2.01.49	Transurethral Water Vapor Thermal Therapy and Transurethral Water Jet Ablation (Aquablation) for Benign Prostatic Hypertrophy		
Original Policy Date:	August 1, 2019	**Effective Date:**	August 1, 2023
Section:	7.0 Surgery	**Page:**	Page 1 of 18

Policy Statement

I. Transurethral water vapor thermal therapy is considered **investigational** as a treatment of benign prostatic hyperplasia.

II. Transurethral waterjet ablation (aquablation) is considered **investigational** as a treatment of benign prostatic hyperplasia.

NOTE: Refer to Appendix A to see the policy statement changes (if any) from the previous version.

Policy Guidelines

A CPT code describes transurethral water vapor thermal therapy:

- **53854**: Transurethral destruction of prostate tissue; by radiofrequency generated water vapor thermotherapy

A Pass Through code was created as a result of an application by Procept for the AquaBeam® System. Per the manufacturer, it is intended for the resection and removal of prostate tissue in males suffering from lower urinary tract symptoms due to benign prostatic hyperplasia.

- **C2596**: Probe, image guided, robotic, waterjet ablation

There is a CPT for ultrasound guided transurethral ablation of prostate tissue for treating prostate cancer using thermotherapy with water vapor generated by high energy direct current.

- **0582T**: Transurethral ablation of malignant prostate tissue by high-energy water vapor thermotherapy, including intraoperative imaging and needle guidance

Description

Transurethral water vapor thermal therapy is a minimally invasive alternative to transurethral resection of the prostate (TURP). 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 procedure uses radiofrequency-generated water vapor (~103°C) thermal energy to ablate prostate tissue. 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.

Related Policies

- N/A

Benefit Application

Benefit determinations should be based in all cases on the applicable contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract

language will control. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

Some state or federal mandates (e.g., Federal Employee Program [FEP]) prohibits plans from denying Food and Drug Administration (FDA)-approved technologies as investigational. In these instances, plans may have to consider the coverage eligibility of FDA-approved technologies on the basis of medical necessity alone.

Regulatory Status

In September 2016, the Rezum System™ (NxThera, Inc) was cleared for marketing by the U.S. Food and Drug Administration through the 510(k) process (K150786). The Food and Drug Administration determined that this device was substantially equivalent to existing devices (Medtronic Prostiva devices). Rezum™ is intended to relieve symptoms, obstructions, and reduce prostate tissue associated with benign prostatic hyperplasia. It is indicated for men > 50 years of age with a prostate volume >30cm^3 and <80cm.^{3} The Rezum System™ is also indicated for the treatment of prostate with hyperplasia of the central zone and/or a median lobe.

Rationale

Background

Benign prostatic hyperplasia (BPH) is a common condition in older men, affecting to some degree 40% of men in their 50s, 70% of those between ages 60 and 69, and almost 80% of those ages 70 and older.[1,] BPH is a histologic diagnosis defined as an increase in the total number of stromal and glandular epithelial cells within the transition zone of the prostate gland. In some men, BPH results in prostate enlargement which can, in turn, lead to benign prostate obstruction and bladder outlet obstruction, which are often associated with lower urinary tract symptoms including urinary frequency, urgency, irregular flow, weak stream, straining, and waking up at night to urinate. Lower urinary tract symptoms is the most commonly presenting urological complaint and can have a significant impact on the quality of life.[1,]

BPH does not necessarily require treatment. The decision on whether to treat BPH is based on an assessment of the impact of symptoms on quality of life along with the potential side effects of treatment. Options for medical treatment include alpha-1-adrenergic antagonists, 5-alpha-reductase inhibitors, anticholinergic agents, and phosphodiesterase-5 inhibitors. Medications may be used as monotherapy or in combination.[2,]

Patients with persistent symptoms despite medical treatment may be considered for surgical treatment. The traditional standard treatment for BPH is transurethral resection of the prostate.

Transurethral water vapor thermal therapy has been investigated as a minimally invasive alternative to transurethral resection of the prostate. The procedure uses radiofrequency-generated water vapor (~103°C) thermal energy to ablate prostate tissue.[3,]

Literature Review

Evidence reviews assess the clinical evidence to determine whether the use of technology improves the net health outcome. Broadly defined, health outcomes are the length of life, quality of life, and ability to function including benefits and harms. Every clinical condition has specific outcomes that are important to patients and managing the course of that condition. Validated outcome measures are necessary to ascertain whether a condition improves or worsens; and whether the magnitude of that change is clinically significant. The net health outcome is a balance of benefits and harms.
To assess whether the evidence is sufficient to draw conclusions about the net health outcome of technology, 2 domains are examined: the relevance, and quality and credibility. To be relevant,

studies must represent 1 or more intended clinical use of the technology in the intended population and compare an effective and appropriate alternative at a comparable intensity. For some conditions, the alternative will be supportive care or surveillance. The quality and credibility of the evidence depend on study design and conduct, minimizing bias and confounding that can generate incorrect findings. The randomized controlled trial (RCT) is preferred to assess efficacy; however, in some circumstances, nonrandomized studies may be adequate. Randomized controlled trials are rarely large enough or long enough to capture less common adverse events and long-term effects. Other types of studies can be used for these purposes and to assess generalizability to broader clinical populations and settings of clinical practice.

