MEDICAL POLICY

POLICY TITLE	TREATMENTS OF THE PROSTATE
POLICY NUMBER	MP 4.043

CLINICAL BENEFIT	☐ MINIMIZE SAFETY RISK OR CONCERN. ☒ MINIMIZE HARMFUL OR INEFFECTIVE INTERVENTIONS. ☐ ASSURE APPROPRIATE LEVEL OF CARE. ☐ ASSURE APPROPRIATE DURATION OF SERVICE FOR INTERVENTIONS. ☒ ASSURE THAT RECOMMENDED MEDICAL PREREQUISITES HAVE BEEN MET. ☐ ASSURE APPROPRIATE SITE OF TREATMENT OR SERVICE.
Effective Date:	**5/1/2025**

I. POLICY

Urethral Lift

Use of a prostatic urethral lift in individuals 45 years of age or older with lower urinary tract symptoms due to benign prostatic hyperplasia may be considered **medically necessary** when all of the following criteria are met:

- The individual has failed a trial of satisfactory voiding with medication (alpha blocker and/or alpha-reductase inhibitor) or intolerance to medication (alpha blocker and/or 5-alpha-reductase inhibitor); **and**
- Prostate volume of 30-80cc **and**
- Prostate anatomy demonstrates normal bladder neck without an obstructive or protruding median lobe; **and**
- Individual does not have urinary retention, urinary tract infection, or recent prostatitis (within past year); **and**
- The individual has normal renal function **and**
- Individual has had appropriate testing to exclude diagnosis of prostate cancer; **and**
- The patient has no known allergy to nickel, titanium, or stainless steel.

The prostatic urethral lift procedure is considered **investigational** for all other indications. There is insufficient evidence to support a general conclusion concerning the health outcomes or benefits associated with this procedure.

Water Vapor Thermal Therapy

Water vapor thermal therapy (e.g. Rezūm™) is considered **investigational** for all indications. There is insufficient evidence to support a general conclusion concerning the health outcomes or benefits associated with this procedure.

Hydrogel Rectal Spacer

Hydrogel Rectal Spacer is considered **investigational** for all indications. There is insufficient evidence to support a general conclusion concerning the health outcomes or benefits associated with this procedure.

Transurethral Waterjet Ablation (aquablation)

Transurethral waterjet ablation (aquablation) is considered **investigational** for all indications. There is insufficient evidence to support a general conclusion concerning the health outcomes or benefits associated with this procedure.

High-Intensity Focused Ultrasound

HIFU is considered **investigational** for all indications. There is insufficient evidence to support a general conclusion concerning the health outcomes or benefits associated with this procedure.

Investigational Interventions:

The following are considered **investigational**

- Temporary prostatic urethral stents/implants
- Focal laser ablation
- Prostate Artery Embolization
- Use of any other focal therapy modality not listed

There is insufficient evidence to support a general conclusion concerning the health outcomes or benefits associated with this procedure.

Cross-Reference:
MP 5.053 Magnetic Resonance–Guided Focused Ultrasound

II. PRODUCT VARIATIONS

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This policy is only applicable to certain programs and products administered by Capital Blue Cross. Please see additional information below, and subject to benefit variations as discussed in Section VI below.

FEP PPO - Refer to FEP Medical Policy Manual. The FEP Medical Policy manual can be found at:

https://www.fepblue.org/benefit-plans/medical-policies-and-utilization-management-guidelines/medical-policies .

III. DESCRIPTION/BACKGROUND

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PROSTATE CANCER

Prostate cancer is the second most common cancer diagnosed among men in the U.S. with over 1 in 10 men diagnosed with prostate cancer over their lifetime According to the National Cancer Institute, nearly 288,300 new cases are estimated to be diagnosed in the U.S. in 2023, associated with around 34,700 deaths. Prostate cancer is more likely to develop in older men and in non-Hispanic Black men. About 6 in 10 cases are diagnosed in men who are ≥65 years of age, and it is rare in men <40 years of age. Autopsy studies in the pre-prostate-specific antigen (PSA) screening era identified incidental cancerous foci in 30% of men 50 years of age, with incidence reaching 75% at age 80 years. However, the National Cancer Institute Surveillance Epidemiology and End Results Program data have shown that age-adjusted cancer-specific mortality rates for men with prostate cancer declined from 40 per 100,000 in 1992 to 19 per 100,000 in 2018. This decline has been attributed to a combination of earlier detection via PSA screening and improved therapies.

