Introduction

Embolization is a procedure to block blood flow. Combined with radiation, it is a way to treat cancer in the liver in some situations. In this procedure a catheter (a long, thin, hollow tube) is inserted in an artery near the groin. It's threaded to the tumor's blood supply. Tiny radioactive particles are released into the artery that feeds the tumor. The particles travel into the tumor and block off — embolize — the blood supply feeding the tumor, causing it to shrink. The radiation works to kill the cancer cells. The radiation dissipates in a few weeks and the particles stay in the liver permanently. The radiation usually doesn’t affect the healthy liver tissue around the tumor very much. This policy describes when radioembolization may be considered medically necessary.

Note: The Introduction section is for your general knowledge and is not to be taken as policy coverage criteria. The rest of the policy uses specific words and concepts familiar to medical professionals. It is intended for providers. A provider can be a person, such as a doctor, nurse, psychologist, or dentist. A provider also can be a place where medical care is given, like a hospital, clinic, or lab. This policy informs them about when a service may be covered.
# Policy Coverage Criteria

<table>
<thead>
<tr>
<th>Service</th>
<th>Medical Necessity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Radioembolization</td>
<td>Radioembolization may be considered medically necessary in the following situations:</td>
</tr>
<tr>
<td></td>
<td>• Treatment of primary hepatocellular carcinoma that is unresectable and limited to the liver (size of 3cm or larger, and patient with good performance status)</td>
</tr>
<tr>
<td></td>
<td>OR</td>
</tr>
<tr>
<td></td>
<td>• Treatment of primary hepatocellular carcinoma as a bridge to liver transplantation</td>
</tr>
<tr>
<td></td>
<td>OR</td>
</tr>
<tr>
<td></td>
<td>• Treatment of primary intrahepatic cholangiocarcinoma in patients with unresectable tumors</td>
</tr>
<tr>
<td></td>
<td>OR</td>
</tr>
<tr>
<td></td>
<td>• Treatment of hepatic metastases from neuroendocrine tumors (carcinoid and noncarcinoid) with diffuse and symptomatic disease when systemic therapy has failed to control symptoms. (symptoms related to excess hormone production)</td>
</tr>
<tr>
<td></td>
<td>OR</td>
</tr>
<tr>
<td></td>
<td>• Treatment of unresectable hepatic metastases</td>
</tr>
<tr>
<td></td>
<td>o From breast, colorectal or melanoma (ocular or cutaneous) AND</td>
</tr>
<tr>
<td></td>
<td>o That are progressive and unresectable in patients with liver dominant disease AND</td>
</tr>
<tr>
<td></td>
<td>o That are refractory to chemotherapy or are not candidates for chemotherapy</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Service</th>
<th>Investigational</th>
</tr>
</thead>
<tbody>
<tr>
<td>Radioembolization</td>
<td>Radioembolization is considered investigational for all other hepatic metastases except as noted in the Medical Necessity section above.</td>
</tr>
</tbody>
</table>
### Service

<table>
<thead>
<tr>
<th>Investigational</th>
</tr>
</thead>
<tbody>
<tr>
<td>Radioembolization is considered investigational for all other indications not described in the Medical Necessity section above.</td>
</tr>
</tbody>
</table>

### Documentation Requirements

The patient’s medical records submitted for review for all conditions should document that medical necessity criteria are met. The record should include office visit notes that contain the relevant history and physical supporting ANY of the following situations:

- Patient with primary liver cancer that cannot be removed by surgery and limited to the liver (size of 3 cm or larger, and patient with good performance status)
- Treatment for hepatocellular carcinoma before a liver transplant
- Treatment of primary intrahepatic cholangiocarcinoma that cannot be removed by surgery
- Treatment of hepatic metastases from neuroendocrine tumors (carcinoid and noncarcinoid) with diffuse and symptomatic disease when systemic therapy has failed to control symptoms (symptoms related to excess hormone production)
- Treatment of hepatic metastases that cannot be removed by surgery:
  - From breast, colorectal, or melanoma (ocular or cutaneous)
  - That are progressive and unresectable in patients with liver dominant disease
  - Has failed chemotherapy or are not candidates for chemotherapy

### Coding

The coding for radioembolization may depend on the medical specialty providing the therapy.

