



Louisiana

Radioembolization for Primary and Metastatic Tumors of the Liver

Policy # 00110

Original Effective Date: 02/23/2004

Current Effective Date: 05/11/2020

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.****

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.****

©2020 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.



Louisiana

Radioembolization for Primary and Metastatic Tumors of the Liver

Policy # 00110

Original Effective Date: 02/23/2004

Current Effective Date: 05/11/2020

Based on review of available data, the Company may consider radioembolization (RE) to treat primary intrahepatic cholangiocarcinoma (ICC) in patients 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 patients 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.

©2020 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.



Louisiana

Radioembolization for Primary and Metastatic Tumors of the Liver

Policy # 00110

Original Effective Date: 02/23/2004

Current Effective Date: 05/11/2020

Radioembolization should be reserved for patients 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 patients 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.

©2020 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.



Louisiana

Radioembolization for Primary and Metastatic Tumors of the Liver

Policy # 00110

Original Effective Date: 02/23/2004

Current Effective Date: 05/11/2020

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 Food and Drug Administration (FDA) granted premarket approval of SIR-Spheres for use in combination with 5-fluorouridine 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 patients 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.

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^{®†} (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 patients with unresectable hepatocellular carcinoma who can have placement of appropriately positioned hepatic arterial catheters (H980006).

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

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,

©2020 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.



Louisiana

Radioembolization for Primary and Metastatic Tumors of the Liver

Policy # 00110

Original Effective Date: 02/23/2004

Current Effective Date: 05/11/2020

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.

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

For individuals who have unresectable intrahepatic cholangiocarcinoma who receive RE, the evidence includes case series. The relevant outcomes are OS, functional outcomes, QOL, and treatment-related morbidity. Comparisons of these case series to case series of alternative treatments have suggested that RE for primary intrahepatic cholangiocarcinoma has response rates similar to those seen with standard chemotherapy. RE may play a role for patients with unresectable tumors that are chemorefractory or who are unable to tolerate systemic chemotherapy. However, the evidence is not yet sufficiently robust to draw definitive conclusions about treatment efficacy. The evidence is insufficient to determine the effects of the technology on health outcomes.

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. The relevant outcomes are OS, functional outcomes, QOL, and treatment-related morbidity. This evidence has suggested that RE provides outcomes similar to standard therapies and historical controls for patients with neuroendocrine tumor-related symptoms or progression of the liver tumor. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

©2020 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.



Louisiana

Radioembolization for Primary and Metastatic Tumors of the Liver

Policy # 00110

Original Effective Date: 02/23/2004

Current Effective Date: 05/11/2020

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. The relevant outcomes are OS, functional outcomes, QOL, and treatment-related morbidity. RCTs of patients with prior treatment failure have methodologic problems, do not show definitive superiority of RE compared with alternatives but tend to show greater tumor response with RE. The evidence is sufficient to determine that the technology results in a meaningful 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 observational studies. The relevant outcomes are OS, functional outcomes, QOL, 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 the effects of the technology on health outcomes.

Clinical input obtained in 2010, 2011, and 2015 has supported the use of RE for primary hepatocellular carcinoma, intrahepatic cholangiocarcinoma, hepatic metastases from neuroendocrine tumors, chemorefractory colorectal carcinoma, chemorefractory breast cancer, and chemorefractory melanoma, despite the lack of rigorous comparative clinical trials for many of the indications.

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

©2020 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.



Louisiana

Radioembolization for Primary and Metastatic Tumors of the Liver

Policy # 00110

Original Effective Date: 02/23/2004

Current Effective Date: 05/11/2020

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.

2010-2011 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 patients 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 patients with liver metastases from colorectal cancers and support for its use in patients 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 patients 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

National Comprehensive Cancer Network

©2020 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.



Louisiana

Radioembolization for Primary and Metastatic Tumors of the Liver

Policy # 00110

Original Effective Date: 02/23/2004

Current Effective Date: 05/11/2020

Primary Hepatobiliary Carcinoma

The NCCN guidelines (v.1.2019) on the treatment of hepatobiliary 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 non-target treatment.

