

### DISCLAIMER

This Molina Clinical Policy (MCP) is intended to facilitate the Utilization Management process. Policies are not a supplementation or recommendation for treatment; Providers are solely responsible for the diagnosis, treatment, and clinical recommendations for the Member. It expresses Molina's determination as to whether certain services or supplies are medically necessary, experimental, investigational, or cosmetic for purposes of determining appropriateness of payment. The conclusion that a particular service or supply is medically necessary does not constitute a representation or warranty that this service or supply is covered (e.g., will be paid for by Molina) for a particular Member. The Member's benefit plan determines coverage – each benefit plan defines which services are covered, which are excluded, and which are subject to dollar caps or other limits. Members and their Providers will need to consult the Member's benefit plan to determine if there are any exclusion(s) or other benefit plan will govern. In addition, coverage may be mandated by applicable legal requirements of a State, the Federal government or CMS for Medicare and Medicaid Members. CMS's Coverage Determination (LCD) will supersede the contents of this MCP and provide the directive for all Medicare members. References included were accurate at the time of policy approval and publication.

### **OVERVIEW**

**Hepatocellular carcinoma (HCC)**, or primary liver cancer, is becoming more prevalent due to the spread of hepatitis virus infection (Schwartz & Carithers 2025). HCC is usually associated with cirrhosis of the liver and has poor prognosis (Abdalla et al. 2025). Patients with primary liver cancer are categorized as having localized resectable, localized unresectable, or advanced disease. Surgical excision is the preferred treatment for liver tumors; however, many liver tumors are inoperable due to the placement of the tumor within the liver or the presence of concurrent medical conditions such as cirrhosis (Curley et al. 2025). While some of these patients may be candidates for liver transplantation, the restricted availability of donor livers remains a barrier (Tsoulfas et al. 2023). Additional therapy options for nonresectable HCC in the early stage include percutaneous ablation with ethanol injection and radiofrequency ablation (Abdalla et al. 2025).

**Radioembolization**, also known as **selective internal radiation therapy (SIRT)**, is a type of nuclear medicine therapy used to treat primary or metastatic hepatic malignancies utilizing yttrium 90 (Y-90) (Curley et al. 2025; Tsoulfas et al. 2023). Radioembolization, intra-arterial radiation therapy, or trans-arterial radioembolization (TARE) are all locoregional therapies that have the goal of deterring tumor progression. During therapy, a radiation oncologist uses x-ray fluoroscopy to guide a catheter percutaneously via a patient's femoral artery to the correct hepatic artery where a vial containing Y-90 microspheres is then released. The microspheres are selectively delivered through the hepatic vasculature to the target tumor(s). The procedure is performed on an outpatient basis and takes 30 to 60 minutes to complete. Patients are usually discharged within 23 hours. Radioembolization has been proposed as a treatment for a variety of primary and metastatic liver tumors and has been utilized to downstage the cancer or as a bridge therapy prior to resection, surgery, or transplantation (Tsoulfas et al. 2023).

#### **Regulatory Status**

Two forms of Y-90 microspheres have received FDA approval:

- SIR-Spheres (Sirtex Medical) are Y-90 microspheres made of resin. SIR-Spheres microspheres are indicated for the treatment of unresectable metastatic liver tumors from primary colorectal cancer with adjuvant intrahepatic artery floxuridine chemotherapy. FDA premarket approval was granted on March 5, 2002 (FDA 2002).
- 2. TheraSphere (BTG) are Y-90 microspheres made of glass.
  - TheraSphere received approval in 1999 as a neoadjuvant treatment to surgery or transplantation in
    patients with unresectable HCC who can have placement of appropriately positioned hepatic arterial
    catheters through the humanitarian drug exemption (HDE) process for radiotherapy (FDA 1999). In 2006,
    this HDE was expanded to include patients with HCC who have partial or branch portal vein thrombosis
    (FDA 2006).
  - TheraSphere received approval through the PMA process on March 17, 2021, for use as SIRT for local tumor control of solitary tumors (1-8 cm in diameter), in patients with unresectable HCC, Child-Pugh Score A cirrhosis, well-compensated liver function, no macrovascular invasion, and good performance status (FDA 2021).



The U.S Nuclear Regulatory Commission also regulates the usage of TheraSphere and SIR-Spheres by issuing licenses for their application (NRC 2021).

