Introduction

Embolization is 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>
</table>
| Radioembolization | **Radioembolization may be considered medically necessary in the following situations:**  
  - Treatment of primary hepatocellular carcinoma that is unresectable and limited to the liver (size of 3cm or larger, and patient with good performance status)  
  OR  
  - Treatment of primary hepatocellular carcinoma as a bridge to liver transplantation  
  OR  
  - Treatment of primary intrahepatic cholangiocarcinoma in patients with unresectable tumors  
  OR  
  - 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)  
  OR  
  - Treatment of unresectable hepatic metastases  
    o From breast, colorectal or melanoma (ocular or cutaneous)  
    AND  
    o That are progressive and unresectable in patients with liver dominant disease  
    AND  
    o That are refractory to chemotherapy or are not candidates for chemotherapy                                                                                                                                                                            |

<table>
<thead>
<tr>
<th>Service</th>
<th>Investigational</th>
</tr>
</thead>
<tbody>
<tr>
<td>Radioembolization</td>
<td><strong>Radioembolization is considered investigational for all other hepatic metastases except as noted in the Medical Necessity section above.</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Radioembolization is considered investigational for all other</strong></td>
</tr>
</tbody>
</table>
Service
Investigational indications not described in the Medical Necessity section above.

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>77399</td>
<td>Unlisted procedure, medical radiation physics, dosimetry and treatment devices, and special services.</td>
</tr>
<tr>
<td>79445</td>
<td>Radiopharmaceutical therapy, by intra-arterial particulate administration</td>
</tr>
<tr>
<td>HCPCS</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

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.
Definition of Terms

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

**Eastern Cooperative Oncology Group (ECOG):** The ECOG performance status is used to assess the patient’s disease progression and how the disease impacts the patient’s activities of daily living (ADLs). [http://www.ecog.org/](http://www.ecog.org/)

Evidence Review

Background

**Radioembolization**

The use of external beam radiotherapy (EBRT) and the application of more advanced radiotherapy approaches (e.g., intensity-modulated radiotherapy [IMRT]) may be of limited use in patients with diffuse, multiple 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 [RFA]), particle and wave physics (microwave or laser ablation), or arterial embolization therapy including chemoembolization, bland embolization, or RE.

RE, referred to as selective internal radiation therapy or “SIRT in older literature, is the intra-arterial delivery of small beads (microspheres) impregnated with yttrium-90 via the hepatic artery. The microspheres, which become permanently embedded, are delivered to tumor preferentially to normal liver, as 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 RE are initially examined by hepatic angiogram to identify and map the hepatic arterial system, and at that time, a mixture of albumin particles is delivered via the hepatic artery to simulate microspheres. After, single-photon emission computed tomography (SPECT) gamma imaging is
used to detect possible shunting of the albumin particles into gastrointestinal or pulmonary vasculature.

Currently two commercial forms of yttrium-90 microspheres are available: a glass sphere, TheraSphere® (MDS Nordion Inc., Ontario, Canada) and a resin sphere, SIR-Spheres® (Sirtex Medical Limited; Lake Forest, IL). Noncommercial forms are mostly used outside the U.S. 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. Note also that the U.S. Food and Drug Administration (FDA) granted premarket approval of SIR-Spheres® for use in combination with 5-fluorouridine (5-FUDR) chemotherapy by hepatic arterial infusion (HAI) to treat unresectable hepatic metastases from colorectal cancer (CRC). In contrast, TheraSphere® was approved by humanitarian device exemption (HDE) for use as monotherapy to treat unresectable hepatocellular carcinoma (HCC). In January 2007, this HDE was expanded to include patients with HCC 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.

**Summary of Evidence**

For individuals who have hepatocellular carcinoma (HCC) who receive radioembolization (RE) or RE with liver transplant, the evidence includes primarily retrospective and prospective observational studies, with limited evidence from randomized controlled trials (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 HCC, including transarterial chemoembolization (TACE) and TACE 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 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. 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 1 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 shown that RE has similar outcomes 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 (CRC) 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, along with 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 breast cancer or melanoma 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. The evidence is sufficient to determine qualitatively that the technology results in a meaningful improvement in net 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><strong>Hepatocellular carcinoma</strong></td>
<td></td>
<td></td>
<td></td>
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<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>Apr 2017 (ongoing)</td>
</tr>
<tr>
<td>NCT01126645*</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</td>
</tr>
<tr>
<td>NCT01556490*</td>
<td>A Phase III Clinical Trial of Intra-arterial TheraSphere® in the Treatment of Patients With Unresectable Hepatocellular Carcinoma (HCC)</td>
<td>390</td>
<td>Oct 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><strong>Metastatic colorectal cancer</strong></td>
<td></td>
<td></td>
<td></td>
</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</td>
</tr>
<tr>
<td>NCT00724503*</td>
<td>Randomised Comparative Study of Folfox6m Plus SirSpheres® 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</td>
</tr>
<tr>
<td>NCT01483027*</td>
<td>A Phase III Clinical Trial Evaluating TheraSphere® in</td>
<td>-340</td>
<td>Feb 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></td>
<td>Patients With Metastatic Colorectal Carcinoma of the Liver Who Have Failed First Line Chemotherapy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NCT01721954</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>
</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>Apr 2018</td>
</tr>
</tbody>
</table>

NCT: national clinical trial.

