Whole Gland Cryoablation of Prostate Cancer

Policy # 00022
Original Effective Date: 06/24/2002
Current Effective Date: 05/08/2023

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: Focal Treatments for Prostate Cancer are addressed separately in medical policy 00484.

Note: Stereotactic Radiosurgery and Stereotactic Body Radiation Therapy are addressed separately in medical policy 00045.

Note: Proton Beam Therapy are addressed separately in medical policy 00187.

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 whole gland cryoablation of the prostate as treatment of clinically localized (organ-confined) prostate cancer when patient selection criteria are met to be eligible for coverage.**

Patient Selection Criteria
Coverage eligibility for whole gland cryoablation of the prostate as treatment of clinically localized (organ-confined) prostate cancer will be considered when any of the following criteria are met:

- As an initial treatment; or
- As salvage treatment of disease that recurs following radiotherapy.
Whole Gland Cryoablation of Prostate Cancer

Policy # 00022
Original Effective Date: 06/24/2002
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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, the Company considers the use of whole gland cryoablation of the prostate as treatment of clinically localized (organ-confined) prostate cancer when patient selection criteria are not met to be investigational.*

Background/Overview
Prostate Cancer
Prostate cancer is the most commonly diagnosed cancer in men and the second leading cause of cancer death among men in the U. S., with an estimated 268,490 new cases and 34,500 deaths in 2022. The diagnosis and grading of prostate cancer are performed by taking a biopsy of the prostate gland.

Treatment
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 (EBRT). 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 cryoablation usually requires a single treatment.

FDA or Other Governmental Regulatory Approval
U.S. Food and Drug Administration (FDA)
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. FDA.
Whole Gland Cryoablation of Prostate Cancer

Policy # 00022  
Original Effective Date: 06/24/2002  
Current Effective Date: 05/08/2023

Rationale/Source
This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. FDA 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.

Cryoablation, also known as cryotherapy or cryosurgery, is a procedure that attacks cancer cells using extremely cold gas. This technique can be used to treat prostate cancer by percutaneously inserting thin, needle-like cryoprobes into the prostate gland and then sending very cold gas down the cryoprobes to rapidly freeze and thaw the tissue, causing necrosis. This review 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 systematic reviews, 2 randomized controlled trials, and many comparative and noncomparative observational studies. Relevant outcomes are overall survival (OS), disease-specific survival, symptoms, functional outcomes, quality of life (QOL), and treatment-related morbidity. High-quality data comparing cryoablation with external-beam radiotherapy (EBRT), radical prostatectomy, or active surveillance are lacking, but available data have suggested similar OS and disease-specific survival rates compared with radical prostatectomy and EBRT. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have salvage treatment for a recurrence of localized prostate cancer following radiotherapy who receive whole gland cryoablation, the evidence primarily includes case series and a few retrospective studies comparing salvage cryoablation with salvage prostatectomy or brachytherapy. Relevant outcomes are OS, disease-specific survival, symptoms, functional outcomes, QOL, and treatment-related morbidity. High-quality data comparing salvage cryoablation with salvage prostatectomy or brachytherapy are lacking, though limited evidence suggests that salvage cryotherapy may be associated with better survival outcomes than prostatectomy. Men with recurrent localized prostate cancer have limited treatment options and prostatectomy can be difficult
Whole Gland Cryoablation of Prostate Cancer

Policy # 00022
Original Effective Date: 06/24/2002
Current Effective Date: 05/08/2023

in tissue that has been irradiated. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

Additional Information
Input was received from 1 physician specialty society and 4 academic medical centers while this policy was under review in 2009. There was strong agreement that cryoablation should be considered medically necessary as an option in the initial treatment of organ-confined prostate cancer, as well as for use as salvage therapy for disease recurrence after radiotherapy.

