

(70179)

Medical Benefit		Effective Date: 10/01/15	Next Review Date: 07/19
Preauthorization	No	Review Dates: 02/07, 02/08, 05/09, 01/10, 01/11, 01/12, 09/12, 07/13, 07/14, 07/15, 07/16, 07/17, 07/18	

Preauthorization is not required.

The following protocol contains medical necessity criteria that apply for this service. The criteria are also applicable to services provided in the local Medicare Advantage operating area for those members, unless separate Medicare Advantage criteria are indicated. If the criteria are not met, reimbursement will be denied and the patient cannot be billed. Please note that payment for covered services is subject to eligibility and the limitations noted in the patient's contract at the time the services are rendered.

Populations	Interventions	Comparators	Outcomes
Individuals: <ul style="list-style-type: none"> Who are considering initial treatment for localized prostate cancer 	Interventions of interest are: <ul style="list-style-type: none"> Whole gland cryoablation 	Comparators of interest are: <ul style="list-style-type: none"> Radiotherapy Radical prostatectomy Active surveillance 	Relevant outcomes include: <ul style="list-style-type: none"> Overall survival Disease-specific survival Symptoms Functional outcomes Quality of life Treatment-related morbidity
Individuals: <ul style="list-style-type: none"> Who need salvage treatment for recurrence of localized prostate cancer following radiotherapy 	Interventions of interest are: <ul style="list-style-type: none"> Whole gland cryoablation 	Comparators of interest are: <ul style="list-style-type: none"> Radical prostatectomy Brachytherapy 	Relevant outcomes include: <ul style="list-style-type: none"> Overall survival Disease-specific survival Symptoms Functional outcomes Quality of life Treatment-related morbidity

DESCRIPTION

Cryoablation, also known as cryotherapy or cryosurgery, is a cancer-fighting technique that attacks cancer cells with extremely cold gas. This technique can be used to combat prostate cancer by percutaneously inserting thin, needle-like cryoprobes into the prostate gland; then, sending very cold gas down the cryoprobes to rapidly freeze and thaw the tissue, causing necrosis. This protocol evaluates evidence on the use of total (whole gland, definitive therapy) cryoablation.

SUMMARY OF EVIDENCE

For individuals who are considering initial treatment for localized prostate cancer who receive whole gland cryoablation, the evidence includes several systematic reviews, two randomized controlled trials, and many comparative and noncomparative observational studies. Relevant outcomes are overall survival, disease specific survival, symptoms, functional outcomes, quality of life, and treatment-related morbidity. High quality data comparing cryoablation with external-beam radiotherapy, radical prostatectomy, or active surveillance are

lacking, but available data suggest similar overall survival and disease-specific survival rates compared with radical prostatectomy and external-beam radiotherapy. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have salvage treatment for recurrence of localized prostate cancer following radiotherapy who receive whole gland cryoablation, the evidence includes primarily noncomparative case series and a few retrospective studies comparing salvage cryoablation with salvage prostatectomy. Relevant outcomes are overall survival, disease-specific survival, symptoms, functional outcomes, quality of life, and treatment-related morbidity. High-quality data comparing cryoablation to prostatectomy is mixed, and evidence comparing cryotherapy to brachytherapy is lacking. Men in this group have few options and prostatectomy can be difficult in tissue that has been irradiated. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

POLICY

Whole gland cryoablation of the prostate may be considered **medically necessary** as treatment of clinically localized (organ-confined) prostate cancer when performed

- As initial treatment or
- As salvage treatment of disease that recurs following radiotherapy.

MEDICARE ADVANTAGE

For Medicare Advantage, cryosurgery of the prostate gland, also known as cryosurgical ablation, is considered **medically necessary** as primary treatment for patients with clinically localized prostate cancer, Stages T1-T3.

Salvage cryosurgery of the prostate after *radiation failure*, for recurrent cancer, is **medically necessary** for those patients with localized disease who:

1. Have failed a trial of radiation therapy as their primary treatment; and
2. Meet one of the following conditions: Stage T2B or below, Gleason score less than 9, PSA less than 8 ng/mL.

Cryosurgery as salvage therapy is **investigational** after failure of other therapies as the primary treatment.

Cryosurgery as salvage is only **medically necessary** after the failure of a trial of radiation therapy, under the conditions noted above.

