Radioembolization for Primary and Metastatic Tumors of the Liver

Policy # 00110
Original Effective Date: 02/23/2004
Current Effective Date: 05/01/2025

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: Microwave Tumor Ablation is addressed separately in medical policy 00569.

Note: Cryosurgical Ablation of Primary or Metastatic Liver Tumors is addressed separately in medical policy 00220.

Note: Radiofrequency Ablation of Primary or Metastatic Liver Tumors is addressed separately in medical policy 00182.

Note: Transcatheter Arterial Chemoembolization to Treat Primary or Metastatic Liver Malignancies is addressed separately in medical policy 00227.

When Services Are 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 the use of radioembolization (RE) to treat primary hepatocellular carcinoma (HCC) that is unresectable and limited to the liver to be **eligible for coverage**** (see Policy Guidelines section).

Based on review of available data, the Company may consider the use of radioembolization (RE) in primary hepatocellular carcinoma (HCC) as a bridge to liver transplantation to be **eligible for coverage.****

Based on review of available data, the Company may consider radioembolization (RE) to treat primary intrahepatic cholangiocarcinoma (ICC) in individuals with unresectable tumors to be **eligible for coverage.****

Based on review of available data, the Company may consider the use of radioembolization (RE) to treat hepatic metastases from neuroendocrine tumors (carcinoid and noncarcinoid) with diffuse and

symptomatic disease when systemic therapy has failed to control symptoms to be **eligible for coverage.****

Based on review of available data, the Company may consider the use of radioembolization (RE) to treat unresectable hepatic metastases from colorectal carcinoma (CRC), melanoma (ocular or cutaneous), or breast cancer that are both progressive and diffuse, in individuals with liver-dominant disease who are refractory to chemotherapy or are not candidates for chemotherapy or other systemic therapies to be **eligible for coverage.****

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 radioembolization for all other hepatic metastases except as noted above to be **investigational.***

Based on review of available data, the Company considers radioembolization (RE) for all other indications not described as above to be **investigational.***

Policy Guidelines

In general, radioembolization is used for unresectable hepatocellular carcinoma that is greater than 3 cm.

There is little information on the safety or efficacy of repeated radioembolization treatments or on the number of treatments that should be administered.

Radioembolization should be reserved for individuals with adequate functional status (Eastern Cooperative Oncology Group Performance Status 0-2), adequate liver function and reserve, Child-Pugh class A or B, and liver-dominant metastases.

Symptomatic disease from metastatic neuroendocrine tumors refers to symptoms related to excess hormone production.

Background/Overview

Treatments for Hepatic and Neuroendocrine Tumors

The use of external-beam radiotherapy and the application of more advanced radiotherapy approaches (eg, intensity-modulated radiotherapy) may be of limited use in individuals with multiple diffuse lesions due to the low tolerance of the normal liver to radiation compared with the higher doses of radiation needed to kill the tumor.

Various nonsurgical ablative techniques have been investigated that seek to cure or palliate unresectable hepatic tumors by improving locoregional control. These techniques rely on extreme temperature changes (cryosurgery or radiofrequency ablation), particle and wave physics (microwave or laser ablation), or arterial embolization therapy including chemoembolization, bland embolization, or radioembolization.

Radioembolization
Radioembolization (referred to as selective internal radiotherapy in older literature) delivers small beads (microspheres) impregnated with yttrium-90 (Y90) intra-arterially via the hepatic artery. The microspheres, which become permanently embedded, are delivered to tumors preferentially because the hepatic circulation is uniquely organized, whereby tumors greater than 0.5 cm rely on the hepatic artery for blood supply while the normal liver is primarily perfused via the portal vein. Y90 is a pure beta-emitter with a relatively limited effective range and a short half-life that helps focus the radiation and minimize its spread. Candidates for radioembolization are initially examined by hepatic angiogram to identify and map the hepatic arterial system. At that time, a mixture of technetium 99-labeled albumin particles are delivered via the hepatic artery to simulate microspheres. Single-photon emission computed tomography is used to detect possible shunting of the albumin particles into the gastrointestinal or pulmonary vasculature.

