Whole Gland Cryoablation of Prostate Cancer

Policy # 00022
Original Effective Date: 06/24/2002
Current Effective Date: 11/15/2017

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.

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 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.

When Services Are Considered Investigational
Note: 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
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 1 treatment is usually required for total cryoablation.

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

Policy # 00022
Original Effective Date: 06/24/2002
Current Effective Date: 11/15/2017

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.

Centers for Medicare and Medicaid Services (CMS)
The Centers for Medicare & Medicaid Services have indicated 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 failure of other therapies is not covered.

Rationale/Source

PRIMARY PROSTATE CRYOABLATION
Systematic Reviews
This evidence review was informed by a 2001 TEC Assessment that focused on total cryoablation for primary localized prostate cancer. At that time, available evidence was heterogeneous with insufficient information on baseline characteristics of enrolled patients. Where data were available, outcomes appeared to be generally comparable across treatment methods. However, data from cryoablation studies were sparse and did not permit conclusions on oncologic outcomes. Perioperative mortality and acute life-threatening consequences of cryoablation appeared negligible. Patients had the highest likelihood of impotence after cryoablation compared with radical prostatectomy or 3-dimensional conformal radiotherapy (3D-CRT). The frequency of incontinence appeared similar to that after 3D-CRT, and potentially less than that after radical prostatectomy. Adverse gastrointestinal (GI) consequences typical of 3D-CRT were not noted after cryoablation. Long-term consequences of cryoablation were uncertain because follow-up was inadequate.

The conclusions of the 2001 TEC Assessment contrasted with a 2001 analysis from the CMS supporting Medicare’s decision that cryosurgical ablation was eligible for coverage. The TEC Assessment sought data on clinical health outcomes, whereas the CMS assessment used an intermediate outcome, changes in prostate-specific antigen (PSA) levels. As noted in the CMS assessment, “Data shows that a significant number of patients are able to sustain undetectable levels of PSA for a period of time of at least 24 months. This compares favorably with the biopsy data following external beam irradiation.”

A 2007 Cochrane review of cryoablation for localized prostate cancer found no randomized trials comparing cryoablation with other therapies for the primary treatment of localized prostate cancer; studies identified included case series. The patients recruited in the case series (total N=1483 patients) ranged in age from 41 to 84 years, and their conditions were classified by stage: stages T1: 0% to 43%; T2: 24% to 88%; T3: 1% to 41%; and T4: 0% to14%. The mean preoperative PSA level ranged from 9.7 to 39 ng/mL, with Gleason scores less than 7 in 9% to 37% of patients. Reviewers concluded that cryoablation offered a potential alternative to standard therapies for the primary treatment of localized prostate cancer, and that patients who select cryoablation as their therapeutic option should be informed of the relevant data (eg,
Whole Gland Cryoablation of Prostate Cancer

Policy #  00022
Original Effective Date:  06/24/2002
Current Effective Date:  11/15/2017

efficacy, complications, low-grade evidence) associated with such treatment; however, due to the poor quality of the available studies, it was difficult to determine the relative benefits of cryoablation.

A 2008 comparative effectiveness review of therapies for clinically localized prostate cancer from the Agency for Healthcare Research and Quality also found that no randomized trials had evaluated cryoablation. The report noted that, in general, neither overall survival (OS) nor prostate cancer–specific survival was reported for this technique. Progression-free survival (PFS) in patients with T1 or T2 stages ranged from 29% to 100%.

A subsequent systematic review of localized prostate cancer treatments prepared for the Agency for Healthcare Research and Quality was published in late 2011. Reviewers found no studies comparing cryoablation with watchful waiting (surveillance) and no randomized trials or cohort studies evaluating OS or prostate cancer–specific survival outcomes. The available evidence was mostly from uncontrolled studies and found to be very limited and not sufficiently reliable to estimate the benefits or harms of cryoablation.

