



BlueCross BlueShield of Louisiana

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Cryosurgery Ablation of Miscellaneous Solid Tumors other than Liver or Prostate Tumors or Breast Fibroadenomas

Policy # 00023

Original Effective Date: 01/26/2004
Current Effective Date: 03/19/2014

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: Cryoablation of Clinically Localized Prostate Tumors is addressed separately in medical policy 00022; Cryosurgical Ablation of Primary or Metastatic Liver Tumors is addressed separately in medical policy 00220; and Cryosurgery Ablation of Breast Fibroadenomas is addressed separately in medical policy 00235.

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 cryosurgery ablation as a treatment of localized renal cell carcinoma (RCC) to be **eligible for coverage**.

Patient Selection Criterion

Coverage eligibility for the use of cryosurgery ablation to treat localized renal cell carcinoma [RCC] (no more than 4 cm in size) will be considered when the following criterion is met:

- Preservation of kidney function is necessary (i.e., the patient has one kidney or renal insufficiency defined by a glomerular filtration rate [GFR] of < 60 mL/min/m²) and standard surgical approaches would compromise kidney function.

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 cryosurgery ablation to treat localized renal cell carcinoma (RCC) when patient selection criteria are not met to be **investigational.***

Based on review of available data, the Company considers cryosurgical ablation as a treatment of malignant tumors of the breast, lung, pancreas and liver, or other solid tumors other than prostate tumors and breast fibroadenomas to be **investigational.***

Background/Overview

Cryosurgical ablation (hereafter referred to as cryosurgery) involves freezing of target tissues, most often by inserting into the tumor a probe through which coolant is circulated. Cryosurgery may be performed as an open surgical technique or as a closed procedure under laparoscopic or ultrasound guidance.

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The hypothesized advantages of cryosurgery include improved local control and benefits common to any minimally invasive procedure (e.g., preserving normal organ tissue, decreasing morbidity, decreasing length of hospitalization). Potential complications of cryosurgery include those caused by hypothermic damage to normal tissue adjacent to the tumor, structural damage along the probe track, and secondary tumors, if cancerous cells are seeded during probe removal.

Cryosurgical treatment of various tumors including RCCs, malignant and benign breast disease, pancreatic cancer, and lung cancer has been reported in the literature.

Breast Tumors

Early stage primary breast cancers are treated surgically. The selection of lumpectomy, modified radical mastectomy, or another approach is balanced against the patient's desire for breast conservation, the need for tumor-free margins in resected tissue, and the patient's age, hormone receptor status, and other factors. Adjuvant radiation therapy decreases local recurrences, particularly for those who select lumpectomy. Adjuvant hormonal therapy and/or chemotherapy are added, depending on presence and number of involved nodes, hormone receptor status, and other factors. Treatment of metastatic disease includes surgery to remove the primary lesion and combination chemotherapy.

Fibroadenomas are common benign tumors of the breast that can either present as a palpable mass or a mammographic abnormality. These benign tumors are frequently surgically excised to rule out a malignancy.

Lung Tumors

Early stage lung tumors are typically treated surgically. Patients with early stage lung cancer who are not surgical candidates may be candidates for radiation treatment with curative intent. Cryoablation is being investigated in patients who are medically inoperable, with small primary lung cancers or lung metastases. Patients with more advanced local disease or metastatic disease may undergo chemotherapy with radiation following resection. This is rarely curative but rather seeks to retard tumor growth or palliate symptoms.

Pancreatic Cancer

Pancreatic cancer is a relatively rare solid tumor that occurs almost exclusively in adults and is almost always fatal. Surgical resection of tumors contained entirely within the pancreas is currently the only potentially curative treatment. However, the nature of the cancer is such that few tumors are found at such an early and potentially curable stage. Patients with more advanced local disease or metastatic disease may undergo chemotherapy with radiation following resection. This is rarely curative but rather seeks to retard tumor growth or palliate symptoms.

Renal Cell Carcinoma

Localized RCC is treated by radical nephrectomy or nephron-sparing surgery. Prognosis drops precipitously if the tumor extends outside the kidney capsule, since chemotherapy is relatively ineffective against metastatic RCC.