Diagnosis

Different types of localized prostate cancers may appear similar during initial diagnosis. However, the cancer often exhibits varying degrees of risk progression that may not be captured by accepted clinical risk categories (e.g., D'Amico criteria) or prognostic tools based on clinical findings (e.g., PSA titers, Gleason grade, or tumor stage). In studies of conservative management, the risk of localized disease progression based on prostate cancer–specific survival rates at ten (10) years may range from 15% to 20%, ten (10) to perhaps 27% at 20-year follow-up. Among elderly men (greater or less than 70 years) with this type of low-risk disease, comorbidities typically supervene as a cause of death; these men will die from the comorbidities with prostate cancer present rather than from the cancer itself. Other very similar appearing low-risk tumors may progress unexpectedly and rapidly, quickly disseminating and becoming incurable.

A digital rectal exam may detect nodules, induration, or asymmetry, which is then followed by an ultrasound-guided biopsy with an evaluation of the number and grade of positive biopsy cores.

Clinical staging is based on the digital rectal exam and biopsy results. T1 lesions are not palpable while T2 lesions are palpable but appear to be confined to the prostate. T3 lesions extend through the prostatic capsule, and T4 lesions are fixed to or invade adjacent structures.

The most widely used grading scheme for a prostate biopsy is the Gleason system. It is an architectural grading system ranging from 1 (well-differentiated) to 5 (poorly differentiated); the score is the sum of the primary and secondary patterns. A Gleason score of 6 or less is low-grade prostate cancer that usually grows slowly; 7 is an intermediate grade; 8 to 10 is high-grade cancer that grows more quickly. A revised prostate cancer grading system has been adopted by the National Cancer Institute and the World Health Organization. A crosswalk of these grading systems is shown in Table 1.

Table 1. Prostate Cancer Grading Systems

Grade Group	Gleason Score (Primary and Secondary Pattern)	Cells
1	6 or less	Well-differentiated (low grade)
2	7 (3 + 4)	Moderately differentiated (moderate grade)
3	7 (4 + 3)	Poorly differentiated (high grade)
4	8	Undifferentiated (high grade)
5	9-10	Undifferentiated (high grade)

Treatments

The divergent behavior of localized prostate cancers creates uncertainty whether to treat immediately. A patient may choose definitive treatment upfront. Surgery (radical prostatectomy) or external-beam radiotherapy are frequently used to treat patients with localized prostate cancer. Complications most commonly reported with radical prostatectomy or external-beam radiotherapy and with the greatest variability are incontinence (0%-73%) and other genitourinary toxicities (irritative and obstructive symptoms); hematuria (typically less than or equal to5%); gastrointestinal and bowel toxicity, including nausea and loose stools (25%-50%); proctopathy, including rectal pain and bleeding (10%-39%); and erectile dysfunction, including impotence (50%-90%).

American Urological Association guidelines have suggested patients with low- and intermediate-risk disease have the option of entering an “active surveillance” protocol, which takes into account patient age, patient preferences, and health conditions related to urinary, sexual, and bowel function. With this approach, patients forgo immediate therapy but continue regular monitoring until signs or symptoms of disease progression are evident—at which point curative treatment is instituted.

Focal Treatments for Localized Prostate Cancer

Given significant uncertainty in predicting the behavior of individual localized prostate cancers, and the substantial adverse events associated with definitive treatments, investigators have sought a therapeutic middle ground. The latter seeks to minimize morbidity associated with radical treatment in those who may not actually require surgery while reducing tumor burden to an extent that reduces the chances for rapid progression to incurability. This approach is termed focal treatment, in that it seeks to remove using any of several ablative methods described next cancerous lesions at high risk of progression, leaving behind uninvolved glandular parenchyma. The overall goal of any focal treatment is to minimize the risk of early tumor progression and preserve erectile, urinary, and rectal functions by reducing damage to the neurovascular bundles, external sphincter, bladder neck, and rectum. Although focal treatments are offered as an alternative middle approach to manage localized prostate cancer, several key issues must be considered in choosing it. They include patient selection, lesion selection, therapy monitoring, and modalities used to ablate lesions.