In a 2012 comparative effectiveness report from the Prostate Cancer Results Study Group, treatment effectiveness measured by PSA levels following various prostate cancer treatments, including cryoablation, was noted to be difficult to evaluate, because very few studies comparing results from treatment options were identified. Additionally, variations in methods of evaluating outcomes and reporting results complicated the analysis. No recommendations for cryoablation were made by the Prostate Cancer Results Study Group.

A network meta-analysis published in 2014 evaluated the following: the comparative efficacy and safety of radical prostatectomy, several regimens of external-beam radiotherapy (EBRT), cryoablation, and observational management. This analysis incorporated 21 randomized controlled trials (RCTs; total N=7350 patients) that reported OS and prostate cancer–specific survival rates at 5 years, and late GI and late genitourinary (GU) toxicities at 3 years. It used Bayesian network analysis with informative prior distributions based on external evidence for heterogeneity variances to compute odd ratios (ORs) with 95% confidence intervals (CIs) for all pairwise comparisons of interventions. The rank order of superiority of each intervention was compared with all the others using the surface under the cumulative ranking (SUCRA) curve statistic. The SUCRA curve is expressed as a percentage that ranges from 0% if an intervention is certainly the worst to 100% if an intervention is certainly the best. If all interventions are equal, all SUCRA curve values will approximate a percentage of 50%. Overall, the network analysis showed no evidence of the superiority of any treatment for OS (this was based on SUCRA curve values that ranged from 18% [observational management] to 69% [conformal low-dose EBRT]). Cryoablation had a SUCRA curve value of 50%, which yielded a ranking of fourth best treatment. However, the SUCRA curve values for late GI (99%) and GU (77%) events with cryoablation rated this intervention in first place for those specific outcomes. These analyses are consistent with a positive balance of benefits and harms associated with total cryoablation compared with radical prostatectomy, EBRT, and observational management.
Whole Gland Cryoablation of Prostate Cancer

Policy # 00022
Original Effective Date: 06/24/2002
Current Effective Date: 11/15/2017

In 2015, a Health Technology Assessment was reported by the National Institute for Health Research. Reviewers compared the clinical effectiveness of ablative therapies with radical prostatectomy, EBRT, and active surveillance. The search included RCTs and non-RCTs published through March 2013. Meta-analyses were performed using a Bayesian indirect mixed-treatment comparison. Fourteen case series, 1 RCT, and 4 non-RCT comparative studies (total N=3995 patients) evaluated cryoablation. Reviewers included studies of primary and salvage treatment as well as whole and focal cryoablation. All studies were considered at high risk of bias. Only pooled estimates of primary, whole cryoablation are described here. Two publications provided data on OS for cryoablation vs EBRT; there was no evidence of a difference in OS for cryotherapy and EBRT at 4 years. The probability that cryoablation was superior to EBRT was 0.73. The predicted survival rate in the mixed-treatment comparison model at 4 years was 93% for cryoablation and 91% for EBRT. Reviewers concluded that there was insufficient evidence to form any clear recommendations on the use of ablative therapies.

In 2016, Gao et al reported results of a systematic review and meta-analysis comparing cryoablation with radiotherapy and radical prostatectomy for treatment of localized prostate cancer. The search included articles published up to December 2015. Because the pooled estimates combined primary and salvage treatment, we present the individual studies in the following sections and do not present pooled data here. Six studies described primary treatment (2 RCTs, 2 prospective observational, 2 retrospective). Cryotherapy had similar OS and disease-specific survival rates as radiotherapy and radical prostatectomy in trials of primary treatment. There was significantly more sexual bother for cryoablation (compared with radiotherapy) at all times reported (p<0.01).