Promotion of greater diversity and inclusion in clinical research of historically marginalized groups (e.g., People of Color [African-American, Asian, Black, Latino and Native American]; LGBTQIA (Lesbian, Gay, Bisexual, Transgender, Queer, Intersex, Asexual); Women; and People with Disabilities [Physical and Invisible]) allows policy populations to be more reflective of and findings more applicable to our diverse members. While we also strive to use inclusive language related to these groups in our policies, use of gender-specific nouns (e.g., women, men, sisters, etc.) will continue when reflective of language used in publications describing study populations.

Transurethral Water Vapor Thermal Therapy

Clinical Context and Therapy Purpose

The purpose of transurethral water vapor thermal therapy in individuals who have benign prostatic hyperplasia (BPH) and lower urinary tract symptoms (LUTS) is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest is men with BPH and LUTS. Symptoms include urinary frequency, urgency, irregular flow, weak stream, straining, and getting up at night to urinate.

Interventions

The therapy being considered is transurethral water vapor thermal therapy. This procedure involves the transurethral injection of steam into the prostate. Once injected, the steam condenses to water, imparting convective energy to the tissue, causing cell death and damage. The technology uses radiofrequency to boil the water to create the steam that is injected but does not impart radiofrequency directly to the prostate tissue. Patients typically require catheterization for at least 1 week due to post-procedure sloughing of prostatic tissue.

Medical management of pain and anxiety may also be required. In one RCT, 69% of patients received oral sedation only, 21% received a prostate block, and 10% received intravenous sedation.

Comparators

The following practices and therapies are currently being used to make decisions about transurethral water vapor thermal therapy:

- Conservative treatment, including watchful waiting and lifestyle modifications;
- Pharmacotherapy;
- Transurethral resection of the prostate (TURP);
- Prostatic urethral lift.

Outcomes

The general outcomes of interest are symptoms, functional outcomes, quality of life, retreatment rates, and treatment-related morbidity.
The International Prostate Symptom Score (IPSS) is used to assess the severity of BPH symptoms. The first 7 questions address urinary frequency, nocturia, weak urinary stream, hesitancy, intermittence,

incomplete emptying, and urgency each on a scale of 0 to 5. The total score, summed across the 7 items measured, ranges from 0 (no symptoms) to 35 (most severe symptoms). A decrease in score indicates improvement.

Quality of life is assessed with various scales including the IPSS-QoL.
Erectile and ejaculatory function is assessed in sexually active men only. Scales include the International Index of Erectile Function and the Male Sexual Health Questionnaire.
Both short-term (up to 12 months) and long-term (12 months and longer) outcomes should be assessed. Treatment-related morbidity can also be assessed in the immediate post-procedure period.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies;
- To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.

Review of Evidence

Systematic Review

Kang et al (2020) conducted a Cochrane review of transurethral water vapor thermal therapy for management of LUTS in men with BPH.[5] In literature searches conducted through February 2020, the reviewers identified only a single RCT (McVary et al [2015],[6] discussed in the section below). The reviewers concluded that there was moderate-to low-certainty evidence that the procedure appears to improve urologic symptom scores and quality of life compared to a sham procedure. However, there was very low certainty of evidence about the effects of the intervention on major adverse events.

Randomized Controlled Trial

Transurethral water vapor thermal therapy has been evaluated in a single RCT conducted in 197 men (Table 1). Three-month results were reported in McVary et al (2015).[6]
The trial also had an uncontrolled, open-label, crossover phase. After unblinding at 3 months, control subjects who elected to proceed were requalified for the crossover study. A total of 97 patients were followed through 3 years and 90 patients through 4 years. Three-year results were reported in McVary et al (2018)[3], and 4-year results in McVary et al (2019).[7] These results are shown in Table 1.

Table 1. Randomized Controlled Trial of Rezum: Characteristics

Study; Trial	Countries	Sites	Dates	Participants	Interventions	
					Active	*Comparator*
McVary et al 2015,[6] 2018[3], 2019[7], 2021[8] NCT01912339	United States	15	2013-2016	Men with moderate to severe symptomatic BPH, at least 50 years of age (61% were under age 65 years) with IPSS ≥13, a prostate volume of 30 mL to 80 mL, Qmax of ≤15 mL/s, and a measured postvoid residual urine of <250 mL. Exclusion criteria included a prostate-specific antigen >2.5	n=136 Transurethral water vapor thermal therapy (Rezum)	n=61 Sham procedure with rigid cystoscopy and activation of the system generator outside the subject's body to mimic the sound of the active procedure

Study; Trial	Countries	Sites	Dates	Participants	Interventions
				ng/mL with a free prostate specific antigen <25% (unless prostate cancer was ruled out by biopsy) and an active urinary tract infection.	

BPH: benign prostatic hyperplasia; IPSS: International Prostate Symptom Score; NCT: national clinical trial; Qmax: maximum urinary flow rate.

