life.

CONSERVATIVE MEDICAL THERAPY

The medications listed in Table 1 may be used for conservative treatment of BPH.

Table 1. Medications for conservative treatment of BPH

Class	Common Examples
Alpha-1-receptor antagonists	Alfuzosin (Uroxatral, Xatral), doxazosin (Cardura), tamsulosin (Flomax), and terazosin (Hytrin)
5-alpha-reductase inhibitors	Finasteride, dutasteride
Anticholinergics	Fesoterodine (Toviaz), tolterodine (Detrol, Detrol LA), oxybutynin (Ditropan, Ditropan XL), darifenacin (Enablex), solifenacin (Vesicare), trospium (Sanctura, Sanctura XR)

LIST OF INFORMATION NEEDED FOR REVIEW

REQUIRED DOCUMENTATION:

The information below must be submitted for review to determine whether policy criteria are met. If any of these items are not submitted, it could impact our review and decision outcome.

- History and physical/chart notes
- Conservative treatment provided, if any
 - If options for more conservative management are relatively or absolutely contraindicated, those contraindications should be specified.
 - If options for more conservative management previously have been tried and have been ineffective or not tolerated, clinical information regarding those previous treatments should be provided.
- Relevant imaging (ultrasound, etc) reports documenting prostate volume.

CROSS REFERENCES

None

BACKGROUND

Benign prostatic hyperplasia (BPH) is a diagnosis that describes the enlargement of the prostate often associated with a group of obstructive symptoms, termed lower urinary tract

symptoms (LUTS). These symptoms include decreased force of stream, hesitancy, straining, incomplete bladder emptying, and nocturia. The enlargement is caused by the proliferation of epithelial and smooth muscle cells in the transition zone of the prostate. Proliferation generally increases with age, and the initiation of BPH likely begins by the age of 30.^[2] According to a multinational survey, 90% of men ages 50-80 experience BPH, although only 11% of men in the study received medical treatment.^[3]

Standard management of BPH includes watchful waiting (active surveillance) in patients not bothered by their symptoms, medical management, surgery, and a number of new minimally invasive therapies. Surgical treatments include transurethral resection of the prostate (TURP), transurethral vaporization, holmium laser enucleation or resection of the prostate, prostatic artery embolization, and prostatectomy. Minimally invasive therapies include transurethral needle ablation of the prostate (TUNA) and transurethral microwave thermotherapy (TUMT), as well as transurethral water vapor thermal therapy.

Transurethral water vapor thermal therapy is a process by which water vapor is created outside of the body and delivered to the prostate with a needle. The treatment is repeated in multiple locations within the prostate. During the procedure, saline irrigation cools and protects the surface of the urethra. The heat from the vapor disrupts cell membranes in the prostate, which leads to cell death and necrosis.

REGULATORY STATUS

In 2015, the U.S. Food and Drug Administration (FDA) approved the Rezūm System[®] (NxThera, Inc.) under the 510(k) process for use in relieving symptoms and obstructions, and reducing prostate tissue associated with BPH.

EVIDENCE SUMMARY

The primary beneficial outcomes of interest are symptom reduction, measured in various ways, including the International Prostate Symptom Score (IPSS), the benign prostatic impact index (BPHII), and the maximum urinary flow rate (Qmax). Evaluating the safety and effectiveness of transurethral water vapor thermal therapy requires randomized comparisons with standard care. These comparisons are necessary to determine whether the benefits of implantable cardiac monitors outweigh any risks and whether they offer advantages over conventional methods with respect to increasing quality of life and decreasing symptoms.

SYSTEMATIC REVIEWS

A Cochrane systematic review (SR) was reported by Kang in 2020.^[4] The search was limited to parallel-group randomized controlled trials (RCTs), cluster-RCTs, and non-randomized observational prospective studies with concurrent comparison groups, in which men with BPH underwent convective radiofrequency water vapor thermal therapy, another active therapy, or a sham procedure. Only the RCT described below met inclusion criteria. The authors concluded that both urologic symptom scores and quality of life appear to be improved by water vapor thermal therapy, but they were very uncertain about major adverse events and that study limitations and imprecision led to a downgrade of evidence, which ranged from moderate to very low.

RANDOMIZED CONTROLLED TRIALS

A single RCT was identified, with results published in five publications.^[5-9] The trial began with a three month randomized phase followed by an uncontrolled, open-label crossover phase. One-hundred and ninety-seven men experiencing lower urinary tract symptoms associated with benign prostatic hyperplasia were randomized 2:1. The active treatment group received water vapor ablation therapy with the Rezūm® System and the control group underwent a control procedure including rigid cystoscopy with simulated active treatment sounds. After three months, 53 of 61 control subjects who met criteria elected to participate in a crossover active treatment study. The International Prostate Symptom Score (IPSS) was 10.8 (standard deviation [SD] = 6.5) and 17.5 (SD = 7.6) in the active therapy and sham groups, respectively ($p < 0.0001$) at three months post-treatment. The peak flow-rate (Qmax) increased significantly more in the treatment group at three months, to 16.1 (SD \pm 7.3), compared with 10.8 (SD = 4) in the sham group ($p < 0.0001$). Quality of life, as measured by the IPSS-QOL question, was statistically significantly better in the treatment group (2.3; SD = 1.4) than in the sham group (3.5; SD = 1.5; $p < 0.0001$).