Patient Selection

A proportion of men with localized prostate cancer have been reported to have (or develop) serious misgivings and psychosocial problems in accepting active surveillance, sometimes leading to inappropriately discontinuing it. Thus, appropriate patient selection is imperative for physicians who must decide whether to recommend active surveillance or focal treatment for patients who refuse radical therapy or for whom it is not recommended due to the risk/benefit balance.

Lesion Selection

Proper lesion selection is a second key consideration in choosing a focal treatment for localized prostate cancer. Although prostate cancer is a multifocal disease, clinical evidence has shown that between 10% and 40% of men who undergo radical prostatectomy for presumed multifocal disease actually have a unilaterally confined discrete lesion, which, when removed, would “cure” the patient. This view presumably has driven the use of regionally targeted focal treatment variants, such as hemiablation of half the gland containing the tumor, or subtotal prostate ablation via the “hockey stick” method. While these approaches can be curative, the more extensive the treatment, the more likely the functional adverse outcomes would approach those of radical treatments. The concept that clinically indolent lesions comprise most of the tumor burden in organ-confined prostate cancer led to development of a lesion-targeted strategy, which is referred to as “focal therapy” in this evidence review. This involves treating only the largest and highest-grade cancerous focus (referred to as the “index lesion”), which has been shown in pathologic studies to determine clinical progression of disease.

This concept is supported by molecular genetics evidence that suggests a single index tumor focus is usually responsible for disease progression and metastasis. The index lesion approach leaves in place small foci less than 0.5 cm3in volume, with a Gleason score less than 7, that are considered unlikely to progress over a ten (10)- to twenty (20) year period. This also leaves available subsequent definitive therapies as needed should disease progress.

Identification of prostate cancer lesions (disease localization) particularly the index lesion, is critical to the oncologic success of focal therapy; equally important to success is the ability to guide focal ablation energy to the tumor and assess treatment effectiveness. At present, no single modality reliably meets the requirements for all 3 activities (disease localization, focal ablation energy to the tumor, assessment of treatment effectiveness). Systematic transrectal ultrasound–guided biopsy alone has been investigated; however, it has been considered insufficient for patient selection or disease localization for focal therapy. A 5-mm transperineal prostate mapping (TPM) biopsy using a brachytherapy template has been the recommended standard by the European Association of Urology, according to its 2012 guidelines. TPM can provide 3-dimensional coordinates of cancerous lesions and has 87% to 95% accuracy rates in detecting and ruling out clinically significant cancer of all sizes. However, TPM is resource-intensive, requires general anesthesia, and has been associated with adverse events (including urinary retention [6%], prostatitis [4%], and local events such as perineal hematoma, bruising, and pain [5%]). The risk of complications of general anesthesia and the cost of processing multiple biopsy specimens limits the practicality and widespread applicability of this approach.

Multiparametric magnetic resonance imaging (mpMRI), typically including T1-, T2-, diffusion-weighted imaging, and dynamic contrast-enhanced imaging, has been recognized as a promising modality to risk-stratify prostate cancer and select patients and lesions for focal

therapy. Evidence has shown mpMRI can detect high-grade, large prostate cancer foci with performance similar to TPM. For example, for the primary end point definition (lesion, greater than or equal to 4 mm; Gleason score, greater than or equal to3+4), with TPM as the reference standard, sensitivity, negative predictive value, and negative likelihood ratios with mpMRI were 58% to 73%, 84% to 89%, and 0.3 to 0.5, respectively. Specificity, positive predictive value and positive likelihood ratios were 71% to 84%, 49% to 63%, and 2.0 to 3.44, respectively. The negative predictive value of mpMRI appears sufficient to rule out clinically significant prostate cancer and may have clinical use in this setting. However, although mpMRI technology has the capability to detect and risk-stratify prostate cancer, several issues constrain its widespread use for these purposes (e.g., mpMRI requires highly specialized MRI-compatible equipment; biopsy within the MRI scanner is challenging; interpretation of prostate MRI images requires experienced uroradiologists) and it is still necessary to histologically confirm suspicious lesions using TPM.

