MEDICAL POLICY DRAFT FOR REVIEW

MEDICAL POLICY DETAILS

<table>
<thead>
<tr>
<th>Medical Policy Title</th>
<th>MINIMALLY INVASIVE TREATMENTS FOR BENIGN PROSTATIC HYPERPLASIA (BPH)</th>
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<tbody>
<tr>
<td>Policy Number</td>
<td>7.01.104</td>
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<tr>
<td>Category</td>
<td>Technology Assessment</td>
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<tr>
<td>Effective Date</td>
<td></td>
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<td>Revised Date</td>
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</tbody>
</table>

Product Disclaimer

- If a product excludes coverage for a service, it is not covered, and medical policy criteria do not apply.
- If a commercial product (including an Essential Plan product) or a Medicaid product covers a specific service, medical policy criteria apply to the benefit.
- If a Medicare product covers a specific service, and there is no national or local Medicare coverage decision for the service, medical policy criteria apply to the benefit.

POLICY STATEMENT

I. Based upon our criteria and assessment of the peer-reviewed literature, prostatic urethral lift (i.e. UroLift®) has been medically proven to be effective and, therefore, is considered medically necessary for patients with symptomatic benign prostatic hyperplasia (BPH) who meet ALL of the following criteria:
   A. persistent or progressive lower urinary tract symptoms despite medical therapy (e.g., alpha blocker, PDE5 Inhibitor, finasteride/dutasteride) for at least six months or inability to tolerate medical therapy for BPH;
   B. estimated prostate volume less than 80 cc; and
   C. no obstructive median lobe of the prostate identified on cystoscopy.

II. Based upon our criteria and assessment of the peer-reviewed literature, prostatic urethral lift (i.e. UroLift®) has not been medically proven effective and, therefore, is considered investigational for all other indications.

III. Based upon our criteria and assessment of the peer-reviewed literature, transurethral water vapor thermal therapy (i.e. Rezūm®) has not been medically proven effective and, therefore, is considered investigational for the treatment of benign prostatic hyperplasia (BPH).

Refer to Corporate Medical Policy #7.01.28 Transurethral Microwave Thermotherapy.

Refer to Corporate Medical Policy #11.01.03 Experimental and Investigational Services.

POLICY GUIDELINE

I. The number of prostatic urethral lift implants will vary due to the unique characteristics of the prostate and prostatic urethra, but clinical data supports an average of four to five implants per procedure.

II. The Federal Employee Health Benefit Program (FEHBP/FEP) requires that procedures, devices or laboratory tests approved by the U.S. Food and Drug Administration (FDA) may not be considered investigational and thus these procedures, devices or laboratory tests may be assessed only on the basis of their medical necessity.

DESCRIPTION

Benign prostatic hyperplasia (BPH) is one of the most common afflictions in the aging man. It is a histologic diagnosis defined as the proliferation of smooth muscle and epithelial cells within the transition zone of the prostate gland. The enlarged gland has been proposed to contribute to the overall lower urinary tract symptoms (LUTS) complex through direct bladder outlet obstruction (BOO) from enlarged tissue and from increased smooth muscle tone and resistance within the enlarged gland. Voiding symptoms have often been attributed to the physical presence of BOO. BPH does not necessarily require treatment. The decision to treat is based on an assessment of the symptoms on quality of life which can be significant. Patients with persistent symptoms despite medical management may be considered for surgical treatment. The traditional standard treatment is transurethral resection of the prostate (TURP).
The UroLift System® (NeoTract Inc., Pleasanton, CA) is a minimally invasive, prostatic urethral lift (PUL) system that provides anterolateral mechanical traction of the lateral lobes of the prostate, opening the urethral lumen, and reducing urinary obstruction. The delivery device contains a preloaded implant that deploys a permanent tensioning suture. The suture runs from the urethra to the outer prostatic capsule and serves to pull the lateral lobe of the prostate away from the urethra. Implants are delivered bilaterally to separate the encroaching lobes. Four to five implants are typically inserted, but this varies with the size and shape of the prostate. The UroLift® may be used to treat prostate glands measuring less than 80 milliliters (mL) and is generally implanted by a urologist in an outpatient or inpatient setting. The transurethral procedure to insert the UroLift® is performed with the use of local or general anesthesia and oral sedation. In 2013, the FDA granted a de novo classification clearance for the UroLift® System (NeoTract, Inc., Pleasanton, CA). In January 2017, FDA granted 510(k) clearance for UroLift® System (UL400 and UL500) for the treatment of symptoms due to urinary outflow obstruction secondary to BPH, including lateral and median lobe hyperplasia, in men 45 years of age or older.