Metastatic Neuroendocrine Tumors

The NCCN guidelines (v.2.2019) on the treatment of neuroendocrine tumors give a category 2B recommendation for hepatic regional therapy (arterial embolization, chemoembolization, RE) in the setting of advanced locoregional disease.

Metastatic Colon Cancer

The NCCN guidelines (v.2.2019) 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 patients with chemotherapy-resistant/-refractory disease and with predominant hepatic metastases."

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.

©2020 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.



Louisiana

Radioembolization for Primary and Metastatic Tumors of the Liver

Policy # 00110

Original Effective Date: 02/23/2004

Current Effective Date: 05/11/2020

Table 1

NCT No.	Trial Name	Planned Enrollment	Completion Date
Hepatocellular carcinoma			
<i>Ongoing</i>			
NCT01135056	Phase III Multi-Centre Open-Label Randomized Controlled Trial of Selective Internal Radiation Therapy (SIRT) Versus Sorafenib in Locally Advanced Hepatocellular Carcinoma (SIRveNIB)	360	Jul 2018 (ongoing)
NCT01126645 ^a	Evaluation of Sorafenib in Combination With Local Micro-therapy Guided by Gd-EOB-DTPA Enhanced MRI in Patients With Inoperable Hepatocellular Carcinoma	529	Dec 2018 (Completed)
NCT01556490 ^a	A Phase III Clinical Trial of Intra-arterial TheraSphere in the Treatment of Patients With Unresectable	526	Sept 2019

©2020 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.



Louisiana

Radioembolization for Primary and Metastatic Tumors of the Liver

Policy # 00110

Original Effective Date: 02/23/2004

Current Effective Date: 05/11/2020

NCT No.	Trial Name	Planned Enrollment	Completion Date
	Hepatocellular Carcinoma (HCC)		
<i>Unpublished</i>			
NCT01482442	A Prospective Randomized Open-labeled Trial Comparing RADIOEMBOLIZATION With Yttrium 90 Microspheres and Sorafenib in Patients With Advanced Hepatocellular Carcinoma	496	Apr 2016 (completed)
NCT00846131	A Single-Center Proof of Concept Pilot Study to Evaluate the Safety, Efficacy, and Tolerability of Sorafenib Combined With TheraSphere in Subjects With Hepatocellular Carcinoma Awaiting Liver Transplantation	24	Sep 2016 (completed)

©2020 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.



Louisiana

Radioembolization for Primary and Metastatic Tumors of the Liver

Policy # 00110

Original Effective Date: 02/23/2004

Current Effective Date: 05/11/2020

NCT No.	Trial Name	Planned Enrollment	Completion Date
NCT01381211	Transarterial RAdioembolization Versus ChemoEmbolization for the Treatment of HCC: A Multicenter Randomized Controlled Trial (TRACE Trial)	140	Dec 2016 (unknown)
Metastatic colorectal cancer			
NCT01483027 ^a	A Phase III Clinical Trial Evaluating TheraSphere in Patients With Metastatic Colorectal Carcinoma of the Liver Who Have Failed First Line Chemotherapy	420	Sep 2019
NCT01721954 ^a	Assessment of Overall Survival of FOLFOX6m Plus SIR-Spheres Microspheres Versus FOLFOX6m Alone as First-line Treatment in Patients With Non-resectable Liver Metastases From Primary	200	Dec 2019

©2020 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.



Louisiana

Radioembolization for Primary and Metastatic Tumors of the Liver

Policy # 00110

Original Effective Date: 02/23/2004

Current Effective Date: 05/11/2020

NCT No.	Trial Name	Planned Enrollment	Completion Date
	Colorectal Carcinoma in a Randomized Clinical Study		
<i>Unpublished</i>			
ISRCTN83867919	FOXFIRE: An open-label randomized phase III trial of 5-Fluorouracil, OXaliplatin and Folinic acid +/- Interventional Radio-Embolisation as first line treatment for patients with unresectable liver-only or liver-predominant metastatic colorectal cancer	490	Oct 2016 (completed)
NCT00724503 ^a	Randomized Comparative Study of Folfox6m Plus Sir-Spheres Microspheres Versus Folfox6m Alone as First Line Treatment in Patients With Nonresectable Liver Metastases From Primary Colorectal Carcinoma (SIRFLOX)	532	May 2015 (completed)

©2020 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.