Therapy Monitoring

Controversy exists about the proper end points for focal therapy of prostate cancer. The primary end point of focal ablation of clinically significant disease with negative biopsies evaluated at 12 months post treatment is generally accepted according to a European consensus report. The clinical validity of MRI to analyze the presence of residual or recurrent cancer compared with histologic findings is offered as a secondary end point. However, MRI findings alone are not considered sufficient in follow-up.

Finally, although investigators have indicated PSA levels should be monitored, PSA levels are not considered valid end points because the utility of PSA kinetics in tissue preservation treatments has not been established.

Modalities Used to Ablate Lesions

Five ablative methods for which clinical evidence is available are considered herein: focal laser ablation; high-intensity focused ultrasound; cryoablation; radiofrequency ablation; and photodynamic therapy. Each method requires placement of a needle probe into a tumor volume followed by delivery of some type of energy that destroys the tissue in a controlled manner. All methods except focal laser ablation currently rely on ultrasound guidance to the tumor focus of interest; focal laser ablation uses MRI to guide the probe. This evidence review does not cover focal brachytherapy.

Focal Laser Ablation

Focal laser ablation refers to the destruction of tissue using a focused beam of electromagnetic radiation emitted from a laser fiber introduced transperineal or transrectal into the cancer focus. Tissue is destroyed through thermal conversion of the focused electromagnetic energy into heat, causing coagulative necrosis. Other terms for focal laser ablation include photothermal therapy, laser interstitial therapy, and laser interstitial photocoagulation.

High-Intensity Focused Ultrasound

High-intensity focused ultrasound focuses high-energy ultrasound waves on a single location, which increases the local tissue temperature to over 80 °C. This causes a discrete locus of coagulative necrosis of approximately 3x3x10 mm. The surgeon uses a transrectal probe to

plan, perform, and monitor treatment in a real-time sequence to ablate the entire gland or small discrete lesions.

Cryoablation

Cryoablation induces cell death through direct cellular toxicity from disruption of the cell membrane caused by ice-ball crystals and vascular compromise from thrombosis and ischemia secondary to freezing below -30 °C. Using a TPM template, cryoablation is performed by transperineal insertion under transrectal ultrasound guidance of a varying number of cryoprobe needles into the tumor.

Radiofrequency Ablation

Radiofrequency ablation uses energy produced by a 50-watt generator at a frequency of 460 kHz. Energy is transmitted to the tumor focus through 15 needle electrodes inserted transperineally under ultrasound guidance. Radiofrequency ablation produces an increase in tissue temperature causing coagulative necrosis.

Photodynamic Therapy

Photodynamic therapy uses an intravenous photosensitizing agent, which distributes through prostate tissue, followed by light delivered transperineally by inserted needles. The light induces a photochemical reaction that produces reactive oxygen species that are highly toxic and causes functional and structural tissue damage (i.e., cell death). A major concern with photodynamic therapy is that real-time monitoring of tissue effects is not possible, and the variable optical properties of prostate tissue complicate assessment of necrosis and treatment progress.

Hydrogel Spacer

For low-or intermediate-risk prostate cancer, radiation therapy is an option. Because the rectum lies in close proximity to the prostate, the risk of rectal toxicity is high. One approach is to push the rectum away from the prostate, increasing the space and reducing the radiation dose to the rectum. A variety of biomaterials, including polyethylene glycol hydrogels (e.g., SpaceOAR System) have been evaluated as perirectal spacers.

BENIGN PROSTATIC HYPERPLASIA

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. Benign prostatic hyperplasia 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 (LUTS) including urinary frequency, urgency, irregular flow, weak

stream, straining, and waking up at night to urinate. Lower urinary tract symptoms are the most commonly presenting urological complaint and can have a significant impact on quality of life.

Benign prostatic hyperplasia 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.

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 (TURP). 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 1 or more permanent implants into the prostate, which retracts prostatic tissue and maintains an expanded urethral lumen.

Transurethral water vapor thermal therapy and aquablation have been investigated as minimally invasive alternatives to TURP. 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.

Prostatic Urethral Lift

The therapy being considered is PUL. The PUL procedure involves the placement of 1 or more implants in lobes of the prostate using a transurethral delivery device. The implant device is designed to retract the prostate to allow expansion of the prostatic urethra. The implants are retained in the prostate to maintain an expanded urethral lumen. One device, the NeoTract UroLift System, has been cleared for marketing by the FDA (see Regulatory Status section). The device has 2 main components: the delivery device and the implant. Each delivery device comes preloaded with a UroLift implant.

