MEDICAL POLICY

MEDICAL POLICY DETAILS	
Medical Policy Title	**SELECTIVE INTERNAL RADIATION THERAPY (SIRT) FOR HEPATIC TUMORS**
Policy Number	**7.01.69**
Category	**Technology Assessment**
Effective Date	**12/15/05**
Revised Date	**12/21/06, 12/20/07, 07/17/08, 08/20/09, 06/17/10, 06/16/11, 08/18/11, 08/16/12, 07/18/13, 06/19/14, 05/28/15, 04/21/16, 06/15/17, 08/16/18, 07/18/19**
Product Disclaimer	• *If a product excludes coverage for a service, it is not covered, and medical policy criteria do not apply.* • *If a commercial product (including an Essential Plan product) or a Medicaid product covers a specific service, medical policy criteria apply to the benefit.* • *If a Medicare product covers a specific service, and there is no national or local Medicare coverage decision for the service, medical policy criteria apply to the benefit.*

POLICY STATEMENT

I. Based upon our criteria and assessment of peer-reviewed literature, selective internal radiation therapy (SIRT) has been medically proven to be effective and is considered **medically appropriate** as a treatment for:
   A. Primary hepatocellular carcinoma that is unresectable and limited to the liver (See Policy Guidelines); or
   B. Hepatic metastases from neuroendocrine tumors with diffuse and symptomatic disease when systemic therapy has failed to control symptoms; or
   C. As a bridge to transplant for patients with hepatocellular carcinoma who meet liver transplant criteria and are waiting liver transplantation; or
   D. Unresectable hepatic metastases from colorectal carcinoma in patients with liver-dominant disease who are refractory to chemotherapy or who are not candidates for chemotherapy, or other systemic therapies (see Policy Guidelines).

II. Based upon our criteria and assessment of peer-reviewed literature, selective internal radiation therapy (SIRT) has not been medically proven to be effective and is considered **investigational** as a treatment for all other metastatic or primary tumors of the liver.

Refer to Corporate Medical Policy #7.01.03 regarding Cryosurgical Tumor Ablation.

Refer to Corporate Medical Policy # 7.01.78 regarding Peptide Receptor Radionuclide Therapy.

Refer to Corporate Medical Policy #7.02.32 regarding Radiofrequency Tumor Ablation.

Refer to Corporate Medical Policy #11.01.10 regarding Clinical Trials.

Refer to Corporate Medical Policy # 11.01.03 regarding Experimental and Investigational Services.

POLICY GUIDELINES

I. In general, SIRT is used for unresectable HCC that is greater than 3 cm.

II. SIRT should be reserved for patients with adequate functional status (ECOG 0-2), adequate liver function and reserve, Child Pugh score A or B, and liver-dominant metastases. Patients should also have a life expectancy of greater than 3 months.

III. The Federal Employee Health Benefit Program (FEHBP/FEP) requires that procedures, devices or laboratory tests approved by the U.S. Food and Drug Administration (FDA) may not be considered investigational and thus these procedures, devices or laboratory tests may be assessed only on the basis of their medical necessity.

DESCRIPTION

Hepatic tumors can arise either as primary liver cancer or by metastasis to the liver from other tissues or organs. At present, surgical resection with tumor-free margins or liver transplantation are the only potentially curative treatments for hepatic cancer. Unfortunately, most hepatic tumors are not amenable to resection or transplantation at diagnosis, due either to their anatomic location, size, the number of lesions, concurrent nonmalignant liver disease, or insufficient hepatic reserve. Various minimally invasive ablative techniques have been investigated that seek to cure or palliate unresectable hepatic tumors by improving loco-regional control. Examples of these techniques include cryosurgical ablation, radiofrequency ablation and chemoembolization.

Selective internal radiation therapy (SIRT), another minimally invasive ablative method, relies on targeted delivery of small beads (microspheres) impregnated with yttrium-90 (90Y). Yttrium-90 is a beta emitter with a short half-life of 64.2 hours (2.67 days) that limits radiation hazard, while providing a clinically appropriate dose of radiotherapy. In SIRT, the radioactive material is directed into the left, right or common hepatic artery via a percutaneous (femoral or gastroduodenal) arterial catheter or a porta-cath. This allows the delivery of a concentrated dosage of radiation directly into the tumor bed, while conserving the normal liver tissue that surrounds the tumor. The size of the microspheres actually causes them to become entrapped within the tumor vasculature and retained within the tumor. The total radioactivity required by a patient is dependent on the extent and presentation of the tumor tissue. SIRT can usually be performed in an outpatient setting, as there is no radiation exposure to others once the microspheres have been infused.

SIRT has been investigated as a promising new technique due to several factors: 1) the liver parenchyma is sensitive to radiation; 2) the hepatic circulation is uniquely organized, whereby the normal liver derives 75% of its of its blood supply from the portal vein and malignant tumors in the liver derive nearly 100% of their blood supply from the hepatic artery; and 3) 90Y is a pure beta emitter with a relatively limited effective range and short half-life that helps focus the radiation and minimize its spread.