Currently, 2 commercial forms of Y90 microspheres are available: a glass sphere (TheraSphere) and a resin sphere (SIR-Spheres). Noncommercial forms are mostly used outside the U.S. While the commercial products use the same radioisotope (Y90) and have the same target dose (100 gray), they differ in microsphere size profile, base material (ie, resin vs glass), and size of commercially available doses. The physical characteristics of the active and inactive ingredients affect the flow of microspheres during injection, their retention at the tumor site, spread outside the therapeutic target region, and dosimetry calculations. The U.S. Food and Drug Administration (FDA) granted premarket approval of SIR-Spheres for use in combination with 5-floxuridine chemotherapy by hepatic arterial infusion to treat unresectable hepatic metastases from colorectal cancer. In contrast, TheraSphere's glass sphere was approved under a humanitarian device exemption for use as monotherapy to treat unresectable hepatocellular carcinoma. In 2007, this humanitarian device exemption was expanded to include individuals with hepatocellular carcinoma who have partial or branch portal vein thrombosis. For these reasons, results obtained with a product do not necessarily apply to another commercial (or non-commercial) products (see Regulatory Status section).

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)
Currently, 2 forms of Y90 microspheres have been approved by the FDA.

In 1999, TheraSphere®‡ (Boston Scientific; previously manufactured by Nordion, under license by BTG International), a glass sphere system, was approved by the FDA through the humanitarian drug exemption process for radiotherapy or as a neoadjuvant treatment to surgery or transplantation in

individuals with unresectable hepatocellular carcinoma who can have placement of appropriately positioned hepatic arterial catheters (H980006).

On March 17, 2021, TheraSphere received approval through the premarket approval process for use as selective internal radiation therapy (SIRT) for local tumor control of solitary tumors (1 to 8 cm in diameter), in individuals with unresectable hepatocellular carcinoma, Child-Pugh Score A cirrhosis, well-compensated liver function, no macrovascular invasion, and good performance status (P200029).

In 2002, SIR-Spheres®‡ (Sirtex Medical), a resin sphere system, was approved by the FDA through the premarket approval process for the treatment of inoperable colorectal cancer metastatic to the liver (P990065).

FDA product code: NAW.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to regulations, other plan medical policies, and accredited national guidelines.

Radioembolization (RE), also referred to as selective internal radiotherapy, delivers small beads (microspheres) impregnated with yttrium 90 intra-arterially via the hepatic artery. The microspheres, which become permanently embedded, are delivered to tumors preferentially because the hepatic circulation is uniquely organized, whereby tumors greater than 0.5 cm rely on the hepatic artery for blood supply while the normal liver is primarily perfused via the portal vein. Radioembolization has been proposed as a therapy for multiple types of primary and metastatic liver tumors.