Transurethral Water Vapor Thermal Therapy and Transurethral Waterjet Ablation (Aquablation)

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.

Temporary Implanted Devices

Temporarily implanted nitinol devices have been proposed as a minimally invasive alternative to transurethral resection of the prostate (TURP), considered the traditional standard treatment for symptomatic benign prostatic hyperplasia. The device is temporarily implanted into the obstructed prostatic urethra to facilitate tissue reshaping and improve urine outflow. The implant is typically removed after 5 to 7 days of treatment. The AUA provides a conditional recommendation: temporary implanted prostatic devices may be offered as a treatment option for patients with LUTS/BPH provided prostate volume is between 25 and 75 g and lack of obstructive median lobe.

REGULATORY STATUS

Focal Laser Ablation

In 2010, the Visualase® Thermal Therapy System (Medtronic, Minneapolis, MN) and, in 2015, the TRANBERGCLS|Laser fiber (Clinical Laserthermia Systems, Sweden) was cleared for marketing by the FDA through the 510(k) process to necrotize or coagulate soft tissue through interstitial irradiation or thermal therapy under magnetic resonance imaging guidance for multiple indications including urology, at wavelengths from 800 to 1064 nm. FDA product code: LLZ, GEX, FRN.

High-Intensity Focused Ultrasound

In 2015, the Sonablate® 450 (SonaCare Medical, Charlotte, NC) was approved by FDA through a de novo request and classified the device as class II under the generic name “high intensity ultrasound system for prostate tissue ablation”. This device was the first of its kind to be approved in the United States. A similar device, Ablatherm® (EDAP TMS, France), was cleared for marketing by FDA through the 510(k) process shortly thereafter.

Cryoablation

Some cryoablation devices cleared for marketing by FDA through the 510(k) process for cryoablation of the prostate are: Visual-ICE® (Galil Medical, St. Paul, MN), Ice Rod CX, CryoCare® (Galil Medical), IceSphere (Galil Medical), and Cryocare® Systems (Endocare®; HealthTronics, Austin, TX). FDA product code: GEH.

Radiofrequency (RF) Ablation

RF devices have been cleared for marketing by FDA through the 510(k) process for general use for soft tissue cutting and coagulation and ablation by thermal coagulation. Under this general indication, radiofrequency ablation may be used to ablate tumors. FDA product code: GEI.

Photodynamic Therapy

FDA has granted approval to several photosensitizing drugs and light applicators. Photofrin® (porfimer sodium) (Axcan Pharma) and psoralen are photosensitizer ultraviolet lamps used to treat cancer; they were cleared for marketing by FDA through the 510(k) process. FDA product code: FTC.

Transurethral Convective Water Vapor Thermal Ablation

In September 2016, the Rezum™ System (NxThera, Inc., acquired by Boston Scientific in 2018) was cleared for marketing by the U.S. Food and Drug Administration (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 >30cm3 and <80cm3. The Rezum System is also indicated for the treatment of prostate with hyperplasia of the central zone and/or a median lobe.

Prostatic Urethral Lift (PUL)

One implantable transprostatic tissue retractor system has been cleared for marketing by the U.S. Food and Drug Administration (FDA) through the 510(k) process. In 2013, the NeoTract UroLift® System UL400 (NeoTract) was cleared (after receiving clearance through the FDA's de novo classification process in March 2013; K130651/DEN130023). In 2016, the FDA determined that the UL500 was substantially equivalent to existing devices (UL400) for the treatment of symptoms of urinary flow obstruction secondary to BPH in individuals ages 50 years and older. In 2017, the FDA expanded the indication for the UL400 and UL500 to include lateral and median lobe hyperplasia in men 45 years or older. An additional clearance in 2019 (K193269) modified an existing contraindication for use from men with a prostate volume of >80 cc to men with a prostate volume of >100 cc. FDA product code: PEW.

Hydrogel Spacer

In October 2014, SpaceOAR® (Augmenix, a subsidiary of Boston Scientific) was cleared by the FDA through the De Novo process (DEN140030). "SpaceOAR System is intended to temporarily position the anterior rectal wall away from the prostate during radiotherapy for prostate cancer and in creating this space it is the intent of SpaceOAR System to reduce the radiation dose delivered to the anterior rectum."