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FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

There are several cryoablation devices cleared for marketing by the FDA through the 510(k) process for use in open, minimally invasive or endoscopic surgical procedures in the areas of general surgery, urology, gynecology, oncology, neurology, dermatology, proctology, thoracic surgery and ear; nose; and throat. Examples include:

- Cryocare Surgical System by Endocare;
- CryoGen Cryosurgical System by Cryosurgical, Inc.;
- CryoHit by Galil Medical for the treatment of breast fibroadenoma;
- SeedNet System by Galil Medical; and
- Visica System by Sanarus Medical.

Centers for Medicare and Medicaid Services (CMS)

No national coverage determination.

Rationale/Source

The following is a summary of the key literature to date. The literature search identified publications discussing applications of cryosurgery for primary and metastatic tumors outside the liver and prostate. All were uncontrolled case series with varied criteria to select patients for cryosurgery and reported limited data on long-term outcomes.

The following sections summarize those studies that adequately described baseline characteristics of the patient populations and the methods used for cryosurgery and also reported outcomes of treatment for 8 or more patients with the same diagnosis, or 8 or more procedures on the same malignancy. One article discussed cryosurgery in 429 patients with a wide variety of primary and recurrent solid tumors (e.g., head and neck, lung, genital organs, sarcomas). Although the author reported survival for some patient subsets with certain of these malignancies, the article only reported baseline tumor and patient characteristics for those with breast cancer.

Breast Cancer

In 2010, Zhao and Wu reported on a systematic review of minimally-invasive ablative techniques of early-stage breast cancer. The review noted that studies on cryoablation for breast cancer are primarily limited to pilot and feasibility studies in the research setting. Complete ablation of tumors was found to be reported within a wide range of 36-83%. Since there are many outstanding issues, including patient selection criteria and the ability to precisely determine the size of tumors and achieve 100% tumor cell death, the reviewers noted minimally-invasive thermal ablation techniques for breast cancer treatment, including cryoablation, should be limited until results from prospective, randomized clinical trials become available.

Three studies described the outcome of cryosurgery for advanced primary or recurrent breast cancer in 72 patients. Cryosurgery was performed percutaneously with ultrasound guidance (n = 15) or during an open surgical procedure (n = 57). Patients were treated for advanced primary disease (44%) or recurrent tumors (56%). Tanaka reported the largest retrospective series: 9 patients with advanced primary tumors and 40



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with recurrent disease. The author reported 44% survival of primary breast cancer patients (n = 9) at 3 and 5 years but did not report survival duration or other outcomes for those with recurrent or metastatic disease. The report also did not adequately describe selection criteria for those enrolled in the study, details of the procedure, and procedure-related adverse events. The other studies were smaller series of patients and also were inadequate with respect to study design, analysis, and reporting of results. Furthermore, the study by Pfleiderer et al. was a pilot trial to evaluate technical limitations of the procedure. Tumors were excised and evaluated by pathology days to weeks after cryosurgery, and the authors reported incomplete necrosis in tumors greater than 23 mm in diameter.

One case series by Sabel and colleagues explored the role of cryoablation as an alternative to surgical excision as a primary treatment of early stage breast cancer. This Phase I study included 29 patients who underwent cryoablation of primary breast cancers measuring less than 2 cm in diameter, followed up 1 to 4 weeks later by standard surgical excision. Cryoablation was successful in patients with invasive ductal carcinoma less than 1.5 cm in diameter and with less than 25% ductal carcinoma in situ identified in a prior biopsy specimen. In a small series of 11 patients with breast cancer tumors less than 2 cm, Pusztaszeri, et al. found residual tumor present in 6 cases when follow-up lumpectomy was performed approximately 4 weeks after cryoablation.

Since available evidence did not include control groups or compare outcomes of cryosurgery to alternative strategies for managing similar patients, no conclusions can be made on the net health outcomes of cryosurgery for breast cancer. Therefore, cryosurgery for breast cancer is considered investigational.