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPT</td>
<td></td>
</tr>
<tr>
<td>37243</td>
<td>Vascular embolization or occlusion, inclusive of all radiological supervision and interpretation, intraprocedural roadmapping, and imaging guidance necessary to complete the intervention; for tumors, organ ischemia, or infarction.</td>
</tr>
<tr>
<td>75894</td>
<td>Transcatheter therapy, embolization, any method, radiological supervision and interpretation</td>
</tr>
<tr>
<td>79445</td>
<td>Radiopharmaceutical therapy, by intra-arterial particulate administration</td>
</tr>
<tr>
<td>Code</td>
<td>Description</td>
</tr>
<tr>
<td>--------</td>
<td>-----------------------------------------------------------------------------</td>
</tr>
<tr>
<td>S2095</td>
<td>Transcatheter occlusion or embolization for tumor destruction, percutaneous, any method, using yttrium-90 microspheres</td>
</tr>
</tbody>
</table>

**Note:** CPT codes, descriptions and materials are copyrighted by the American Medical Association (AMA). HCPCS codes, descriptions and materials are copyrighted by Centers for Medicare Services (CMS).

**Related Information**

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 about the number of treatments that should be administered.

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.

**Definition of Terms**

**Child-Pugh Score:** This score is used to assess the prognosis of chronic liver disease, usually cirrhosis.

Description

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.

Background

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 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, (radiotherapy in older literature) 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 normal liver is primarily perfused via the portal vein. Yttrium-90 is a pure beta-emitter with a relatively limited effective range and 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 is delivered via the hepatic artery to simulate
microspheres. Single-photon emission computed tomography is used to detect possible shunting of the albumin particles into gastrointestinal or pulmonary vasculature.

Currently 2 commercial forms of yttrium-90 microspheres are available: a glass sphere, (TheraSphere) and a resin sphere (SIR-Spheres). Noncommercial forms are mostly used outside the United States. While the commercial products use the same radioisotope (yttrium-90) and have the same target dose (100 Gy), 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-flourouridine 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 1 product do not necessarily apply to other commercial (or non-commercial) products (see Regulatory Status section).

Summary of Evidence

For individuals who have unresectable hepatocellular carcinoma who receive radioembolization (RE) or RE with liver transplant, the evidence includes primarily retrospective and prospective observational studies, with limited evidence from RCTs. Relevant outcomes are overall survival, functional outcomes, quality of life, 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 demonstrated similar outcomes for RE compared with alternatives. Evidence from observational studies has demonstrated that RE can allow successful liver transplantation in certain patients. The evidence is sufficient to determine that the technology results in a meaningful improvement in net health outcome.

For individuals who have unresectable intrahepatic cholangiocarcinoma who receive RE, the evidence includes case series. Relevant outcomes are overall survival, 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 intrahepatic cholangiocarcinoma has response rates similar to those 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. Relevant outcomes are overall survival, 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 patients with neuroendocrine tumor-related symptoms or progression of liver tumor. The evidence is sufficient to determine that the technology results in a meaningful improvement in 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 overall survival, functional outcomes, quality of life, and treatment-related morbidity. RCTs of patients with prior treatment failure have methodologic problems, do not show definitive superiority of RE compared to alternatives, but tend to show greater tumor response with RE. The evidence is sufficient to determine qualitatively that the technology results in a meaningful improvement in 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. Relevant outcomes are overall survival, functional outcomes, quality of life, and treatment-related morbidity. These studies generally 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.

Despite the lack of rigorous comparative clinical trials for many of the indications, clinical input 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.