Louisiana

Radioembolization for Primary and Metastatic Tumors of the Liver

Policy # 00110

Original Effective Date: 02/23/2004

Current Effective Date: 05/11/2020

NCT No.	Trial Name	Planned Enrollment	Completion Date
Cholangiocarcinoma			
<i>Unpublished</i>			
NCT01912053	An Open-label, Multicenter, Phase II Trial, to Evaluate the Efficacy of Intra-hepatic Administration of Yttrium 90-labeled Microspheres (Therasphere, Nordion) in Association With Intravenous Chemotherapy With Gemcitabine and Cisplatin for the Treatment of Intra-hepatic Cholangiocarcinoma, First Line	41	Nov 2017 (completed)

References

1. Blue Cross and Blue Shield Association, Medical Policy Reference Manual, “Radioembolization for Primary and Metastatic Tumors of the Liver”, Policy 8.01.43, August 2019.
2. Llovet JM, Real MI, Montana X, et al. Arterial embolisation or chemoembolisation versus symptomatic treatment in patients with unresectable hepatocellular carcinoma: a randomised controlled trial. *Lancet*. May 18 2002;359(9319):1734-1739. PMID 12049862.

©2020 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.



Louisiana

Radioembolization for Primary and Metastatic Tumors of the Liver

Policy # 00110

Original Effective Date: 02/23/2004

Current Effective Date: 05/11/2020

3. Lo CM, Ngan H, Tso WK, et al. Randomized controlled trial of transarterial lipiodol chemoembolization for unresectable hepatocellular carcinoma. *Hepatology*. May 2002;35(5):1164-1171. PMID 11981766.
4. Tao R, Li X, Ran R, et al. A mixed analysis comparing nine minimally invasive surgeries for unresectable hepatocellular carcinoma patients. *Oncotarget*. Jan 17 2017;8(3):5460-5473. PMID 27705924.
5. Ludwig JM, Zhang D, Xing M, et al. Meta-analysis: adjusted indirect comparison of drug-eluting bead transarterial chemoembolization versus 90Y-radioembolization for hepatocellular carcinoma. *Eur Radiol*. May 2017;27(5):2031-2041. PMID 27562480.
6. Lobo L, Yakoub D, Picado O, et al. Unresectable hepatocellular carcinoma: radioembolization versus chemoembolization: a systematic review and meta-analysis. *Cardiovasc Intervent Radiol*. Nov 2016;39(11):1580- 1588. PMID 27586657.
7. Facciorusso A, Serviddio G, Muscatiello N. Transarterial radioembolization vs chemoembolization for hepatocarcinoma patients: A systematic review and meta-analysis. *World J Hepatol*. Jun 28 2016;8(18):770-778. PMID 27366304.
8. Vente MA, Wondergem M, van der Tweel I, et al. Yttrium-90 microsphere radioembolization for the treatment of liver malignancies: a structured meta-analysis. *Eur Radiol*. Nov 2009;19(4):951-959. PMID 18989675.
9. Kolligs FT, Bilbao JI, Jakobs T, et al. Pilot randomized trial of selective internal radiation therapy vs. chemoembolization in unresectable hepatocellular carcinoma. *Liver Int*. Jun 2015;35(6):1715-1721. PMID 25443863.
10. Pitton MB, Kloeckner R, Ruckes C, et al. Randomized comparison of selective internal radiotherapy (SIRT) versus drug-eluting bead transarterial chemoembolization (DEB-TACE) for the treatment of hepatocellular carcinoma. *Cardiovasc Intervent Radiol*. Apr 2015;38(2):352-360. PMID 25373796.
11. Padia SA, Johnson GE, Horton KJ, et al. Segmental Yttrium-90 radioembolization versus segmental chemoembolization for localized hepatocellular carcinoma: results of a single-center, retrospective, propensity score-matched study. *J Vasc Interv Radiol*. Jun 2017;28(6):777-785 e771. PMID 28365172.
12. Soydal C, Arslan MF, Kucuk ON, et al. Comparison of survival, safety, and efficacy after transarterial chemoembolization and radioembolization of Barcelona Clinic Liver Cancer stage B-C hepatocellular cancer patients. *Nucl Med Commun*. Jun 2016;37(6):646-649. PMID 26905317.