Transurethral water vapor thermal therapy has been investigated as a minimally invasive alternative to transurethral resection of the prostate. The Rezūm® System (NxThera, Inc., Maple Grove, MN) received FDA 510(k) approval in August 2015. The FDA indications for use state: The Rezūm® 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 ≥ 30 cm³ and ≤ 80 cm³. The Rezūm® System is also indicated for treatment of prostate with hyperplasia of the central zone and/or median lobe. Transurethral water vapor thermal therapy is a transurethral needle ablation technique which injects radiofrequency-generated, sterile water vapor (~103 degrees C) into enlarged prostate tissue. As the steam comes into contact with prostatic tissue, it condenses back into water, releasing large amounts of thermal energy, disrupting the prostatic cell membranes, and leading to cell death a necrosis. It takes approximately three months for the body to reabsorb dead tissue, decreasing prostate volume and relieving LUTS. The thermal energy is confined to the prostate which reduces the risk of injury to other parts of the body. The procedure in performed under local anesthesia in an office or outpatient setting.

RATIONALE

Prostatic Urethral Lift

In 2013, Roehrborn et al. reported results of the L.I.F.T. trial, the first multicenter, randomized, double-blinded trial of the prostatic urethral lift (PUL) for the treatment of lower urinary tract symptoms secondary to BPH. Nineteen centers in three countries (United States, Canada, and Australia) enrolled 206 men who were randomized 2:1 to treatment with either the PUL (n=140) or sham control (n=66) consisting of rigid cystoscopy. The primary endpoint was the reduction in AUASI at three months. Secondary measures included QOL, Benign Prostatic Hyperplasia Impact Index (BPHII), International Index of Erectile Function (IIEF), Male Sexual Health Questionnaire for Ejaculatory Dysfunction (MSHQ-EjD), Qmax, and PVR. Participants were followed for 12 months with 23 PUL subjects included in the 12-month analysis. The primary endpoint was met with the PUL AUASI reduction 88% greater than sham control, 11.1 vs. 5.9 respectively (p=0.003) and sustained at one year. Qmax (peak urinary flow rate) increased 4.4 ml per second at 3 months and was sustained at 4.0 ml per second at 12 months which was both clinically and statistically significant. Erectile function remained stable after the procedure. There were two serious adverse events, one clot retention and one bladder stone. Less serious AEs (postoperative dysuria, hematuria, pain/discomfort and urgency) were typically mild to moderate and resolved within two weeks. The authors conclude the prostatic urethral lift provides a clinically meaningful improvement in LUTS secondary to BPH and urinary flow and can be performed under local anesthesia with low morbidity and preservation of sexual function.

Roehrborn et al. (2017) reported five year results of the L.I.F.T. study. At five years of follow-up data were available for 104 of 140 PUL subjects (74.3%). A total of 18 were lost to follow-up, nine died of unrelated causes; nine exited the study for other reasons. Surgical retreatment for failure to cure was 13.6% with 4.3% receiving additional PUL implants and 9.3% undergoing TURP or laser ablation. The authors reported on two analyses, a per-protocol (PP) analysis and an intention-to-treat (ITT) analysis. A total of 72 patients were included in the per-protocol analysis after exclusion for protocol violations, additional BPH procedures, or treatment with BPH medication. Sustained improvements were
reported based on the PP analysis in symptoms (36% IPSS), quality of life (50% QOL, 52% BPHII) and urinary flow rate (44% Qmax). No differences were seen between ITT and PP populations.