**Ongoing and Unpublished Clinical Trials**

Some currently unpublished trials that might influence this review are listed in Table 1.
### Table 1. Summary of Key Trials

<table>
<thead>
<tr>
<th>NCT No.</th>
<th>Trial Name</th>
<th>Planned Enrollment</th>
<th>Completion Date</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><strong>Hepatocellular carcinoma</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Ongoing</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NCT01135056</td>
<td>Phase III Multi-Centre Open-Label Randomized Controlled Trial of Selective Internal Radiation Therapy (SIRT) Versus Sorafenib in Locally Advanced Hepatocellular Carcinoma (SIRveNIB)</td>
<td>360</td>
<td>Jul 2018 (ongoing)</td>
</tr>
<tr>
<td>NCT01126645(^a)</td>
<td>Evaluation of Sorafenib in Combination With Local Micro-therapy Guided by Gd-EOB-DTPA Enhanced MRI in Patients With Inoperable Hepatocellular Carcinoma</td>
<td>529</td>
<td>Mar 2018 (ongoing)</td>
</tr>
<tr>
<td>NCT01556490(^a)</td>
<td>A Phase III Clinical Trial of Intra-arterial TheraSphere® in the Treatment of Patients With Unresectable Hepatocellular Carcinoma (HCC)</td>
<td>526</td>
<td>Apr 2019</td>
</tr>
<tr>
<td></td>
<td><strong>Unpublished</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NCT01482442</td>
<td>A Prospective Randomized Open-labeled Trial Comparing RADIOEMBOLIZATION With Yttrium 90 Microspheres and Sorafenib in Patients With Advanced Hepatocellular Carcinoma</td>
<td>496</td>
<td>Apr 2016 (completed)</td>
</tr>
<tr>
<td>NCT00846131</td>
<td>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</td>
<td>24</td>
<td>Sep 2016 (completed)</td>
</tr>
<tr>
<td>NCT01381211</td>
<td>Transarterial Radioembolization Versus ChemoEmbolization for the Treatment of HCC: A Multicenter Randomized Controlled Trial (TRACE Trial)</td>
<td>140</td>
<td>Dec 2016 (unknown)</td>
</tr>
<tr>
<td></td>
<td><strong>Metastatic colorectal cancer</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Ongoing</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NCT01483027(^a)</td>
<td>A Phase III Clinical Trial Evaluating TheraSphere® in Patients With Metastatic Colorectal Carcinoma of the Liver Who Have Failed First Line Chemotherapy</td>
<td>420</td>
<td>Sep 2019</td>
</tr>
<tr>
<td>NCT01721954(^a)</td>
<td>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 Colorectal Carcinoma in a Randomised Clinical Study</td>
<td>200</td>
<td>Dec 2019</td>
</tr>
<tr>
<td>NCT No.</td>
<td>Trial Name</td>
<td>Planned Enrollment</td>
<td>Completion Date</td>
</tr>
<tr>
<td>--------------</td>
<td>-----------------------------------------------------------------------------</td>
<td>--------------------</td>
<td>-----------------------</td>
</tr>
<tr>
<td>Unpublished</td>
<td>FOXFIRE: An open-label randomised 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</td>
<td>490</td>
<td>Oct 2016 (completed)</td>
</tr>
<tr>
<td>NCT00724503a</td>
<td>Randomised 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)</td>
<td>532</td>
<td>Nov 2016 (completed)</td>
</tr>
<tr>
<td>Cholangiocarcinoma</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unpublished</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NCT01912053</td>
<td>An Open-label, Multicenter, Phase II Trial, to Evaluate the Efficacy of Intra-hepatic Administration of Yttrium 90-labelled Microspheres (Therasphere®, Nordion) in Association With Intravenous Chemotherapy With Gemcitabine and Cisplatin for the Treatment of Intra-hepatic Cholangiocarcinoma, First Line</td>
<td>41</td>
<td>Nov 2017 (completed)</td>
</tr>
</tbody>
</table>

NCT: national clinical trial.

*a* Denotes industry-sponsored or cosponsored trial.