©2020 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.



Louisiana

Radioembolization for Primary and Metastatic Tumors of the Liver

Policy # 00110

Original Effective Date: 02/23/2004

Current Effective Date: 05/11/2020

13. Oladeru OT, Miccio JA, Yang J, et al. Conformal external beam radiation or selective internal radiation therapy-a comparison of treatment outcomes for hepatocellular carcinoma. *J Gastrointest Oncol.* Jun 2016;7(3):433-440. PMID 27284477.
14. El Fouly A, Ertle J, El Dorry A, et al. In intermediate stage hepatocellular carcinoma: radioembolization with yttrium 90 or chemoembolization? *Liver Int.* Feb 2015;35(2):627-635. PMID 25040497.
15. Gramenzi A, Golfieri R, Mosconi C, et al. Yttrium-90 radioembolization vs sorafenib for intermediate-locally advanced hepatocellular carcinoma: a cohort study with propensity score analysis. *Liver Int.* Mar 2015;35(3):1036-1047. PMID 24750853.
16. Carr BI, Kondragunta V, Buch SC, et al. Therapeutic equivalence in survival for hepatic arterial chemoembolization and yttrium 90 microsphere treatments in unresectable hepatocellular carcinoma: a two- cohort study. *Cancer.* Mar 1 2010;116(5):1305-1314. PMID 20066715.
17. Kulik L, Heimbach JK, Zaiem F, et al. Therapies for patients with hepatocellular carcinoma awaiting liver transplantation: A systematic review and meta-analysis. *Hepatology.* Jan 2018;67(1):381-400. PMID 28859222.
18. Salem R, Gordon AC, Mouli S, et al. Y90 Radioembolization significantly prolongs time to progression compared with chemoembolization in patients with hepatocellular carcinoma. *Gastroenterology.* Dec 2016;151(6):1155- 1163 e1152. PMID 27575820.
19. Kulik L, Vouche M, Koppe S, et al. Prospective randomized pilot study of Y90+/-sorafenib as bridge to transplantation in hepatocellular carcinoma. *J Hepatol.* Aug 2014;61(2):309-317. PMID 24681342.
20. Tohme S, Sukato D, Chen HW, et al. Yttrium-90 radioembolization as a bridge to liver transplantation: a single- institution experience. *J Vasc Interv Radiol.* Nov 2013;24(11):1632-1638. PMID 24160821.
21. Ramanathan R, Sharma A, Lee DD, et al. Multimodality therapy and liver transplantation for hepatocellular carcinoma: a 14-year prospective analysis of outcomes. *Transplantation.* Jul 15 2014;98(1):100-106. PMID 24503764.
22. Lewandowski RJ, Kulik LM, Riaz A, et al. A comparative analysis of transarterial downstaging for hepatocellular carcinoma: chemoembolization versus radioembolization. *Am J Transplant.* Aug 2009;9(8):1920-1928. PMID 19552767.
23. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology. Hepatobiliary Cancers. Version 2.2018. https://www.nccn.org/professionals/physician_gls/pdf/hepatobiliary.pdf. Al-Adra DP, Gill RS, Axford SJ, et al. Treatment of unresectable intrahepatic cholangiocarcinoma with yttrium-90

©2020 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.



