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><strong>Radioembolization</strong></td>
<td><strong>Radioembolization may be considered medically necessary in the following situations:</strong></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><strong>OR</strong></td>
</tr>
<tr>
<td></td>
<td>• Treatment of primary hepatocellular carcinoma as a bridge to liver transplantation</td>
</tr>
<tr>
<td></td>
<td><strong>OR</strong></td>
</tr>
<tr>
<td></td>
<td>• Treatment of primary intrahepatic cholangiocarcinoma in patients with unresectable tumors</td>
</tr>
<tr>
<td></td>
<td><strong>OR</strong></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><strong>OR</strong></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)</td>
</tr>
<tr>
<td></td>
<td><strong>AND</strong></td>
</tr>
<tr>
<td></td>
<td>o That are progressive and unresectable in patients with liver dominant disease</td>
</tr>
<tr>
<td></td>
<td><strong>AND</strong></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><strong>Radioembolization</strong></td>
<td><strong>Radioembolization is considered investigational for all other hepatic metastases except as noted in the Medical Necessity section above.</strong></td>
</tr>
</tbody>
</table>
Radioembolization is considered investigational for all other indications not described in the Medical Necessity section above.

### 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)
    - AND
  - That are progressive and unresectable in patients with liver dominant disease
    - AND
- 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>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>37243</td>
<td>Transcatheter therapy, embolization, any method, radiological supervision and interpretation</td>
</tr>
<tr>
<td>75894</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.


**Evidence Review**
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-floxuridine chemotherapy by hepatic arterial infusion to treat unresectable hepatic metastases from colorectal cancer. In contrast, TheraSphere’s glass sphere was approved under a humanitarian device exemption for use as monotherapy to treat unresectable hepatocellular carcinoma. In 2007, this humanitarian device exemption was expanded to include 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>
<thead>
<tr>
<th>NCT No.</th>
<th>Trial Name</th>
<th>Planned Enrollment</th>
<th>Completion Date</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hepatocellular carcinoma</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Ongoing</strong></td>
<td></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 LocallyAdvanced Hepatocellular Carcinoma (SIRveNIB)</td>
<td>360</td>
<td>Jul 2018 (ongoing)</td>
</tr>
<tr>
<td>NCT01126645a</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>NCT01556490a</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><strong>Unpublished</strong></td>
<td></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>
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<tr>
<td><strong>Metastatic colorectal cancer</strong></td>
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<td></td>
<td></td>
</tr>
<tr>
<td><strong>Ongoing</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NCT01483027a</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>NCT01721954a</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>
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</tr>
<tr>
<td>ISRCTN83867919</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>
</tbody>
</table>

**Cholangiocarcinoma**

<table>
<thead>
<tr>
<th>NCT No.</th>
<th>Trial Name</th>
<th>Planned Enrollment</th>
<th>Completion Date</th>
</tr>
</thead>
<tbody>
<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.²²

**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.⁷⁴

**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.”⁵⁵

**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.


### 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>
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<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. Clinical Trials and NCCN Guidelines updated.</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>
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<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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  - 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 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 509F, HHH Building
Washington, D.C. 20201, 1-800-368-1019, 800-537-7697 (TDD)

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).

Oromoo (Cushite):

Français (French):

Kreyòl ayisyen (Creole):
Avi sila a gen Enfômsasyon Enpòtan la. Avi sila a kapab genyen enfômsasyon enpòtan konsénan aplikasyon w lan oswa konsénan kouvèti asirans lan atravé Premera Blue Cross. Kapab genyen dat ki enpòtan nan avi sila a. Ou ka gan pou pran kék aksyon avan sèten dat limit pou ka kennbe kouvèti asirans sante w la oswa pou yo ka ede w avèk depans yo. Se dwa w pou resewva enfômsasyon sa a ak asistans nan lang ou pale a, san ou pa gan pou peye pou sa. Rate nan 800-722-1471 (TTY: 800-842-5357).

Deutsche (German):

Hmoob (Hmong):
Tsab ntawv tshaj xo no muaj cov ntshiab lus tseem ceeb. Tej zaum tsab ntawv tshaj xo no muaj cov ntsiab lus tseem ceeb bjoq koj dain tntawv thov kev pab los yoy kyo chov kev pab cuam los ntawv Premera Blue Cross. Tej zaum tuaj cov hnb tseem ceeb uas sau rau hauv daim ntawv no. Tej zaum koj kuj yuav tau uu qeem yam uu peb koj uu taip lib dhuav cov caij nyoy uas teev taip rau hauv daim ntawv no mas koj thiay yuav taui bas kev pab cuam kho hmo los yoy kev pab tem tej nji kho mo ntawv. Koj muaj cai kom laww muab cov ntshiab lus no uas tau muab sau uu koj hom lus pub dawb rau koj. Hu rau 800-722-1471 (TTY: 800-842-5357).