Sonksen et al., (2015) conducted a randomized trial known as the BPH6 study, comparing PUL to TURP to determine LUTS improvement, recovery, worsening of erectile and ejaculatory function, continence, and safety. A total of 80 men across 10 European centers received either PUL (n=45) or TURP (n=35). One patient in the PUL group was excluded from analysis for violation of the active urinary retention exclusion criteria. At 12-month follow-up, the PUL group demonstrated an average decrease of 11.4 in IPSS, while IPSS improvement after TURP was 15.4. PUL patients consistently had more rapid recovery than TURP patients (82% vs. 53% respectively). Significant improvements in IPSS, IPSS QoL, BPH II, and Qmax were observed in both arms over time. Erectile function was preserved in both PUL and TURP groups as measured by SHIM scores. The PUL group experienced an improvement in average ejaculatory score (MSHQ EjD) from baseline (p = 0.03), but the TURP group suffered from a significant decline. For the BPH6 ejaculatory assessment, the response for the PUL group was 100%, significantly better than the 60.6% response for the TURP group (p < 0.0001). Continence preservation was comparable between the groups. The number of patients who experienced grade 2 and 3 adverse events was similar between groups. Participants who met the original BPH6 primary endpoint was 34.9% for the PUL group and 8.6% for the TURP group. For the modified BPH6 primary endpoint, 52.3% of PUL and 20.0% of TURP patients met. Reintervention for failure to cure occurred in 6.8% (3/44) of PUL and 5.7% (2/35) of TURP patients (not significant). The authors conclude PUL and TURP groups achieved significant symptom relief compared to baseline, with a superior symptom relief rate for TURP while PUL was superior to TURP in terms of quality of recovery and preservation of ejaculatory function. Limitations include the short-medium follow-up, small sample size, and lack of blinding.

In 2017, Gratzke et al. reported two-year follow-up results from the BPH6 study. Over the two year follow-up, six patients (13.6%) in the PUL arm and two (5.7%) in the TURP arm underwent secondary treatment for LUTS. Three additional patients discontinued study participation resulting in 37 PUL patients and 32 TURP patients included in the 2 year analysis. Significant improvements in International Prostate Symptom Score (IPSS), IPSS quality of life (QoL), BPH Impact Index (BPHII), and maximum urinary flow rate (Qmax) were observed in both arms throughout the two year follow up. Change in IPSS and Qmax in the TURP arm were superior to the PUL arm. Improvements in IPSS QoL and BPHII score were not statistically different between the study arms. PUL resulted in superior quality of recovery, ejaculatory function preservation and performance on the composite BPH6 index. Ejaculatory function bother scores did not change significantly in either treatment arm. TURP significantly compromised continence function at two weeks and three months. Only PUL resulted in statistically significant improvement in sleep.

In summary, based on the BPH6 study, PUL was noninferior to TURP based on the study’s composite endpoint and superior to TURP in preserving ejaculatory function. TURP was superior to PUL in managing lower urinary tract symptoms, specifically IPSS and Qmax, although PUL did significantly improve symptoms over two years. The LIFT study compared PUL to sham treatment in an RCT of 206 men and demonstrated meaningful improvements in LUTS and urinary flow without compromising sexual function. Five-year results from the LIFT study showed sustained improvements in symptoms (36% IPSS), quality of life (50% QOL, 52% BPHII) and urinary flow rate (44% Qmax). The MedLift study demonstrated promising results when PUL was used to treat median lobes in 45 patients with significant improvements in IPSS, QoL, BPHII and Qmax up to one year. Both the BPH6 and LIFT studies excluded men with median lobe obstruction. Published evidence supports a clinically meaningful improvement in net health outcome.

Transurethral Water Vapor Thermal Therapy

McVary et al. (2016a) reported the results of a multicenter, randomized, controlled study (Rezum II study) using transurethral prostate convective water vapor thermal energy to treat LUTS associated with BPH. A total of 197 men 50 yrs and older were randomized 2:1 to thermal therapy, n=136, and control (insertion of a rigid cystoscope), n=61. The primary endpoint was an IPSS reduction at three months greater than 125% in the treatment group as compared to the control. Results showed IPSS was reduced by 50% compared with 20% reduction for controls. Therapy outcomes for the treatment group, including Qmax, QoL (p < 0.0001) and BPHII (p= 0.0003), were significantly improved compared to control and sustained throughout 12 months. Two treatment subjects had 3 serious AEs adjudicated as procedure related: extended urinary retention and nausea and vomiting. The authors conclude convective water vapor energy ablation of
prostate adenomas provides statistically significant and clinically meaningful improvements within two weeks after treatment for LUTS due to BPH. Limitations include the short follow up period and small sample size.