In the patients that crossed over to the treatment group after unblinding at three months, improvements in IPSS, IPSS-QOL, and Qmax were all reported to be statistically significant compared to baseline values at 3, 6, 12, 24, 36, and 48 months ($p < 0.0001$). Sexual function scores (IIEF-EF and MSHQ function) remained unchanged at two years, but declined at four years (-7.6% change, $p = 0.0333$ and -14.2% change, $p = 0.0038$, respectively).

Adverse events reported include one treated patient each who experienced nausea, vomiting, and de-novo urinary retention. In addition, among active treatment patients, 17% reported dysuria, 15% reported hematuria, 7% reported urinary frequency, and 7% reported hematospermia. At four years, 45 subjects were excluded from the analysis. Of these, seven were excluded due to use of BPH medication. Additionally, further surgical intervention was performed in six patients. This study is limited by duration of follow-up, with no control group present after three months of follow-up, and a lack of comparison to alternative treatments. Additionally, there was a high loss to follow-up, with data available for the primary outcome at four years from 90 of 197 patients.

NONRANDOMIZED STUDIES

Garden (2021) published a retrospective analysis of Rezūm outcomes in men with prostates \geq 80 cc (large prostate group; $n = 36$) versus $<$ 80 cc (small prostate group; $n = 168$).^[10] For individuals with large prostates, there were significant improvements in Qmax and post-void residual volume (PVR) postoperatively ($p = 0.039$ and $p = 0.009$, respectively), but no changes in AUA-Symptom Score (AUA-SS) or Sexual Health Inventory for Men (SHIM) were reported ($p = 0.29$ and $p = 0.825$, respectively). For men with prostates $<$ 80 cc, the study reported improved PVR (89.51 to 62.72, $p = 0.027$) and AUA-SS (16.59 to 11.21, $p = 0.003$), but not in Qmax (9.47 to 10.90, $p = 0.187$). Passing trial void (large prostate 94.44%, small prostate 93.45%), postoperative UTI (large prostate 19.44%, small prostate 10.12%), ED visits (large prostate 22.22%, small prostate 17.86%), readmissions (large prostate 8.33%, small prostate 4.76%), and retreatment (large prostate 8.33%, small prostate 4.76%) were not significantly different between groups. Mean days to foley removal (large prostate 9, small prostate 5.71, $p = 0.003$) and urosepsis rates (large prostate 5.56%, small prostate 0.00%, $p = 0.002$) were significantly different between groups. No Clavien grade \geq III complications were reported.

Bole (2020) reported a retrospective analysis of Rezūm for large prostates.^[11] A total of 182 patients were identified as having undergone Rezūm, 25.8% of whom had prostate volume

over 80cc. In this group, mean prostate volume was 119 cc and 55.3% were catheter dependent. AUA-SS improved from 22 pre-treatment to 13.4 following Rezūm ($p=0.04$). The improvement in peak flow rate was also statistically significant (7.7 to 12.7 mL/second; $p=0.002$).

Alegorides (2020) reported outcomes of 62 men with BPH treated with convective radiofrequency water vapor thermal therapy.^[12] The IPSS decreased significantly from baseline at six months post-treatment, and the decrease persisted at one year (12-point decrease, $p<0.001$). Also at one year, the QoL score decreased by 3.2 points ($p<0.001$), the Qmax improved by 6mL/s ($p<0.001$), and there was a 2.1% rate of surgical retreatment. No serious side effects (>Clavien II) and no cases of de novo erectile dysfunction were reported.

McVary (2020) reported on a retrospective case series of water vapor thermal therapy for nonneurogenic complete urinary retention associated with BPH.^[13] A total of 38 men with complete urinary retention and catheter-dependence were treated with water vapor thermal therapy using the Rezūm™ System. Of the 37 men available for follow-up, 26 voided spontaneously and were catheter free at a median of 26 days (range 4 to 65) following the procedure. Median follow-up for the catheter-free patients was 15.8 months. Adverse events included dysuria ($n=5$), gross hematuria ($n=4$), and UTIs in patients with indwelling catheters ($n=2$).

Mollengard (2018) published a retrospective review of 129 patients with BPH who underwent Rezūm. Minimum follow-up was four months. IPSS, and Qmax improved from baseline at the 91-180 day follow-up (18.3 to 6.9 and 10.5 to 16.8 mL/s, respectively; $p<0.001$). PVR also significantly improved over that time span (108.0 to 73.1, $p=0.005$). The most commonly reported adverse events were urinary tract infections (17%) and transient urinary retention (14%).