Louisiana

Radioembolization for Primary and Metastatic Tumors of the Liver

Policy # 00110

Original Effective Date: 02/23/2004

Current Effective Date: 05/11/2020

- radioembolization: A systematic review and pooled analysis. *Eur J Surg Oncol*. Jan 2015;41(1):120-127. PMID 25449754.
24. Mouli S, Memon K, Baker T, et al. Yttrium-90 radioembolization for intrahepatic cholangiocarcinoma: safety, response, and survival analysis. *J Vasc Interv Radiol*. Aug 2013;24(8):1227-1234. PMID 23602420.
 25. Hoffmann RT, Paprottka PM, Schon A, et al. Transarterial hepatic yttrium-90 radioembolization in patients with unresectable intrahepatic cholangiocarcinoma: factors associated with prolonged survival. *Cardiovasc Intervent Radiol*. Feb 2012;35(1):105-116. PMID 21431970.
 26. Saxena A, Bester L, Chua TC, et al. Yttrium-90 radiotherapy for unresectable intrahepatic cholangiocarcinoma: a preliminary assessment of this novel treatment option. *Ann Surg Oncol*. Feb 2010;17(2):484-491. PMID 19876691.
 27. Boehm LM, Jayakrishnan TT, Miura JT, et al. Comparative effectiveness of hepatic artery based therapies for unresectable intrahepatic cholangiocarcinoma. *J Surg Oncol*. Feb 2015;111(2):213-220. PMID 25176325.
 28. Chan LS, Sze DY, Poultides GA, et al. Yttrium-90 radioembolization for unresectable combined hepatocellular- cholangiocarcinoma. *Cardiovasc Intervent Radiol*. Sep 2017;40(9):1383-1391. PMID 28432387.
 29. Jia Z, Paz-Fumagalli R, Frey G, et al. Resin-based Yttrium-90 microspheres for unresectable and failed first-line chemotherapy intrahepatic cholangiocarcinoma: preliminary results. *J Cancer Res Clin Oncol*. Mar 2017;143(3):481-489. PMID 27826686.
 30. Mosconi C, Gramenzi A, Ascanio S, et al. Yttrium-90 radioembolization for unresectable/recurrent intrahepatic cholangiocarcinoma: a survival, efficacy and safety study. *Br J Cancer*. Jul 26 2016;115(3):297-302. PMID 27336601.
 31. Rayar M, Sulpice L, Edeline J, et al. Intra-arterial yttrium-90 radioembolization combined with systemic chemotherapy is a promising method for downstaging unresectable huge intrahepatic cholangiocarcinoma to surgical treatment. *Ann Surg Oncol*. Sep 2015;22(9):3102-3108. PMID 25623598.
 32. Haug AR, Heinemann V, Bruns CJ, et al. 18F-FDG PET independently predicts survival in patients with cholangiocellular carcinoma treated with 90Y microspheres. *Eur J Nucl Med Mol Imaging*. Jun 2011;38(6):1037- 1045. PMID 21308371.
 33. Ibrahim SM, Mulcahy MF, Lewandowski RJ, et al. Treatment of unresectable cholangiocarcinoma using yttrium- 90 microspheres: results from a pilot study. *Cancer*. Oct 15 2008;113(8):2119-2128. PMID 18759346.

©2020 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.