Lung Cancer

Lee and colleagues conducted a systematic review of endoscopic cryoablation of lung and bronchial tumors. Included in the review were 15 case studies and one comparative, observational study. Cryoablation was performed for inoperable, advanced lung and bronchial cancers in most studies. Some studies included patients with co-morbid conditions and poor general health that would not be considered surgical candidates. Complications occurred in 11.1% of patients from 10 studies and consisted of hemorrhage, mediastinal emphysema, atrial fibrillation, and dyspnea. Within 30 days of the procedure, death from hemoptysis and respiratory failure, considered to be most likely related to disease progression, occurred in 7.1% of patients. Improvements in pulmonary function and clinical symptoms occurred in studies reporting these outcomes. Because the studies in the review did not include control groups or compare outcomes of cryosurgery to alternative strategies for managing similar patients, no conclusions can be made on the net health outcomes of cryosurgery for lung cancer. Therefore, cryosurgery for lung cancer is considered investigational.

Pancreatic Cancer

In 2012, Tao and colleagues reported on a systematic review of cryoablation for pancreatic cancer. The authors identified 29 studies from the literature search and included 5 of these studies in the review. The 5 studies were all case series and considered to be of low quality. Adverse events, when mentioned in the studies, included delayed gastric emptying (0% to 40.9% in 3 studies), pancreatic leak (0% to 6.8% in 4 studies), biliary leak (0% to 6.8% in 3 studies), and one instance of upper gastrointestinal hemorrhage. Pain



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relief was reported in 3 studies and ranged from 66.7% to 100%. Median survival times reported in 3 studies ranged from 13.4 to 16 months. One-year total survival rates reported in 2 studies were 57.5% and 63.6%.

Kovach et al. reported 10 cryosurgical ablations in 9 patients with unresectable pancreatic cancer using intraoperative ultrasound guidance during laparotomy. The authors report no intraoperative morbidity or mortality and adequate pain control in all patients postoperatively. At the time of publication, all patients were dead at an average of 5 months postoperatively (range: 1–11 months).

A pilot study on the combination of cryosurgery and (125) iodine seed implantation for treatment of locally advanced pancreatic cancer was reported by Xu et al. Forty-nine patients were enrolled, 12 with liver metastases. Twenty patients received regional chemotherapy. At 3 months after therapy, most patients showed tumor necrosis with 20.4% of patients having complete response. Overall, the 6-, 12-, 24-, and 36-month survival rates were 94.9%, 63.1%, 22.8%, and 9.5%, respectively.

Li and colleagues reported on a retrospective study of 142 patients with unresectable pancreatic cancer treated with palliative bypass with (n = 68) or without cryoablation (n = 74) from 1995 to 2002. Median dominant tumor sizes decreased from 4.3 cm to 2.4 cm in 36 of 55 patients (65%) 3 months after cryoablation. Survival rates were not significantly different between groups, with the cryoablation group surviving a median of 350 days versus 257 days in the group that did not receive cryoablation.

Complications overall were not significantly different between the 2 groups. However, a higher percentage of delayed gastric emptying occurred in the cryoablation group compared to the group that did not receive cryoablation (36.8% vs. 16.2%, respectively).

Because these studies did not include control groups or compare outcomes of cryosurgery to alternative strategies for managing similar patients, no conclusions can be made on the net health outcomes of cryosurgery for pancreatic cancer. Therefore, cryosurgery for pancreatic cancer is considered investigational.

Renal Cell Carcinoma

In a 2010 Cochrane review, Nabi and colleagues review evidence on the management of localized RCC. No randomized trials comparing cryoablation to open radical or partial nephrectomy were identified. One nonrandomized study compared laparoscopic partial nephrectomy with laparoscopic cryoablation using a matched paired-analysis and 3 retrospective studies. The review notes percutaneous cryoablation can successfully destroy small RCC and may be considered a treatment option in patients with serious comorbidities that pose surgical risks. The review concluded that high-quality, randomized controlled trials (RCTs) are required in the management of localized RCC and that one area of emphasis should be the role of renal surgery compared to minimally invasive techniques for small tumors (< 4 cm).

Long et al. reported on a 2011 systematic review comparing percutaneous cryoablation to surgical cryoablation of small renal masses. A total of 42 studies treating small renal masses (pooled total of 1,447

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lesions) were reviewed including 28 articles on surgical cryoablation and 14 articles on percutaneous cryoablation. The authors concluded percutaneous and surgical cryoablation for small renal masses have similar, acceptable short-term oncologic outcomes, and each technique is relatively equivalent. Long-term data are needed to ultimately compare ablation techniques to the gold standard of partial or radical nephrectomy.