Results of the RCT are shown in Table 2. The primary outcome was the difference in the change from baseline between the treatment and control arms at 3 months post-treatment. The secondary outcome was the percentage of responders at 3 months. Response was defined as a 30% or greater improvement (reduction) in the IPSS at 3 months compared to baseline. The Rezum group showed an 11.2-point decrease in IPSS, versus a 4.3-point decrease in the sham group (p<.001). There were more responders (defined as 30% or more improvement in the IPSS) in the Rezum group. Notably, more than half of the patients in the control group were classified as responders at 3 months. There were significant differences in other measures of LUTS and quality of life.

One hundred thirty of the 197 participants (70.0%) reported being sexually active at baseline and were assessed for erectile function. There were no significant changes in erectile or ejaculatory function at follow-up and no differences between groups. That is, the treatment was not associated with adverse effects on erectile or ejaculatory function. A *post hoc* subgroup analysis of 125 Rezum-treated subjects who were sexually active at baseline found that sexual function continued to be unimpacted at 5 years.[9,] However, only 67 of these participants (53.6%) had follow-up data at this timepoint.

Two patients in the Rezum group experienced 3 serious procedure-related adverse events: 1 patient had de novo extended urinary retention and another had nausea and vomiting due to alprazolam and was hospitalized overnight for observation.

Table 2. Randomized Controlled Trial of Rezum: Results

Study	IPSS change from baseline	Responders (30% improvement in IPSS)	IPSS QoL	Qmax (mL/s)	BPHII	IIEF-EF	MSHQ-EjD function	MSHQ-EjD bother	Serious AEs
McVary et al (2015)[6,]									
N analyzed	197	197	197	194	195	130	130	130	197
Rezum	-11.2 (7.6)	106/136 (77.9%)	-2.1 (1.6)	6.2 (7.1)	-3.4 (3.5)	0.1 (7.4)	0.3 (4.3)	-0.4 (1.9)	66/136 (48.5%)
Sham	-4.3 (6.9)	21/61 (59.5%)	-0.9 (1.5)	0.5 (4.2)	-1.5 (3.0)	-1.5 (3.0)	-0.2 (3.2)	-0.2 (1.9)	4/61 (6.6%)
p-value	<.0001	<.0001	<.0001	<.0001	<.0003	.0003	.443	.623	NR

AE: adverse events; BPHII: benign prostatic hyperplasia Impact Index; IIEF: International Index of Erectile Function; IPSS: International Prostate Symptom Score; MSHQ-EjD: Male Sexual Health Questionnaire for Ejaculatory Dysfunction; NR: not reported; Qmax: peak urinary flow rate; QoL: quality of life.

The trial also had an uncontrolled, open-label, crossover phase, reported in McVary et al (2018), McVary et al (2019), and McVary et al (2021). After unblinding at 3 months, control subjects who elected to proceed were requalified for the crossover study. A total of 98 patients were followed through 60 months. These results are shown in Table 3. Urinary symptoms and quality of life remained significantly improved from baseline up to 5 years. Over 5 years, the surgical retreatment rate was 4.4% and the medication retreatment rate was 11.1%.[8,]

Table 3. Randomized Controlled Trial of Rezum: Results of Open-label Uncontrolled Crossover Phase (McVary et al [2018][3], McVary et al [2019][7], and McVary et al [2021])[8]

Outcome, mean change from baseline (SD)	3 months	6 months	12 months	24 months	36 months	48 months	60 months[1]
IPSS							
N	134	129	121	109	97	90	
Change	-11.3 (7.6)	-12.2 (7.6)	-11.6 (7.3)	-11.2 (7.3)	-11.0 (7.1)	-10.1 (7.6)	-11.1 (7.8)
p-value	<.0001	<.0001	<.0001	<.0001	<.0001	<.0001	
IPSS QoL							
N	134	129	121	109	97	90	
Change	-2.1 (1.6)	-2.3 (1.6)	-2.2 (1.6)	-2.2 (1.5)	-2.2 (1.6)	-2.0 (1.7)	-2.2 (1.4)
p-value	<.0001	<.0001	<.0001	<.0001	<.0001	<.0001	
Qmax							
N	125	119	112	99	80	81	
Change	6.4 (7.2)	5.7 (6.2)	5.5 (6.4)	4.8 (6.1)	3.5 (4.7)	4.2 (5.7)	4.1
p-value							
PVR volume							
N	133	125	118	106	92	89	
Change	-10.6 (68.3)	-8.4 (75.8)	-3.9 (82.7)	-0.3 (85.3)	-26.4 (63.9)	-9.2 (72.2)	NR
p-value	.3459	.3721	.8943	.6549	.0004		
BPHII							
N	143	129	121	109	97	90	
Change	-3.4 (3.5)	-4.1 (3.0)	-3.9 (3.3)	-3.8 (3.1)	-3.7 (3.3)	-3.5 (3.4)	-2.2 (1.4)
p -value	<.0001	<.0001	<.0001	<.0001	<.0001	<.0001	
IIEF-EF							
N	90	84	77	71	62	58	
Change	0.1 (7.4)	-0.3 (6.4)	-0.3 (7.5)	-1.2 (7.6)	-1.9 (8.2)	-2.5 (8.7)	-2.4 ± 9.2
p-value	.8927	.8816	.8709	.4080	.1119	.03333	
MSHQ-EjD Function							
N	90	83	78	70	63	56	
change	0.3 (4.3)	0.1 (3.6)	-0.3 (3.5)	-0.5 (4.2)	-1.4 (3.8)	-1.8 (4.4)	NR
p-value	.5612	.7451	.2778	.3505	.0033	.0038	
MSHQ-EjD Bother							
N	90	84	79	70	63	56	
change	-0.3 (1.9)	-0.4 (1.9)	-0.7 (1.8)	-0.5 (1.7)	-0.5 (1.6)	-0.1 (1.8)	NR
p-value	.776	.951	.0015	.0129	.0060	.6495	