Louisiana

Radioembolization for Primary and Metastatic Tumors of the Liver

Policy # 00110

Original Effective Date: 02/23/2004

Current Effective Date: 05/11/2020

34. King J, Quinn R, Glenn DM, et al. Radioembolization with selective internal radiation microspheres for neuroendocrine liver metastases. *Cancer*. Sep 1 2008;113(5):921-929. PMID 18618495.
35. Devcic Z, Rosenberg J, Braat AJ, et al. The efficacy of hepatic 90Y resin radioembolization for metastatic neuroendocrine tumors: a meta-analysis. *J Nucl Med*. Sep 2014;55(9):1404-1410. PMID 25012459.
36. Engelman ES, Leon-Ferre R, Naraev BG, et al. Comparison of transarterial liver-directed therapies for low-grade metastatic neuroendocrine tumors in a single institution. *Pancreas*. Mar 2014;43(2):219-225. PMID 24518499.
37. Rhee TK, Lewandowski RJ, Liu DM, et al. 90Y Radioembolization for metastatic neuroendocrine liver tumors: preliminary results from a multi-institutional experience. *Ann Surg*. Jun 2008;247(6):1029-1035. PMID 18520231.
38. Cao CQ, Yan TD, Bester L, et al. Radioembolization with yttrium microspheres for neuroendocrine tumour liver metastases. *Br J Surg*. Apr 2010;97(4):537-543. PMID 20205229.
39. Kennedy AS, Dezarn WA, McNeillie P, et al. Radioembolization for unresectable neuroendocrine hepatic metastases using resin 90Y-microspheres: early results in 148 patients. *Am J Clin Oncol*. Jun 2008;31(3):271- 279. PMID 18525307.
40. Memon K, Lewandowski RJ, Mulcahy MF, et al. Radioembolization for neuroendocrine liver metastases: safety, imaging, and long-term outcomes. *Int J Radiat Oncol Biol Phys*. Jul 1 2012;83(3):887-894. PMID 22137020.
41. Paprottka PM, Hoffmann RT, Haug A, et al. Radioembolization of symptomatic, unresectable neuroendocrine hepatic metastases using yttrium-90 microspheres. *Cardiovasc Intervent Radiol*. Apr 2012;35(2):334-342. PMID 21847708.
42. Peker A, Cicek O, Soydal C, et al. Radioembolization with yttrium-90 resin microspheres for neuroendocrine tumor liver metastases. *Diagn Interv Radiol*. Jan-Feb 2015;21(1):54-59. PMID 25430526.
43. Jia Z, Paz-Fumagalli R, Frey G, et al. Single-institution experience of radioembolization with yttrium-90 microspheres for unresectable metastatic neuroendocrine liver tumors. *J Gastroenterol Hepatol*. Sep 2017;32(9):1617-1623. PMID 28132407.
44. Fan KY, Wild AT, Halappa VG, et al. Neuroendocrine tumor liver metastases treated with yttrium-90 radioembolization. *Contemp Clin Trials*. Sep 2016;50:143-149. PMID 27520932.
45. Tice J. Selective internal radiation therapy or radioembolization for inoperable liver metastases from colorectal cancer San Francisco, CA: California Technology Assessment Forum; 2010.

©2020 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.



Louisiana

Radioembolization for Primary and Metastatic Tumors of the Liver

Policy # 00110

Original Effective Date: 02/23/2004

Current Effective Date: 05/11/2020

46. Saxena A, Bester L, Shan L, et al. A systematic review on the safety and efficacy of yttrium-90 radioembolization for unresectable, chemorefractory colorectal cancer liver metastases. *J Cancer Res Clin Oncol.* Apr 2014;140(4):537-547. PMID 24318568.
47. Gray B, Van Hazel G, Hope M, et al. Randomised trial of SIR-Spheres plus chemotherapy vs. chemotherapy alone for treating patients with liver metastases from primary large bowel cancer. *Ann Oncol.* Dec 2001;12(12):1711-1720. PMID 11843249.
48. Hendlisz A, Van den Eynde M, Peeters M, et al. Phase III trial comparing protracted intravenous fluorouracil infusion alone or with yttrium-90 resin microspheres radioembolization for liver-limited metastatic colorectal cancer refractory to standard chemotherapy. *J Clin Oncol.* Aug 10 2010;28(23):3687-3694. PMID 20567019.
49. Rosenbaum CE, Verkooijen HM, Lam MG, et al. Radioembolization for treatment of salvage patients with colorectal cancer liver metastases: a systematic review. *J Nucl Med.* Nov 2013;54(11):1890-1895. PMID 24071510.
50. Van Hazel G, Blackwell A, Anderson J, et al. Randomised phase 2 trial of SIR-Spheres plus fluorouracil/leucovorin chemotherapy versus fluorouracil/leucovorin chemotherapy alone in advanced colorectal cancer. *J Surg Oncol.* Nov 1 2004;88(2):78-85. PMID 15499601.
51. Townsend A, Price T, Karapetis C. Selective internal radiation therapy for liver metastases from colorectal cancer. *Cochrane Database Syst Rev.* Oct 07 2009(4):CD007045. PMID 19821394.
52. Van Hazel GA, Heinemann V, Sharma NK, et al. SIRFLOX: randomized phase III trial comparing first-line mFOLFOX6 (plus or minus bevacizumab) versus mFOLFOX6 (plus or minus bevacizumab) plus selective internal radiation therapy in patients with metastatic colorectal cancer. *J Clin Oncol.* May 20 2016;34(15):1723- 1731. PMID 26903575.
53. Salem R, Lewandowski RJ, Mulcahy MF, et al. Radioembolization for hepatocellular carcinoma using Yttrium-90 microspheres: a comprehensive report of long-term outcomes. *Gastroenterology.* Jan 2010;138(1):52-64. PMID 19766639.
54. Seidensticker R, Denecke T, Kraus P, et al. Matched-pair comparison of radioembolization plus best supportive care versus best supportive care alone for chemotherapy refractory liver-dominant colorectal metastases. *Cardiovasc Intervent Radiol.* Oct 2012;35(5):1066-1073. PMID 21800231.
55. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology. Colon Cancer Version 2 2018. https://www.nccn.org/professionals/physician_gls/pdf/colon.pdf. Kennedy AS, Salem R. Radioembolization (yttrium-90 microspheres) for primary and metastatic hepatic malignancies. *Cancer J.* Mar-Apr 2010;16(2):163-175. PMID 20404614.