Summary of Evidence

For individuals who have unresectable hepatocellular carcinoma (HCC) who receive radioembolization (RE) or RE with a liver transplant, the evidence includes primarily retrospective and prospective nonrandomized studies, with limited evidence from randomized controlled trials (RCTs). Relevant outcomes are overall survival (OS), functional outcomes, quality of life, and treatment-related morbidity. Nonrandomized studies have suggested that RE has high response rates compared with historical controls. Two small pilot RCTs have compared RE with alternative therapies for HCC, including transarterial chemoembolization and transarterial chemoembolization with drug-eluting beads. Both trials reported similar outcomes for RE compared with alternatives. Evidence from nonrandomized studies has demonstrated that RE can permit successful liver transplantation in certain individuals. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have unresectable intrahepatic cholangiocarcinoma (ICC) who receive RE, the evidence includes phase 2 studies and case series. Relevant outcomes are OS, functional outcomes, quality of life, and treatment-related morbidity. Comparisons of these case series to case series of alternative treatments have suggested that RE for primary ICC has response rates similar to those seen with standard chemotherapy. Due to high study heterogeneity, it is difficult to identify individuals that are most likely to benefit from treatment. A phase 2 study of RE with chemotherapy in the first-line setting reported a response rate of 39% and a disease control rate of 98%. The efficacy of RE in the neoadjuvant setting is being evaluated in an ongoing follow-up RCT. Another phase 2 study evaluating RE with or without subsequent chemotherapy in individuals without prior treatment with chemotherapy or radiation found overall response rates of 25% and 16.7% in those who received RE with and without chemotherapy, respectively; the disease control rates were 75% and 58.3% amongst those who received RE with and without chemotherapy, respectively. However, at this time, the evidence is not yet sufficiently robust to draw definitive conclusions about treatment efficacy. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have unresectable neuroendocrine tumors who receive RE, the evidence includes an open-label phase 2 study, retrospective reviews, and case series, some of which have compared RE with other transarterial liver-directed therapies. Relevant outcomes are OS, functional outcomes, quality of life, and treatment-related morbidity. This evidence has suggested that RE provides outcomes similar to standard therapies and historical controls for individuals with neuroendocrine tumor-related symptoms or progression of the liver tumor. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have unresectable intrahepatic metastases from colorectal cancer and prior treatment failure who receive RE, the evidence includes several small- to moderate-sized RCTs, prospective trials, and retrospective studies using a variety of comparators, as well as systematic reviews of these studies. Relevant outcomes are OS, functional outcomes, quality of life, and treatment-related morbidity. While studies of individuals with prior chemotherapy failure have methodologic problems and have not shown definitive superiority of RE compared with alternatives in terms of survival benefit, they tend to show greater tumor response and significantly delayed disease progression, particularly with combined use of RE and chemotherapy. For example, the Efficacy Evaluation of TheraSphere Following Failed First Line Chemotherapy in Metastatic Colorectal Cancer (EPOCH) RCT found significantly prolonged primary endpoints of progression-free survival (PFS) (hazard ratio [HR], 0.69; 95% confidence interval [CI], 0.54 to 0.88) and hepatic PFS (HR, 0.59; 95% CI, 0.46 to 0.77) with combined RE and chemotherapy in individuals who had progressed on first-line chemotherapy. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have unresectable intrahepatic metastases from other cancers (eg, breast, melanoma, pancreatic) who receive RE, the evidence includes nonrandomized studies. Relevant outcomes are OS, functional outcomes, quality of life, and treatment-related morbidity. These

studies have shown significant tumor response; however, improvement in survival has not been demonstrated in controlled comparative studies. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Supplemental Information

Clinical Input From Physician Specialty Societies and Academic Medical Centers

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.

2015 Input

In response to requests, input was received from 3 physician specialty societies (with 5 individual responses) and 1 academic medical center (with 4 individual responses), for a total of 9 respondents, while this policy was under review in 2015. There was consensus supporting the use of radioembolization (RE) for hepatic metastases from melanoma, particularly ocular melanoma, and breast cancer. There was also consensus supporting the use of RE for treatment of primary intrahepatic cholangiocarcinoma. There was less consensus on the use of RE for hepatic metastases from other specific tumor types, including pancreatic cancer. However, many reviewers supported the use of RE for treatment of other radiosensitive tumors metastatic to the liver with the liver-limited or liver-dominant disease for symptom palliation or prolongation of survival.

2010 to 2011 Input

In response to requests, input was received from 2 physician specialty societies (with 5 individual responses) and 6 academic medical centers, for a total of 11 respondents, while this policy was under review in 2010 and again in 2011. For the 2011 review, input was received from 2 physician specialty societies and 3 academic medical centers; all but 1 academic medical center had provided input in 2010. There was strong support for the use of RE in individuals with primary hepatocellular carcinoma, as a bridge to liver transplant in hepatocellular carcinoma, and in neuroendocrine tumors. There was also strong support for use of RE in individuals with liver metastases from colorectal cancers and support for its use in individuals with liver metastases from other cancers but with less consensus than for colorectal metastases. Those providing input were split as to whether RE should be used as monotherapy or in combination with other agents.

The support for the use of RE in individuals with chemotherapy-refractory colorectal metastases was primarily to prolong time to tumor progression and subsequent liver failure (a major cause of morbidity and mortality in this patient population), potentially prolonging survival. Additional support for the use of RE in this setting was for the palliation of symptoms from tumor growth and tumor bulk.

Support for the use of RE for liver metastases from tumors other than colorectal or neuroendocrine was generally limited to a number of specific tumor types, in particular, ocular melanoma, cholangiocarcinoma, breast, and pancreas.

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.

