Medical Coverage Policy | Radioembolization for Primary and Metastatic Tumors of the Liver

EFFECTIVE DATE: 10|06|2009
POLICY LAST UPDATED: 11|03|2015

OVERVIEW

Radioembolization (RE), referred to as selective internal radiation therapy or "SIRT" in older literature has been developed for the treatment of unresectable primary and secondary liver cancer.

MEDICAL CRITERIA

Radioembolization may be considered **medically necessary** as a treatment for any of the following:

- Primary hepatocellular carcinoma that is unresectable and limited to the liver.
- In primary hepatocellular carcinoma as a bridge to liver transplantation.
- Hepatic metastases from neuroendocrine tumors (carcinoid and noncarcinoid) with diffuse and symptomatic disease when systemic therapy has failed to control symptoms.
- Unresectable hepatic metastases from colorectal carcinoma melanoma (ocular or cutaneous), or breast cancer that are both progressive and diffuse, in patients with liver-dominant disease who are refractory to chemotherapy or are not candidates for chemotherapy.
- Primary intrahepatic cholangiocarcinoma in patients with unresectable tumors.

PRIOR AUTHORIZATION

Prior authorization is required for BlueCHiP for Medicare members and recommended for Commercial products.

POLICY STATEMENT

BlueCHiP for Medicare and Commercial Products

Radioembolization is considered medically necessary when the medical criteria have been met.
Radioembolization is considered not medically necessary for all other indications.

COVERAGE

Benefits may vary between groups and contracts. Please refer to the appropriate Benefit Booklet, Evidence of Coverage, or Subscriber Agreement for the applicable radiology benefits.

BACKGROUND

The use of external beam radiotherapy and the application of more advanced radiotherapy approaches (e.g., intensity-modulated radiotherapy) 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.

Radioembolization (RE), referred to as selective internal radiation therapy (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. At that time, a mixture of technetium 99-labelled albumin particles is delivered via the hepatic artery to simulate microspheres. Single photon emission computed tomography imaging 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® (manufactured by Nordion, Ontario, Canada, under license by BTG International) and a resin sphere, SIR-Spheres® (Sirtex Medical, Lake Forest, IL). 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 (i.e., 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. FDA granted premarket approval (PMA) of SIR-Spheres for use in combination with 5-floxuridine chemotherapy by hepatic arterial infusion (HAI) to treat unresectable hepatic metastases from 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 noncommercial) products.

Most patients with HCC present with unresectable disease, and treatment options are limited secondary to the chemoresistance of HCC and the intolerance of normal liver parenchyma to tumoricidal radiation doses. Results of 2 (RCTs have shown a survival benefit for TACE therapy compared with supportive care in patients with unresectable HCC.1,2 In 1 study, patients were randomly assigned to TACE, transarterial embolization (TAE), or supportive care. One-year survival rates for TACE, TAE, and supportive care were 82%, 75%, and 63%, respectively, and 2-year survival rates were 63%, 50%, and 27%, respectively. Targeted therapies have been investigated for HCC. For example, sorafenib was associated with improved OS in a randomized phase 3 trial with 602 patients.

Unresectable Intrahepatic Cholangiocarcinoma
Cholangiocarcinomas are tumors that arise from the epithelium of the bile duct and are separated into intrahepatic and extrahepatic types. Intrahepatic cholangiocarcinomas appear in the hepatic parenchyma and are also known as peripheral cholangiocarcinomas. Resection is the only treatment with the potential for cure, and 5-year survival rates have been in the range of 20% to 43 %. Patients with unresectable disease may select among fluoropyrimidine-based or gemcitabine-based chemotherapy, fluoropyridimine chemoradiation or best supportive care.