©2020 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.



Louisiana

Radioembolization for Primary and Metastatic Tumors of the Liver

Policy # 00110

Original Effective Date: 02/23/2004

Current Effective Date: 05/11/2020

56. Smits ML, Prince JF, Rosenbaum CE, et al. Intra-arterial radioembolization of breast cancer liver metastases: a structured review. *Eur J Pharmacol.* Jun 5 2013;709(1-3):37-42. PMID 23545356.
57. Pieper CC, Meyer C, Wilhelm KE, et al. Yttrium-90 radioembolization of advanced, unresectable breast cancer liver metastases-a single-center experience. *J Vasc Interv Radiol.* Sep 2016;27(9):1305-1315. PMID 27461588.
58. Gordon AC, Gradishar WJ, Kaklamani VG, et al. Yttrium-90 radioembolization stops progression of targeted breast cancer liver metastases after failed chemotherapy. *J Vasc Interv Radiol.* Oct 2014;25(10):1523-1532, 1532 e1521-1522. PMID 25156827.
59. Saxena A, Kapoor J, Meteling B, et al. Yttrium-90 radioembolization for unresectable, chemoresistant breast cancer liver metastases: a large single-center experience of 40 patients. *Ann Surg Oncol.* Apr 2014;21(4):1296- 1303. PMID 24337647.
60. Cianni R, Pelle G, Notarianni E, et al. Radioembolisation with (90)Y-labelled resin microspheres in the treatment of liver metastasis from breast cancer. *Eur Radiol.* Jul 2013;23(1):182-189. PMID 22836160.
61. Haug AR, Tiega Donfack BP, Trumm C, et al. 18F-FDG PET/CT predicts survival after radioembolization of hepatic metastases from breast cancer. *J Nucl Med.* Feb 2012;53(3):371-377. PMID 22331219.
62. Jakobs TF, Hoffmann RT, Fischer T, et al. Radioembolization in patients with hepatic metastases from breast cancer. *J Vasc Interv Radiol.* May 2008;19(5):683-690. PMID 18440456.
63. Bangash AK, Atassi B, Kaklamani V, et al. 90Y radioembolization of metastatic breast cancer to the liver: toxicity, imaging response, survival. *J Vasc Interv Radiol.* May 2007;18(5):621-628. PMID 17494843.
64. Coldwell DM, Kennedy AS, Nutting CW. Use of yttrium-90 microspheres in the treatment of unresectable hepatic metastases from breast cancer. *Int J Radiat Oncol Biol Phys.* Nov 1 2007;69(3):800-804. PMID 17524567.
65. Xing M, Prajapati HJ, Dhanasekaran R, et al. Selective internal Yttrium-90 radioembolization therapy (90Y-SIRT) versus best supportive care in patients with unresectable metastatic melanoma to the liver refractory to systemic therapy: safety and efficacy cohort studys. *Am J Clin Oncol.* Feb 2017;40(1):27-34. PMID 25089529.
66. Eldredge-Hindy H, Ohri N, Anne PR, et al. Yttrium-90 microsphere brachytherapy for liver metastases from uveal melanoma: clinical outcomes and the predictive value of fluorodeoxyglucose positron emission tomograph. *Am J Clin Oncol.* Apr 2016;39(2):189-195. PMID 24441583.