BACKGROUND

Whole gland (also known as total) cryoablation is one of several methods used to treat clinically localized prostate cancer and may be considered an alternative to radical prostatectomy or external-beam radiotherapy. Additionally, whole gland cryoablation may be used for salvage of nonmetastatic relapse following initial therapy for clinically localized disease. Using percutaneously inserted cryoprobes, the glandular tissue is rapidly frozen and thawed to cause tissue necrosis. Cryosurgical ablation is less invasive than radical prostatectomy and recovery time may be shorter. External-beam radiotherapy requires multiple treatments, whereas only one treatment is usually required for total cryoablation.

REGULATORY STATUS

Cryoablation of prostate cancer is a surgical procedure that uses previously approved and available cryoablation systems; and as a surgical procedure, it is not subject to regulation by the U.S. Food and Drug Administration.

RELATED PROTOCOLS

Charged-Particle (Proton or Helium Ion) Radiotherapy for Neoplastic Conditions

Stereotactic Radiosurgery and Stereotactic Body Radiotherapy

Services that are the subject of a clinical trial do not meet our Technology Assessment Protocol criteria and are considered investigational. *For explanation of experimental and investigational, please refer to the Technology Assessment Protocol.*

It is expected that only appropriate and medically necessary services will be rendered. We reserve the right to conduct prepayment and postpayment reviews to assess the medical appropriateness of the above-referenced procedures. **Some of this protocol may not pertain to the patients you provide care to, as it may relate to products that are not available in your geographic area.**

REFERENCES

We are not responsible for the continuing viability of web site addresses that may be listed in any references below.

1. Blue Cross and Blue Shield Association Technology Evaluation Center (TEC). Cryoablation for the primary treatment of clinically localized prostate cancer. TEC Assessments. 2001;Volume16:Tab 6.
2. Centers for Medicare and Medicaid Services. National Coverage Determination (NCD) for Cryosurgery of Prostate (230.9). 2001; <http://www.cms.gov/medicare-coverage-database/details/nccdetails.aspx?NCDId=123&bc=AgAAQAAAAAAAA&ncdver=1>. Accessed August 15, 2017.
3. Shelley M, Wilt TJ, Coles B, et al. Cryotherapy for localised prostate cancer. Cochrane Database Syst Rev. Jul 18 2007(3):CD005010. PMID 17636783
4. Wilt TJ, Shamlivan T, Taylor B, et al. Comparative Effectiveness of Therapies for Clinically Localized Prostate Cancer (Report No. 08-EHC010-EF). Rockville (MD): Agency for Healthcare Research and Quality; 2008
5. Chou R, Dana T, Bougatsos C, et al. Treatments for Localized Prostate Cancer: Systematic Review to Update the 2002 U.S. Preventive Services Task Force Recommendation (Report No. 12-05161-EF-1). Rockville (MD): Agency for Healthcare Research and Quality; 2011.
6. Grimm P, Billiet I, Bostwick D, et al. Comparative analysis of prostate-specific antigen free survival outcomes for patients with low, intermediate and high risk prostate cancer treatment by radical therapy. Results from the Prostate Cancer Results Study Group. BJU Int. Feb 2012;109 Suppl 1:22-29. PMID 22239226
7. Xiong T, Turner RM, Wei Y, et al. Comparative efficacy and safety of treatments for localised prostate cancer: an application of network meta-analysis. BMJ Open. May 15 2014;4(5):e004285. PMID 24833678
8. Ramsay CR, Adewuyi TE, Gray J, et al. Ablative therapy for people with localised prostate cancer: a systematic review and economic evaluation. Health Technol Assess. Jul 2015;19(49):1-490. PMID 26140518
9. Gao L, Yang L, Qian S, et al. Cryosurgery would be an effective option for clinically localized prostate cancer: a meta-analysis and systematic review. Sci Rep. Jun 07 2016;6:27490. PMID 27271239
10. Chin JL, Ng CK, Touma NJ, et al. Randomized trial comparing cryoablation and external beam radiotherapy for T2C-T3B prostate cancer. Prostate Cancer Prostatic Dis. 2008;11(1):40-45. PMID 17579613