[1]Some outcomes were presented graphically only and did not include number analyzed, P-values, or change from baseline.
BPHII: Benign Prostatic Hyperplasia Impact Index; IIEF-EF: International Index of Erectile Function; IPSS: International Prostate Symptom Score; MSHQ-EjD: Male Sexual Health Questionnaire for Ejaculatory Dysfunction; NR: not reported; PVR: postvoid residual urine volume; Qmax: peak urinary flow rate; QoL: quality of life; SD: standard deviation.

Notable relevance and study design and conduct limitations of the RCT reported by McVary et al are summarized in Tables 4 and 5. The major limitations were the short follow-up duration in the sham-controlled phase, and lack of blinding, no control group, and high loss to follow-up in the follow-up phase. Additionally, no studies have compared Rezum to medical management, TURP, or other minimally invasive procedures. Because LUTS in men with BPH may improve spontaneously over time, it is important for future studies to include a longer follow-up period with a control group.

Table 4. Study Relevance Limitations

Study	Population[a]	Intervention[b]	Comparator[c]	Outcomes[d]	Follow-Up[e]
McVary et al (2015)[6]			Sham procedure; no comparison to	Clinically significant difference on	1, 2: 3 months

Study	Population[a]	Intervention[b]	Comparator[c]	Outcomes[d]	Follow-Up[e]
			alternative treatments	symptoms not prespecified	
McVary et al (2018)[3], McVary et al (2019)[7], and McVary et al (2021)[8],			No control group (comparison to baseline only)	Clinically significant difference in symptom outcomes not prespecified	

The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
[a] Population key: 1. Intended use population unclear; 2. Clinical context is unclear; 3. Study population is unclear; 4. Study population not representative of intended use.
[b] Intervention key: 1. Not clearly defined; 2. Version used unclear; 3. Delivery not similar intensity as comparator; 4.Not the intervention of interest.
[c] Comparator key: 1. Not clearly defined; 2. Not standard or optimal; 3. Delivery not similar intensity as intervention; 4. Not delivered effectively.
[d] Outcomes key: 1. Key health outcomes not addressed; 2. Physiologic measures, not validated surrogates; 3. No CONSORT reporting of harms; 4. Not establish and validated measurements; 5. Clinical significant difference not prespecified; 6. Clinical significant difference not supported.
[e] Follow-Up key: 1. Not sufficient duration for benefit; 2. Not sufficient duration for harms.

Table 5. Study Design and Conduct Limitations

Study	Allocation[a]	Blinding[b]	Selective Reporting[c]	Data Completeness[d]	Power[e]	Statistical[f]
McVary et al (2015)[6],						
McVary et al (2018)[3], McVary et al (2019)[7], and McVary et al (2021)[8],		1, 2, 3: open label		High loss to follow-up (97/197 [49%] had 3-year data on primary outcome), 90/197 (46%) had 4-year data), 98/197 (50%) had 5-year data		

The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
[a] Allocation key: 1. Participants not randomly allocated; 2. Allocation not concealed; 3. Allocation concealment unclear; 4. Inadequate control for selection bias.
[b] Blinding key: 1. Not blinded to treatment assignment; 2. Not blinded outcome assessment; 3. Outcome assessed by treating physician.
[c] Selective Reporting key: 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication.
[d] Data Completeness key: 1. High loss to follow-up or missing data; 2. Inadequate handling of missing data; 3. High number of crossovers; 4. Inadequate handling of crossovers; 5. Inappropriate exclusions; 6. Not intent to treat analysis (per protocol for noninferiority trials).
[e] Power key: 1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on clinically important difference.
[f] Statistical key: 1. Analysis is not appropriate for outcome type: (a) continuous; (b) binary; (c) time to event; 2. Analysis is not appropriate for multiple observations per patient; 3. Confidence intervals and/or p values not reported; 4. Comparative treatment effects not calculated.

Section Summary: Transurethral Water Vapor Thermal Therapy

Rezum effectively reduced symptoms of BPH compared to sham treatment in one RCT with 5 years of follow-up; however, comparisons to TURP or other active therapies are lacking.

Transurethral Waterjet Ablation (Aquablation)

Clinical Context and Therapy Purpose

The purpose of aquablation in individuals who have BPH and LUTS is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The following PICO was used to select literature to inform this review.

Populations
The relevant population of interest is men with BPH and LUTS. Symptoms include urinary frequency, urgency, irregular flow, weak stream, straining, and getting up at night to urinate.