Randomized Controlled Trials
Chin et al (2008, 2012) reported on a randomized trial of cryoablation comparing with EBRT in patients with clinical stage T2C-T3B prostate cancer. These patients had node-negative disease and had received 6 months of hormonal therapy, starting 3 months before treatment. Only 64 of the planned 150 patients were accrued; entry was limited due to changes in practice and difficulty beginning cryoablation at one of the sites. Twenty-one (64%) of 33 in the cryoablation group and 14 (45%) of 31 in the EBRT-treated group were classified as treatment failures. The mean biochemical disease-free survival (bDFS) was 41 months for the EBRT group and 28 months for the cryoablation group. The 4-year bDFS rate for the EBRT and cryoablation groups were 47% and 13%, respectively. The 8-year bDFS rate for the EBRT and cryoablation groups were 59.1% and 17.4%, respectively. Disease-specific survival rates and OS rates were very similar and, at the 8-year follow-up, the rates still did not differ significantly. Serious complications were uncommon in both groups. EBRT patients exhibited adverse GI effects more frequently. The trialists concluded that taking into account the relative deficiency in numbers and the original trial design, this prospective randomized trial indicated that the results of cryoablation were less favorable than those of EBRT and that cryoablation was suboptimal primary therapy in locally advanced prostate cancer.

Donnelly et al (2010) reported on a randomized trial of 244 patients with newly diagnosed localized prostate cancer, during the period from 1997 through 2003, to compare cryoablation with EBRT. All patients began neoadjuvant antiandrogen therapy before local treatment and continued for a period of 3 to 6 months. The
Whole Gland Cryoablation of Prostate Cancer

Policy # 00022
Original Effective Date: 06/24/2002
Current Effective Date: 11/15/2017

median follow-up was 100 months. At 36 months, the biochemical failure rate (PSA nadir + 2 ng/mL) was 17.1% in the cryoablation group and 13.2% in the radiotherapy group. The OS rate at 5 years was 89.7% in the cryoablation group, and 88.3% in the radiotherapy group; the two did not differ statistically (p=0.78). At 36 months, radiotherapy patients had significantly more positive prostate biopsies (22/76 patients) than the cryoablation group (7/91 patients; p<0.001). Observed failure rates at 60 months were similar in both groups but were less likely with cryoablation at 84 months. Using National Cancer Institute of Canada Common Toxicity Criteria, 12 cryoablation patients experienced 13 grade 3 adverse events vs 16 grade 3 adverse events in 14 radiotherapy patients. Urinary retention was the most common grade 3 adverse event in both treatment arms. The trialists were unable to establish that cryoablation was noninferior to radiotherapy at 36 months due to the wide confidence interval. The trialists also noted several issues that limited interpretation of trial results, including the use of uncommonly low radiation dosages (68 gray [Gy], 70 Gy, 73.5 Gy, respectively), and early trial closure due to lack of patient enrollment.

In a second article from the Donnelly trial (2010), Robinson et al (2009) reported on quality of life outcomes in the same 244 patients. With few exceptions, Robinson et al found study participants reported quality of life at high levels in both the cryoablation and radiotherapy treatment arms. Acute urinary dysfunction, which eventually resolved, occurred more often with cryoablation, as measured using the University of California at Los Angeles (UCLA) Prostate Cancer Index (mean urinary function after cryoablation was 69.4 vs 90.7 after EBRT; p<0.001; higher scores indicate better function and less bother). UCLA Prostate Cancer Index sexual function decreased in both arms at 3 months. However, reduced sexual function was reported more in the cryoablation arm (mean cryoablation, 7.2 vs mean EBRT, 32.9; p<0.001). Decreased sexual function continued at the 3-year evaluation, with the mean score 15 points lower in the cryoablation group.

Nonrandomized Comparative Studies
Many nonrandomized studies have reported on cryoablation for localized prostate cancer. In 2002, the largest single-institution series reported on the 7-year actuarial rate of bDFS for 590 consecutively treated patients. However, 59% of the patients were treated using an older liquid nitrogen system, which the authors asserted “… yields inferior results compared with the argon-based cryomachines we now use….” Even so, reported results combined outcomes obtained from both systems.