Supplemental Information
Clinical Input From Physician Specialty Societies and Academic Medical Centers
In response to requests, input was received from 1 physician specialty society and 4 academic medical centers while this policy was under review in 2009. There was strong agreement that cryoablation should be considered medically necessary as an option in the initial treatment of organ-confined prostate cancer, as well as for use as salvage therapy for disease recurrence after radiotherapy.

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.

National Comprehensive Cancer Network
The National Comprehensive Cancer Network (NCCN) guidelines (v.4 2022) for prostate cancer indicate cryosurgery and high-intensity focused ultrasound are options for radiotherapy recurrence in patients who have no evidence of metastatic disease. NCCN does not recommend cryotherapy as routine primary therapy for localized prostate cancer due to limited long-term data comparing cryotherapy with radiation or radical prostatectomy.
American Urological Association et al
In 2022, the American Urological Association and the American Society for Radiology Oncology issued a joint, updated guideline on the treatment of clinical localized prostate cancer; the guideline was additionally endorsed by the Society of Urologic Oncology. In the guideline, treatment recommendations are stratified according to risk group, and ablative techniques are discussed in general with no recommendations specific to whole-gland cryoablation (Table 1).

Table 1. Treatment Recommendations Related to Cryoablation by Prostate Cancer Risk Group

<table>
<thead>
<tr>
<th>Severity/Risk Group</th>
<th>Risk Definition</th>
<th>Treatment Recommendation</th>
<th>LOE</th>
<th>GOE</th>
<th>Clinical Considerations</th>
</tr>
</thead>
</table>
| Low-risk disease    | PSA <10 ng/mL AND Grade Group 1 AND clinical stage T1-T2a | For patients with low-risk prostate cancer, clinician should recommend active surveillance as the preferred management option | Strong | A   | The Panel believes that the benefits of aggressive treatment do not outweigh the risk of treatment-related harms for most patients with low-risk disease. The Panel acknowledges that select patients with low-risk disease may elect definitive local therapy after an informed discussion between

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Whole Gland Cryoablation of Prostate Cancer

| Intermediate-risk disease | PSA 10-20 ng/mL OR Grade Group 2-3 OR clinical stage T2b-c | 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 | --- | The Panel believes that ablation maybe considered in select, appropriately informed patients (with clinical trial enrollment prioritized).

Patients considering ablation should be counseled regarding side effects and recurrence risk and should be followed post-ablation with PSA, DRE, MRI, and biopsy tailored to their specific health and cancer characteristics.

Clinicians should not recommend whole gland or focal ablation for patients with high-risk prostate | Expert opinion | --- | There is a lack of data supporting treatment of high-risk disease with ablation. |
Whole Gland Cryoablation of Prostate Cancer

Policy # 00022
Original Effective Date: 06/24/2002
Current Effective Date: 05/08/2023

<table>
<thead>
<tr>
<th>OR clinical stageT3</th>
<th>cancer outside of a clinical trial</th>
</tr>
</thead>
</table>

DRE: digital rectal exam; GOE: grade of evidence; HIFU: high-intensity focused ultrasound; LOE: level of evidence; MRI: magnetic resonance imaging; PSA: prostate-specific antigen.

U.S. Preventive Services Task Force Recommendations
A systematic review of localized prostate cancer treatments was prepared by Fenton et al (2018) for the Agency for Healthcare Research and Quality, updating the 2002 U.S. Preventive Services Task Force recommendation. Reviewers found no studies comparing cryoablation with watchful waiting and no randomized trials or cohort studies evaluating overall survival or prostate cancer-specific mortality outcomes. The available evidence was mostly from uncontrolled studies, found to be very limited, and not sufficiently reliable to estimate the benefits or harms of cryoablation.

Medicare National Coverage
The Centers for Medicare & Medicaid Services have determined that total cryotherapy is medically necessary and appropriate as primary treatment for clinically localized prostate cancer in stages T1 to T3. Salvage cryoablation is only medically necessary and appropriate in localized disease when radiotherapy has failed as primary treatment, and the patient meets 1 of 3 criteria: stage T2B or below, Gleason score less than 9, or prostate-specific antigen level of less than 8 ng/mL. Salvage cryoablation after the failure of other therapies is not covered.