Interventions
The therapy being considered is transurethral waterjet ablation, known as aquablation. Aquablation cuts tissue by using a pressurized jet of fluid delivered to the prostatic urethra. The device is able to image the treatment area, or pairs with an imaging modality, to monitor treatment progress.

Comparators
The following practices and therapies are currently being used to make decisions about aquablation:

- Conservative treatment, including watchful waiting and lifestyle modifications;
- Pharmacotherapy;
- TURP;
- Prostatic urethral lift.

Outcomes
The general outcomes of interest are symptoms, functional outcomes, quality of life, retreatment rates, and treatment-related morbidity.

The IPSS is used to assess the severity of BPH symptoms. The first 7 questions address urinary frequency, nocturia, weak urinary stream, hesitancy, intermittence, incomplete emptying, and urgency each on a scale of 0 to 5. The total score, summed across the 7 items measured, ranges from 0 (no symptoms) to 35 (most severe symptoms). A decrease in score indicates improvement. Quality of life is assessed with various scales including the IPSS-QoL.

Erectile and ejaculatory function is assessed in sexually active men only. Scales include the International Index of Erectile Function and the Male Sexual Health Questionnaire.
Both short-term (up to 12 months) and long-term (12 months and longer) outcomes should be assessed. Treatment-related morbidity can also be assessed in the immediate post-procedure period.

Study Selection Criteria
Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies;
- To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.

Review of Evidence

Systematic Review

Elterman et al (2021) performed a meta-analysis of individual patient data from 4 prospective, multicenter trials (N=425) with aquablation in the management of symptomatic BPH (Tables 6 to 8).[10,] The 4 studies were WATER (an RCT), WATER II (a prospective single-arm study), OPEN WATER (a prospective single-arm study), and FRANCAIS WATER (an observational study). Each study had at least 1 year of follow-up. Pooled results from all 4 studies showed improvement from baseline in IPSS, IPSS-QoL, maximum urine flow rate, and postvoid residual volume. There were no new cases of erectile dysfunction postoperatively, but 10.8% of men reported new ejaculatory dysfunction.

Table 6. Comparison of Trials/Studies Included in Systematic Review and Meta-Analysis

	Elterman et al (2021)[10,]
Gilling et al (2019)[11,]; WATER	●
Bhojani et al (2019)[12,]; WATER II	●
Misrai et al (2019)[13,]; FRANCAIS WATER	●
Bach et al (2020)[14,]; OPEN WATER	●

Table 7. Systematic Review & Meta-Analysis Characteristics

Study	Dates	Trials	Participants	N (Range)	Design	Duration
Elterman et al (2021)[10,]	2015-2019	4	Men treated with Aquablation for BPH	425 (30 to 178)	1 RCT, 2 uncontrolled cohorts, 1 observational study	At least 1 year

BPH: benign prostatic hyperplasia; RCT: randomized controlled trial.

Table 8. Systematic Review & Meta-Analysis Results

Study	IPSS change from baseline (points)	IPSS-QoL change from baseline (points)	Qmax change from baseline (mL/s)	PVR change from baseline (mean, mL)
Elterman et al (2021)[10,]				
425	425	425	425	425
Pooled effect	-16	-3.3	9.4	-62

IPSS: International Prostate Symptom Score; PVR: postvoid residual urine volume; Qmax: peak urinary flow rate; QoL: quality of life.

Randomized Controlled Trial

Aquablation for treatment of BPH has been assessed in a single RCT, known as WATER (Waterjet Ablation Therapy for Endoscopic Resection of Prostate Tissue).[11,] WATER was a noninferiority trial comparing aquablation with TURP in 181 participants at 17 sites in 4 countries (Table 9). Participants were men ages 45 to 80 years with moderate-to-severe LUTS, defined as an IPSS 10 score ≥12, and prostate size between 30 and 80 mL. The primary efficacy endpoint was the difference between groups in the change in IPSS at 6 months, and the primary safety endpoint was the development of Clavien-Dindo persistent grade 1, or 2 or higher operative complications at 3 months. Primary endpoint results were reported by Gilling et al in 2018,[11,] 12-month results in Gilling et al (2019),[15,], 3-year results in Gilling et al (2020) [16,], and 5-year results in Gilling et al (2022)[17,] Additionally, a synthesis of the trial results up to 12 months was reported in a Cochrane systematic review conducted by Hwang et al (2019).[18,]

On the primary efficacy outcome in WATER, aquablation was noninferior to TURP. At 6 months, mean IPSS decreased from baseline by 16.9 points for aquablation and 15.1 points for TURP (mean difference, 1.8 points; p<.0001 for noninferiority and p=.1347 for superiority). The primary safety endpoint rate was lower in the aquablation group compared to the TURP group (26% vs. 42% ; p=.0149). The rate of grade 2 and greater events was similar in the 2 groups (20% for aquablation and 23% for TURP; p=.3038).

