

MEDICAL POLICY

| Medical Policy Details | |
|-------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Medical Policy Title | Focal Therapies for Prostate Cancer Treatment |
| Policy Number | 7.01.01 |
| Category | Technology Assessment |
| Original Effective Date | 09/16/99 |
| Committee Approval Date | 04/19/01, 11/15/01, 10/16/02, 08/21/03, 07/15/04, 07/21/05, 07/20/06, 07/19/07, 07/17/08, 07/16/09, 08/19/10, 08/18/11, 08/16/12, 08/15/13, 08/21/14, 08/20/15, 07/21/16, 07/20/17, 07/19/18, 07/18/19, 06/18/20, 04/15/21, 02/17/22, 02/16/23, 02/22/24, 08/22/24 |
| Current Effective Date | 08/22/24 |
| Archived Date | N/A |
| Archive Review Date | N/A |
| Product Disclaimer | <ul style="list-style-type: none"> • Services are contract dependent; if a product excludes coverage for a service, it is not covered, and medical policy criteria do not apply. • If a commercial product (including an Essential Plan or Child Health Plus product), medical policy criteria apply to the benefit. • If a Medicaid product covers a specific service, and there are no New York State Medicaid guidelines (eMedNY) criteria, medical policy criteria apply to the benefit. • If a Medicare product (including Medicare HMO-Dual Special Needs Program (DSNP) product) covers a specific service, and there is no national or local Medicare coverage decision for the service, medical policy criteria apply to the benefit. • If a Medicare HMO-Dual Special Needs Program (DSNP) product DOES NOT cover a specific service, please refer to the Medicaid Product coverage line. |

POLICY STATEMENT

- I. Based upon our criteria and assessment of the peer-reviewed literature, local therapy options (i.e., cryosurgery and high-intensity focused ultrasound (HIFU)) for recurrent prostate cancer have been proven to be effective and, therefore, are considered **medically appropriate** for individuals when **BOTH** the following criteria have been met:
 - A. Recurrence of prostate cancer after radiation therapy (as evidence by positive, repeat biopsy); **and**
 - B. Absence of metastatic disease.
- II. Based upon our criteria and assessment of the peer-reviewed literature, cryotherapy or other local therapies (i.e., HIFU) performed for routine primary therapy for localized prostate cancer have not been medically proven to be effective and, therefore, are considered **investigational**.
- III. Based upon our criteria and assessment of the peer-reviewed literature, additional focal therapies for the routine treatment of prostate cancer have not been medically proven to be effective, and, therefore, are considered **investigational**. These treatments include, but are not limited to, the following:
 - A. Vascular-Targeted Photodynamic, therapy (VTP);
 - B. Irreversible Electroporation (IRE);
 - C. Nano Knife for tissue ablation;
 - D. Laser Interstitial Thermal Therapy (LITT);
 - E. Transurethral Ultrasound Ablation (TULSA);
 - F. Magnetic field induction (NanoTherm therapy);
 - G. High energy water vapor thermotherapy.

Refer to Corporate Medical Policy #6.01.16 Brachytherapy or Radioactive Seed Implantation for Prostate Cancer

Refer to Corporate Medical Policy #8.01.06 Photodynamic Therapy for Malignant Disease

Refer to Corporate Medical Policy #11.01.03 Experimental or Investigational Services

Medical Policy: Focal Therapies for Prostate Cancer Treatment

Policy Number: 7.01.01

Page: 2 of 6

DESCRIPTION

Cryosurgical ablation of the prostate is an alternative method of treatment for prostate cancer. The cryoablation technique involves the use of transrectal, ultrasound-guided, percutaneous placement of cryoprobes to freeze prostate tissue to produce well-demarcated areas of cell injury and destruction. Refinements in the technique, with transrectal ultrasonography, improved cryosurgical instrumentation, and the use of commercial urethral warmers have decreased the complications associated with the early attempts at cryosurgery. The benefits of cryosurgery of the prostate include a shorter surgical procedure time with minimal blood loss.