DuraSeal® Exact (Integra) was approved by the FDA through the premarket approval process as a spine and cranial sealant (dura mater) and has been used off-label as a perirectal spacer.

Waterjet Ablation

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.

Magnetic Nanoparticles

MagForce® USA, Inc. is conducting a clinical study evaluating NanoTherm® under an FDA Investigational Device Exemption (IDE) (NCT05010759). NanoTherm uses magnetic nanoparticles and an alternating magnetic field to create heat and local ablation in the ablation of prostate cancer.

Irreversible electroporation

The NanoKnife System was approved by the FDA through the 510(k) premarket approval process (K183385) in 2019 for the surgical ablation of soft tissue. NanoKnife has not received clearance for the treatment of any specific disease. NanoKnife has not received clearance for the treatment of any specific disease.

III. RATIONALE

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Summary of Evidence: Focal Treatment Overview

For individuals who have primary localized prostate cancer who receive focal therapy using laser ablation, high-intensity focused ultrasound, cryoablation, radiofrequency ablation, or photodynamic therapy, the evidence includes a high-quality systematic review, studies from a registry cohort, and numerous observational studies. Relevant outcomes are overall survival, disease-specific survival, symptoms, change in disease status, functional outcomes, quality of life, and treatment-related morbidity. The evidence is highly heterogeneous and inconsistently reports clinical outcomes. No prospective, comparative evidence was found for focal ablation techniques vs current standard treatment of localized prostate cancer, including radical prostatectomy, external-beam radiotherapy, or active surveillance. Methods have not been standardized to determine which and how many identified cancerous lesions should be treated for best outcomes. No evidence supports which, if any, of the focal techniques leads to better functional outcomes. Although high disease-specific survival rates have been reported, the short follow-up periods and small sample sizes preclude conclusions on the effect of any of these techniques on overall survival rates. The adverse event rates associated with focal therapies appear to be superior to those associated with radical treatments (e.g., radical prostatectomy, external-beam radiotherapy); however, the evidence is limited in its quality, reporting, and scope. The evidence is insufficient to determine the effects of the technology on health outcomes.

Summary of Evidence: Transurethral Convective Water Vapor Thermal Ablation Overview

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.

Summary of Evidence: Prostatic Urethral Lift

For individuals who have lower urinary tract obstruction symptoms due to BPH who do not have sufficient response to medical therapy or are experiencing significant side effects with medical therapy and receive a PUL, the evidence includes systematic reviews, RCTs, and noncomparative studies. Relevant outcomes are symptoms, functional outcomes, health status measures, quality of life, and treatment-related morbidity. One RCT, the BPH6 study, compared the PUL procedure with TURP and reported that the PUL procedure was noninferior for the study's composite endpoint, which required concurrent fulfillment of 6 independently validated measures of symptoms, safety, and sexual health. While TURP was superior to PUL in managing lower urinary tract symptoms, PUL did provide significant symptom improvement over 2 years. Prostatic urethral lift was further superior to TURP in preserving ejaculatory function. These findings were corroborated by another RCT (the LIFT study), which compared PUL with sham control. Patients underwent washout of BPH medications before enrollment. LIFT reported that patients with the PUL procedure, compared with patients who had sham surgery and no BPH medication, had greater improvements in lower urinary tract symptoms without worsened sexual function at 3 months. After 3 months, patients were given the option to have PUL surgery; 80% of the patients with sham procedures chose that option. Publications from this trial reported these findings were preserved in a subset of patients over 3 to 5 years; however, a high number of patients were either excluded or lost to follow-up during this time. The BPH6 and LIFT RCTs included men with a prostate volume up to 80 cm3 and excluded men with median lobe obstruction. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have lower urinary tract obstruction symptoms due to BPH who have had a prior PUL procedure who are treated with a repeat PUL, the evidence includes long-term follow-up data from the LIFT study, a systematic review, and reports on care setting real world experience. Relevant outcomes are symptoms, functional outcomes, health status measures, quality of life, and treatment-related morbidity. Clinical data on the occurrence of repeat PUL, and consensus on clinically relevant definitions of retreatment/reintervention and subsequent outcomes are lacking. The 5-year surgical reintervention rate in the LIFT study was reported as 13.6%, while a meta-analysis concluded that the surgical reintervention rate following PUL is