Aus (2008) reported that cryoablation is now using third-generation equipment and that long-term follow-up from these newer devices, which emerged around 2000, would be needed. The newer devices use more ultra-thin probes and argon gas (as opposed to liquid nitrogen) and create smaller ice balls. Lian et al (2011) reported on early results of cryoablation using third-generation technology as a primary treatment for 102 patients with localized prostate cancer during the period of 2006 through 2009. Only 1 patient developed biopsy-confirmed prostate cancer recurrence. PSA levels were elevated in 7 patients; however, biopsies were negative. Mild incontinence, urethral sloughing, and erectile dysfunction occurred in 4%, 4.9%, and 64%, respectively.

Ball et al (2006) reported on quality of life outcomes on a subset of 719 patients with localized prostate cancer treated with various techniques including cryosurgical ablation. They reported that, in an older
population, the tissue destruction resulting from cryoablation appeared to relieve obstructive and irritative urinary symptoms but at the sacrifice of sexual function compared with palladium 103 brachytherapy.

**Registry Studies**
Williams et al (2012) compared data from the U.S. Surveillance, Epidemiology, and End Results (SEER) Medicare-linked data on 10,928 patients with localized prostate cancer treated with primary cryoablation or brachytherapy. Urinary and erectile dysfunction occurred significantly more frequently after cryoablation (41.4% and 34.7%) than brachytherapy (22.2% and 21%), respectively. Androgen-deprivation therapy was also used significantly more often after cryoablation than after brachytherapy, suggesting a higher rate of recurrence after cryoablation (1.4 vs 0.5 per 100 person-years). Bowel complications, however, occurred significantly more frequently with brachytherapy (19%) than cryoablation (12.1%).

The Cryo Online Data (COLD) Registry is a database established and supported by a cryoablation manufacturer. The data are maintained independently. Physicians submit standardized forms to the database and participation is voluntary. The Registry contains case report forms of pretreatment and posttreatment information for patients undergoing whole gland or partial gland (focal) prostate cryoablation. Patients are stratified into low-, intermediate-, and high-risk groups. Jones et al (2008) reported initial outcome for 1198 men with primary whole gland prostate cryoablation. Mean follow-up was 24.4 months; 136 men had 5-year data. The 5-year bDFS rate (Phoenix definition) for the entire population was 73%; rates by category were 91%, 79%, and 62%, for the low-, intermediate-, and high-risk groups, respectively. The rectal fistula rate was 0.4%. Incontinence was reported by 5% of men, with 3% of men using pads. Twenty-five percent of men reported having sexual intercourse, but only 9% did so without pharmaceutical or device assistance. In 2016, outcomes for 300 men in the COLD Registry who underwent primary whole gland cryotherapy for high-grade (Gleason score ≥8), localized prostate cancer were published. Mean follow-up was 28.4 months. The estimated 2- and 5-year bDFS rates were 77% (95% CI, 71% to 88%) and 59% (95% CI, 50% to 67%), respectively. At 12-month follow-up, complete continence was reported by 91% of men and potency by 17% of men. The incidence of recto-urethral fistulae was 1.3%. Urinary retention requiring intervention beyond temporary catheterization was reported by 3% of men.

**Section Summary: Primary Prostate Cryoablation**
Evidence for the use of whole gland cryoablation to treat localized prostate cancer comes from several systematic reviews, 2 RCTs, and many comparative and noncomparative observational studies. High-quality data comparing cryoablation with other treatments are lacking, but available data suggest similar OS and disease-specific survival rates compared with radical prostatectomy and EBRT.

**SALVAGE PROSTATE CRYOABLATION**
Studies have described results from using cryoablation in men with recurrent, localized prostate cancer following radiotherapy.
Whole Gland Cryoablation of Prostate Cancer

Policy # 00022
Original Effective Date: 06/24/2002
Current Effective Date: 11/15/2017

Systematic Reviews
The 2015 Health Technology Assessment (described previously) identified 2 studies (Chin et al, 2001; Robinson et al, 2006) assessing salvage whole gland cryoablation. Both were single-arm studies. One reported 1- and 4-year bDFS rates of 71% and 54%, respectively. Both reported functional outcomes. With a median follow-up of 19 months, the incontinence rate was 20%, bladder neck stenosis rate was 25%, and the recto-urethral fistula rate was 3%. The sexual dysfunction rate was 69% at 1 year, and 52% at 2 years.