©2020 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.



Louisiana

Radioembolization for Primary and Metastatic Tumors of the Liver

Policy # 00110

Original Effective Date: 02/23/2004

Current Effective Date: 05/11/2020

67. Gonsalves CF, Eschelmann DJ, Sullivan KL, et al. Radioembolization as salvage therapy for hepatic metastasis of uveal melanoma: a single-institution experience. *AJR Am J Roentgenol.* Feb 2011;196(2):468-473. PMID 21257902.
68. Kennedy AS, Nutting C, Jakobs T, et al. A first report of radioembolization for hepatic metastases from ocular melanoma. *Cancer Invest.* Jul 2009;27(6):682-690. PMID 19219675.
69. Klingenstein A, Haug AR, Zech CJ, et al. Radioembolization as locoregional therapy of hepatic metastases in uveal melanoma patients. *Cardiovasc Intervent Radiol.* Feb 2013;36(1):158-165. PMID 22526099.
70. Piduru SM, Schuster DM, Barron BJ, et al. Prognostic value of 18f-fluorodeoxyglucose positron emission tomography-computed tomography in predicting survival in patients with unresectable metastatic melanoma to the liver undergoing yttrium-90 radioembolization. *J Vasc Interv Radiol.* Jul 2012;23(7):943-948. PMID 22609292.
71. Michl M, Haug AR, Jakobs TF, et al. Radioembolization with Yttrium-90 microspheres (SIRT) in pancreatic cancer patients with liver metastases: efficacy, safety and prognostic factors. *Oncology.* Jan 2014;86(1):24-32. PMID 24401529.
72. Miller MD, Sze DY, Padia SA, et al. Response and overall survival for yttrium-90 radioembolization of hepatic sarcoma: a multicenter retrospective study. *J Vasc Interv Radiol.* Jun 2018;29(6):867-873. PMID 29724518.
73. National Comprehensive Cancer Network. Hapatobiliary carcinoma. Version 2.2019. https://www.nccn.org/professionals/physician_gls/pdf/hepatobiliary.pdf.
74. National Comprehensive Cancer Network. Neuroendocrine tumors. Version 1.2019. https://www.nccn.org/professionals/physician_gls/pdf/neuroendocrine.pdf.
75. National Comprehensive Cancer Network. Colon Cancer. Version 2.2019. https://www.nccn.org/professionals/physician_gls/pdf/colon.pdf.

Policy History

Original Effective Date: 02/23/2004

Current Effective Date: 05/11/2020

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.

©2020 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.



Louisiana

Radioembolization for Primary and Metastatic Tumors of the Liver

Policy # 00110

Original Effective Date: 02/23/2004

Current Effective Date: 05/11/2020

- 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

©2020 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.



Louisiana

Radioembolization for Primary and Metastatic Tumors of the Liver

Policy # 00110

Original Effective Date: 02/23/2004

Current Effective Date: 05/11/2020

- 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
- 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.

Next Scheduled Review Date: 04/2021

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 2019

©2020 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.



Louisiana

Radioembolization for Primary and Metastatic Tumors of the Liver

Policy # 00110

Original Effective Date: 02/23/2004

Current Effective Date: 05/11/2020

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:

Code Type	Code
CPT	37243, 75894, 77399, 77778, 79445
HCPCS	A9543, C2616, S2095
ICD-10 Diagnosis	C22.1, C22.9, C43.0-C43.9, C50.011-C50.929, C78.7, C79.81, D03.0-D03.9, D05.00- D05.92, D09.3, D09.8

*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

©2020 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.



Louisiana

Radioembolization for Primary and Metastatic Tumors of the Liver

Policy # 00110

Original Effective Date: 02/23/2004

Current Effective Date: 05/11/2020

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.

****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.

©2020 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.



Louisiana

Radioembolization for Primary and Metastatic Tumors of the Liver

Policy # 00110

Original Effective Date: 02/23/2004

Current Effective Date: 05/11/2020

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.

©2020 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.