Ilokano (Ilocano):
Daytoy a Pakdaar ket naglaon iti Napateg nga Impomrsion. Daytoy a pakdaar mabalini nga adda ket naglaon iti napateg nga impomrsion maihanggip iti aplikasyonu yowo coverage babaen iti Premera Blue Cross. Daytoy ket mabalini dagiti importante a pelta iti daytoy a pakdaar. Mabalini nga adda rumbeng nga aramidenyu nga addang sakbay dagiti paticular a naituding nga adda taip tapo mapagatalndeyo ti coverage ti salan-atyo yowo tulong kados gastos. Adda karbengayo a mangala iti daytoy nga impomrsion ken tulong iti bokydo a pagasasng nga awan ti bayadanyo. Tumawag iti numero nga 800-722-1471 (TTY: 800-842-5357).

Italiano (Italian):

中文 (Chinese):
本通知有重要的訊息。本通知可能有關於您透過Premera Blue Cross提交的申請或保險的相關重要訊息，本通知可能有重要的日期。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。請接電話800-722-1471 (TTY: 800-842-5357)。
한국어 (Korean):

본 통지서에는 중요한 정보가 들어 있습니다. 즉 이 통지서는 귀하의 신청에
관하여 그리고 Premera Blue Cross를 통해 커버리지에 관한 정보를
포함하고 있습니다. 본 통지서에는 핵심이 되는 날짜들이 있을 수 있습니다.
귀하의 귀하의 신청 커버리지를 계속 유지하거나 바꾸려면 철저히 알아야
함께 설정한 마감까지 조치를 취해야 할 필요가 있을 수 있습니다.
귀하의 이러한 정보와 더욱 귀하의 안녕을 위해 부담없이 읽을 수 있는
권리가 있습니다. 800-722-1471 (TTY: 800-842-5357)로 전화하시십시오.

Română (Romanian):
Premiza notificare conține informații importante. Această notificare poate conține informații importante privind cererea sau acoperirea asigurării
dumneavoastră de sănătate prin Premera Blue Cross. Po exista date cheie
în această notificare. Este posibil să fie nevoie să acționați până la anumite
terme care limită pentru a vă menține acoperirea asigurării de sănătate sau
asistenta prívitoare la costuri. Aveți dreptul de a obține gratuit aceste
informații și ajutor în limba dumneavoastră. Sunăți la 800-722-1471
(TTY: 800-842-5357).

Русский (Russian):
Настоящее уведомление содержит важную информацию. Это
уведомление может содержать важную информацию о вашем
заявлении или страховом покрытии через Premera Blue Cross. В
настоящем уведомлении могут быть ключевые даты. Вам,
возможно, потребуется принять меры к определенным предельным
срокам для сохранения страховочного покрытия или помощи с
расходами. Вы имеете право на бесплатное получение этой
информации и помощь на вашем языке. Звоните по телефону 800-722-1471
(TTY: 800-842-5357).

Español (Spanish):
Este Aviso contiene información importante. Es posible que este aviso
contenga información importante acerca de su solicitud o cobertura a
través de Premera Blue Cross. Es posible que haya fechas claves en este
aviso. Es posible que deba tomar alguna medida antes de determinadas
fechas para mantener su cobertura médica o ayuda con los costos. Usted
tiene derecho a recibir esta información y ayuda en su idioma sin costo

Tagalog (Tagalog):
Ang Paunawa na ito ay naglalaman ng mahalagang impormasyon. Ang
paunawa na ito ay naglalaman ng mahalagang impormasyon tungkol sa iyong aplikasyon o pagsakop sa pamamagitan ng Premera Blue Cross.
Maaaring may mga mahalagang petsa dito sa paunawa. Maaring paunawa na ito ay maaaring naglalaman ng mahalagang impormasyon at tulong sa iyong wika ng walang gastos. Tumawag sa 800-722-1471 (TTY: 800-842-5357).

ไทย (Thai):
ประกาศนี้มีข้อมูลสําคัญและอาจมีกําหนดการในประกาศนี้
ที่จะสําหรับการประกันสุขภาพของคุณหรือการช่วยเหลือที่
คุณมีซึ่งคุณมีสิทธิที่จะได้รับข้อมูลและการช่วยเหลือในภาษาต่างๆที่
คุณต้องการ 800-722-1471 (TTY: 800-842-5357).

Український (Ukrainian):
Це повідомлення містить важливу інформацію. Це повідомлення
може містити важливу інформацію про Ваше звернення щодо
страховального покриття через Premera Blue Cross. Зверніть увагу на
ключові дати, які можуть бути вказані у цьому повідомленні. Існує
імовірність того, що Вам треба буде здійснити певні кроки у конкретні
кінцеві строки для того, щоб зберегти Ваше медичне страхування або
отримати фінансову допомогу. У Вас є право на отримання цієї
інформації та допомоги безкоштовно на Вашій рідній мові. Дозвоніть
за номером телефону 800-722-1471 (TTY: 800-842-5357).