In 2012, Mouraviev et al reviewed literature published between 1991 and 2012 to compare salvage cryoablation for radio-recurrent prostate cancer with other salvage treatments. They found comparisons difficult to make because no prospective, randomized studies were identified and PSA failure was defined in various ways. However, they noted that studies had reported salvage cryoablation outcomes as being comparable to those for salvage radical prostatectomy (for an intermediate term). The following criteria were identified as favorable prognostic factors for defining patients for salvage cryoablation: a PSA level less than 10 ng/mL, a Gleason score 8 or less, and a clinical stage T1c or T2 before salvage cryoablation therapy. In a 2013 systematic review, Punnen et al evaluated management approaches, including cryoablation, for salvage treatment (biochemical recurrence) after primary treatment for localized prostate cancer. Reviewers noted, while there was limited evidence, cryoablation was a possible treatment option for salvage therapy although randomized trials are needed.

Nonrandomized Comparative Studies
Peters et al (2013) reported on results of retrospective data from 129 men from 5 high-volume Dutch centers. Forty-four men underwent salvage prostatectomy, 54 underwent salvage cryoablation, and 31 underwent salvage brachytherapy. The mean follow-up was 29 months, 22 months, and 14 months, respectively. Biochemical failure occurred in 25 (81%) men in the brachytherapy group, 29 (66%) men in the prostatectomy group, and 33 (61%) men in the cryosurgery group. Severe GU and GI toxicity (grade >3) using Common Toxicity Criteria for Adverse events (v.3.0), definition was observed in up to 30% of patients in all 3 groups. There were 12 (27%), 5 (9%), and 14 (45%) deaths, respectively.

Pisters et al (2009) compared retrospective data between groups; the first group consisted of 38 men who underwent salvage radical prostatectomy at a U.S. clinic between 1990 and 1999; the second group consisted of 34 men who underwent salvage cryoablation at U.S. cancer center between 1992 and 1995. Mean follow-up was 7.8 years in the prostatectomy group and 5.5 years in the cryoablation group. The bDFS rate was 42% for cryoablation and 66% for prostatectomy at 5 years (p=0.002). The OS rate at 5 years was 85% for cryoablation and 95% for prostatectomy (p=0.001). There was no significant difference in disease-specific survival rates at 5 years (96% cryoablation vs 98% prostatectomy, p=0.283).

Nonrandomized Noncomparative Studies
Wenske et al (2013) reported on salvage cryoablation in a series of 396 consecutively treated patients who had failed cryoablation or radiotherapy. Data were analyzed from 328 patients, with a median follow-up of 47.8 months (range, 1.6-203.5 months). Fifty-five (16.7%) of these patients received subtotal (focal) salvage cryoablation. At the 5- and 10-year follow-ups, disease-free survival was 63% and 35%, disease-specific...
Whole Gland Cryoablation of Prostate Cancer

Policy # 00022
Original Effective Date: 06/24/2002
Current Effective Date: 11/15/2017

survival was 91% and 79%, and OS was 74% and 45%, respectively. After salvage cryoablation, the median PSA nadir was 0.2 ng/mL (range, 0.01-70.70 ng/mL) at a median follow-up of 2.6 months (range, 2.0-67.3 months). PSA nadir was the only predictor of recurrence and disease-specific survival based on multivariate analyses (p<0.001 and p=0.012, respectively). Complications occurred in 0.6% to 4.6% of patients.