6% per year. An analysis of clinical care setting real world experience reported the overall retreatment rate at 1 and 2 years to be 5.2% (95% CI, 4.2 to 6.1) and 11.9% (95% CI, 10.1 to 13.6), respectively, following an initial PUL. A retrospective healthcare system database analysis of endoscopic procedures for BPH found that patients treated with PUL were almost twice as likely to be retreated at 2-year follow-up compared to those receiving TURP (OR, 1.78; p<.01). The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Summary of Evidence: Hydrogel Spacer

For individuals who have prostate cancer and are undergoing radiation therapy who receive a hydrogel spacer, the evidence includes a pivotal randomized controlled trial (RCT) with a 3-year follow-up for the SpaceOAR system, a pivotal RCT with up to 6-month follow-up for the Barrigel, observational studies, and systematic reviews of these studies. Relevant outcomes include symptoms, quality of life, and treatment-related morbidity. The combined evidence indicates that the hydrogel spacer can reduce the radiation dose to the rectum with a statistically significant decrease in Grade 1 or greater late toxicity and a number needed to treat (NNT) of 14.3. There were few events of greater than Grade 1 toxicity in either group across all trials, and the NNT for a reduction in clinically significant Grade 2 toxicity has been reported as 68 for SpaceOar. Patient-reported declines in rectal and urinary quality of life at 3 years in the SpaceOAR studies were statistically lower in the spacer group and met the threshold for a clinically significant difference, although patients were not blinded to treatment at the longer-term follow-up. The NNT for late improvement in rectal and urinary quality of life was 6.3 to 6.7, respectively, for SpaceOAR analysis. Limitations to all RCTs include the lack of blinding and the exclusion of patients who might be at greater risk of rectal toxicity. Evidence from observational studies is inconclusive but generally shows a decrease in radiation dose to the rectum with the insertion of a hydrogel spacer. However, the potential benefits of the hydrogel spacer must be balanced against the risks of an additional procedure. Additional studies are needed to corroborate the findings of the pivotal RCTs, to identify the factors that increase the risk of rectal toxicity, and to determine who is likely to benefit from the use of a spacer. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Summary of Evidence: Aquablation

For individuals who have benign prostatic hyperplasia and lower urinary tract symptoms who receive aquablation, the evidence includes one noninferiority RCT of aquablation compared to TURP in 187 patients with 3 years of follow-up. The outcomes of interest are symptoms, quality of life, and treatment-related morbidity. The primary efficacy endpoint was the difference between groups in the change in International Prostate Symptom Score (IPSS) at 6 months, and the primary safety end point was the development of Clavien-Dindo persistent grade 1, or 2 or higher operative complications at 3 months. At 6 months, mean I-PSS 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 3 years, improvements remained similar between groups. 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.

Summary of Evidence: Prostate Artery Embolization (PAE)

PAE is not recommended by AUA. Current data does not support this and the benefit over risk is unclear. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Summary of Evidence: Temporary Implanted Devices

For individuals who have benign prostatic hyperplasia (BPH) with lower urinary tract symptoms who receive a temporarily implanted nitinol device (e.g., iTind), the evidence includes a meta-analysis, 1 randomized controlled trial (RCT), and 2 single-arm, multicenter, international prospective studies. Relevant outcomes are symptoms, functional outcomes, health status measures, quality of life, and treatment-related morbidity. One network meta-analysis compared the safety and efficacy of various minimally invasive treatments for lower urinary tract symptoms associated with BPH, finding that iTind may result in worse urologic symptoms scores compared to TURP at short-term follow-up. One RCT compared the iTind device with a sham procedure and reported an improvement of at least 3 points on the IPSS scale at 3 months in 78.6% versus 60% of participants, respectively (p=.029). However, corresponding changes in overall IPSS, IPSS QoL, Qmax, SHIM, and IIEF scores were not significantly different between groups. One single-arm study reported significant improvements in symptoms and functional outcomes through 3 years. A subsequent single-arm study enrolling men desiring to preserve ejaculatory function reported no significant change in the SHIM total score and a statistically significant improvement on the MSHQ-EjD questionnaire at 6 months. No studies have directly compared iTind to established alternatives; however, an RCT comparing iTind with the UroLift prostratic urethral lift procedure is currently ongoing. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

IV. DEFINITIONS

TOP

IMRT refers to Intensity Modulated Radiation Therapy.