**Clinical Input Received 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 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*

**Primary Hepatocellular Carcinoma**

National Comprehensive Cancer Network (NCCN) guidelines (v.2.2018) 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 nontarget treatment.19

**Metastatic Neuroendocrine Tumors**

NCCN guidelines (v.2.2018) 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.21

**Metastatic Colon Cancer**

NCCN guidelines (v.2.2018) 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.”22

**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.

**Regulatory Status**

Currently, 2 forms of yttrium-90 microspheres have been approved by FDA.
In 1999, TheraSphere® (manufactured by Nordion, Ontario, under license by BTG International), a glass sphere system, was approved by FDA through the humanitarian drug exemption process for radiotherapy or as a neoadjuvant 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 FDA through the premarket approval process for the treatment of inoperable colorectal cancer metastatic to the liver (P990065).

FDA product code: NAW.

References


45. Tice J. Selective internal radiation therapy or radioembolization for inoperable liver metastases from colorectal cancer San Francisco, CA: California Technology Assessment Forum; 2010.


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**History**

<table>
<thead>
<tr>
<th>Date</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>03/30/04</td>
<td>Add to Therapy Section - New Policy</td>
</tr>
<tr>
<td>03/08/05</td>
<td>Replace Policy - Policy reviewed; reference added; policy statement unchanged.</td>
</tr>
<tr>
<td>03/14/06</td>
<td>Replace Policy - Policy reviewed; reference added; policy statement unchanged.</td>
</tr>
<tr>
<td>06/02/06</td>
<td>Scope and Disclaimer Update - No other changes.</td>
</tr>
<tr>
<td>11/14/06</td>
<td>Replace Policy - Policy reviewed by Oncology Advisory panel and recommended for adoption on October 26, 2006.</td>
</tr>
<tr>
<td>04/10/07</td>
<td>Cross Reference Update - No other changes.</td>
</tr>
<tr>
<td>06/15/07</td>
<td>Cross Reference Update - No other changes.</td>
</tr>
<tr>
<td>03/19/08</td>
<td>Code Update - ICD-9 diagnosis code 197.7 added.</td>
</tr>
<tr>
<td>11/11/08</td>
<td>New PR Policy - Policy updated with literature search. Policy statement changed to medically necessary with bulleted criteria. This was changed to keep consistent with the TACE (8.01.505) policy statement. Reviewed and recommended by OAP on August 21, 2008. Policy status changed from BC to PR, replacing BC.8.01.43.</td>
</tr>
<tr>
<td>08/11/09</td>
<td>Replace Policy - Policy updated with literature search; no change to the policy</td>
</tr>
<tr>
<td>Date</td>
<td>Comments</td>
</tr>
<tr>
<td>------------</td>
<td>-------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>12/14/10</td>
<td>Replace Policy - Policy updated with literature search; no change to policy statement. NCCN 2010 reference added. Reviewed and recommended by OAP November 18, 2010.</td>
</tr>
<tr>
<td>10/11/11</td>
<td>Replace Policy – Policy updated with literature review; no change in policy statement.</td>
</tr>
<tr>
<td>02/27/12</td>
<td>Related Policies updated; 7.01.133 added.</td>
</tr>
<tr>
<td>05/22/12</td>
<td>Replace policy. Policy updated with literature review through February 2012; no change in policy statements. Physician specialty society input and references added.</td>
</tr>
<tr>
<td>05/28/13</td>
<td>Replace policy. Policy updated with literature review. Policy reorganized. No change in policy statements. References added, removed, renumbered. ICD-10 codes added.</td>
</tr>
<tr>
<td>07/16/13</td>
<td>Update Related Policies. Add 8.01.528.</td>
</tr>
<tr>
<td>12/23/13</td>
<td>Coding Update. CPT code 37204 discontinued effective 12/31/13.</td>
</tr>
<tr>
<td>03/14/14</td>
<td>Coding update. CPT code 37243, effective 1/1/14, added to the policy.</td>
</tr>
<tr>
<td>03/27/14</td>
<td>Coding update; CPT codes 37243 removed from policy. It does not apply to this policy, see 8.01.521.</td>
</tr>
<tr>
<td>09/03/14</td>
<td>Annual Review. Added a policy statement indicating all other indications not listed as medically necessary are investigational. Policy Guidelines added including Definition of Terms. Policy updated with literature review through June, 2014. Rationale section reformatted. References 15-16, 22-23, 32, 42-43, 48, 51 added. References 4-6 and 49-51 updated; others renumbered/removed. Policy statement added as noted. Coding update: CPT code 77776 added to the policy; ICD-9 and ICD-10 codes removed from policy – they are not utilized in adjudication of the policy.</td>
</tr>
<tr>
<td>09/11/14</td>
<td>Update Related Policies. Add 7.01.95.</td>
</tr>
<tr>
<td>10/13/15</td>
<td>Annual Review. Policy updated with literature review. Medically necessary indications were added for the treatment of hepatocellular carcinoma as a bridge to hepatic transplant. The indications for treatment of hepatic metastases from breast cancer or melanoma with liver dominant disease and intrahepatic cholangiocarcinoma were moved from medically necessary to investigational. These changes harmonize the medical necessity indications for this policy and 8.01.505- Transcatheter Arterial Chemoembolization (TACE) as a Treatment for Primary or Metastatic Liver Malignancies. References updated.</td>
</tr>
<tr>
<td>Date</td>
<td>Comments</td>
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<tr>
<td>------------</td>
<td>------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td></td>
<td>carcinomas. Discussion section clarified to support policy. Clinical trials section simplified.</td>
</tr>
<tr>
<td>07/08/16</td>
<td>Minor edit to investigational statement for clarity; intent is unchanged.</td>
</tr>
<tr>
<td>10/01/16</td>
<td>Interim Review, approved September 13, 2016. Policy updated with literature review through June 10, 2016; references 12-13, 47, and 49 added. Investigational statement added for previously untreated metastatic colorectal cancer. CPT codes 77776 and 77778 removed; deleted code as of 1/1/16 and reviewed by AIM, respectively.</td>
</tr>
<tr>
<td>10/01/17</td>
<td>Annual Review, approved September 5, 2017. No changes to policy statements. Policy updated with literature review through June 2017: references added 8-11, 15, 21, 31-32 and 56.</td>
</tr>
<tr>
<td>03/01/18</td>
<td>Coding update, removed CPT code 77399.</td>
</tr>
</tbody>
</table>