Ng et al (2007) reported on a series of 187 patients with locally recurrent prostate cancer after radiotherapy who underwent salvage cryoablation, with a mean follow-up of 39 months. Serum PSA level at cryoablation was a predictive factor for biochemical recurrence on univariate and multivariate analyses (p<0.001). Patients with a precryoablation PSA level less than 4 ng/mL had 5- and 8-year biochemical recurrence-free survival (bRFS) rates of 56% and 37%, respectively. In contrast, patients with precryoablation PSA levels of 10 ng/mL or greater had 5- and 8-year bRFS rates of only 1% and 7%, respectively. Patients with precryoablation PSA levels ranging from 4 to 9.99 ng/mL had intermediate survival outcomes. Overall 5- and 8-year survival rates were 97% and 92%, respectively. The authors concluded that salvage cryoablation was a viable treatment option for patients with prostate cancer for whom radiotherapy has failed; they further concluded that salvage cryoablation should be performed when the serum PSA level is still relatively low because, in these patients, the procedure may potentially be curative.

Ismail et al (2007) reported on 100 patients treated between 2000 and 2005 with cryoablation for recurrent prostate cancer after radiotherapy; the mean follow-up was 33.5 months. All patients had biopsy-confirmed recurrent prostate cancer. The definition for bRFS was defined using a PSA level of less than 0.5 ng/mL and by applying the American Society for Therapeutic Radiology and Oncology definition for biochemical failure. Patients were stratified into 3 risk groups: high-risk (68 men), intermediate-risk (20 men), and low-risk (12 men). There was no surgery- or cancer-related deaths; the 5-year actuarial bRFS rates were 73%, 45%, and 11% for the low-, intermediate- and high-risk groups, respectively. Complications included incontinence (13%), erectile dysfunction (86%), lower urinary tract symptoms (16%), prolonged perineal pain (4%), urinary retention (2%), and recto-urethral fistula (1%). The authors concluded that salvage cryoablation was a safe and effective treatment for localized prostate cancer recurrence after radiotherapy.

Williams et al (2011) retrospectively reviewed 176 patients receiving salvage cryoablation for locally recurrent prostate cancer during the period of 1995 to 2004. Patients were followed a mean of 7.46 years, with 52 patients having been followed for more than 10 years. The 10-year disease-free survival rate was 39%. The authors found certain risk factors for prostate cancer recurrence following salvage cryoablation, and these risk factors were: presalvage PSA levels, preradiation, and presalvage Gleason scores. Early recurrence was highly predicted by a PSA nadir greater than 1.0 ng/dL after salvage cryoablation.

In 2016, Siddiqui et al reported long-term outcomes for 157 men undergoing salvage cryoablation for biopsy-proven, localized radio-recurrent prostate cancer at a single institution from 1995 to 2004. Median follow-up was 117 months (interquartile range, 55-154 months). OS rates at 5 and 10 years were 93% and 76%, respectively. The bDFS rates at 10 and 15 years were 35% and 23%, respectively. Recto-urethral
fistula developed in 2.5% of patients and successfully repaired in all cases. Fifty-two percent of men reported no incontinence while 44% required 0 or 1 pad per day.

Registry Studies
Friedlander et al (2014) compared salvage cryoablation with salvage radical prostatectomy in 440 men retrospectively identified in the SEER database who were treated between 1992 and 2009. The authors used propensity score analyses to compare overall and prostate cancer–specific mortality. Overall mortality was significantly higher (21.6 vs 6.1 deaths/100 person years, p<0.001) for prostatectomy than for cryoablation. Prostate cancer–specific death rates were numerically higher for prostatectomy than for cryoablation (6.5 vs 1.4 deaths/100 person years, p=0.061).

In 2013, Spiess et al reported outcomes for 156 men who underwent salvage cryoablation without neoadjuvant hormonal ablative therapy from the COLD Registry. The bDFS rates at 1, 2, and 3 years were 89.0%, 73.7%, and 66.7%, respectively. For men with presalvage PSA levels less than 5 ng/mL, the bDFS rates were 95.3%, 86.7%, and 78.3% vs 81.4%, 58.4%, and 52.9% for those with PSA levels of 5 ng/mL or more.