Ongoing and Unpublished Clinical Trials
Some currently ongoing and unpublished trials that might influence this review are listed in Table 2.

Table 2. Summary of Key Trials

<table>
<thead>
<tr>
<th>NCT No.</th>
<th>Trial Name</th>
<th>Planned Enrollment</th>
<th>Completion Date</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ongoing</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NCT01727284</td>
<td>Technical Success, Safety, and Short and Long-Term Efficacy for MR-Guided Cryoablation of Prostate Bed Recurrences</td>
<td>100</td>
<td>Dec 2023</td>
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</tbody>
</table>

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Whole Gland Cryoablation of Prostate Cancer

Policy # 00022
Original Effective Date: 06/24/2002
Current Effective Date: 05/08/2023

<table>
<thead>
<tr>
<th>Unpublished</th>
<th>Study Description</th>
<th>NCT</th>
<th>Last Updated</th>
</tr>
</thead>
<tbody>
<tr>
<td>NCT01398657</td>
<td>Cryotherapy With or Without Short-term Adjvant Androgen-Deprivation Therapy for High-Risk Localized Prostate Cancer - Open-Label Randomized Clinical Study</td>
<td>182</td>
<td>Jun 2016 (Unknown; last updated Nov 2012)</td>
</tr>
<tr>
<td>NCT02615223</td>
<td>A Prospective Multi-Center Study to Compare the QOL and Efficacy of Endocrine Therapy with or without Cryoablation for Stage IV Prostate Cancer</td>
<td>120</td>
<td>Dec 2018 (Unknown; last updated Jun 2017)</td>
</tr>
<tr>
<td>NCT02605226</td>
<td>A Prospective Multi-Center Study to Compare the QOL and Efficacy of External Beam Radiation Therapy or Cryoablation Therapy for Stage III Prostate Cancer (CRYO-PCA-III)</td>
<td>240</td>
<td>Dec 2018 (Unknown; last updated Jun 2017)</td>
</tr>
<tr>
<td>NCT03348722</td>
<td>START (Active Surveillance or Radical Treatment for Newly Diagnosed Patients with a Localized, Low Risk, Prostate Cancer): an Epidemiological Study of the Oncology Network of Piemonte and Valle d’Asosta, Italy</td>
<td>3000</td>
<td>Nov 2019 (Unknown; last updated Nov 2017)</td>
</tr>
</tbody>
</table>

NCT: national clinical trial.

References
Whole Gland Cryoablation of Prostate Cancer

Policy # 00022
Original Effective Date: 06/24/2002
Current Effective Date: 05/08/2023


Whole Gland Cryoablation of Prostate Cancer

Policy # 00022
Original Effective Date: 06/24/2002
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Whole Gland Cryoablation of Prostate Cancer

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Page 11 of 16
Whole Gland Cryoablation of Prostate Cancer

Policy # 00022
Original Effective Date: 06/24/2002
Current Effective Date: 05/08/2023


Policy History

Original Effective Date: 06/24/2002
Current Effective Date: 05/08/2023

06/20/2002 Medical Policy Committee review
06/24/2002 Managed Care Advisory Council approval. Format revision. No substance change to policy.
08/31/2004 Medical Director review
09/21/2004 Medical Policy Committee review. Format revision. No substance change to policy.
09/27/2004 Managed Care Advisory Council approval
09/07/2005 Medical Director review
09/20/2005 Medical Policy Committee review. Format revision. Coverage eligibility unchanged. The following clarification statement was added: “Based on review of available data, the Company considers other uses of cryoablation of the prostate to be investigational.”
09/22/2005 Quality Care Advisory Council approval
07/07/2006 Format revision, including addition of FDA and or other governmental regulatory approval and rationale/source. Coverage eligibility unchanged.
10/04/2006 Medical Director review
10/18/2006 Medical Policy Committee approval. Format revision, including addition of information added to FDA and or other governmental regulatory approval. References updated and additional references added. Coverage eligibility unchanged.
11/07/2007 Medical Director review
11/15/2007 Medical Policy Committee approval. No change to coverage eligibility.
11/05/2008 Medical Director review
11/18/2008 Medical Policy Committee approval. No change to coverage eligibility. Rationale updated.
Whole Gland Cryoablation of Prostate Cancer