Table 9. Summary of Key Randomized Controlled Trial Characteristics

Trial	Countries	Sites	Dates	Participants	Interventions	
					Active	*Comparator*
WATER[11,16,17,] NCT02505919	US, UK, Australia, New Zealand	17	October 2015-December 2016	Men age 45 to 80 years with a prostate size between 30 to 80 mL, moderate-to	Aquablation n=65	TURP n=116

Trial	Countries	Sites	Dates	Participants	Interventions
				severe LUTS (IPSS 10 to ≥12), and Qmax <15 mL/s.	

IPSS: International Prostate Symptom Score; LUTS: lower urinary tract symptoms; Qmax: peak urinary flow rate; TURP: transurethral resection of the prostate; WATER: Waterjet Ablation Therapy for Endoscopic Resection of Prostate Tissue.

WATER trial results at 12 months, as summarized in the Cochrane review, are shown in Table 10. The reviewers assessed the certainty of the evidence for each outcome using the GRADE approach.[18,] The reviewers concluded that up to 12 months, aquablation likely results in a similar improvement in urologic symptom scores to TURP and may result in similar quality of life when compared to TURP. The authors also concluded that aquablation may result in little to no difference in major adverse events, but considered the evidence for this finding very low certainty due to study limitations and imprecision of estimates.

Table 10. WATER Trial Results at 12 months (Adapted from Hwang et al [2019][18,])

Outcome at 12 months	N Analyzed	Mean Difference (95% CI)	Certainty of the Evidence (Reason for downgrading)
IPSS	174	-0.6 (-2.51 to 2.39)	Moderate (study limitations)
IPSS QoL	174	0.27 (-0.024 to 0.78)	Low (imprecision)
Major adverse events	181	15 fewer per 1000 (-64 to 116) RR 0.84 (0.31 to 2.26)	Very low (high risk of performance bias, unclear risk of reporting bias, wide CI crosses assumed threshold of minimal clinically important difference)
Retreatment	181	10 more per 1000 (13 fewer to 228 more) RR 1.68 (0.18 to 15.83)	Very low (imprecision and high risk of performance and attrition bias)
Erectile function	64	2.31 (-0.63 to 5.25)	Very low (imprecision and high risk of performance and attrition bias)
Ejaculatory function	121	2.57 (0.6 to 4.53)	Very low (imprecision: CI crosses assumed threshold of minimal clinically important difference, high risk of performance and attrition bias)

Source: adapted from Hwang et al (2019)[18,]
CI: confidence interval; IPSS: International Prostate Symptom Score; QoL: quality of life; RR: relative risk; WATER: Waterjet Ablation Therapy for Endoscopic Resection of Prostate Tissue.

Gilling et al (2020) and Gilling et al (2022) reported WATER trial results at 3 and 5 years, respectively (Table 11).[16,17,] Improvements in symptoms and quality of life were maintained through 3 years in both treatment groups, and the rate of serious adverse events did not differ between groups any any time point. Efficacy was maintained through 5 years as well, but safety results were not reported beyond 3 years.

Table 11. WATER Trial Results at 3 and 5 Years

Study	Mean IPSS reduction	Mean % reduction in IPSS	Improvement at least 5 points from baseline	IPSS QoL improvement	Qmax (mL/s)	Retreatment Rate	Serious AEs Subjects (%)
WATER[16,17], NCT02505919							
3 year results							
Aquablation	14.4 (6.8)	64%	78%	3.2 (1.8)	11.6	5/116 (4.3%)	0 to 3 months: 7 (6.0%) 3 months to 1 year: 5 (4.3%) 1 to 2 years: 8 (6.9%) 2 to 3 years: 4 (3.4%)
TURP	13.9 (8.6)	61%	82%	3.2 (1.7)	8.2	1/65 (1.5%)	0 to 3 months: 4 (6.2%) 3 months to 1 year: 5 (7.7%) 1 to 2 years: 2 (3.1%) 2 to 3 years: 1 (1.5%)
Difference	0.6 (-3.3 to 2.2)	3%	4%	0	3.3 (-0.5 to 7.1)	2.8%	
p-value	.6848	NS	NS	.7845	.0848	.4219	NS at any time point
5 year results							
Aquablation	15.1 (6.6)	NR	NR	NR	8.7 (9.1)	6.0%	NR
TURP	13.2 (8.2)	NR	NR	NR	6.3 (7.5)	12.3%	NR
Difference	1.9	NR	NR	NR	NR	6.3%	NR
p-value	.2764	NR	NR	NR	NR	NR	NR

AE: adverse events; IPSS: International Prostate Symptom Score; NS: not significant; Qmax: peak urinary flow rate; QoL: quality of life; TURP: transurethral resection of the prostate; WATER: Waterjet Ablation Therapy for Endoscopic Resection of Prostate Tissue.

Study design and conduct limitations of the WATER trial are displayed in Tables 12 and 13. Limitations included a lack of blinding of treating clinicians and baseline evaluators, but blinding of study participants makes this less of a concern. Adverse events were adjudicated up to 1 year, but not after 1 year.