Unresectable Metastatic CRC
About 50% to 60% of patients with colorectal cancer (CRC) will develop metastases, either synchronously or metachronously. Select patients with liver-only metastases that are surgically resectable can be cured, with some reports showing 5-year survival rates exceeding 50%. Emphasis on treating these patients with potentially curable disease is on complete removal of all tumor with negative surgical margins. Most patients diagnosed with metastatic colorectal disease are initially classified as having unresectable disease. In patients with metastatic disease limited to the liver, preoperative chemotherapy is sometimes used in an attempt to downsize the metastases to convert the metastatic lesions to a resectable status (conversion chemotherapy).

In patients with unresectable disease that cannot be converted to resectable disease, the primary treatment goal is palliative, with survival benefit shown with both second- and third-line systemic chemotherapy. Recent

advances in chemotherapy, including oxaliplatin, irinotecan, and targeted antibodies like cetuximab, have doubled the median survival in this population from less than 1 year to more than 2 years. Palliative chemotherapy by combined systemic and hepatic arterial infusion (HAI) may increase disease-free intervals for patients with unresectable hepatic metastases from colorectal cancer.

Radiofrequency ablation (RFA) has been shown to be inferior to resection in local recurrence rates and 5-year overall survival (OS) and is generally reserved for patients with potentially resectable disease that cannot be completely resected due to patient comorbidities, location of metastases (i.e., adjacent to a major vessel), or an estimate of inadequate liver reserve following resection. RFA is generally recommended to be used with the goal of complete resection with curative intent. The role of local (liver-directed) therapy (including RE, chemoembolization, and conformal radiation therapy) in debulking unresectable metastatic disease remains controversial.

Unresectable Metastatic Neuroendocrine Tumors

Neuroendocrine tumors are an uncommon, heterogeneous group of mostly slow-growing, hormone-secreting malignancies, with an average patient age of 60 years. Primary neuroendocrine tumors vary in location, but most are either carcinoids (which most commonly arise in the mid gut) or pancreatic islet cells. Carcinoid tumors, particularly if they metastasize to the liver, can result in excessive vasoactive amine secretion including serotonin and are commonly associated with the carcinoid syndrome (diarrhea, flush, bronchoconstriction, right valvular heart failure).

Although they are considered to be indolent tumors, at the time of diagnosis, up to 75% of patients have liver metastases, and with metastases to the liver, 5-year survival rates are less than 20%. Surgical resection of the metastases is considered the only curative option; however, less than 10% of patients are eligible for resection, as most patients have diffuse, multiple lesions.

Conventional therapy is largely considered to be palliative supportive care to control, eradicate, or debulk hepatic metastases, often to palliate carcinoid syndrome or local pain from liver capsular stretching. Therapies for unresectable metastatic neuroendocrine tumors include medical (somatostatin analogs like octreotide), systemic chemotherapy, ablation (radiofrequency or cryotherapy), TAE or TACE, or radiation. Although patients often achieve symptom relief with octreotide, the disease eventually becomes refractory, with a median duration of symptom relief of approximately 13 months, with no known effect on survival. Systemic chemotherapy for these tumors has shown modest response rates of limited duration, is better for pancreatic neuroendocrine tumors compared with carcinoids, and is frequently associated with significant toxicity. Chemoembolization has shown response rates of nearly 80%, but the effect is of short duration and a survival benefit has not been demonstrated.

Miscellaneous Metastatic Tumors

Small case reports have been published on the use of RE in many other types of cancer with hepatic metastases, including breast, melanoma, head, and neck (including parotid gland), pancreaticobiliary, anal, thymic, thyroid, endometrial, lung, kidney, gastric, small bowel, esophageal, ovarian, cervical, prostatic, bladder, and for sarcoma and lymphoma.

CODING

BlueCHiP for Medicare and Commercial Products

There are no specific CPT codes describing radioembolization therapy. Providers should file using the unlisted CPT code:

77399

RELATED POLICIES

None

PUBLISHED

Provider Update, January 2016
Provider Update, February 2015
Provider Update, January 2014
Provider Update, December 2012
Provider Update, March 2011

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