QALY refers to Quality Adjusted Life Year.

QoL refers to Quality of Life.

V. BENEFIT VARIATIONS

TOP

The existence of this medical policy does not mean that this service is a covered benefit under the member's health benefit plan. Benefit determinations are based on the applicable health benefit plan language. Medical policies do not constitute a description of benefits. Members and providers should consult the member's health benefit plan for information or contact Capital Blue Cross for benefit information.

VI. DISCLAIMER

TOP

Capital Blue Cross' medical policies are developed to assist in administering a member's benefits. These medical policies do not constitute medical advice and are subject to change. Treating providers are solely responsible for medical advice and treatment of members. Members should discuss any medical policy related to their coverage or condition with their provider and consult their benefit information to determine if the service is covered. If there is a discrepancy between this medical policy and a member's benefit information, the benefit information will govern. If a provider or a member has a question concerning the application of this medical policy to a specific member's plan of benefits, please contact Capital Blue Cross' Provider Services or Member Services. Capital Blue Cross considers the information contained in this medical policy to be proprietary and it may only be disseminated as permitted by law.

VII. CODING INFORMATION

TOP

Note: This list of codes may not be all-inclusive, and codes are subject to change at any time. The identification of a code in this section does not denote coverage as coverage is determined by the terms of member benefit information. In addition, not all covered services are eligible for separate reimbursement.

Investigational when used to describe Focal Treatments for Prostate Cancer

Procedure Codes							
0582T	0655T	0941T	0942T	0943T	51721	53865	53866
55881	55882	55899					

Investigational for aquablation

Procedure Codes							
0421T	C2596						

Investigational for high intensity-focused ultrasound (HIFU)

Procedure Codes							
55880	55899						

Investigational for radiofrequency water vapor (steam) thermal therapy

Procedure Codes							
53854							

Investigational for Hydrogel Therapy

Procedure Codes							
55874							

POLICY TITLE	TREATMENTS OF THE PROSTATE
POLICY NUMBER	MP 4.043

Covered when Medically Necessary for Prostatic Urethral Lift

Procedure Codes								
52441	52442	C9739	C9740					

ICD-10-CM Diagnosis Code	Description
D29.1	Benign Neoplasm of Prostate
N40.1	Enlarged Prostate with lower urinary tract symptoms
N40.3	Nodular Prostate with lower urinary tract symptoms

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IX. POLICY HISTORY

TOP

MP 4.043	**04/03/2020 Consensus Review**. Policy Statement unchanged. ICD codes: N13.8; R33.8; R39.15; R39.16 added and updated. References reviewed and updated. Variations updated.
	07/16/2020 Minor Review. Policy Statement changed to include the Hydrogel Spacer. Variation Statement updated. References reviewed, updated and Hydrogel Spacer references added. Coding reviewed. New codes added: 55874; C61; C79.82; D07.5; D40.0; D49.59.

	11/18/2020 Administrative Update. Added code 55880. Effective 01/01/2021
	12/14/2020 Administrative Update. Deleted code C9747. Effective 01/01/2021.
	03/10/2021 Administrative Update. Revised Code C9761. Effective 04/01/2021.
	09/08/2021 Minor Review. Addition of aquablation as INV. Update to include titanium and stainless-steel allergy. Updated coding, references, background, and rationale.
	06/24/2022 Administrative Update. C9761 removed.
	12/02/2022 Minor Review. Aquablation moved to NMN. HIFU now NMN, Updated to Urethral Lift criteria. Updated INV list to include PAE and temporary urethral stents. Updates and clarification to multiple other criteria statements. References, background, rationale and coding updated.
	11/22/2023 Consensus Review. Updated background and rationale. New references.
	10/31/2024 Major Review. Policy statement changed from MN to INV for water vapor thermal therapy and hydrogel rectal spacer. Changed all policy language from not medically necessary to INV. Added codes 0600T, 0601T, and 0739T to investigational table. Moved codes 53854 and 55874 to investigational table. Updated background and references.
	12/13/2024 Administrative Update. Added codes 0941T-0943T, 51721, 53865, 53866, 55881, 55882. Effective 01/01/2025.

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