High intensity focused ultrasound (HIFU) is a noninvasive approach that uses precisely delivered ultrasound energy to achieve tumor cell necrosis without radiation or surgical excision. This technique is also referred to as ultrasonic ablation, sonablation or focal ultrasound surgery. HIFU involves the use of a transrectal probe to plan, perform, and monitor treatment in a real-time sequence to ablate the entire prostate gland or small discrete lesions. HIFU is a promising treatment for prostate cancer especially in patients with low and intermediate risk disease who chose to not undergo open surgery. HIFU is a minimally invasive, outpatient, radiation free procedure that patients can undergo then return home. This advancement in the treatment of prostate cancer is making it possible for patients with earlier stages of the disease to maintain their quality of life without open surgery. HIFU can also be used if disease recurs, despite what earlier treatment methods were deployed.

Vascular-targeted photodynamic therapy (VTP) or photodynamic therapy (PDT) is a tissue-preserving treatment for low-risk prostate cancer which consists of intravenous 4 mg/kg padeliporfin over 10 min and optical fibers inserted into the prostate to cover the desired treatment zone and subsequent activation by laser light. For treating prostate cancer, the photosensitizer **TOOKAD soluble (WST11)** is used. The technical term for this treatment is **TOOKAD Soluble vascular-targeted photodynamic (VTP) therapy**.

Irreversible electroporation (IRE) is used as focal therapy to target areas of significant tumor burden to ablate tumors in situ or improve margins of resection. Primarily being used for pancreas, kidney, liver and prostate tumors. IRE destroys cancerous tumors with short electrical pulses without thermal heat disrupting permeabilization of cell membrane phospholipids. The NanoKnife System which became commercially available for research purposes in 2009 is being solely used for the surgical ablation of soft tissue tumors.

Laser interstitial thermotherapy (LITT) treatment produces focal thermal ablation leading to lesion cytoreduction through tissue coagulation, necrosis, and cellular apoptosis.

Trans-urethral ultrasound ablation (TULSA) is a transurethral prostate tissue ablation system that uses real-time MRI, robotically driven, directional thermal ultrasound and closed-loop temperature feedback control software. It provides incision- and radiation-free, whole or partial prostate gland ablation, protecting the urethra and rectum to preserve men's functional abilities.

Magnetic field induction (NanoTherm therapy) - The NanoTherm liquid containing the magnetic nanoparticles is specifically injected into the tumor or applied at the resection cavity wall in the course of the tumor resection. The particles, which contain iron oxide, are then activated during six one-hour sessions in the NanoActivator by an externally applied, rapidly alternating magnetic field, which generates heat. This either destroys the tumor cells or sensitizes them to additional treatment approaches such as radiotherapy and/or chemotherapy (MagForce USA, Inc).

Transurethral water vapor thermal therapy is a transurethral needle ablation technique which injects radiofrequency-generated, sterile water vapor (~103 degrees C) into enlarged prostate tissue. As the steam encounters the prostatic tissue, it condenses back into water, releasing large amounts of thermal energy, disrupting the prostatic cell membranes and leading to cell death and necrosis. It takes approximately three months for the body to reabsorb dead tissue, decreasing prostate volume and relieving LUTS. The thermal energy is confined to the prostate, which reduces the risk of injury to other parts of the body. The procedure is performed under local anesthesia in an office or outpatient setting. Currently there is no literature or professional society that supports this therapy for prostate cancer.

Medical Policy: Focal Therapies for Prostate Cancer Treatment

Policy Number: 7.01.01

Page: 3 of 6

RATIONALE

Published studies have demonstrated that patients with low volume, localized, primary prostate cancer undergoing cryosurgery remain biochemically disease-free up to three years. Surgically related morbidities of cryosurgery of the prostate have compared favorably to those reported for radical prostatectomy and radiation therapy. The available data suggest that select patients with radioresistant cancer have benefited from the use of cryosurgery as a salvage therapy. To date, case studies indicate that, at least in the short-term, cryosurgery is better tolerated than open salvage surgery and can be considered a treatment option for men who would not be candidates for open surgery. Complication rates can be minimized with improvements in technique and instrumentation and the use of experienced cryosurgeons.