Table 12. Study Relevance Limitations

Study	Population[a]	Intervention[b]	Comparator[c]	Outcomes[d]	Follow-Up[e]
WATER[11,16,17], NCT02505919				**Adverse events occurring after month 12 were not adjudicated by the clinical events committee**	

The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
[a] Population key: 1. Intended use population unclear; 2. Clinical context is unclear; 3. Study population is unclear; 4. Study population not representative of intended use.
[b] Intervention key: 1. Not clearly defined; 2. Version used unclear; 3. Delivery not similar intensity as comparator; 4.Not the intervention of interest.
[c] Comparator key: 1. Not clearly defined; 2. Not standard or optimal; 3. Delivery not similar intensity as intervention; 4. Not delivered effectively.
[d] Outcomes key: 1. Key health outcomes not addressed; 2. Physiologic measures, not validated surrogates; 3. No

CONSORT reporting of harms; 4. Not establish and validated measurements; 5. Clinical significant difference not prespecified; 6. Clinical significant difference not supported.
[e] Follow-Up key: 1. Not sufficient duration for benefit; 2. Not sufficient duration for harms.

Table 13. Study Design and Conduct Limitations

Study	Allocation[a]	Blinding[b]	Selective Reporting[c]	Data Completeness[d]	Power[e]	Statistical[f]
WATER[11,16,17,] NCT02505919		Baseline evaluation and study surgeons were not blinded; patients and outcome assessors were blinded	Unclear - secondary outcomes not prespecified			

The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
[a] Allocation key: 1. Participants not randomly allocated; 2. Allocation not concealed; 3. Allocation concealment unclear; 4. Inadequate control for selection bias.
[b] Blinding key: 1. Not blinded to treatment assignment; 2. Not blinded outcome assessment; 3. Outcome assessed by treating physician.
[c] Selective Reporting key: 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication.
[d] Data Completeness key: 1. High loss to follow-up or missing data; 2. Inadequate handling of missing data; 3. High number of crossovers; 4. Inadequate handling of crossovers; 5. Inappropriate exclusions; 6. Not intent to treat analysis (per protocol for noninferiority trials).
[e] Power key: 1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on clinically important difference.
[f] Statistical key: 1. Analysis is not appropriate for outcome type: (a) continuous; (b) binary; (c) time to event; 2. Analysis is not appropriate for multiple observations per patient; 3. Confidence intervals and/or p values not reported; 4. Comparative treatment effects not calculated.

Section Summary: Transurethral Waterjet Ablation (Aquablation)

Aquablation was compared to TURP in the WATER trial, with follow-up until 5 years. Aquablation was superior to TURP for the primary safety endpoint at 6 months, but few safety results beyond 6 months are available. At 3 years and 5 years, there were no significant differences between groups in IPSS scores.

Supplemental Information

The purpose of the following information is to provide reference material. Inclusion does not imply endorsement or alignment with the evidence review conclusions.

Practice Guidelines and Position Statements

Guidelines or position statements will be considered for inclusion in 'Supplemental Information' if they were issued by, or jointly by, a US professional society, an international society with US representation, or National Institute for Health and Care Excellence (NICE). Priority will be given to guidelines that are informed by a systematic review, include strength of evidence ratings, and include a description of management of conflict of interest.

American Urological Association

In 2021, the American Urological Association published guidelines on the surgical evaluation and treatment of lower urinary tract symptoms (LUTS) attributed to benign prostatic hyperplasia (BPH) and included the following recommendations related to the interventions included in this evidence review:[19,]

- Water vapor thermal therapy should be considered as a treatment option for patients with LUTS/BPH provided prostate volume is 30 to 80 mL. (Moderate Recommendation; Evidence Level: Grade C)
- Water vapor thermal therapy may be offered as a treatment option to eligible patients who desire preservation of erectile and ejaculatory function. (Conditional Recommendation; Evidence Level: Grade C)
- Robotic waterjet treatment may be offered as a treatment option to patients with LUTS/BPH provided prostate volume is 30 to 80 mL. (Conditional Recommendation; Evidence Level: Grade C)

National Institute for Health and Care Excellence
In 2020, the NICE issued the following guidance on Rezum for treatment of LUTS secondary to BPH:[20,]
"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."

"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^3 and 80 cm^3)."

In 2018, NICE issued the following guidance on transurethral water jet ablation for LUTS caused by BPH:
"The evidence on transurethral water jet ablation for lower urinary tract symptoms caused by benign prostatic hyperplasia raises no major safety concerns. The evidence on efficacy is limited in quantity. Therefore, this procedure should only be used with special arrangements for clinical governance, consent, and audit or research."[21,]

The guidance also states, "NICE encourages further research into transurethral water jet ablation for LUTS caused by BPH and may update the guidance on publication of further evidence. Further research should report long-term follow-up and include reintervention rates."[21,]

A Medtech innovation briefing was released by NICE in January 2023 but guidance specific to Aquablation is awaiting development as of March 7, 2023.[22,]

U.S. Preventive Services Task Force Recommendations
Not applicable.

Medicare National Coverage
There is no national coverage determination. In the absence of a national coverage determination, coverage decisions are left to the discretion of local Medicare carriers.

Ongoing and Unpublished Clinical Trials
Ongoing trials that might influence this review are listed in Table 14.