American College of Radiology et al
In 2021, the American College of Radiology issued a practice parameter jointly developed with the American Brachytherapy Society, the American College of Nuclear Medicine, the American Society for Radiation Oncology, the Society of Interventional Radiology, and the Society of Nuclear Medicine and Molecular Imaging addressing the use of RE for the treatment of liver malignancies with glass- or resin-based yttrium-90 microspheres. The guidelines provided indications and contraindications for treatment as follows:

- "Indications for both agents include but are not limited to the following:
    1. The presence of unresectable or inoperable primary or secondary liver malignancies (particularly colorectal cancer and neuroendocrine tumor metastases). The tumor burden should be liver dominant, not necessarily exclusive to the liver. Individuals should also have a performance status that will allow them to benefit from such therapy.
    2. A life expectancy of at least 3 months."
- "Absolute contraindications include the following:
    1. Inability to catheterize the hepatic artery
    2. Fulminant liver failure
    3. Initial mapping angiography and/or technetium-99m macroaggregated albumin (MAA) hepatic arterial perfusion scintigraphy demonstrating nontarget deposition to the gastrointestinal organs that cannot be corrected by angiographic techniques.
    4. Pretreatment hepatic arterial administration with technetium-99m MAA demonstrative of unfavorable (or unacceptable) shunt function between the liver and the pulmonary parenchyma. This shunt fraction must not be greater than acceptable limits specific to each brachytherapy device.
    5. Active hepatic infection
    6. Therapy during pregnancy may possibly be an option in extraordinary circumstances and with multidisciplinary consult and considerations."

- "Relative contraindications include the following:
    1. Excessive tumor burden in the liver with greater than 50 to 70% of the parenchyma replaced by tumor. In the setting of more extensive tumor burden, treatment can be considered if synthetic hepatic function is preserved.
    2. Total bilirubin greater than 2 mg/dL (in the absence of obstructive cause), which indicates severe liver function impairment. Nonobstructive bilirubin elevations may indicate that liver metastases have caused liver impairment to the degree that risks outweigh benefits for this therapy. In contrast, individuals with hepatocellular carcinoma (HCC) and elevated bilirubin may be treated with radioembolization if a segmental or subsegmental infusion can be performed.
    3. Prior radiation therapy to the liver or upper abdomen that included a significant volume of the liver (clinical judgment by the [authorized user] required).
    4. Care must be employed when individuals are on systemic therapies that may potentiate or may alter the impact of radioembolization and should use caution when combining therapies."

American Society of Clinical Oncology
The 2023 American Society of Clinical Oncology (ASCO) guidelines for the treatment of metastatic colorectal cancer (mCRC) makes the following relevant recommendation:

- "SIRT [selective internal radiation therapy] is not routinely recommended for individuals with mCRC and unilobar or bilobar metastases of the liver (Type: Evidence-based, harms outweigh benefits; Evidence quality: Low; Strength of recommendation: Weak)."

National Comprehensive Cancer Network
Primary Hepatocellular Carcinoma
The National Comprehensive Cancer Network (NCCN) guidelines (v.1.2024) on the treatment of hepatocellular carcinoma indicate that the use of arterially directed therapies, including transarterial bland embolization, transarterial chemoembolization, and drug-eluting beads transarterial chemoembolization, and RE with yttrium-90 microspheres may be appropriate provided that the arterial blood supply can be isolated without excessive nontarget treatment. Individuals should be considered for locoregional therapy if they are not candidates for potential curative treatments (resection, transplantation, and for small lesions, ablative strategies). RE with yttrium-90 microspheres has an increased risk of radiation-induced liver disease in individuals with bilirubin levels greater than 2 mg/dL. Delivery of 205 Gy or more to the tumor may be associated with increased overall survival. A dose of greater than 400 Gy to 25% of the liver or less in individuals with Child-Pugh A liver function is recommended. For anatomically limited disease, radiation segmentectomy with yttrium-90 or ablative dose stereotactic body radiation therapy should be considered. RE may be more appropriate in some individuals with advanced HCC, specifically individuals with segmental or lobar portal vein, rather than main portal vein thrombosis.

Metastatic Neuroendocrine Tumors
The NCCN guidelines (v.1.2023) on the treatment of neuroendocrine tumors recommend consideration of transarterial radioembolization (TARE) for lobar or segmental disease distribution and in individuals with prior Whipple surgery or biliary tract instrumentation.TARE is better tolerated than transarterial embolization/transarterial chemoembolization, but late radioembolization-induced chronic hepatotoxicity may occur in long-term survivors, and is particularly a concern among individuals undergoing bilobar radioembolization.