Patient relevant outcome data such as disease free- and metastasis free- survival are now becoming available in the United States as more studies are completed, therefore post-treatment prostate biopsy data and the adverse event profile of HIFU are more available. HIFU currently remains experimental and investigational for primary treatment for localized prostate cancer.

The National Comprehensive Cancer Network (NCCN) guidelines for Prostate Cancer Version 4.2024 recommends only cryosurgery and high-intensity focused ultrasound (HIFU) as local therapy options for RT recurrence in the absence of metastatic disease. Cryotherapy or other local therapies are not recommended as routine primary therapy for localized prostate cancer due to lack of longterm data comparing these treatments to radiation or radical prostatectomy.

National Institute for Health and Care Excellence (NICE) notes that current evidence on the safety and efficacy of IRE for treating prostate cancer is inadequate in quantity and quality.

Based on an ECRI systematic review (2019), (ECRI is a designated Evidence-based Practice Center by the U.S. Agency for Healthcare Research and Quality and a federally certified Patient Safety Organization by the U.S. Department of Health and Human Services), the available evidence on laser interstitial thermal therapy (LITT) is inconclusive as a minimally invasive alternative treatment for the treatment of localized prostate cancer.

The TULSA procedure received FDA clearance August 16, 2019 to begin marketing for the ablation of prostate tissue. Treatment (primary or salvage therapy) of prostate cancer is considered investigational as its effectiveness has not been established.

The American Urological Association (AUA) and American Society for Radiation Oncology (ASTRO) and endorsed by the Society of Urologic Oncology (SUO) released 2022 guidelines for clinically localized prostate cancer. The guidelines offer the following recommendations regarding focal therapies:

1. Clinicians should inform patients with intermediate-risk prostate cancer considering whole gland or focal ablation that there are a lack of high-quality data comparing ablation outcomes to radiation therapy, surgery, and active surveillance. (Expert Opinion)
2. Clinicians should not recommend whole gland or focal ablation for patients with high-risk prostate cancer outside of a clinical trial. (Expert Opinion)

CODES

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

CPT Codes

| Code | Description |
|-------|-------------------------------------------------------------------------------------|
| 55873 | Cryosurgical ablation of the prostate (includes ultrasonic guidance and monitoring) |

Medical Policy: Focal Therapies for Prostate Cancer Treatment

Policy Number: 7.01.01

Page: 4 of 6

| Code | Description |
|-------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 55880 | Ablation of malignant prostate tissue, transrectal, with high intensity-focused ultrasound (HIFU), including ultrasound guidance |
| 55899 | Unlisted procedure, male genital system |
| 0582T (E/I) | Transurethral ablation of malignant prostate tissue by high-energy water vapor thermotherapy, including intraoperative imaging and needle guidance |
| 0600T (E/I) | Ablation, irreversible electroporation; 1 or more tumors per organ, including imaging guidance, when performed, percutaneous |
| 0601T (E/I) | Ablation, irreversible electroporation; 1 or more tumors, including Fluoroscopic and ultrasound guidance, when performed, open |
| 0655T (E/I) | Transperineal focal laser ablation of malignant prostate tissue, including transrectal imaging guidance, with MR-fused images or other enhanced ultrasound imaging |
| 0738T (E/I) | Treatment planning for magnetic field induction ablation of malignant prostate tissue, using data from previously performed magnetic resonance imaging (MRI) examination |
| 0739T (E/I) | Ablation of malignant prostate tissue by magnetic field induction, including all intraprocedural, transperineal needle/catheter placement for nanoparticle installation and intraprocedural temperature monitoring, thermal dosimetry, bladder irrigation, and magnetic field nanoparticle activation |

Copyright © 2024 American Medical Association, Chicago, IL

HCPCS Codes

| Code | Description |
|-------|----------------------------|
| C2618 | Probe/needle, cryoablation |

ICD10 Codes

| Code | Description |
|--------|-------------------------------------------------------------------|
| C61 | Malignant neoplasm of prostate |
| C79.82 | Secondary malignant neoplasm of genital organs |
| D07.5 | Carcinoma in situ of prostate |
| R97.21 | Rising PSA following treatment for malignant neoplasm of prostate |
| Z85.46 | Personal history of malignant neoplasm of prostate |
| Z92.3 | Personal history of irradiation |

REFERENCES

Abreu AL, et al. High intensity focused ultrasound hemigland ablation for prostate cancer: Initial outcomes of a United States series. J Urol 2020 Oct;204(4):741-747.