**Disclaimer:** This medical policy is a guide in evaluating the medical necessity of a particular service or treatment. The Company adopts policies after careful review of published peer-reviewed scientific literature, national guidelines and local standards of practice. Since medical technology is constantly changing, the Company reserves the right to review and update policies as appropriate. Member contracts differ in their benefits. Always consult the member benefit booklet or contact a member service representative to determine coverage for a specific medical service or supply. CPT codes, descriptions and materials are copyrighted by the American Medical Association (AMA). ©2018 Premera All Rights Reserved.

**Scope:** Medical policies are systematically developed guidelines that serve as a resource for Company staff when determining coverage for specific medical procedures, drugs or devices. Coverage for medical services is subject to the limits and conditions of the member benefit plan. Members and their providers should consult the member benefit booklet or contact a customer service representative to determine whether there are any benefit limitations applicable to this service or supply. This medical policy does not apply to Medicare Advantage.
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Premera Blue Cross complies with applicable Federal civil rights laws and does not discriminate on the basis of race, color, national origin, age, disability, or sex. Premera does not exclude people or treat them differently because of race, color, national origin, age, disability or sex.

Premera:
- Provides free aids and services to people with disabilities to communicate effectively with us, such as:
  - Qualified sign language interpreters
  - Written information in other formats (large print, audio, accessible electronic formats, other formats)
- Provides free language services to people whose primary language is not English, such as:
  - Qualified interpreters
  - Information written in other languages

If you need these services, contact the Civil Rights Coordinator.

If you believe that Premera has failed to provide these services or discriminated in another way on the basis of race, color, national origin, age, disability, or sex, you can file a grievance with:
- Civil Rights Coordinator - Complaints and Appeals
  PO Box 91102, Seattle, WA 98111
  Toll free 855-332-4535, Fax 425-918-5592, TTY 800-842-5357
  Email AppealsDepartmentInquiries@Premera.com

You can also file a grievance in person or by mail, fax, or email. If you need help filing a grievance, the Civil Rights Coordinator is available to help you.