Darson (2017) reported the results of a case series of 131 patients treated with transurethral convective radiofrequency water-vapor thermal therapy with LUTS associated with BPH.^[14] Not all values were reported for all patients at all time-points. Statistical significance of changes from baseline was determined using a longitudinal general estimation-equation model using an exchangeable working correlation structure, which takes into account the correlation within a subject over time. IPSS at baseline, three to six months, and 12 months was 19.9 (SD = 6.7), 9.8 (SD = 6.9), and 10.1 (SD = 7.2). The three to six- and 12-month values were significantly lower than baseline ($p<0.001$). Qmax values at baseline, three to six, and 12 months were 8.7 (SD = 4.7), 11.6 (SD = 7.7), and 10 (SD = 5). The three- to six-month value was significantly different from baseline, but the 12-month value was not ($p=0.04$ and $p=0.4$, respectively). Improvement in IPSS-QOL scores from baseline to three-month follow-up was statistically significant, from 4.3 (SD = 1.2) to 2.3 (SD = 1.5; $p<0.0001$), and this statistically significant improvement was maintained at the 12-month follow-up. Urinary frequency, urgency, frequency and urgency, hematuria and nocturia were reported in less or equal to 4% of patients.

Dixon (2015 and 2016) reported the results of a case series in two publications.^[15, 16] A total of 65 men at or above the age of 45 experiencing LUTS secondary to BPH received convective radiofrequency thermal therapy. Results were gathered as self-administered questionnaires as well as measurements taken at scheduled follow-up visits over the following two years. Not all values were reported for all patients at all time-points. Statistical differences were calculated using a paired Student's *t*-test for each measure. IPSS at one, three, 12, and 24 months was

14.8 (SD = 8.4), 8.3 (SD = 5.8), 9.2 (SD = 6.5), and 9.6 (SD = 6.5), respectively. All values were significantly improved compared to baseline (21.7 SD = 5.5; $p < 0.001$). Qmax at one, three, 12, and 24 months was 9.9 (SD = 3.9), 12.8, 12.7 (SD = 6.3), and 12 (SD = 6.2). These values were also values were significantly improved compared to baseline (7.9 SD \pm 3.2; $p < 0.001$ except 24 months, where $p = 0.001$). Improvement in IPSS-QOL scores from baseline to each time point reported were statistically significant ($p < 0.001$). Adverse events reported were hematuria (14%), UTIs (20%), dysuria (22%), and urinary urgency (20%). All were mild to moderate transient events and 75% were reported within the first 30 days.

Section Summary

The evidence regarding transurethral water vapor thermal therapy of the prostate for the treatment of BPH includes one RCT and two case series. These studies report clinically significant improvements in several measures of urinary symptoms and quality of life. Limitations of the published evidence include limited comparative follow-up and lack of studies with no industry associations. Despite the limitations, water vapor thermal therapy appears to improve urologic symptom scores and quality of life.

PRACTICE GUIDELINE SUMMARY

American Urological Association

The American Urological Association (AUA) published a 2018 (updated in 2019 and 2020) evidence-based clinical practice guideline “Surgical Management of Lower Urinary Tract Symptoms Attributed to Benign Prostatic Hyperplasia: AUA Guideline,” which includes the following recommendations:^[17, 18]

- “Water vapor thermal therapy may be offered to patients with LUTS attributed to BPH provided prostate volume $< 80\text{g}$ (Moderate Recommendation; Evidence Level: Grade C).”
- “Water vapor thermal therapy may be offered to eligible patients who desire preservation of erectile and ejaculatory function. (Conditional Recommendation; Evidence Level: Grade C).”

A conditional recommendation is described as:

- Balance between Benefits & Risks/Burdens unclear
- Alternative strategies may be equally reasonable
- Better evidence likely to change confidence

SUMMARY

It appears that transurethral water vapor thermal therapy of the prostate may improve urinary symptoms for some people with benign prostatic hyperplasia. In addition, clinical practice guidelines based on evidence recommend transurethral water vapor thermal therapy of the prostate for certain individuals with benign prostatic hyperplasia. Therefore, transurethral water vapor thermal therapy of the prostate may be considered medically necessary when criteria are met. In all other situations, there is not enough evidence to show that transurethral water vapor thermal therapy of the prostate improves health outcomes.

Therefore, transurethral water vapor thermal therapy of the prostate is considered investigational when criteria are not met.

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CODES

Codes	Number	Description
CPT	53854	Transurethral destruction of prostate tissue; by radiofrequency generated water vapor thermotherapy
	53899	Unlisted procedure, urinary system
HCPCS	None	

Date of Origin: December 2018