In another 2011 systematic review, Klatte and colleagues reviewed 98 studies published through December 2010 to compare treatment of small renal masses with laparoscopic cryoablation or partial nephrectomy. Partial nephrectomy was performed in 5,347 patients and laparoscopic cryoablation was performed in 1,295 patients. Renal cell carcinoma was proven in 159 (2.9%) of patients. After cryoablation, local tumor progression of the RCC occurred at a rate of 8.5% (70 of 821; range: 0–17.7%). After partial nephrectomy, 1.9% (89 of 4,689; range: 0–4.8%), experienced local tumor progression. Distant metastasis occurred more frequently in partial nephrectomy patients than cryoablation patients although not significantly (91 vs. 9 patients, respectively; $p = 0.126$). However, mean tumor size for cryoablation patients was smaller than the partial nephrectomy patients (2.4 vs. 3.0 cm; $p < 0.001$). Fewer patients receiving cryoablation experienced perioperative complications than partial nephrectomy patients (17% [range: 0–42%] vs. 23.5% [range: 8–66%]; $p < 0.001$).

In 2011, Van Poppel et al. conducted a review of the literature on localized RCC treatment published between 2004 and May 2011. In this review, the authors concluded cryoablation is a reasonable treatment option for low-grade renal tumors less than 4 cm (mostly less than 3 cm) in patients who are not candidates for surgical resection or active surveillance. The authors noted the need for long-term prospective studies to compare ablative techniques for renal ablation, such as radiofrequency ablation (RFA) versus cryoablation.

In 2012, El Dib and colleagues conducted a meta-analysis evaluating cryoablation and RFA for small renal masses. Included in the review were 20 cryoablation (totaling 457 patients) and 11 RFA (totaling 426 patients) case series studies published through January 2011. Mean tumor size was 2.5 cm (range from 2 to 4.2 cm) in the cryoablation group and 2.7 cm (range from 2 to 4.3 cm) in the RFA group. Mean follow-up times for the cryoablation group and RFA group were 17.9 and 18.1 months, respectively. Clinical efficacy, defined as cancer-specific survival rate, radiographic success, no evidence of local tumor progression, or distant metastases, was not significantly different between groups. The pooled proportion of clinical efficacy for cryoablation was 89% (95% confidence interval [CI]: 0.83–0.94) and 90% (95% CI: 0.86–0.93) for RFA. Kunkle and Uzzo conducted a comparative meta-analysis evaluating cryoablation and RFA as primary treatment for small renal masses in 2008. Forty-seven case series representing 1,375 renal tumors were analyzed. Of 600 lesions treated with cryoablation, 494 were biopsied before treatment versus 482 of 775 treated with RFA. The incidence of RCC with known pathology was 72% in the cryoablation group and 90% in the RFA group. The mean duration of follow-up after cryoablation was 22.5 months. Most studies used contrast enhanced imaging to determine treatment effect. Local tumor progression was reported in 31 of 600 (5%) lesions after cryoablation and in 100 of 775 (13%) lesions after RFA. Progression to metastatic disease was described in 6 of 600 (1%) lesions after cryoablation versus 19 of 775 (2.5%) after RFA. The authors caution that minimally invasive ablation generally has been performed selectively on older patients with smaller tumors, possibly resulting in selection bias; series of ablated lesions tend to have shorter post-



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treatment follow-up compared with tumors managed by surgical excision or active surveillance, and treatment efficacy may be overestimated in series that include tumors with unknown pathology.

A number of studies reported intermediate-term outcomes for cryoablation with RCC. Weld and colleagues reported on 3-year follow-up of 36 renal tumors (22 were malignant) treated with laparoscopic cryoablation. In this series, the 3-year cancer-specific survival rate was 100%, and no patient developed metastatic disease. The authors concluded that these intermediate-term data seemed equivalent to results obtained with extirpative therapy. Hegarty and co-workers reported results on 164 laparoscopic cryoablations and 82 percutaneous RFAs for localized renal tumors. Mean tumor size was 2.5 cm. Cancer-specific survival following cryotherapy was 98% at a median follow-up of 3 years and 100% for RFA at just 1-year median follow-up. The authors noted that cryoablation and RFA are developmental nephron-sparing options and that early results are encouraging in terms of early oncologic control, preservation of renal function, and low complication rates. Studies are also reporting results with small numbers of patients comparing laparoscopic cryoablation with laparoscopic partial nephrectomy for treatment of renal masses.

Matin and Ahrar reviewed studies of cryoablation and RFA with at least 12-month follow-up and found that recently published 3- and 5-year outcomes show 93–98% cancer-specific survival in small cohorts. They caution that, while studies suggest satisfactory outcomes, given the limitations of imaging and the indolent nature of the tumors, stringent selection criteria and rigorous follow-up is required.

Strom and colleagues reported on a retrospective comparison of 145 patients who underwent laparoscopic (n = 84) or percutaneous (n = 61) cryoablation of small renal masses at 5 academic medical centers in the United States. These patients were offered cryoablation because they were considered to be at higher risk for complications from partial nephrectomy or were not surgical candidates due to comorbidities. Mean tumor size was 2.7 cm in the laparoscopic group versus 2.5 cm in the percutaneous group. Patients were followed for a longer period of time in the laparoscopic group (mean of 42.3 ± 21.2 months) compared to the percutaneous group (31.0 ± 15.9 months [$p = 0.008$]). Complications in both treatment groups were similar and did not occur with any significant difference in frequency. At a mean intermediate follow-up of 37.6 months, local tumor recurrence was significantly more frequent in the percutaneous group at 16.4% (10/61) compared to 5.9% (5/84) in the laparoscopic group. However, disease-free survival and overall survival were not significantly different at last follow-up in the laparoscopic group compared to the percutaneous group (91.7% and 89.3% vs. 93.7% and 88.9%, respectively).

In a prospective, single-institution study, Rodriguez et al. reported on 113 patients consecutively treated with percutaneous cryoablation for 117 renal lesions. The average size of renal lesions in the study was 2.7 ± 2.4 cm (83 or 71% were RCC). Patients were selected for cryoablation over surgery when tumors were equal to or less than 4 cm and percutaneously approachable or if the patient could not tolerate surgery when tumors were greater than 4–7 cm. Technical success was reported to be 100% with 93% of patients having no complications or only mild complications. At a median follow-up of 2 years with 59 patients, efficacy was 98.3% and 92.3% at 3 years with 13 patients. Metastatic disease did not occur in any of the patients during the follow-up period, and cancer-specific survival was 100%.



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Nguyen et al. evaluated options for salvage of ipsilateral tumor recurrence after previous ablation. Recurrence rates at their center were 13 of 175 (7%) after cryoablation and 26 of 104 (25%) after RFA. Extensive perinephric scarring was encountered in all salvage operations following cryoablation, and the authors conclude that cryoablation in particular can lead to extensive perinephric fibrosis, which can complicate attempts at salvage.

The available evidence supports a role for cryoablation for patients with small renal tumors less than 4 cm in size. Since longer-term cancer-specific outcomes are unknown, cryoablation of renal tumors should be limited to patients considered to be poor candidates for the standard surgical approach.

Other Cancers

Meller et al. report a retrospective analysis of a single center experience of 440 bone tumor cryosurgery procedures performed between 1988 and 2002, two-thirds of them for primary benign-aggressive and low-grade malignant lesions, and one-third for primary high-grade and metastatic bone tumors. At median follow-up of 7 years (range 3–18 years), overall recurrence rate was 8%. Based on their experience, the authors suggest that the ideal case for cryosurgery is a young adult with involvement of long bone, a benign-aggressive or low-grade malignant bone tumor, a good cavity with greater than 75% thick surrounding walls, none or minimal soft tissue component, and at least +/-1 cm of subchondral bone left near a joint surface after curettage and burr drilling.

Other articles identified in the literature search related to use of cryoablation in other cancers either involved small numbers of patients or limited follow-up.

Ongoing Clinical Trials

A search of online site ClinicalTrials.gov in June 2012 found no RCTs. Several ongoing non-randomized clinical trials addressing cryoablation in breast, bone, lung, pancreatic and renal tumors were identified.

Clinical Input Received through Physician Specialty Societies and Academic Medical Centers

In response to requests, input was received from 2 Physician Specialty Societies (5 reviews) and from 2 Academic Medical Centers (3 reviews) while this policy was under review for February 2009. While the various Physician Specialty Societies and Academic Medical Centers may collaborate with and make recommendations during this process, through the provision of appropriate reviewers, input received does not represent an endorsement or position statement by the Physician Specialty Societies or Academic Medical Centers, unless otherwise noted. There was strong reviewer support for use of cryoablation in the treatment of select patients with renal tumors. There also was support for use in the treatment of benign breast disease. Reviewers generally agreed this was investigational in the treatment of pancreatic cancer.

Summary

Cryosurgical ablation involves freezing of target tissues, most often by inserting into the tumor a probe through which coolant is circulated. Cryosurgery may be performed as an open surgical technique or as a closed procedure under laparoscopic or ultrasound guidance.



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The literature on the use of cryosurgical ablation of tumors addressed in this policy consists primarily of reports of single-center case series; however, evidence is accumulating that cryoablation provides short-term tumor control and perhaps survival benefit for carefully selected patients with small RCCs. Based on the scientific data (large numbers of patients treated with follow-up) and the clinical input received, cryoablation of small (4 cm or less) renal cancers may be considered medically necessary in those patients who are not surgical candidates due to comorbid conditions or who have baseline renal insufficiency such that standard surgical procedures would impair their kidney function.

The current evidence on cryoablation for all other indications consists largely of non-comparative, case series and is insufficient to permit conclusions concerning the effect of cryoablation on health outcomes. Therefore, cryoablation is considered investigational for all other indications. Comparative studies with larger numbers of subjects and longer follow-up are needed.

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

Code Type	Code
CPT	0340T, 19105, 50250, 50542, 50593
HCPSC	C2618
ICD-9 Diagnosis	All relative diagnoses
ICD-9 Procedure	55.32, 55.33, 55.34, 55.35, 85.20



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Cryosurgery Ablation of Miscellaneous Solid Tumors other than Liver or Prostate Tumors or Breast Fibroadenomas

Policy # 00023

Original Effective Date: 01/26/2004

Current Effective Date: 03/19/2014

Policy History

Original Effective Date: 01/26/2004

Current Effective Date: 03/19/2014

10/21/2003	Medical Policy Committee review
01/26/2004	Managed Care Advisory Committee approval
12/07/2005	Medical Director review
12/20/2005	Medical Policy Committee review. Format revision. FDA approval information added to policy.
02/23/2006	Quality Care Advisory Council approval
10/10/2007	Medical Director review
10/17/2007	Medical Policy Committee approval. No change to coverage eligibility.
03/04/2009	Medical Director review
03/18/2009	Medical Policy Committee approval. Changed localized renal cell carcinoma from investigational to eligible for coverage with criteria. Breast fibroadenomas removed from this policy and made into a separate policy.
03/05/2010	Medical Policy Committee review
03/19/2010	Medical Policy Implementation Committee approval. Added benign tumors of the breast to be investigational.
03/03/2011	Medical Policy Committee review
03/16/2011	Medical Policy Implementation Committee approval. Renal cell carcinomas in patients who are surgical candidates was added as investigational.
03/01/2012	Medical Policy Committee review
03/21/2012	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
03/07/2013	Medical Policy Committee review
03/20/2013	Medical Policy Implementation Committee approval. Title changed from "Cryosurgery Ablation of Miscellaneous Solid Tumors other than Liver or Prostate" to "Cryosurgery Ablation of Miscellaneous Solid Tumors Other than Liver or Prostate Tumors or Breast Fibroadenomas". Removed the second criteria bullet for treatment of renal cell carcinoma requiring that the patient not be considered as a surgical candidate due to co-morbid disease. Lung cancer added to investigational statement. The investigational statement was revised for clarification.
03/06/2014	Medical Policy Committee review
03/19/2014	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.

Next Scheduled Review Date: 03/2015

*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 the Blue Cross and Blue Shield Association technology assessment program (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.

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**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.

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