You can also file a civil rights complaint with the U.S. Department of Health and Human Services, Office for Civil Rights, electronically through the Office for Civil Rights Complaint Portal, available at:
- https://ocrportal.hhs.gov/ocr/portal/lobby.jsf, or by mail or phone at:
  U.S. Department of Health and Human Services
  200 Independence Avenue SW, Room S09F, HHH Building
  Washington, D.C. 20201, 1-800-368-1019, 800-537-7697 (TDD)
  Complaint forms are available at
  https://ocrportal.hhs.gov/ocr/portal/lobby.jsf, or by mail or phone at:
  U.S. Department of Health and Human Services
  200 Independence Avenue SW, Room S09F, HHH Building
  Washington, D.C. 20201, 1-800-368-1019, 800-537-7697 (TDD)
  Email AppealsDepartmentInquiries@Premera.com

Getting Help in Other Languages

This Notice has Important Information. This notice may have important information about your application or coverage through Premera Blue Cross. There may be key dates in this notice. You may need to take action by certain deadlines to keep your health coverage or help with costs. You have the right to get this information and help in your language at no cost. Call 800-722-1471 (TTY: 800-842-5357).

Arabic (Amharic):
لا يوجد هذا الإشعار ملازمة. قد يكون هذا الإشعار معلوماتًا مهمة لمعرفة طبيك أو
العملية التي تزيد الصعوبة عليها من خلال
Premera Blue Cross. قد تكون هناك توجيهات
تمكّنك من النزاع. لا تتجاوز إجراء في توضيح
園يحتي على تنفيذك صحة العادة. في هذا الإشعار. وتنبيه
يمكنك أن تضغط أداة على هذه المعلومات والمساعدة
يمكنك أن تضغط أداة على هذه المعلومات.
800-722-1471 (TTY: 800-842-5357) للحصول على
800-722-1471 (TTY: 800-842-5357) للحصول على

Chinese (Chinese):
本通知有重要的讯息。本通知可能有關於您透過 Premera Blue Cross 提交的
申請或保險的重要訊息。本通知可能有重要日期。您可能需要在截止日期
之前採取行動。以保留您的健康保險或費用補貼。您有權利免費以您的母
語得到本訊息和幫助。請撥電話 800-722-1471 (TTY: 800-842-5357)。

Oromo (Cushite):
Beekisini kun odeefannoo barbaachissa qaba. Beekisini kun sagantaa
youkan karaa Premera Blue Cross tiin tajaalii keessaan ilaalchisee
odeefannoo barbaachissa qabaachuu danda’a. Guyyaawaan murtaa
sa’an beekisaa kana keessatti ilaala. Tarii kaffalldiinaa deeggarmuun
youkan tajaalii fayyaa keessanifi guyyaa dhumaar iratti wamii raawwatan
jiraachuu danda’a. Kaffalii iraa bilisa haala ta’an afaan keessanin
odeefannoo argabuun fi deeggara argachuu miga ni qabaaatu.
Lakkoofsa bilbilaa 800-722-1471 (TTY: 800-842-5357) ti bilbilaa.

Français (French):
Cet avis a d’importantes informations. Cet avis peut avoir d’importantes
informations sur votre demande ou la couverture par l’intermédiaire de
Premera Blue Cross. Le présent avis peut contenir des dates clés. Vous
devrez peut-être prendre des mesures par certains délais pour maintenir
votre couverture de santé ou d’aide avec les coûts. Vous avez le droit
d’obtenir cette information et de l’aider dans votre langue à aucun coût.
Appelez le 800-722-1471 (TTY: 800-842-5357).

Kreyòl ayisyen (Creole):
Avi sila a gen Enfòmasyon Enpòtan idann. Avi sila a kapab genyen
enfòmasyon enpòtan konsén aplan ayisyen w l oswa konsèn kouvèti
asirans lan atravé Premera Blue Cross. Kapab genyen dat ki en pòtan nan
avi sila a. Ou ka gen pou pouan kòk akson avan séten dat limit pou ka
kenbe kouvèt asirans sante w la ayisyen pou yo ka ede w avek desans yo.
Se dwa w pou resewwa enfòmasyon sa a ak asistans nan lang ou pale a,
san ou pa gen pou peye pou sa. Rate nan 800-722-1471
(TTY: 800-842-5357).