Table 14. Summary of Key Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
Ongoing			
NCT04838769	Water Vapor Thermotherapy vs. Combination Pharmacotherapy for Symptomatic Benign Prostatic Hyperplasia Refractory to	394	Jul 2026

NCT No.	Trial Name	Planned Enrollment	Completion Date
	Alpha Blocker Monotherapy in Sexually Active Men: A Multicenter Randomized Controlled Trial		
NCT05762198	A Randomized Controlled Trial Comparing Water Vapour Thermal Therapy (Rezūm) and TURP in Men With Benign Prostatic Hyperplasia in Refractory Urinary Retention	108	Jun 2026
NCT04338776[a]	C.L.E.A.R. - Comparing UroLift Experience Against Rezum	120	Dec 2024
NCT04801381	WATER III: A Randomized, Controlled Trial of Aquablation vs. Transurethral Laser Enucleation of Large Prostates (80 - 180 mL) in Benign Prostatic Hyperplasia	200	Dec 2027

[a]Denotes industry sponsored or cosponsored trial
NCT: National Clinical Trial

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Documentation for Clinical Review

- No records required

Coding

This Policy relates only to the services or supplies described herein. Benefits may vary according to product design; therefore, contract language should be reviewed before applying the terms of the Policy.

The following codes are included below for informational purposes. Inclusion or exclusion of a code(s) does not constitute or imply member coverage or provider reimbursement policy. Policy Statements are intended to provide member coverage information and may include the use of some codes for clarity. The Policy Guidelines section may also provide additional information for how to interpret the Policy Statements and to provide coding guidance in some cases.

Type	Code	Description
CPT®	0582T	Transurethral ablation of malignant prostate tissue by high-energy water vapor thermotherapy, including intraoperative imaging and needle guidance
	53854	Transurethral destruction of prostate tissue; by radiofrequency generated water vapor thermotherapy
	55899	Unlisted procedure, male genital system
HCPCS	C2596	Probe, image guided, robotic, waterjet ablation

Policy History

This section provides a chronological history of the activities, updates and changes that have occurred with this Medical Policy.

Effective Date	Action
08/01/2019	BCBSA Medical Policy adoption
03/01/2020	Coding update
08/01/2023	Policy reactivated. Previously archived from 07/01/2020 to 07/31/2023.

Definitions of Decision Determinations

Medically Necessary: Services that are Medically Necessary include only those which have been established as safe and effective, are furnished under generally accepted professional standards to treat illness, injury or medical condition, and which, as determined by Blue Shield, are: (a) consistent with Blue Shield medical policy; (b) consistent with the symptoms or diagnosis; (c) not furnished primarily for the convenience of the patient, the attending Physician or other provider; (d) furnished at the most appropriate level which can be provided safely and effectively to the patient; and (e) not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of the Member's illness, injury, or disease.

Investigational/Experimental: A treatment, procedure, or drug is investigational when it has not been recognized as safe and effective for use in treating the particular condition in accordance with generally accepted professional medical standards. This includes services where approval by the federal or state governmental is required prior to use, but has not yet been granted.

Split Evaluation: Blue Shield of California/Blue Shield of California Life & Health Insurance Company (Blue Shield) policy review can result in a split evaluation, where a treatment, procedure, or drug will be considered to be investigational for certain indications or conditions, but will be deemed safe and effective for other indications or conditions, and therefore potentially medically necessary in those instances.

Prior Authorization Requirements and Feedback (as applicable to your plan)

Within five days before the actual date of service, the provider must confirm with Blue Shield that the member's health plan coverage is still in effect. Blue Shield reserves the right to revoke an authorization prior to services being rendered based on cancellation of the member's eligibility. Final determination of benefits will be made after review of the claim for limitations or exclusions.

Questions regarding the applicability of this policy should be directed to the Prior Authorization Department at (800) 541-6652, or the Transplant Case Management Department at (800) 637-2066 ext. 3507708 or visit the provider portal at www.blueshieldca.com/provider.

We are interested in receiving feedback relative to developing, adopting, and reviewing criteria for medical policy. Any licensed practitioner who is contracted with Blue Shield of California or Blue Shield of California Promise Health Plan is welcome to provide comments, suggestions, or concerns. Our internal policy committees will receive and take your comments into consideration.

For utilization and medical policy feedback, please send comments to: MedPolicy@blueshieldca.com

Disclaimer: This medical policy is a guide in evaluating the medical necessity of a particular service or treatment. Blue Shield of California may consider published peer-reviewed scientific literature, national guidelines, and local standards of practice in developing its medical policy. Federal and state law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over medical policy and must be considered first in determining covered services. Member contracts may differ in their benefits. Blue Shield reserves the right to review and update policies as appropriate.

Appendix A

POLICY STATEMENT	
BEFORE	**AFTER** **Blue font: Verbiage Changes/Additions**
Reactivated Policy **Policy Statement:** N/A	**Transurethral Water Vapor Thermal Therapy and Transurethral Water Jet Ablation (Aquablation) for Benign Prostatic Hypertrophy** **2.01.49** **Policy Statement:** I. Transurethral water vapor thermal therapy is considered **investigational** as a treatment of benign prostatic hyperplasia. II. Transurethral waterjet ablation (aquablation) is considered **investigational** as a treatment of benign prostatic hyperplasia.