McVary et al. (2019) reported four year outcomes of the randomized controlled trial of water vapor thermal therapy study. Out of the original 135 subjects who underwent water vapor therapy, 90 (66.7%) were included in the 48 month per protocol analysis. IPSS improvements from baseline remained consistent from the early response at 3 months (49.9%) to years 1 (52.2%), 2 (50.7%), 3 (49.7%) and 4 (46.7%). Flowrate improvements were sustained relative to baseline, remaining significant, although an increase of 5.5 at 1 year to a mean 4.2 mL/s at 4 years was noted. Men with moderate and severe LUTS had symptomatic relief with similar IPSS improvements at 4 years of 46.1% and 46.9% and Qmax of 45% and 51.3%, respectively. QOL and BPH Impact Index remained improved at 43% and 52% respectively, P <.0001. Throughout 4 years, urinary incontinence scores decreased significantly. Sexual function throughout 2 years after treatment shows that erectile function (IIEF) and ejaculatory function (MSHQ-EjD) scores remained unchanged, but worsened at four years. At four years, surgical intervention was performed in six of 135 subjects (4.4%) including four subjects in whom a median lobe was identified but not treated. Comparatively, surgical retreatment rates for TUNA are 19.1% at 3 years and 14%-51% at 5 years. TUMT retreatment at 5 years is 8.9%-21%, and prostatic urethral lift procedure has reported surgical retreatment of 10.6% at 3 years and 13.6% at 5 years. The authors conclude water vapor thermal therapy provides effective symptom relief and improved QOL that remained durable throughout four years.

In summary, the evidence for transurethral water vapor thermal therapy mostly consists of one small, short term, sham controlled RCT with a four year uncontrolled follow-up phase. LUTS improved more in the intervention group (50%) compared to sham (20%) at three months. Improvements were sustained through four years of follow-up. No adverse events on erectile or ejaculatory function were observed with scores unchanged through two years of follow-up. However, the evidence is limited by the small sample size, short term duration, lack of blinding for longer-term outcomes, and lack of comparison to alternative procedures such as TURP. The evidence is insufficient to determine the effects on health outcomes.

**CODES**

- Eligibility for reimbursement is based upon the benefits set forth in the member’s subscriber contract.
- CODES MAY NOT BE COVERED UNDER ALL CIRCUMSTANCES. PLEASE READ THE POLICY AND GUIDELINES STATEMENTS CAREFULLY.
- Codes may not be all inclusive as the AMA and CMS code updates may occur more frequently than policy updates.
- Code Key: Experimental/Investigational = (E/I)

### CPT Codes

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<tr>
<td>52442</td>
<td>Cystourethroscopy, with insertion of permanent adjustable transprostatic implant; each additional permanent adjustable transprostatic implant (List separately in addition to code for primary procedure)</td>
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<td>Transurethral destruction of prostate tissue; by radiofrequency generated water vapor thermotherapy</td>
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### HCPCS Codes

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ICD10 Codes

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<td>N40.1</td>
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REFERENCES


*Key Article

**KEY WORDS**

Rezūm, UroLift, transurethral water vapor thermal therapy, prostatic urethral lift

**CMS COVERAGE FOR MEDICARE PRODUCT MEMBERS**

There is currently a Local Coverage Determination (LCD), Water Vapor Thermal Therapy, for Rezūm® Water Vapor Therapy. Please refer to the following LCD website for Medicare Members: https://www.cms.gov/medicare-coverage-database/details/lcd-details.aspx?LCDId=37808&ver=17&SearchType=Advanced&CoverageSelection=Both&NCSelection=NCA%7cCAL%7cNCD%7cMEDCAC%7cTA%7cMCD&ArticleType=SAD&PolicyType=Both&s=41&KeyWord=rezum&KeyWordLookUp=Doc&KeyWordSearchType=Exact&kq=true&bc=MAAAABAAAAA&A

Based on our review, prostatic urethral lift is not addressed in National or Regional Medicare coverage determinations or policies.