MEDICAL POLICY

MEDICAL POLICY DETAILS	
Medical Policy Title	**Selective Internal Radiation Therapy (SIRT) for Hepatic Tumors**
Policy Number	**7.01.69**
Category	**Technology Assessment**
Original Effective Date	**12/15/05**
Committee Approval 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, 08/20/20, 08/19/21, 02/17/22, 02/16/23, 02/22/24**
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Archived Date	**N/A**
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Product Disclaimer	• *Services are contract dependent; 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 or Child Health Plus product), medical policy criteria apply to the benefit.* • *If a Medicaid product covers a specific service, and there are no New York State Medicaid guidelines (eMedNY) criteria, medical policy criteria apply to the benefit.* • *If a Medicare product (including Medicare HMO-Dual Special Needs Program (DSNP) 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.* • *If a Medicare HMO-Dual Special Needs Program (DSNP) product DOES NOT cover a specific service, please refer to the Medicaid Product coverage line.*

POLICY STATEMENT

I. Based upon our criteria and assessment of the peer-reviewed literature, selective internal radiation therapy (SIRT), using radioactive Yttrium-90 (90Y) microspheres has been medically proven to be effective and, therefore, is considered **medically necessary** as a treatment for:
   A. Unresectable and/or medically inoperable primary or metastatic liver malignancies from **ANY** of the following: (*Refer to Policy Guidelines*)
      1. Unresectable primary hepatocellular carcinoma (HCC);
      2. Unresectable hepatic metastases from neuroendocrine tumors (e.g., carcinoids, pancreatic islet cell tumors, endocrine tumor) with diffuse and symptomatic disease, when systemic therapy has failed to control symptoms;
      3. As a bridge to transplant for patients with HCC who meet liver transplant criteria and are waiting liver transplantation;
      4. Unresectable metastatic liver tumors from primary colorectal cancer; **or**
      5. Treatment of unresectable hepatic metastases from colorectal carcinoma, breast carcinoma, ocular melanoma, cutaneous melanoma, or intrahepatic cholangiocarcinoma in patients with liver-dominant disease who are refractory to chemotherapy or who are not candidates for chemotherapy, or other systemic therapies.

II. Based upon our criteria and assessment of the peer reviewed literature, repeat radioembolization (SIRT) has been medically proven to be effective and, therefore, is considered **medically necessary** as a treatment for a new, progressive primary or metastatic liver cancer (*Refer to Policy Guidelines*) when **ALL** of the following criteria are met;
   A. A previous satisfactory response to an initial radioembolization treatment as evidenced by results of a computed tomography (CT) scan or positron emission tomography (PET)-CT scan, performed 3 months following the

previous procedure, has been completed, and response should be graded according to the revised Response Evaluation Criteria in Solid Tumors (RECIST) guideline (Version 1.1);

B. The disease must still be liver dominant;
C. There are no other effective systemic or liver-directed treatment options available;
D. The individual has compensated liver function tests (LFTs);
E. Estimated lung dose and combined lung dose from previous embolizations are within acceptable dose volume constraints; **and**
F. Treatment should be given to a targeted tumor volume.

III. Based upon our criteria and assessment of the peer-reviewed literature, a third radioembolizton treatment (SIRT) has not been medically proven to be effective and, therefore, is considered **not medically necessary**.

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

This policy does not address arterially directed therapies other than SIRT

Refer to Corporate Medical Policy #11.01.10 Clinical Trials

Refer to Corporate Medical Policy #11.01.03 Experimental or Investigational Services

Refer to Corporate Medical Policy #7.02.07 Liver Transplantation

POLICY GUIDELINES

I. SIRT should be reserved for patients with an Eastern Coorperative Oncology Group (ECOG) performance status no greater than 2 or Karnofsky Performance Status (KPS) of 70 or above, adequate liver function and reserve, and liver-dominant metastases. Patients should also have a life expectancy of greater than three (3) months.

II. Radioactive Yttrium-90 (90Y) microspheres treatment is allowed only in the outpatient setting unless the documentation supports the medical necessity of inpatient treatment.

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 and 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, tumor 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.

SIRT, which is 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), which 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 technique due to several factors: (1) the liver parenchyma is sensitive to radiation; (2) the hepatic circulation is uniquely organized, in that 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, which helps focus the radiation and minimize its spread.

RATIONALE

There are currently two types of Yttrium microspheres (glass and resin) that have been approved by the FDA: TheraSpheres (Theragenics; Atlanta, GA) and SIR-Spheres (Sirtex Medical Limited; Lake Forest, IL). The 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, the FDA approved TheraSpheres under the humanitarian device exemption (HDE) in 1999 for use as monotherapy to treat unresectable hepatocellular carcinoma (HCC). In January 2007, the HDE for TheraSpheres was expanded to include patients with hepatocellular carcinoma who have partial or branch portal vein thrombosis. In March of 2021, the FDA granted approval of the TheraSphere Y-90 Glass Microspheres, developed for the treatment of patients with hepatocellular carcinoma (HCC). The approval expands access to this life-prolonging therapy for a greater number of patients, which, to date, has been utilized under a humanitarian device exemption (HDE) – an FDA classification which required institutional review board approval and limited the number of patients treated with the therapy per year. TheraSphere is now the only radioembolization technology indicated for the treatment of unresectable HCC in the U.S.

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 Tumors

While studies investigating SIRT for neuroendocrine tumors have limitations such as heterogeneous patient populations, studies 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).

Bridge Therapy

The National Comprehensive Cancer Network's V.2.2023 Guidelines for Hepatocellular Carinoma recommends SIRT as bridge therapy to decrease tumor progression and the dropout rate from the liver transplantation waiting list. The guidelines reference a 2006 study (Kulil, et al) of 150 patients with unresectable HCC treated with TheraSphere with the intent of downstaging to resection, radiofrequency ablation or liver transplantation. Results demonstrated that 56% of patients were successfully downstaged from T3 to T2 following their treatment, with authors concluding that intra-arterial 90 Y microspheres can be used as a bridge to transplantation.

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.*
- *Code Key: Experimental/Investigational = (E/I), Not medically necessary/ appropriate = (NMN).*

CPT Codes

Code	Description
No CPT codes specific to SIRT, but the following could be used*: **This policy does not address arterially directed therapies other than SIRT.*	
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
77778	Interstitial radiation source application, complex, includes supervision, handling, loading of radiation source, when performed (*effective 01/01/2016*)
79445	Radiopharmaceutical therapy, by intra-arterial particulate administration

HCPCS Codes

Code	Description
A9543	Yttrium Y-90 ibritumomab tiuxetan, therapeutic, per treatment dose, up to 40 mCi
C2616	Brachytherapy source, nonstranded, yttrium-90, per source
S2095	Transcatheter occlusion or embolization for tumor destruction, 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
C18.9	Malignant neoplasm of colon, unspecified
C22.0	Liver cell carcinoma
C22.1	Intrahepatic bile duct carcinoma
C22.2	Hepatoblastoma

Code	Description
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, Selective Internal Radiation Therapy is not addressed in National or Regional Medicare coverage determinations or policies.