* 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 to address the use of RE for liver metastases from tumors other than CRC and neuroendocrine tumors and for primary hepatic cholangiocarcinoma. There was consensus supporting the use of 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 expressed support for 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 for July 2010 and again for March 2011 to specifically readdress metastases from CRC and other metastatic tumors besides neuroendocrine tumors. 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 HCC, as a bridge to liver transplant in HCC, and in neuroendocrine tumors. There was also strong support for use of RE in patients with liver metastases from CRCs 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.2.2017) for the treatment of primary HCC mention the use of arterially directed therapies, including transarterial bland embolization, transarterial chemoembolization (TACE), and drug-eluting beads TACE, and RE
with yttrium-90 microspheres for specific categories of patients. The guidelines did not distinguish between the different arterially directed therapies, and all statements were category 2A recommendations.

**Primary Cholangiocarcinoma**

NCCN guidelines for the treatment of primary intrahepatic cholangiocarcinoma lists locoregional therapy as an option for unresectable or metastatic disease, or for residual local disease after resection (category 2B recommendation), although primary treatment is fluoropyrimidine-based or gemcitabine-based chemotherapy (category 1 recommendation). The guidelines note that no RCTs of radiofrequency ablation, TACE, or RE exist.

**Metastatic Neuroendocrine Tumors**

NCCN guidelines (v.2.2017) for the treatment of metastatic neuroendocrine tumors give a category 2B recommendation for hepatic regional therapy (arterial embolization, chemoembolization, RE) in certain clinical situations.

**Metastatic Colon Cancer**

NCCN guidelines (v.2.2017) for the treatment of colon cancer state: “The use of arterial-directed therapies 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.”

**Metastatic Breast Cancer**

NCCN guidelines (v.2.2017) for the treatment of breast cancer do not address the use of RE in the treatment of metastatic breast cancer.

**Metastatic Melanoma**

NCCN guidelines (v.2.2017) for the treatment of melanoma do not address the use of RE in the treatment of metastatic melanoma.
**RE Brachytherapy Oncology Consortium**

The Radioembolization Brachytherapy Oncology Consortium was convened as independent group of experts in interventional radiology, radiation oncology, nuclear medicine, medical oncology, and surgical oncology. In 2007, the panel made 14 recommendations with level 2A evidence (panel consensus with low-level evidence). Some of the consortium’s recommendations about specific indications for RE therapy were as follows:

- The panel believes that there is sufficient evidence to support the safety and effectiveness of yttrium-90 (Y90) microsphere therapy in selected patients.

- Candidates for radioembolization are patients with unresectable primary or metastatic hepatic disease with liver-dominant tumor burden and a life expectancy greater than 3 months.

- Absolute contraindications to Y90 microsphere treatment include pretreatment 99mTc macroaggregated albumin (MAA) scan demonstrating the potential of 30 Gy radiation exposure to the lung or flow to the gastrointestinal tract that cannot be corrected by catheter techniques.

- Relative contraindications to Y90 microsphere treatment include limited hepatic reserve, irreversibly elevated bilirubin levels, compromised portal vein (unless selective or superselective radioembolization can be performed), and prior radiation therapy involving the liver.

**Medicare National Coverage**

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 HCC who can have placement of appropriately positioned hepatic arterial catheters (H980006).

In 2002, SIR-Spheres® (Sirtex Medical, Lake Forest, IL), 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


### 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 statement. References added. Reviewed and recommended by OAP August 2009.</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>Date</td>
<td>Comments</td>
</tr>
<tr>
<td>------------</td>
<td>-------------------------------------------------------------------------------------------------------------------------------------------</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>
</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>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 Update, 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>Date</td>
<td>Comments</td>
</tr>
<tr>
<td>-----------</td>
<td>---------------------------------------------------------------------------</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>
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</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). ©2017 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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  • 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

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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.

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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 ensfomyas enpòtan lidann. Avi sila a kapab genyen enfomays enpòtan konsènplan aplikasyon w lan oswa konsènplan kouvètli asirans lan atravé Premera Blue Cross. Kapab genyen dat ki enpòtan nan avi sila a. Ou ka gen pou pran kék aksyon avan sèten dat limit pou ka Jenbe kouvètli asirans sante w la oswa pou yo ka ede w avèk depans yo. Se dwa w pou resewwa enfomaysan 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):

Hmoob (Hmong):

Ilokano (Ilocano):
Daytoy a Pakdaa ket naglaon iti Napateg nga Impormasion. Daytoy a pakdaa mabalin nga adda ket naglaon iti napateg nga impormasion maipanggep iti aplikasyon yangen coverage babaen iti Premera Blue Cross. Daytoy ket mabalin dagiti importante a petai iti daytoy a pakdaar. Mabalin nga adda rumbeng nga aramidenyo nga addang sakkay dagiti particular a naituding nga aldaw tapno mapagtalaineyo ti coverage ti salun-atyo wenno tulong kadagiti gastos. Adda karbenganyo a mangala iti daytoy nga impormasion ken tulong iti bukodyo a pagasao nga awan ti bayadanyo. Tumawag ti 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 提交的申請或保費的重要訊息。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)。