LOUISIANA BLUE

Transurethral Water Vapor Thermal Therapy (Rezum) and Transurethral Water Jet Ablation (Aquablation) for Benign Prostatic Hypertrophy

Policy # 00684
Original Effective Date: 12/01/2019
Current Effective Date: 02/01/2025

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

Note: Prostatic Urethral Lift is addressed separately in medical policy 00480.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Company may consider water vapor energy ablation (Rezum) for the treatment of benign prostatic hyperplasia (BPH) to be **eligible for coverage**** when ALL of the following criteria are met:

Patient Selection Criteria

Coverage eligibility will be considered when all of the following criteria are met:

- Moderate to severe lower urinary tract symptoms related to BPH (i.e., IPSS $\geq$ 12 and Qmax $\leq$ 15 mL/s; see Policy Guidelines); **AND**
- $\geq$ 50 years of age; **AND**
- Failure or inability to tolerate medical therapy (α1-adrenergic antagonists maximally titrated, 5α-reductase inhibitors, or combination medication therapy maximally titrated) over a trial period of no less than 6 months; **AND**
- Prostate volume 30-80 (g) cm^3 by transrectal ultrasound; **AND**
- Absence of all the following:
    - Active urinary tract infection (UTI or prostatitis)
    - Current treatment of chronic prostatitis
    - Known or suspected prostate cancer or a prostate specific antigen (PSA) > 10 ng/mL unless there has been a negative prostate biopsy within the last 6 months.

Based on review of available data, the Company may consider transurethral waterjet ablation (aquablation with the Aquabeam system) for the treatment of benign prostatic hyperplasia (BPH) to be **eligible for coverage**** when ALL of the following criteria are met:

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Patient Selection Criteria
Coverage eligibility will be considered when all of the following criteria are met:

- Moderate to severe lower urinary tract symptoms related to BPH causing bladder outlet obstruction (i.e., IPSS ≥ 12 and a Qmax ≤ 15 mL/s); **AND**
- Age from 45 to 80 years; **AND**
- Failure or inability to tolerate medical therapy (α1-adrenergic antagonists maximally titrated, 5α-reductase inhibitors, or combination medication therapy maximally titrated) over a trial period of no less than 6 months; **AND**
- Prostate volume 30-150 (g) cm^3 by transrectal ultrasound; **AND**
- Absence of all the following:
    - Active urinary tract (UTI or prostatitis) or systemic infection
    - Current treatment of chronic prostatitis
    - Body mass index (BMI) ≥ 42 kg/m2
    - Known or suspected prostate cancer or a prostate specific antigen (PSA) > 10 ng/mL unless there has been a negative prostate biopsy within the last 6 months
    - Current or suspected bladder cancer, or actively treated bladder cancer within the past 2 years
    - Bladder calculus or clinically significant bladder diverticulum (pouch size > 20% of full bladder size)
    - Diagnosis of urethral stricture, meatal stenosis, or bladder neck contracture.

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, water vapor energy ablation (Rezum) for all other indications, including but not limited to use in individuals with a diagnosis of prostate cancer, use after other minimally invasive procedures for BPH (e.g. prostatic urethral lift), and repeat use of transurethral water vapor thermal therapy is considered to be **investigational.***

Based on review of available data, transurethral waterjet ablation (aquablation with Aquabeam) for all other indications, including but not limited to use in individuals with a diagnosis of prostate cancer, use after other minimally invasive procedures for BPH, and repeat aquablation is considered to be **investigational.***

Policy Guidelines

The International Prostate Symptom Score (IPSS) can be utilized to measure the severity of lower urinary tract symptoms. It was adopted by the World Health Organization in 1993 and is a validated, reproducible scoring system to assess disease severity and response to therapy. It is a modification

of the American Urological Association (AUA) Symptom Index. The questionnaire assesses degree of lower urinary tract symptoms and quality of life. A score of 7 or less is mildly symptomatic, 8-19 is moderately symptomatic, and 20 to 35 is severely symptomatic. Both the AUA index and the IPSS questionnaire are sensitive enough to be used in evaluating symptoms and selecting treatment. IPSS $\geq$ 12 (13) was used for inclusion criteria in clinical trials for Aquabeam and Rezum.

Uroflowmetry is noninvasive screening tool for urethral obstruction. The principal determinants of urine flow rate are the strength of bladder contraction and the resistance of the bladder outlet. In general, peak flow rates (Qmax) greater than 15-20 mL/second and a bell-shaped curve are considered normal in young men and rates < 10 mL/second are abnormal. Numbers decline approximately 1-2 mL/second every 5 years and maximum flow rate at age 80 is 5.5 mL/second. Flow rate is not accurate when voided volume is less than 150 mL. This test cannot distinguish between weak detrusor contraction and obstruction. Qmax < 15 mL/second was used for inclusion criteria in clinical trials for Aquabeam and Rezum.