Metastatic Colon Cancer
The NCCN guidelines (v.3.2024) on the treatment of colon cancer provides a consensus recommendation that: "…arterial-directed catheter therapy, in particular yttrium-90 microsphere selective internal radiation, is an option in highly selected individuals with chemotherapy-resistant/-refractory disease and with predominant hepatic metastases." RE may also be considered "when hepatic metastatic disease is not optimally resectable based on insufficient remnant liver volume..." The guidelines also note that "further investigation is necessary to identify the role of radioembolization at earlier stages of disease, particularly in individuals with right-sided primary origin."

Metastatic Uveal Melanoma
The NCCN guidelines (v.1.2024) on the treatment of uveal melanoma state the following regarding RE: "Further study is required to determine the appropriate individuals for and risks and benefits of this approach."

National Institute for Health and Care Excellence

Primary Hepatobiliary Carcinoma
The July 2013 NICE interventional procedures guidance on selective internal radiation therapy for primary hepatocellular carcinoma states that the evidence for efficacy and safety are adequate for use with normal arrangements. However, "uncertainties remain about its comparative effectiveness, and clinicians are encouraged to enter eligible individuals into trials comparing the procedure against other forms of treatment."

In March 2021, a NICE technology appraisal guidance on selective internal radiation therapies (SIRTs) for treating hepatocellular carcinoma was published, providing specific evidence-based recommendations for the use of SIR-Spheres (Sirtex), TheraSphere (Boston Scientific), and QuiremSpheres (Quirem Medical). The guidance states that RE with SIR-Spheres or TheraSphere is recommended as an option for treating unresectable advanced hepatocellular carcinoma in adults only if "used for people with Child-Pugh grade A liver impairment when conventional transarterial therapies are inappropriate, and the company provides [the microspheres] according to the commercial arrangement." The guidance also stated that "clinical trial data for these SIRTs compared with other treatment options are limited. But, compared with sorafenib, SIRTs may have fewer and more manageable adverse effects, which can improve quality of life." The use of QuiremSpheres,

imageable holmium-166 microspheres, was not recommended due to reduced clinical efficacy compared to sorafenib and higher cost. QuiremSpheres received its CE mark in April 2015 in Europe and is not commercially available in the U.S.

Primary Intrahepatic Cholangiocarcinoma
The October 2018 NICE interventional procedures guidance on selective internal radiation therapy for unresectable primary intrahepatic cholangiocarcinoma state that there are "well-recognized, serious but rare safety concerns. Evidence on its efficacy is inadequate in quantity and quality. Therefore, this procedure should only be used in the context of research."

Metastatic Colon Cancer
The March 2020 NICE interventional procedures guidance on selective internal radiation therapy for unresectable colorectal metastases in the liver states that "in people who cannot tolerate chemotherapy or have liver metastases that are refractory to chemotherapy, there is evidence of efficacy but this is limited, particularly for important outcomes such as quality of life. Therefore, in these people, this procedure should only be used with special arrangements for clinical governance, consent, and audit or research."

U.S. Preventive Services Task Force Recommendations
Not applicable.

Medicare National Coverage
There is no national coverage determination. In the absence of a national coverage determination, coverage decisions are left to the discretion of local Medicare carriers.

Ongoing and Unpublished Clinical Trials
Some currently ongoing and unpublished trials that might influence this review are listed in Table 1.

Table 1. Summary of Key Trials

NCT No.	Name	Planned Enrollment	Completion Date
Hepatocellular Carcinoma			
Ongoing			
NCT06040099[a]	Phase II Single-Arm Study of Durvalumab and Bevacizumab Following Transarterial Radioembolization Using Yttrium-90 Glass Microspheres (TheraSphere™)‡ in Unresectable Hepatocellular Carcinoma Amenable to Locoregional Therapy	100	Jul 2026 (recruiting)