Ahn H, et al. Diagnostic performance of MRI for prediction of recurrent prostate cancer after high-intensity focused ultrasound: a systematic review and meta-analysis. Prostate Int 2023 Jun;11(2):59-68.

*Bahn D, et al. Focal cryotherapy for clinically unilateral, low-intermediate risk prostate cancer in 73 men with a median follow-up of 3.7 years. Eur Urol 2012 Jul;62(1):55-63.

Bates AS, et al. A systematic review of focal ablative therapy for clinically localised prostate cancer in comparison with standard management options: limitations of the available evidence and recommendations for clinical practice and further research. Eur Urol Oncol 2021 Jun;4(3):405-423.

Medical Policy: Focal Therapies for Prostate Cancer Treatment

Policy Number: 7.01.01

Page: 5 of 6

- *Cheetham P, et al. Long-term cancer-specific and overall survival for men followed more than 10 years after primary and salvage cryoablation of the prostate. J Endourol 2010 Jun;24(7):1123-9.
- Chin JL, et al. Long-term outcomes of whole gland salvage cryotherapy for locally recurrent prostate cancer following radiation therapy: A combined analysis of two centers. J Urol 2021 Sep;206(3):646-654.
- *Chou R, et al. Treatments for localized prostate cancer: systematic review to update the 2002 U.S. Preventive Services Task Force Recommendation. Rockville (MD) 2011 Oct.
- Dahm P, et al. Therapies for clinically localized prostate cancer [Internet]. Rockville (MD): Agency for Healthcare Research and Quality (US) 2020 Sep. Report No.: 20-EHC022. PMID: 32986341.
- *Dhar N, et al. Primary full-gland prostate cryoablation in older men (> age of 75 years): results from 860 patients traced with the COLD Registry. BJU Int 2011 Aug;108(4):508-12.
- *Donnelly BJ, et al. A randomized trial of external beam radiotherapy versus cryoablation in patients with localized prostate cancer. Cancer 2010;116:323–30.
- *Durand M, et al. Focal cryoablation: a treatment option for unilateral low-risk prostate cancer. BJU Int 2014 Jan;113(1):56-64.
- Duwe G, et al. Single-center, prospective phase 2 trial of high-intensity focused ultrasound (HIFU) in patients with unilateral localized prostate cancer: good functional results but oncologically not as safe as expected. World J Urol 2023 May;41(5):1293-1299.
- Eastham JA, et al. Clinically Localized Prostate Cancer: AUA/ASTRO Guideline. 2022 [<https://auanet.org/guidelines-and-quality/guidelines/clinically-localized-prostate-cancer-aua/astro-guideline-2022>] accessed 07/22/24.
- Guo RQ, et al. Cryoablation, high-intensity focused ultrasound, irreversible electroporation, and vascular-targeted photodynamic therapy for prostate cancer: a systemic review and meta-analysis. Int J Clin Oncol 2021 Mar;26(3):461-484.
- He Y, et al. The primary treatment of prostate cancer with high-intensity focused ultrasound: A systematic review and meta-analysis. Medicine (Baltimore) 2020 Oct 9;99(41):e22610.
- Mäkelä P, et al. Acute and subacute prostate MRI findings after MRI-guided transurethral ultrasound ablation of prostate cancer. Acta Radiol 2021 Dec;62(12):1687-1695.
- Mäkelä P, et al. Safety and efficacy of MRI-guided transurethral ultrasound ablation for radiorecurrent prostate cancer in the presence of gold fiducial markers. Acta Radiol 2023 Mar;64(3):1228-1237.
- *Malcolm JB, et al. Quality of life after open or robotic prostatectomy cryoablation or brachytherapy for localized prostate cancer. J Urol 2010 May;183:1822-9.
- Morozov A, et al. A systematic review of irreversible electroporation in localised prostate cancer treatment. Andrologia 2020 Aug 12:e13789.
- *Mouraviev V, et al. Cryoablation for locally recurrent prostate cancer following primary radiotherapy. Eur Urol 2012;61:1204-11.
- National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: prostate cancer. Version 4.2024. [https://www.nccn.org/professionals/physician_gls/pdf/prostate.pdf] accessed 07/22/24.
- Nogueira L, et al. Developments in vascular-targeted photodynamic therapy for urologic malignancies. Molecules 2020 Nov 19;25(22):5417.
- *Parekh A, et al. Cancer control and complications of salvage local therapy after failure of radiotherapy for prostate cancer: a systematic review. Semin Radiat Oncol 2013 Jul;23(3):222-34.