Background/Overview

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. 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.

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.

Individuals with persistent symptoms despite medical treatment may be considered for surgical treatment. The traditional standard treatment for BPH is transurethral resection of the prostate. TURP is generally considered the reference standard for comparisons of BPH procedures. Several minimally invasive prostate ablation procedures have also been developed, including transurethral microwave thermotherapy, transurethral needle ablation of the prostate, urethromicroablation phototherapy, and photoselective vaporization of the prostate. The prostatic urethral lift procedure involves the insertion of one or more permanent implants into the prostate, which retracts prostatic tissue and maintains an expanded urethral lumen.

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Transurethral water vapor thermal therapy and aquablation have been investigated as minimally invasive alternatives to transurethral resection of the prostate. Transurethral water vapor thermal therapy uses radiofrequency-generated water vapor (~103°C) thermal energy based on the thermodynamic properties of convective vs conductive heat transfer to ablate prostate tissue. Aquablation cuts tissue by using a pressurized jet of fluid delivered to the prostatic urethra.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

In September 2016, the Rezum™‡ System (NxThera, Inc, acquired by Boston Scientific in 2018) was cleared for marketing by the U.S. FDA through the 510(k) process (K150786). The FDA 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.

In April 2017, the Aquabeam®‡ System (Procept Robotics Corporation) was cleared for marketing by the FDA through the 513(f)(2) (de novo) classification process (DEN170024). The device is intended for the resection and removal of prostate tissue in males suffering from LUTS due to benign prostatic hyperplasia , based on WATER trial.

FDA notes to not use the Aquabeam system in patients with:

- Active urinary tract or systemic infection
- Known allergy to device materials
- Inability to safely stop anticoagulants or antiplatelet agents perioperatively
- Diagnosed or suspected cancer of the prostate.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

Transurethral water vapor thermal therapy and transurethral waterjet ablation (aquablation) have been investigated as minimally invasive alternatives to transurethral resection of the prostate (TURP), considered the traditional standard treatment for benign prostatic hyperplasia (BPH). Transurethral water vapor thermal therapy uses radiofrequency-generated water vapor (~103°C) thermal energy based on the thermodynamic properties of convective versus conductive heat transfer

to ablate prostate tissue. Aquablation cuts tissue by using a pressurized jet of fluid delivered to the prostatic urethra.

Summary of Evidence
For individuals who have benign prostatic hypertrophy (BPH) and lower urinary tract symptoms (LUTS) who receive transurethral water vapor thermal therapy, the evidence includes a single 3-month, sham-controlled, randomized trial of 197 patients with a 5-year uncontrolled follow-up phase and 1 multicenter, prospective, single-arm study. The outcomes of interest are symptoms, functional outcomes, quality of life, and treatment-related morbidity. At 3 months, LUTS improved more in the intervention group compared to the sham procedure. No adverse effects on erectile or ejaculatory function were observed, and improvements were sustained through 5 years of follow-up. The evidence is limited by the small sample size, lack of blinding of longer-term outcomes, and lack of comparison to alternative treatments such as transurethral resection of the prostate (TURP). The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have BPH and LUTS who receive aquablation, the evidence includes a single noninferiority randomized controlled trial (RCT) of aquablation compared to TURP in 187 patients with 5 years of follow-up, and several multicenter, prospective, single-arm studies. The outcomes of interest are symptoms, functional outcomes, quality of life, and treatment-related morbidity. The primary efficacy endpoint in the RCT was the difference between groups in the change in International Prostate Symptom Score (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. 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; $p=.3038$). Over 5 years, improvements remained similar between groups with no new safety signals. Confidence in these conclusions is reduced due to imprecision of estimates and a lack of additional supportive trials, especially with regard to comparative adverse events. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Supplemental Information

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:

- Water vapor thermal therapy should be considered as a treatment option for individuals with LUTS/BPH provided prostate volume is 30 to 80 cc. (Moderate Recommendation; Evidence Level: Grade C)
- Water vapor thermal therapy may be offered as a treatment option to eligible individuals 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 individuals with LUTS/BPH provided prostate volume is 30 to 80 cc. (Conditional Recommendation; Evidence Level: Grade C)

National Institute for Health and Care Excellence
In 2020, the National Institute for Health and Care Excellence (NICE) issued the following guidance on Rezum for treatment of LUTS secondary to BPH:

"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 2023, NICE updated guidance on transurethral water jet ablation for LUTS caused by BPH. The following recommendations were made:
"Transurethral water-jet ablation for lower urinary tract symptoms caused by BPH may be used if standard arrangements are in place for clinical governance, consent, and audit. For auditing the outcomes of this procedure, the main efficacy and safety outcomes identified in this guidance can be entered into NICE's interventional procedure outcomes audit tool (for use at local discretion)."
A Medtech innovation briefing was released by NICE in January 2023 but guidance specific to Aquablation is awaiting development.