11. Chin JL, Al-Zahrani AA, Autran-Gomez AM, et al. Extended followup oncologic outcome of randomized trial between cryoablation and external beam therapy for locally advanced prostate cancer (T2c-T3b). *J Urol.* Oct 2012;188(4):1170-1175. PMID 22901586
12. Ball AJ, Gambill B, Fabrizio MD, et al. Prospective longitudinal comparative study of early health-related quality-of-life outcomes in patients undergoing surgical treatment for localized prostate cancer: a short-term evaluation of five approaches from a single institution. *J Endourol.* Oct 2006;20(10):723-731. PMID 17094746
13. Elkjaer MC, Borre M. Oncological outcome after primary prostate cryoablation compared with radical prostatectomy: a single-centre experience. *Scand J Urol.* Feb 2014;48(1):27-33. PMID 23597178
14. Gould RS. Total cryosurgery of the prostate versus standard cryosurgery versus radical prostatectomy: comparison of early results and the role of transurethral resection in cryosurgery. *J Urol.* Nov 1999;162(5):1653-1657. PMID 10524891
15. Hubosky SG, Fabrizio MD, Schellhammer PF, et al. Single center experience with third-generation cryosurgery for management of organ-confined prostate cancer: critical evaluation of short-term outcomes, complications, and patient quality of life. *J Endourol.* Dec 2007;21(12):1521-1531. PMID 18186694
16. Donnelly BJ, Saliken JC, Brasher PM, et al. A randomized trial of external beam radiotherapy versus cryoablation in patients with localized prostate cancer. *Cancer.* Jan 15 2010;116(2):323-330. PMID 19937954
17. Robinson JW, Donnelly BJ, Siever JE, et al. A randomized trial of external beam radiotherapy versus cryoablation in patients with localized prostate cancer: quality of life outcomes. *Cancer.* Oct 15 2009;115(20):4695-4704. PMID 19691092
18. Bahn DK, Lee F, Badalament R, et al. Targeted cryoablation of the prostate: 7-year outcomes in the primary treatment of prostate cancer. *Urology.* Aug 2002;60(2 Suppl 1):3-11. PMID 12206842
19. Donnelly BJ, Saliken JC, Ernst DS, et al. Prospective trial of cryosurgical ablation of the prostate: five-year results. *Urology.* Oct 2002;60(4):645-649. PMID 12385926
20. Ellis DS. Cryosurgery as primary treatment for localized prostate cancer: a community hospital experience. *Urology.* Aug 2002;60(2 Suppl 1):34-39. PMID 12206846
21. Long JP, Bahn D, Lee F, et al. Five-year retrospective, multi-institutional pooled analysis of cancer-related outcomes after cryosurgical ablation of the prostate. *Urology.* Mar 2001;57(3):518-523. PMID 11248631
22. Onik G. Image-guided prostate cryosurgery: state of the art. *Cancer Control.* Nov-Dec 2001;8(6):522-531. PMID 11807422
23. Robinson JW, Donnelly BJ, Saliken JC, et al. Quality of life and sexuality of men with prostate cancer 3 years after cryosurgery. *Urology.* Aug 2002;60(2 Suppl 1):12-18. PMID 12206843
24. Aus G, Pileblad E, Hugosson J. Cryosurgical ablation of the prostate: 5-year follow-up of a prospective study. *Eur Urol.* Aug 2002;42(2):133-138. PMID 12160583
25. De La Taille A, Benson MC, Bagiella E, et al. Cryoablation for clinically localized prostate cancer using an argon-based system: complication rates and biochemical recurrence. *BJU Int.* Feb 2000;85(3):281-286. PMID 10671882
26. Han KR, Cohen JK, Miller RJ, et al. Treatment of organ confined prostate cancer with third generation cryosurgery: preliminary multicenter experience. *J Urol.* Oct 2003;170(4 Pt 1):1126-1130. PMID 14501706
27. Prepelica KL, Okeke Z, Murphy A, et al. Cryosurgical ablation of the prostate: high risk patient outcomes. *Cancer.* Apr 15 2005;103(8):1625-1630. PMID 15747374
28. Aus G. Cryosurgery for prostate cancer. *J Urol.* Nov 2008;180(5):1882-1883. PMID 18801502
29. Lian H, Guo H, Gan W, et al. Cryosurgery as primary treatment for localized prostate cancer. *Int Urol Nephrol.* Dec 2011;43(4):1089-1094. PMID 21475948
30. Williams SB, Lei Y, Nguyen PL, et al. Comparative effectiveness of cryotherapy vs. brachytherapy for localized prostate cancer. *BJU Int.* Jul 2012;110(2 Pt 2):E92-98. PMID 22192688
31. Jones JS, Rewcastle JC, Donnelly BJ, et al. Whole gland primary prostate cryoablation: initial results from the cryo on-line data registry. *J Urol.* Aug 2008;180(2):554-558. PMID 18550117