Deutsche (German):
Diese Benachrichtigung enthält wichtige Informationen. Diese
Benachrichtigung enthält unter Umständen wichtige Informationen
bezüglich Ihres Antrags auf Krankenversicherungsschutz durch Premera
Blue Cross. Suchen Sie nach eventuellen wichtigen Terminen in dieser
Benachrichtigung. Sie könnten bis zu bestimmten Stichtagen handeln
müssen, um Ihren Krankenversicherungsschutz oder Hilfe mit den Kosten
zu behalten. Sie haben das Recht, kostenlose Hilfe und Informationen
in Ihrer Sprache zu erhalten. Rufen Sie an unter 800-722-1471
(TTY: 800-842-5357).

Hmoob (Hmong):
Tsab ntaww tshaj xo no muaj cov ntsiab lus tseem ceeb. Tjaj zaun
tsab ntaww tshaj xo no muaj cov ntsiab lus tseem ceeb toog xoj daim ntaww
thov këb pab los yoj kog qhov këb pab cuam los ntaww Premera Blue Cross.
Tjaj zaun cov hvub tseem ceeb uas rau hauv daim ntaww no.
Tjaj zaun cov hj kou yuav tau ua qee yam uas peb kor xoj uas tsip pub
thau cov caij nyong uas teev tsig rau hauv daim ntaww no mas kou hj
yuav tau baiss këb pab cuam kou kho los yoj këb pab sox tej zaun xoj kou
kou yuav tau baiss këb pab cuam kou kho los yoj këb pab sox tej zaun kou kho
ntaww. Koi kou yuav kai comm lawv muab cov ntsiab lus uas tau muab sau
uas kou hom lus pub dawb rau kou. Hu rau 800-722-1471
(TTY: 800-842-5357).

Iloko (Ilocano):
Daytoy a Pakdaar ket naglaon iti Napateg nga Impomarsion. Daytoy a
pakdaar magbasa nga adda ket naglaon iti napateg nga impomarsion
maipanggepp iti aplikasyonyo wenn coverage babaen iti Premera Blue Cross.
Daytoy ket magbasa dagiti importante a petsa iti daytoy a pakdaar.
Magbasa nga adda rembang nga aramidenyo nga adda sangkay dagiti
partikular a naituding nga aldaw tiin tajaajila keessan ilaalchisee
Premera Blue Cross. Piyong daytoy a Pakdaar ket naglaon iti Napateg nga
Impomarsion. Adda karbenganyo a mangala iti daytoy nga impomarsion
ken tula nga bukodyo a pagasao nga awan ti bayaadanyo.
Tumawtii numero nga 800-722-1471 (TTY: 800-842-5357).

Italiano (Italian):
Questo avviso contiene informazioni importanti. Questo avviso può contenere
informazioni importanti sulla tua domanda o copertura attraverso Premera
Blue Cross. Potrebbero esserci date chiave in questo avviso. Potrebbe
essere necessario un tuo intervento entro una scadenza determinata per
consentirti di mantenere la tua copertura o sovvenzione. Hai il diritto
di ottenere queste informazioni e assistenza nella tua lingua gratuitamente.
Chiama 800-722-1471 (TTY: 800-842-5357).
Premera Blue Cross is providing important information.

Este Aviso contiene información importante.

Ваше страхование Premera Blue Cross содержит важную информацию.

Указаній у відомленні можуть бути інформаційні матеріали.

Положительное уведомление содержит важную информацию.

Предоставление информации о страховании Premera Blue Cross предоставляет важную информацию.

Ang Paunawa na ito ay naglalaman ng mahalagang impormasyon.

Ваше страхование Premera Blue Cross содержит важную информацию.

Ưu đ motivating message contains important information.

 우리의 보험사 Premera Blue Cross는 중요한 메시지를 제공합니다.