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 1.

Table 1. Summary of Key Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
Ongoing			
NCT04838769[a]	Water Vapor Thermotherapy vs. Combination Pharmacotherapy for Symptomatic Benign Prostatic Hyperplasia Refractory to Alpha Blocker Monotherapy in Sexually Active Men: A Multicenter Randomized Controlled Trial	394	Jul 2026
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	May 2025
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 2028

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

References

1. National Institute for Health and Care Excellence. Rezum for treating lower uninary tract symptoms secondary to benign prostatic hyperplasia. June 2020.
2. Rezūm Water Vapor Thermal Therapy for Lower Urinary Tract Symptoms Associated With Benign Prostatic Hyperplasia: 4-Year Results From Randomized Controlled Study https://www.goldjournal.net/article/S0090-4295(19)30070-6/fulltext
3. Trade/Device Name: Rezum System https://www.accessdata.fda.gov/cdrh_docs/pdf19/K191505.pdf

4. DE NOVO CLASSIFICATION REQUEST FOR AQUABEAM SYSTEM DEN170024.pdf
5. International Prostate Symptom Score. International Review of Neurobiology, 2017. https://www.sciencedirect.com/topics/medicine-and-dentistry/international-prostate-symptom-score#:~:text=A%20score%20of%207%20or%20less%20is,used%20in%20evaluating%20symptoms%20and%20selecting%20treatment.
   International Prostate Symptom Score (IPSS)
6. Medscape. Assess severity of symptoms in benign prostatic hypertrophy https://reference.medscape.com/calculator/338/international-prostate-symptom-score-ipss
7. Uroflowmetry. Uroflowmetry is the measurement of voided urine (in milliliters) per unit of time (in seconds). Abernathy's Surgical Secrets (Sixth Edition), 2009 https://www.sciencedirect.com/topics/medicine-and-dentistry/uroflowmetry#:~:text=In%20general%2C%20in%20men%20peak,80%20is%205.5%20ml/second.

Policy History

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09/05/2019	Medical Policy Committee review
09/11/2019	Medical Policy Implementation Committee approval. New policy.
11/05/2020	Medical Policy Committee review
11/11/2020	Medical Policy Implementation Committee approval. Coverage changed from investigational to eligible for coverage.
11/04/2021	Medical Policy Committee review
11/10/2021	Medical Policy Implementation Committee approval. Title changed. Added "Based on review of available data, Transurethral waterjet ablation (aquablation) as a treatment of benign prostatic hyperplasia is considered to be investigational."
11/03/2022	Medical Policy Committee review
11/09/2022	Medical Policy Implementation Committee approval. No change to coverage.
11/02/2023	Medical Policy Committee review
11/08/2023	Medical Policy Implementation Committee approval. No change to coverage.
01/04/2024	Medical Policy Committee review
01/10/2024	Medical Policy Implementation Committee approval. Added "Based on review of available data, the Company may consider transurethral waterjet ablation (aquablation with the Aquabeam system) for the treatment of benign prostatic hyperplasia (BPH) to be eligible for coverage with criteria." Repeat aquablation is considered to be investigational.
11/07/2024	Medical Policy Committee review
11/13/2024	Medical Policy Implementation Committee approval. Patient selection criteria extensively revised. Added Policy Guidelines. Title changed from "Transurethral Water Vapor Thermal Therapy and Transurethral Water Jet Ablation (Aquablation)

for Benign Prostatic Hypertrophy" to "Transurethral Water Vapor Thermal Therapy (Rezum) and Transurethral Water Jet Ablation (Aquablation) for Benign Prostatic Hypertrophy."

Coding

The five character codes included in the Louisiana Blue Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology (CPT®)‡, copyright 2023 by the American Medical Association (AMA). CPT is developed by the AMA as a listing of descriptive terms and five character identifying codes and modifiers for reporting medical services and procedures performed by physician.

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Codes used to identify services associated with this policy may include (but may not be limited to) the following:

Code Type	Code
CPT	0421T, 53854, 55899
HCPCS	C2596
ICD-10 Diagnosis	N40.0-N40.1

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and

whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or

B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
    1. Consultation with technology evaluation center(s);
    2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
    3. Reference to federal regulations.

**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and 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 that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

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NOTICE: If the Patient's health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

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NOTICE: 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 eligibility for coverage.