32. Tay KJ, Polascik TJ, Elshafei A, et al. Primary cryotherapy for high-grade clinically localized prostate cancer: oncologic and functional outcomes from the COLD Registry. *J Endourol.* Jan 2016;30(1):43-48. PMID 26414656
33. Chin JL, Pautler SE, Mouraviev V, et al. Results of salvage cryoablation of the prostate after radiation: identifying predictors of treatment failure and complications. *J Urol.* Jun 2001;165(6 Pt 1):1937-1941; discussion 1941-1932. PMID 11371885
34. Robinson JW, Donnelly BJ, Coupland K, et al. Quality of life 2 years after salvage cryosurgery for the treatment of local recurrence of prostate cancer after radiotherapy. *Urol Oncol.* Nov-Dec 2006;24(6):472-486. PMID 17138127
35. Mouraviev V, Spiess PE, Jones JS. Salvage cryoablation for locally recurrent prostate cancer following primary radiotherapy. *Eur Urol.* Jun 2012;61(6):1204-1211. PMID 22421081
36. Punnen S, Cooperberg MR, D'Amico AV, et al. Management of biochemical recurrence after primary treatment of prostate cancer: a systematic review of the literature. *Eur Urol.* Dec 2013;64(6):905-915. PMID 23721958
37. Peters M, Moman MR, van der Poel HG, et al. Patterns of outcome and toxicity after salvage prostatectomy, salvage cryosurgery and salvage brachytherapy for prostate cancer recurrences after radiation therapy: a multicenter experience and literature review. *World J Urol.* Apr 2013;31(2):403-409. PMID 22903773
38. Pisters LL, Leibovici D, Blute M, et al. Locally recurrent prostate cancer after initial radiation therapy: a comparison of salvage radical prostatectomy versus cryotherapy. *J Urol.* Aug 2009;182(2):517-525; discussion 525-517. PMID 19524984
39. Wenske S, Quarrier S, Katz AE. Salvage cryosurgery of the prostate for failure after primary radiotherapy or cryosurgery: long-term clinical, functional, and oncologic outcomes in a large cohort at a tertiary referral centre. *Eur Urol.* Jul 2013;64(1):1-7. PMID 22840351
40. Ng CK, Moussa M, Downey DB, et al. Salvage cryoablation of the prostate: followup and analysis of predictive factors for outcome. *J Urol.* Oct 2007;178(4 Pt 1):1253-1257; discussion 1257. PMID 17698104
41. Ismail M, Ahmed S, Kastner C, et al. Salvage cryotherapy for recurrent prostate cancer after radiation failure: a prospective case series of the first 100 patients. *BJU Int.* Oct 2007;100(4):760-764. PMID 17662081
42. Williams AK, Martinez CH, Lu C, et al. Disease-free survival following salvage cryotherapy for biopsy-proven radio-recurrent prostate cancer. *Eur Urol.* Sep 2011;60(3):405-410. PMID 21185115
43. Siddiqui KM, Billia M, Al-Zahrani A, et al. Long-term oncologic outcomes of salvage cryoablation for radio recurrent prostate cancer. *J Urol.* Oct 2016;196(4):1105-1111. PMID 27157372
44. Friedlander DF, Gu X, Prasad SM, et al. Population-based comparative effectiveness of salvage radical prostatectomy vs. cryotherapy. *Urology.* Mar 2014;83(3):653-657. PMID 24581527
45. Spiess PE, Levy DA, Pisters LL, et al. Outcomes of salvage prostate cryotherapy stratified by pre-treatment PSA: update from the COLD registry. *World J Urol.* Dec 2013;31(6):1321-1325. PMID 23179729
46. Mottet N, Bellmunt J, Bolla M, et al. EAU-ESTRO-SIOG Guidelines on Prostate Cancer. Part 1: Screening, Diagnosis, and Local Treatment with Curative Intent. *Eur Urol.* Apr 2017;71(4):618-629. PMID 27568654
47. National Cooperative Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Prostate cancer. Version 2.2017. http://www.nccn.org/professionals/physician_gls/pdf/prostate.pdf. Accessed August 10, 2017.
48. American Urological Association. Best practice policy statement on cryosurgery for the treatment of localized prostate cancer. Linthicum (MD): American Urological Association Education and Research; 2008.
49. National Coverage Determination (NCD) for CRYOSURGERY of PROSTATE (230.9), Effective Date of this Version 7/1/2001.