RATIONALE

There are currently 2 types of Yttrium microspheres (glass and resin) that have been approved by the U.S. Food and Drug Administration (FDA): TheraSpheres® (Theragenics; Atlanta, GA) and SIR-Spheres® (Sirtex Medical Limited; Lake Forest, IL). The U.S. Food and Drug Administration (FDA) granted premarket approval of SIR-Spheres® in 2002 for use in combination with 5-floxuridine (5-FUDR) chemotherapy by HAI to treat unresectable hepatic metastases from colorectal cancer. In contrast, TheraSpheres® were approved by humanitarian device exemption (HDE) in 1999 for use as monotherapy to treat unresectable HCC. In January 2007, the HDE for TheraSpheres® was expanded to include patients with hepatocellular carcinoma who have partial or branch portal vein thrombosis.

HCC:
Studies have demonstrated that SIRT/radioembolization is comparable to chemoembolization (which is considered to be therapy of choice) for patients with unresectable HCC in terms of tumor response and overall survival (e.g., Kulil, et al. 2008; Salem, et al, 2010; Carr, et al. 2010; Hilgard, et al. 2010; Edeline, et al. 2016; Ettore, et al. 2017). Disadvantages of chemoembolization include the necessity of multiple treatment sessions and hospitalization, its contraindication in patients with portal vein thrombosis, and its poorer tolerance by patients.

Neuroendocrine:
While studies investigating SIRT for neuroendocrine tumors have limitations such as heterogeneous patient populations, studies do report relief of symptoms from carcinoid syndrome in a proportion of patients. Surgical debulking of liver metastases has shown palliation of hormonal symptoms; debulking by radioembolization may lead to symptom relief in some patients (e.g., Sato, et al. 2008; Kennedy, et al. 2009; Cao, et al. 2010; Cramer, et al. 2016).

Metastatic colorectal cancer:
A major cause of morbidity and mortality in patients with colorectal disease metastatic to the liver is liver failure, as this disease tends to progress to diffuse, liver-dominant involvement. Therefore, the use of SIRT/radioembolization to decrease tumor bulk and/or halt the time to tumor progression and liver failure, may lead to prolonged progression free and overall survival in patients with no other treatment options (e.g., those with chemotherapy refractory liver-dominant

disease). Other uses include palliation of symptoms from tumor bulk (e.g., Kennedy, et al, 2009, 2016; Mulcahy, et al. 2009; Cianni, et al. 2010; Hendlisz, et al. 2010; Damm, et al. 2016; Jakobs, et al 2017).

Miscellaneous:
There is insufficient evidence to support the use of SIRT for liver metastases from other sites such as breast, pancreatic and cholangiocarcinoma. The outcome data from literature are inadequate at this time to draw positive conclusions related to the safety and efficacy of SIRT for these patient populations (e.g., Atassi, et al. 2008, Jakobs, et al. 2008, Saxena, et al. 2010, Cianni, et al. 2013).

CODES

- *Eligibility for reimbursement is based upon the benefits set forth in the member's subscriber contract.*
- *CODES MAY NOT BE COVERED UNDER ALL CIRCUMSTANCES. PLEASE READ THE POLICY AND GUIDELINES STATEMENTS CAREFULLY.*
- *Codes may not be all inclusive as the AMA and CMS code updates may occur more frequently than policy updates.*

CPT Codes

Code	Description
No CPT codes specific to SIRT, but the following could be used:	
37243	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 infraction
75894	Transcatheter therapy, embolization, any method, radiological supervision and interpretation
79445	Radiopharmaceutical therapy, by intra-arterial particulate administration

HCPCS Codes

Code	Description
C2616	Brachytherapy source, nonstranded, yttrium-90, per source
S2095	Transcatheter occlusion or embolization for tumor obstruction, percutaneous, any method, using yttrium-90 microspheres

ICD10 Codes

Code	Description
C18.0	Malignant neoplasm of cecum
C18.1	Malignant neoplasm of appendix
C18.2	Malignant neoplasm of ascending colon
C18.3	Malignant neoplasm of hepatic flexure
C18.4	Malignant neoplasm of transverse colon
C18.5	Malignant neoplasm of splenic flexure
C18.6	Malignant neoplasm of descending colon
C18.7	Malignant neoplasm of sigmoid colon
C18.8	Malignant neoplasm of overlapping sites of colon

Code	Description
C18.9	Malignant neoplasm of colon, unspecified
C22.0	Liver cell carcinoma
C22.1	Intrahepatic bile duct carcinoma
C22.2	Hepatoblastoma
C22.3	Angiosarcoma of liver
C22.4	Other sarcomas of liver
C22.7	Other specified carcinomas of liver
C22.8	Malignant neoplasm of liver, primary, unspecified as to type
C22.9	Malignant neoplasm of liver, not specified as primary or secondary
C78.7	Secondary malignant neoplasm of liver and intrahepatic bile duct

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*Key Article

KEY WORDS

Radioembolization, Sir-Spheres, Theraspheres, Transarterial Radioembolization (TARE)

CMS COVERAGE FOR MEDICARE PRODUCT MEMBERS

Based on our review, there is no specific national or regional coverage determination for selective internal radiation therapy.