NCT06166576	An Open-label, Prospective, Multi-center Clinical Trial to Evaluate the Efficacy and Safety of Ablative Radioembolization Using Yttrium-90 Glass Microspheres in Patients With Locally-advanced Hepatocellular Carcinoma	30	Nov 2027 (recruiting)
NCT05953337[a]	Radioembolization Oncology Trial Utilizing Transarterial Eye90 (ROUTE 90) for the Treatment of Hepatocellular Carcinoma (HCC)	120	Oct 2025 (recruiting)
NCT04736121[a]	A Prospective, Multicenter, Open-label Single Arm Study Evaluating the Safety & Efficacy of Selective Internal Radiation Therapy Using SIR-Spheres®‡ Y-90 Resin Microspheres on DoR & ORR in Unresectable Hepatocellular Carcinoma Patients (DOORwaY90)	100	Jun 2025 (recruiting)
NCT04522544[a]	A Phase II Study of Immunotherapy With Durvalumab (MEDI4736) and Tremelimumab in Combination With Either Y-90 SIRT or TACE for Intermediate Stage HCC With Pick-the-winner Design	55	Sep 2025 (recruiting)
NCT04069468[a]	A Prospective, Post Approval, Multiple Centre, Open-Label, Non-Interventional, Registry Study to Evaluate Effectiveness of TheraSphere®‡ in Clinical Practice in France (PROACTIF)	500	Jan 2025 (active)
NCT05377034[a]	A Multinational, Double-blind, Placebo-Controlled, Parallel Randomized Arms, Phase II Trial to Compare Safety and Efficacy of Selective Internal Radiation Therapy (Y-90 Resin Microspheres) Followed by Atezolizumab Plus Bevacizumab) Versus Selective Internal Radiation Therapy (SIRT-Y90) Followed by Placebo in Patients With Locally Advanced Hepatocellular Carcinoma (HCC) (STRATUM)	176	Oct 2026 (recruiting)
NCT05063565[a]	An Open-Label, Prospective, Multi-Center Clinical Trial to Evaluate the Efficacy and Safety of TheraSphere™‡ Followed by Durvalumab (Imfinzi®)‡ With Tremelimumab	100	June 2027 (recruiting)

	(Imjudo®)‡ for Hepatocellular Carcinoma (HCC)		
Unpublished			
NCT04090645	A Humanitarian Device Exemption Treatment Protocol of TheraSphere for Treatment of Unresectable Primary or Unresectable Secondary Liver Cancer	187	Apr 2021 (completed)
NCT01176604	Protocol for Use of TheraSphere®‡ for Treatment of Unresectable Hepatocellular Carcinoma	299	Apr 2021 (completed)
NCT01556490[a]	A Phase III Clinical Trial of Intra-arterial TheraSphere® ‡in the Treatment of Patients With Unresectable Hepatocellular Carcinoma (HCC) (STOP-HCC)	526	Apr 2022 (completed)
NCT02072356	A Humanitarian Device Exemption Treatment Protocol of TheraSphere®‡ For Treatment of Unresectable Hepatocellular Carcinoma	290	Jun 2021 (completed)
Metastatic Colorectal Cancer			
NCT05195710[a]	Preoperative Y-90 Radioembolization for Tumor Control and Future Liver Remnant Hypertrophy in Patients With Colorectal Liver Metastases	50	Mar 2024 (recruiting)
Intrahepatic Cholangiocarcinoma			
Ongoing			
NCT06375915	Single Arm, Multicenter Phase II Study Investigating the Efficacy and Safety of a Novel Therapeutic Scheme in Patients With Unresectable CholAngiocarcinoma: RadioEmbolization in Combination With CisGem and Durvalumab (MEDI4736)	33	Jan 2026 (recruiting)
Unpublished			
NCT02807181[a]	SIRT Followed by CIS-GEM Chemotherapy Versus CIS-GEM Chemotherapy Alone as 1st Line Treatment of Patients With Unresectable Intrahepatic Cholangiocarcinoma (SIRCCA)	89	Oct 2022 (completed)

Neuroendocrine Tumors			
NCT04362436[a]	A Phase II Assessment of the Safety and Efficacy of TheraSphere®‡ Selective Internal Radiation Therapy (SIRT) in the Treatment of Metastatic (Liver) Neuroendocrine Tumours (NETs) (ArTisaN)	24	Sep 2024 (recruiting)
Metastatic Uveal Melanoma			
NCT02936388	Transarterial Radioembolisation in Comparison to Transarterial Chemoembolisation in Uveal Melanoma Liver Metastasis (SirTac)	108	Dec 2022 (unknown status)
Metastatic Breast Cancer			
NCT06142344	The Added Value of 166Ho Trans-arterial Radioembolization to Systemic Therapy in Liver Metastatic Breast Cancer Patients	13	Jan 2026 (recruiting)

NCT: national clinical trial.
[a] Denotes industry-sponsored or cosponsored trial.