Medical Policy: Focal Therapies for Prostate Cancer Treatment

Policy Number: 7.01.01

Page: 6 of 6

Rakauskas A, et al. Focal therapy for prostate cancer: Complications and their treatment. Frontiers in Surgery vol. 8 696242. 12 Jul. 2021.

Reddy D, et al. Comparative Healthcare Research Outcomes of Novel Surgery in prostate cancer (IP4-CHRONOS): A prospective, multi-centre therapeutic phase II parallel Randomised Control Trial. Contemp Clin Trials 2020 Jun;93:105999.

Reddy D, et al. Cancer control outcomes following focal therapy using high-intensity focused ultrasound in 1379 men with nonmetastatic prostate cancer: a multi-institute 15-year experience. Eur Urol 2022 Apr;81(4):407-413.

Saouli A, et al. Salvage Radical Prostatectomy for Recurrent Prostate Cancer: A Systematic Review (French ccAFU). Cancers (Basel) 2023 Nov 20;15(22):5485.

Shah TT, et al. Focal therapy compared to radical prostatectomy for non-metastatic prostate cancer: a propensity score-matched study. Prostate Cancer Prostatic Dis 2021 Jan 28.

*Shelley M, et al. Cryotherapy for localised prostate cancer. Cochrane Database Syst Rev 2007;(3):CD005010.

Simmerman E, et. al., Application of irreversible electroporation ablation as adjunctive treatment for Margin enhancement: safety and efficacy. J Surg Res 2020 Feb;246:260-268.

Tan YG, et al. Patient-reported functional outcomes and oncological control after primary focal cryotherapy for clinically significant prostate cancer: A Phase II mandatory biopsy-monitored study. Prostate 2023 Jun;83(8):781-791.

*Ullal AV, et al. A report on major complications and biochemical recurrence after primary and salvage Cryosurgery for prostate cancer in patients with prior resection of benign prostatic hyperplasia: a single-center experience. Urology 2013 Sep;82(3):648-52.

Valle LF, et al. A systematic review and meta-analysis of local salvage therapies after radiotherapy for prostate cancer (MASTER). Eur Urol 2021 Sep;80(3):280-292.

*Ward JF, et al. Cryoablation for locally advanced clinical stage T3 prostate cancer: a report from the Cryo-Online database (COLD) Registry. BJU Int 2014 May;113(5):714-8.

*Ziglioli F, et al. Oncologic outcome, side effects and comorbidity of high-intensity focused ultrasound (HIFU) for localized prostate cancer. A review. Ann Med Surg (Lond) 2020;56:110-115. Published 2020 May 30.

*Key Article

KEY WORDS

Cryoablation of the prostate, high intensity focused ultrasound, vascular-targeted photodynamic therapy, irreversible electroporation, laser interstitial thermotherapy, trans-urethral ultrasound ablation

CMS COVERAGE FOR MEDICARE PRODUCT MEMBERS

There is currently a National Coverage Determination (NCD) for Cryosurgery of the Prostate (230.9). Please refer to the following NCD website for Medicare Members:

[<https://www.cms.gov/medicare-coverage-database/details/ncd-details.aspx?NCDId=123>] accessed 07/22/24.

Based on our review, Salvage High-intensity Focused Ultrasound (HIFU) Treatment in Prostate Cancer is not addressed in National or Regional Medicare coverage determinations or policies.