Section Summary: Salvage Prostate Cryoablation
The evidence for the use of salvage prostate cryoablation in men with localized, recurrent prostate cancer following radiotherapy includes primarily noncomparative case series. A small number of retrospective comparative studies have compared salvage cryoablation with salvage prostatectomy but with contradictory findings. Men in this group have few other options and prostatectomy can be difficult in tissue that has been irradiated.

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, 2 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.

References


©2017 Blue Cross and Blue Shield of Louisiana

Blue Cross and Blue Shield of Louisiana is an independent licensee of the Blue Cross and Blue Shield Association and incorporated as Louisiana Health Service & Indemnity Company.

No part of this publication may be reproduced, stored in a retrieval system, or transmitted, in any form or by any means, electronic, mechanical, photocopying, or otherwise, without permission from Blue Cross and Blue Shield of Louisiana.

©2017 Blue Cross and Blue Shield of Louisiana

Blue Cross and Blue Shield of Louisiana is an independent licensee of the Blue Cross and Blue Shield Association and incorporated as Louisiana Health Service & Indemnity Company.

No part of this publication may be reproduced, stored in a retrieval system, or transmitted, in any form or by any means, electronic, mechanical, photocopying, or otherwise, without permission from Blue Cross and Blue Shield of Louisiana.
Whole Gland Cryoablation of Prostate Cancer

Policy # 00022
Original Effective Date: 06/24/2002
Current Effective Date: 11/15/2017


Policy History
Original Effective Date: 06/24/2002
Current Effective Date: 11/15/2017

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.
05/07/2009 Medical Director review
05/20/2009 Medical Policy Committee approval. Revisions 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.

©2017 Blue Cross and Blue Shield of Louisiana

Blue Cross and Blue Shield of Louisiana is an independent licensee of the Blue Cross and Blue Shield Association and incorporated as Louisiana Health Service & Indemnity Company.

No part of this publication may be reproduced, stored in a retrieval system, or transmitted, in any form or by any means, electronic, mechanical, photocopying, or otherwise, without permission from Blue Cross and Blue Shield of Louisiana.
Whole Gland Cryoablation of Prostate Cancer

Policy # 00022
Original Effective Date: 06/24/2002
Current Effective Date: 11/15/2017

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.
Next Scheduled Review Date: 11/2018

Coding
The five character codes included in the Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology (CPT®), copyright 2016 by the American Medical Association (AMA). CPT is developed by the AMA as a listing of descriptive terms and five character identifying codes and modifiers for reporting medical services and procedures performed by physician.

The responsibility for the content of Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines is with Blue Cross and Blue Shield of Louisiana and no endorsement by the AMA is intended or should be implied. The AMA disclaims responsibility for any consequences or liability attributable or related to any use, nonuse or interpretation of information contained in Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines. Fee schedules, relative value units, conversion factors and/or related components are not assigned by the AMA, are not part of CPT, and the AMA is not recommending their use. The AMA does not directly or indirectly practice medicine or dispense medical services. The AMA assumes no liability for data contained or not contained herein. Any use of CPT outside of Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines should refer to the most current Current Procedural Terminology which contains the complete and most current listing of CPT codes and descriptive terms. Applicable FARS/DFARS apply.

CPT is a registered trademark of the American Medical Association.

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>C61 C79.82 D07.5 Z85.46</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. 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.
Whole Gland Cryoablation of Prostate Cancer

Policy # 00022
Original Effective Date: 06/24/2002
Current Effective Date: 11/15/2017

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 the Blue Cross and Blue Shield Association TEC or other nonaffiliated technology evaluation center(s);
2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
3. Reference to federal regulations.

**Medically Necessary (or “Medical Necessity”) - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:
A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

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

‡ Indicated trademarks are the registered trademarks of their respective owners.

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.