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Policy History

Original Effective Date: 02/23/2004
Current Effective Date: 05/01/2025

01/31/2004	Medical Director review.
02/17/2004	Medical Policy Committee review.
02/23/2004	Managed Care Advisory Council approval.
02/01/2006	Medical Director review
02/15/2006	Medical Policy Committee review. Format revisions, Rationale/Source.
02/23/2006	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.
03/14/2007	Medical Director review.
03/21/2007	Medical Policy Committee approval. Coverage eligibility unchanged.
04/02/2009	Medical Director review.
04/15/2009	Medical Policy Committee approval. Added "(SIRT)" to title. Revised investigational statement from "Based on review of available data, the Company considers the use of internal radiation therapy for all indications including, but not limited to, the treatment of primary or metastatic tumors of the liver, to be investigational*" to "Based on review of available data, the Company considers selective internal radiation therapy using intra-arterial injection of radiolabeled microspheres to treat primary or metastatic liver tumors to be investigational.*" Coverage eligibility unchanged.
09/09/2010	Medical Policy Committee review.

09/15/2010	Medical Policy Implementation Committee approval. policy statement and title ("selective internal radiation therapy" changed to "radioembolization"). Policy statements changed to indicate that selective cases of hepatocellular carcinoma and metastatic neuroendocrine tumors may be considered medically necessary. Title changed to reflect current procedure name.
04/07/2011	Medical Policy Committee review.
04/13/2011	Medical Policy Implementation Committee approval. Added that "radioembolization to treat unresectable hepatic metastases from colorectal cancer that are both progressive and diffuse, in patients with liver-dominant disease who are refractory to chemotherapy or are not candidates for chemotherapy is eligible for coverage.
04/05/2012	Medical Policy Committee review.
04/18/2012	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
10/11/2012	Medical Policy Committee review.
10/31/2012	Medical Policy Implementation Committee approval. Investigational statement for unresectable hepatic metastases from colorectal carcinoma removed, since it is eligible for coverage.
10/03/2013	Medical Policy Committee review
10/16/2013	Medical Policy Implementation Committee approval. New investigational statement on intrahepatic cholangiocarcinoma added.
03/25/2014	Coding update due to codes added and deleted from policy
11/06/2014	Medical Policy Committee review
11/21/2014	Medical Policy Implementation Committee approval, Added "Based on review of available data, the Company considers radioembolization for all other indications not described as above to be investigational."
08/03/2015	Coding update: ICD10 Diagnosis code section added; ICD9 Procedure code section removed.
10/29/2015	Medical Policy Committee review
11/16/2015	Medical Policy Implementation Committee approval. Melanoma (ocular or cutaneous), or breast cancer added to eligibility statement for unresectable hepatic metastases.
11/03/2016	Medical Policy Committee review
11/16/2016	Medical Policy Implementation Committee approval. Medically necessary statements added for unresectable metastatic breast cancer and melanoma with liver-dominant disease and unresectable intrahepatic cholangiocarcinoma.
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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11/13/2019	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
04/02/2020	Medical Policy Committee review
04/08/2020	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
04/01/2021	Medical Policy Committee review
04/14/2021	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
04/07/2022	Medical Policy Committee review
04/13/2022	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
04/06/2023	Medical Policy Committee review
04/12/2023	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
03/28/2024	Coding update
04/04/2024	Medical Policy Committee review
04/10/2024	Medical Policy Implementation Committee approval. Patients changed to individuals.
04/03/2025	Medical Policy Committee review
04/07/2025	Coding update
04/09/2025	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.

Next Scheduled Review Date: 04/2026

Coding

The five character codes included in the Louisiana Blue Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology (CPT®)‡, copyright 2024 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.

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Radioembolization for Primary and Metastatic Tumors of the Liver

Policy # 00110
Original Effective Date: 02/23/2004
Current Effective Date: 05/01/2025

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:

Code Type	Code
CPT	37243, 75894, 77399, 77778, 79445
HCPCS	A9543, C2616, C9797, S2095 Delete code effective 05/01/2025: C8004
ICD-10 Diagnosis	All Related Diagnoses

*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
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: 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.

NOTICE: Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage.