Geisinger

Geisinger Health Plan Policies and Procedure Manual

Policy: MP208

Section: Medical Benefit Policy

Subject: Selective Internal Radiation Therapy (aka, Intrahepatic Radioembolization)

Applicable Lines of Business

Commercial	**X**	**CHIP**	**X**
Medicare	**X**	**ACA**	**X**
Medicaid	**X**		

I. Policy: Selective Internal Radiation Therapy (aka, Intrahepatic Radioembolization)

II. Purpose/Objective:

To provide a policy of coverage regarding Selective Internal Radiation Therapy (aka, Intrahepatic Radioembolization)

III. Responsibility:

A. Medical Directors

B. Medical Management Department

IV. Required Definitions

1. Attachment – a supporting document that is developed and maintained by the policy writer or department requiring/authoring the policy.
2. Exhibit – a supporting document developed and maintained in a department other than the department requiring/authoring the policy.
3. Devised – the date the policy was implemented.
4. Revised – the date of every revision to the policy, including typographical and grammatical changes.
5. Reviewed – the date documenting the annual review if the policy has no revisions necessary.

V. Additional Definitions

Medical Necessity or Medically Necessary means Covered Services rendered by a Health Care Provider that the Plan determines are:

a. appropriate for the symptoms and diagnosis or treatment of the Member's condition, illness, disease or injury;
b. provided for the diagnosis, and the direct care and treatment of the Member's condition, illness disease or injury;
c. in accordance with current standards of good medical treatment practiced by the general medical community;
d. not primarily for the convenience of the Member, or the Member's Health Care Provider; and the most appropriate source or level of service that can safely be provided to the Member. When applied to hospitalization, this further means that the Member requires acute care as an inpatient due to the nature of the services rendered or the Member's condition, and the Member cannot receive safe or adequate care as an outpatient.

Medicaid Business Segment

Medically Necessary — A service, item, procedure, or level of care that is necessary for the proper treatment or management of an illness, injury, or disability is one that:

- Will, or is reasonably expected to, prevent the onset of an illness, condition, injury or disability.
- Will, or is reasonably expected to, reduce or ameliorate the physical, mental or developmental effects of an illness, condition, injury or disability.

- Will assist the Member to achieve or maintain maximum functional capacity in performing daily activities, taking into account both the functional capacity of the Member and those functional capacities that are appropriate for Members of the same age

DESCRIPTION:
Selective Internal Radiation Therapy (aka, Intrahepatic Radioembolization) involves the use of Intra-hepatic microspheres which are radio-labeled particles composed of glass or resin polymers. The spheres are tagged with Y-90 and injected via the hepatic artery to target radiation directly to liver tumors. Evidence suggests that the microspheres are selectively deposited in vascular tumor tissue, which allows much higher radiation doses while sparing the injury and morbidity that accompanies external beam radiation

INDICATIONS:
Selective Internal Radiation with Y-90 microspheres may be considered medically necessary for members with the following criteria:

1. a. Unresectable primary Hepatocellular Carcinoma; or
   b. Unresectable liver tumors from primary colorectal cancer; or
   c. Unresectable intrahepatic cholangiocarcinoma
   d. Treatment of unresectable liver-only or liver dominant metastases from neuroendocrine cancers when other systemic therapy has failed to control symptoms
   and
2. There is documentation of:
   a. adequate hematological and hepatic function; and
   b. Eastern Cooperative Oncology Group (ECOG) performance status of 0-2*

Repeat radioembolization may be considered medically necessary in liver dominant disease when the following criteria are met:

- The member has had a previous response to the initial radioembolization; and
- ECOG performance status of 0-2; and
- No other liver-directed or systemic treatment options are available

CONTRAINDICATIONS:

- Disseminated extra-hepatic disease
- Abnormal vascular anatomy that would result in reflux of hepatic arterial blood to the stomach, pancreas, bowel, etc. as evidenced by angiogram
- Shunting of hepatic artery blood flow to the lungs greater than 20% evidenced by a technetium macroaggregated albumin lung perfusion scan
- Portal vein thrombosis (relative contraindication for SIR Microspheres, but not Theraspheres)

ECOG PERFORMANCE STATUS*

Grade	ECOG
0	Fully active, able to carry on all pre-disease performance without restriction
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work
2	Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours
3	Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours
4	Completely disabled. Cannot carry on any selfcare. Totally confined to bed or chair
5	Dead

* As published in Am. J. Clin. Oncol.:
Oken, M.M., Creech, R.H., Tormey, D.C., Horton, J., Davis, T.E., McFadden, E.T., Carbone, P.P.: Toxicity And Response Criteria Of The Eastern Cooperative Oncology Group. Am J Clin Oncol 5:649-655, 1982.

Eastern Cooperative Oncology Group, Robert Comis M.D., Group Chair.

For Medicaid Lines of Business:
Selective Internal Radiation Therapy is not on the MA fee schedule and is therefore not covered for Medicaid except through a Program Exception.

EXCLUSIONS:
The Plan considers the use of Selective Internal Radiation for the treatment of all other conditions to be **unproven and NOT COVERED.**

Note: A complete description of the process by which a given technology or service is evaluated and determined to be experimental, investigational or unproven is outlined in **MP 15 - Experimental Investigational or Unproven Services or Treatment.**

Medicaid Business Segment:
Any requests for services, that do not meet criteria set in the PARP, may be evaluated on a case by case basis.

CODING ASSOCIATED WITH: Selective Internal Radiation Therapy
The following codes are included below for informational purposes and may not be all inclusive. Inclusion of a procedure or device code(s) does not constitute or imply coverage nor does it imply or guarantee provider reimbursement. Coverage is determined by the member specific benefit plan document and any applicable laws regarding coverage of specific services. Please note that per Medicare coverage rules, only specific CPT/HCPCS Codes may be covered for the Medicare Business Segment. Please consult the CMS website at www.cms.gov or the local Medicare Administrative Carrier (MAC) for more information on Medicare coverage and coding requirements

S2095 Transcatheter occlusion or embolization for tumor destruction, percutaneous, any method, using yttrium-90 microspheres
C2616 Brachytherapy source, Yttrium 90, per source
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 infarction
77263 Therapeutic radiology treatment planning; complex
77370 Special medical radiation physics consultation
77399 Unlisted procedure, medical radiation physics, dosimetry and treatment devices, and special services
77778 Interstitial radiation source application; complex
77790 Supervision, handling, loading of radiation source
75894 Transcatheter therapy, embolization, any method, radiological supervision and interpretation
79445 Radiopharmaceutical therapy, by intra-arterial particulate administration

LINE OF BUSINESS:
Eligibility and contract specific benefits, limitations and/or exclusions will apply. Coverage statements found in the line of business specific benefit document will supersede this policy. For Medicare, applicable LCD's and NCD's will supercede this policy. For PA Medicaid Business segment, this policy applies as written.

REFERENCES:
Geisinger Technology Assessment Committee Triage Group. Yttrium-90 (Y-90) microspheres . Aug. 2007.

Geisinger Technology Assessment Committee. Intrahepatic Microsphere Therapy. April 2010.

Geisinger Technology Assessment Committee Triage Group. Selective Internal Radiation Therapy, May 2011

MDS Nordion. TheraSphere (package insert) yttrium 90 glass microspheres. [TheraSphere Web site]. 2006. Available at: http://www.mds.nordion.com/therasphere/physicians/packageinsert.asp.

Steel J, Baum A, Carr B. Quality of life in patients diagnosed with primary hepatocellular carcinoma: hepatic arterial infusion of Cisplatin versus 90-yttrium microspheres (Therasphere). *Psychooncology.* 2004;13(2):73-79.

Salem R, Thurston KG, Carr BI, et al. Yttrium-90 microspheres: Radiation therapy for unresectable liver cancer. *J Vasc Interv Radiol.* 2002;13(9):S223-S229.

Van Hazel G, Blackwell A, Anderson J, et al. Randomized phase 2 trial of SIR-Spheres plus fluorouracil/leucovorin chemotherapy versus fluorouracil/leucovorin chemotherapy alone in advanced colorectal cancer. *J Surg Oncol.* 2004;88(2):78-85.

Gray B, Van Hazel G, Hope M, et al. Randomized trial of SIR-Spheres plus chemotherapy vs. chemotherapy alone for treating patients with liver metastases from primary large bowel cancer. *Ann Oncol.* 2001;12(12):1711-1720.

Center for Devices and Radiologic Health. SIR-Spheres (package insert).Yttrium-90 microspheres. [US Food and Drug Administration (FDA) Web site)]. 01/23/03. Available at: http://www.fda.gov/cdrh/pdf2/p990065c.pdf. Accessed May 8, 2006.

Center for Devices and Radiologic Health. TheraSphere Yttrium-90 Glass Microspheres [package insert]. [US Food and Drug Administration (FDA) Web site)]. 02/10/00. Available at: http://www.fda.gov/cdrh/pdf/h980006c.pdf. Accessed May 8, 2006.

National Institute for Clinical Excellence (NICE). Selective internal radiation therapy for colorectal liver metastases. Interventional Procedure Consultation Document. London, UK: NICE; January 2004. Available at: http://www.nice.org.uk/cms/htm/default/en/IP_228/ip228consultation/article.aspx.

Sirtex Medical Inc. SIR-Spheres (Yttrium-90 microspheres). Product Labeling. Rockville, MD: U.S. Food and Drug Administration, Center for Devices and Radiological Health; March 5, 2005. Available at: http://www.fda.gov/cdrh/pdf/p990065.html.

Kulik LM, Atassi B, van Holsbeeck L, et al. Yttrium-90 microspheres (TheraSphere) treatment of unresectable hepatocellular carcinoma: Downstaging to resection, RFA and bridge to transplantation. J Surg Oncol. 2006;94(7):572-586.

ECRI. Target Database (Online) Intrhepatic yttrium-90 microsphere therapy for primary liver cancer. Plymouth Meeting, PA; ECRI Institute June 2006

ECRI. Target Database (Online) Intrhepatic yttrium-90 microsphere therapy for metastatic colorectal cancer. Plymouth Meeting, PA; ECRI Institute June 2006.

Atassi B, Bangash AK, Lewandowski RJ, Ibrahim S, Kulik L, Mulcahy MF, Murthy R, Ryu RK, Sato KT, Miller FH, Omary RA, Salem R. Biliary sequelae following radioembolization with yttrium-90 microspheres. J Vasc Interv Radiol. 2008;19(5):691-7.

Kulik LM, Carr BI, Mulcahy MF, Lewandowski RJ, Atassi B, Ryu RK, Sato KT, Benson A 3rd, Nemcek AA Jr, Gates VL, Abecassis M, Omary RA, Salem R. Safety and efficacy of 90Y radiotherapy for hepatocellular carcinoma with and without portal vein thrombosis. Hepatology. 2008;47(1):71-81.

Tice, JA. Selective internal radiation therapy for radioembolization for inoperable liver metastases from colorectal cancer. California Technology Assessment Forum (CTAF). February 17, 2010.

Winifred S. Hayes, Inc. Medical Technology Directory. Radioactive Yttrium-90 microspheres for treatment of primary liver cancer. update search September 2016

Winifred S. Hayes, Inc. Medical Technology Directory. Radioactive Yttrium-90 microspheres for treatment of secondary liver cancer. update search March 2017

Gulec SA, Wheeler J, Pennington K. et al. Chemotherapy with yttrium 90 microsphere selective internal radiation treatment in patients with metastatic pancreatic cancer. J Inter Onoc 2009;2(1):84-92.

Ibrahim SM, Lewandowski RJ, Sato KT et al. Radioembolization for the treatment of unresectable hepatocellular carcinoma: A clinical review. World J Gastroenterol 2008:14(11);1664-1669.

Dubel, GJ and Soares GM. Regional infusion – radioembolization. Surg Oncol Clin N Am 2008:17;957-985.

Jakobs TF, Hoffmann RT, Dehm K, et al. Hepatic yttrium-90 radioembolization of chemotherapy-refractory colorectal cancer liver metastases. *J Vasc Interv Radiol.* Aug 2008;19(8):1187-1195.

Gulec SA, Fong Y. Yttrium 90 microsphere selective internal radiation treatment of hepatic colorectal metastases. *Arch Surg.* Jul 2007;142(7):675-682.

Vente MA, Wondergem M, van der Tweel I, et al. Yttrium-90 microsphere radioembolization for the treatment of liver malignancies: a structured meta-analysis. *Eur Radiol.* Apr 2009;19(4):951-959.

Sato K, Lewandowski RJ, Bui JT, et al. Treatment of unresectable primary and metastatic liver cancer with yttrium-90 microspheres (TheraSphere): assessment of hepatic arterial embolization. *Cardiovasc Intervent Radiol.* Jul-Aug 2006;29(4):522-529.

Kennedy A, Nag S, Salem R, et al. Recommendations for radioembolization of hepatic malignancies using yttrium-90 microsphere brachytherapy: a consensus panel report from the radioembolization brachytherapy oncology consortium. *Int J Radiat Oncol Biol Phys.* May 1 2007;68(1):13-23.

Hoffmann RT, Jakobs TF, Kubisch CH, et al. Radiofrequency ablation after selective internal radiation therapy with Yttrium90 microspheres in metastatic liver disease-Is it feasible? *Eur J Radiol.* Mar 6 2009.

The international liver congress (2009). The 44th annual European Association for the study of the Liver. Retrived April 6, 2011 http://www.easl.eu/assets/application/files/5b0c67e7cc76a88_file.pdf

National Electronic Library of Medicines (NeLM) reviewed November 6, 2009. Accessed April 6, 2011 http://www.nelm.nhs.uk/en/NeLM-Area/Evidence/Medicines-Q--A/What-is-the-Child-Pugh-score/

Carr, BI, Kondragunta, V, Buch, SC, and Branch, RA. Therapeutic equivalence in survival for hepatic arterial chemoembolization and yttrium 90 microsphere treatments in unresectable hepatocellular carcinoma: a Two-Cohort Study. *Cancer*. 2010.

Salem, R, Lewandowski, RJ, Kulik, L, et al. Radioembolization results in longer time-to-progression and reduced toxicity compared with chemoembolization in patients with hepatocellular carcinoma. *Gastroenterology*. 2011;140(2):497-507.

Salem, R, Lewandowski, RJ, et al. Radioembolization for hepatocellular carcinoma using yttrium-90 microspheres: a comprehensive report of long-term outcomes. *Gastroenterology*. 2009.

Cao CQ, Yan TD, et al. Radioembolization wit yttrium microspheres for nueroendocrine tumour liver metastases. Br J Surg. 2010 Mar 4; 97 (4): 537-543

Hilgard, P, Hamami, et. al. Radioembolization with yttrium-90 glass microspheres in hepatocellular carcinoma: European experience on safety and long-term survival. Hepatology. 2010;52(5):1741-1749.

Inarrairaegui, M, Bilbao, JI, et. al. Liver radioembolization using 90 y resin microspheres in elderly patients: tolerance and outcome. Hosp Pract (Minneap). 2010;38(5):103-109.

Kooby, DA, Egnatashvili, V, et. al. Comparison of yttrium-90 radioembolization and transcatheter arterial chemoembolization for the treatment of unresectable hepatocellular carcinoma. J Vasc Interv Radiol. 2010;21(2):224-230.

National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology, Colon cancer. v3.2024

National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology. Hepatobiliary cancers. v1.2024

National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology. Neuroendocrine and Adrenal tumors. v1.2024

American Association for the Study of Liver Diseases. Bruix J, Sherman M. Management of hepatocellular carcinoma: an update. 2010 Jul.

Oken, M.M., Creech, R.H., Tormey, D.C., Horton, J., Davis, T.E., McFadden, E.T., Carbone, P.P.: Toxicity And Response Criteria Of The Eastern Cooperative Oncology Group. Am J Clin Oncol. 1982;5:649-655.

Tsai AL, Burke CT, et al. Use of yttrium-90 microspheres in patients with advanced hepatocellular carcinoma and portal vein thrombosis. J Vasc Interv Radiol. 2010 Sep;21(9):1377-84

Georgiades CS, Hong K, D'Angelo M, Geschwind JF. Safety and efficacy of transarterial chemoembolizationin patients with unresectable hepatocellular carcinoma and portal vein thrombosis. J Vasc Interv Radiol. 2005;16(12):1653-1659

Salem R, Lewandowski R, Roberts C, et al. Use of Yttrium-90 glass microspheres (TheraSphere) for the treatment of unresectable hepatocellular carcinoma in patients with portal vein thrombosis. J Vasc Interv Radiol. 2004;15(4):335-345.

American College of Radiology. ACR Appropriateness Criteria. Radiologic Management of Hepatic Malignancy. https://acsearch.acr.org/docs/69379/Narrative/

Vouche M, Habib A, Ward TJ, et al. Unresectable solitary hepatocellular carcinoma not amenable to radiofrequency ablation: multicenter radiology-pathology correlation and survival of radiation segmentectomy. Hepatology. 2014; 60(1):192-201.

Saxena A, Bester L, Shan L, et al. A systematic review on the safety and efficacy of yttrium-90 radioembolization for unresectable, chemorefractory colorectal cancer liver metastases. J Cancer Res Clin Oncol. 2014; 140(4):537-547.

Kolligs FT, Bilbao JI, Jakobs T, et al. Pilot randomized trial of selective internal radiation therapy vs. chemoembolization in unresectable hepatocellular carcinoma. Liver Int. 2015; 35(6):1715-1721

Zacharias AJ, Jayakrishnan TT, Rajeev R, et al. Comparative effectiveness of hepatic artery based therapies for unresectable colorectal liver metastases: a meta-analysis. PLoS One. 2015;10(10).

Braat MN, Samim M, van den Bosch MA, Lam MG. The role of (90)Y-radioembolization in downstaging primary and secondary hepatic malignancies: a systematic review. Clin Transl Imaging. 2016; 4:283-295.

Lobo L, Yakoub D, Picado O, et al. Unresectable hepatocellular carcinoma: radioembolization versus chemoembolization: a systematic review and meta-analysis. Cardiovasc Intervent Radiol. 2016; 39(11):1580-1588

Facciorusso A, Serviddio G, Muscatiello N. Transarterial radioembolization vs chemoembolization for hepatocarcinoma patients: a systematic review and meta-analysis. World J Hepatol. 2016; 8(18):770-778

Mosconi C, et al. Yttrium-90 radioembolization for unresectable/recurrent intrahepatic cholangiocarcinoma: a survival, efficacy and safety study. Br J Cancer 2016 July 26;115(3):297-302

Jakobs TF, et al. Robust evidence for long-term survival with 90Y radioembolization in chemorefractory liver-predominant metastatic colorectal cancer. Eur Radiol 2017 Jan;27(1):113-119.

Rim CH, et al. Comparison of radiation therapy modalities for hepatocellular carcinoma with portal vein thrombosis: a meta-analysis and systematic review. Radiother Oncol 2017 Dec 9

Wasan HS, et al. First-line selective internal radiotherapy plus chemotherapy versus chemotherapy alone in patients with liver metastases from colorectal cancer (FOXFIRE, SIRFLOX, and FOXFIRE-Global): a combined analysis of three multicenter, randomized, phase 3 trials. Lancet Oncol 2017 Sep;18(9):1159-1171.

Padia SA. Y90 Clinical Data Update: Cholangiocarcinoma, Neuroendocrine Tumor, Melanoma, and Breast Cancer Metastatic Disease. Tech Vasc Interv Radiol. 2019 Jun;22(2):81-86

White J, Carolan-Rees G, Dale M, et al. Yttrium-90 transarterial radioembolization for chemotherapy-refractory intrahepatic cholangiocarcinoma: a prospective, observational study. J Vasc Interv Radiol. 2019 Aug;30(8):1185-1192.

Egger ME, Armstrong E, Martin RC, et al. Transarterial chemoembolization vs radioembolization for neuroendocrine liver metastases: a multi-institutional analysis. Journal of the American College of Surgeons. 2020 Apr;230(4):363-70.

Buettner S, Braat AJAT, Margonis GA, et al. Yttrium-90 radioembolization in intrahepatic cholangiocarcinoma: a multicenter retrospective analysis. J Vasc Interv Radiol. 2020 Jul;31(7):1035-1043.e2.

Abdel-Rahman O, Elsayed Z. Yttrium-90 microsphere radioembolisation for unresectable hepatocellular carcinoma. Cochrane Database Syst Rev. 2020 Nov 16;11:CD011313

Gabr A, Kulik L, Mouli S, et al. Liver transplantation following yttrium-90 radioembolization: 15-year experience in 207-patient cohort. Hepatology. 2021 Mar;73(3):998-1010.

Fruscione M, Pickens RC, Baker EH, et al. Conversion therapy for intrahepatic cholangiocarcinoma and tumor downsizing to increase resection rates: a systematic review. Curr Probl Cancer. 2021 Feb;45(1):100614
Schartz D, Porter M, Schartz E, et al. Transarterial yrittrium-90 radioembolization for unresectable intrahepatic cholangiocarcinoma: a systematic review and meta-analysis. J Vasc Interv Radiol. 2022 Feb 24

Schaarschmidt BM, Kloeckner R, Dertnig T, et al. Real-life experience in the treatment of intrahepatic cholangiocarcinoma by 90y radioembolization: a multicenter retrospective study. J Nucl Med. 2023 Apr;64(4):529-535.

This policy will be revised as necessary and reviewed no less than annually.

Devised: 12/07

Revised: 04/10 (ref. added), 6/11 (added indications), 8/12 (removed cirrhosis limitation), 12/14 (added contraindication); 7/22 (add Unresectable intrahepatic cholangiocarcinoma indication); 7/24 (add repeat tx criteria)

Reviewed: 6/12**,** 8/13, 8/14; 8/15; 7/16, 7/17, 6/18, 7/19, 7/20, 7/21, 7/23

CMS UM Oversight Committee Approval: 12/23, 7/24