Policy #  00022
Original Effective Date:  06/24/2002
Current Effective Date:  05/08/2023

05/07/2009  Medical Director review
05/20/2009  Medical Policy Committee approval. Revised two criteria bullets in coverage section as follows:
  • “As an initial treatment of clinically localized (organ-confined) primary prostate cancer; or
  • As salvage treatment of recurrent (following radiation therapy) localized prostate cancer.”
Added investigational statement as follows, “Based on review of available data, the Company considers subtotal prostate cryoablation in the treatment of prostate cancer to be investigational.*”

06/03/2010  Medical Policy Committee review
06/16/2010  Medical Policy Implementation Committee approval
05/05/2011  Medical Policy Committee review
05/18/2011  Medical Policy Implementation Committee approval. No change.
05/03/2012  Medical Policy Committee review
05/16/2012  Medical Policy Implementation Committee approval. No change to coverage.
06/06/2013  Medical Policy Committee review
06/25/2013  Medical Policy Implementation Committee approval. No change to coverage.
06/05/2014  Medical Policy Committee review
06/18/2014  Medical Policy Implementation Committee approval. No change to coverage. Added FDA section.
08/03/2015  Coding update: ICD10 Diagnosis code section added; ICD9 Procedure code section removed.
09/03/2015  Medical Policy Committee review
09/23/2015  Medical Policy Implementation Committee approval. No change to coverage.
11/03/2016  Medical Policy Committee review
11/16/2016  Medical Policy Implementation Committee approval. Title change, policy statements adjusted to address whole gland treatment.
01/01/2017  Coding update: Removing ICD-9 Diagnosis Codes
11/02/2017  Medical Policy Committee review
11/15/2017  Medical Policy Implementation Committee approval. No change to coverage.
11/08/2018  Medical Policy Committee review
11/21/2018  Medical Policy Implementation Committee approval. No change to coverage.
11/07/2019  Medical Policy Committee review

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Whole Gland Cryoablation of Prostate Cancer

Policy # 00022
Original Effective Date: 06/24/2002
Current Effective Date: 05/08/2023

11/13/2019  Medical Policy Implementation Committee approval. No change to coverage.
04/02/2020  Medical Policy Committee review
04/08/2020  Medical Policy Implementation Committee approval. No change to coverage.
04/01/2021  Medical Policy Committee review
04/14/2021  Medical Policy Implementation Committee approval. No change to coverage.
04/07/2022  Medical Policy Committee review
04/13/2022  Medical Policy Implementation Committee approval. No change to coverage.
04/06/2023  Medical Policy Committee review
04/12/2023  Medical Policy Implementation Committee approval. No change to coverage.

Next Scheduled Review Date: 04/2024

Coding

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Whole Gland Cryoablation of Prostate Cancer

Policy # 00022  
Original Effective Date: 06/24/2002  
Current Effective Date: 05/08/2023

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

<table>
<thead>
<tr>
<th>Code Type</th>
<th>Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPT</td>
<td>55873</td>
</tr>
<tr>
<td>HCPCS</td>
<td>C2618</td>
</tr>
<tr>
<td>ICD-10 Diagnosis</td>
<td>All related diagnoses</td>
</tr>
</tbody>
</table>

*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
Whole Gland Cryoablation of Prostate Cancer

Policy #  00022
Original Effective Date:  06/24/2002
Current Effective Date:  05/08/2023

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.