# **RELATED POLICIES**

Liver Transplantation: Policy No. 114 Pre-Transplant and Transplant Evaluations: Policy No. 459 Radiation Therapy Services: Policy No. 463

#### COVERAGE POLICY

Radioembolization (i.e., TheraSphere, SIR-Spheres) of the liver may be **considered medically necessary** when <u>ALL</u> the following criteria are met:

- 1. The therapy is intended to treat <u>ONE</u> of the following:
  - a. Unresectable primary hepatocellular carcinoma (HCC)
  - b. Unresectable intrahepatic cholangiocarcinoma
  - c. Primary HCC as a bridge to liver transplantation or other curative therapies
  - d. ONE of the following metastatic hepatic disease states:
    - i. Diffuse symptomatic metastases from a neuroendocrine tumor (carcinoid or non-carcinoid) when systemic therapy has failed
      - ii. Unresectable metastases from colorectal tumor
      - iii. Liver dominant metastases
- 2. ECOG performance score of 0-2\*
- 3. Child Pugh Score of A or B\*
- 4. Life expectancy of at least 3 months
- 5. Absence of <u>ALL</u> the following absolute contraindications:
  - a. Inability to catheterize the hepatic artery
  - b. Prior radiation therapy involving the liver
  - c. Technetium-99m MAA hepatic arterial perfusion scintigraphy demonstrating <u>ANY</u> of the following:
    - i. Significant reflux to the gastrointestinal organs that cannot be corrected by angiographic techniques such as embolization
    - ii. 30 Gy radiation absorbed dose to the lungs
    - iii. Lung shunting of the hepatic artery blood flow > 20%
  - d. Encephalopathy
  - e. Biliary obstruction
  - f. Impaired liver function causing hyperbilirubinemia (may be a relative or absolute contraindication depending on the disease burden, hepatic distribution requiring treatment and treatment goals)
  - g. ECOG > 2 score (poor performance status)\*
  - h. Child-Pugh score of C (severely compromised liver function)\*

\*Note: See supplemental information section for scoring definitions

#### Continuation of Therapy

There is limited data on the safety and efficacy of repeated radioembolization treatments, as well as the optimal number of treatments.

DOCUMENTATION REQUIREMENTS. Molina Healthcare reserves the right to require that additional documentation be made available as part of



its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational, or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

# SUMMARY OF MEDICAL EVIDENCE

### Randomized Controlled Trials

Garin et al. (2021) published the DOSISPHERE-01 trial a randomized, multicenter, open-label Phase II study conducted in France to evaluate the efficacy of personalized versus standard dosimetry in Yttrium-90 (Y-90) radioembolization for patients with unresectable, locally advanced hepatocellular carcinoma. A total of 60 patients were randomized: 31 to receive personalized dosimetry (≥205 Gy to the index lesion) and 29 to receive standard dosimetry (120 ± 20 Gy to the perfused lobe). The primary endpoint was the objective response rate (ORR) in the index lesion at 3 months, as assessed by investigators using the European Association for the Study of the Liver (EASL) criteria, in the modified intention-to-treat population. This ORR was significantly higher in the personalized group at 71% (95% CI 51–87) compared to 36% (95% CI 19–56) in the standard group (p=0.0074). Serious adverse events occurred in 20% of patients in the personalized group and 33% in the standard group. Grade 3 or higher adverse events were generally comparable between groups, with lymphopenia being the most common. One treatment-related death occurred in each group. The study concluded that personalized dosimetry significantly improved tumor response and may enhance clinical outcomes, supporting its use in future selective internal radiation therapy protocols.

#### Systematic Reviews and Meta-Analyses

Zeng et al. (2023) completed a systematic review and meta-analysis to compare the efficacy and safety of SIRT, sorafenib, and a combination therapy of SIRT and sorafenib (SIRT+sorafenib). The analysis included 9 studies (6 retrospective and 3 RCTs) with a total of 1954 patients. The outcomes measured included overall survival (OS), progression free survival (PFS), and adverse events (AEs). For OS, the retrospective studies showed SIRT to be superior to sorafenib alone and SIRT+sorafenib (HR 0.60, 95% CI 0.42-0.87; I<sup>2</sup> = 56%) while the RCTs showed no significant difference between any of the groups (HR 0.92, 95% CI 0.79–1.08;  $l^2 = 0\%$ ). The overall comparison including the retrospective studies and RCTs showed a statistically significant difference in OS between SIRT and sorafenib (HR 0.73, 95% CI 0.56-0.94; p = 0.01). PFS was only included in 3 studies but showed no significant difference between any of the groups (HR 0.87, 95% CI 0.62-1.22). In terms of AEs, sorafenib alone was found to lead to a higher incidence rate of grade 3 or higher AEs when compared to SIRT alone. The most common AEs when comparing SIRT alone and sorafenib alone were weight loss (SIRT=0.60%, sorafenib=1.83%), diarrhea (SIRT=1.33%, sorafenib=5.95%), and rash or desguamation (SIRT=0.47%, sorafenib=3.15%). The most common AEs when comparing SIRT+sorafenib and sorafenib alone were fatigue (SIRT+sorafenib=1.92%, sorafenib=7.21%), rash or desquamation (SIRT+sorafenib=0.93%, sorafenib=3.15%), and liver dysfunction (SIRT+sorafenib=0.47%, sorafenib=6.51%). Researchers noted that SIRT+sorafenib did not raise the risk of grade 3 or higher AEs but potentially introduced more AEs than either SIRT or sorafenib alone. Researchers also noted that SIRT alone was superior to SIRT+sorafenib and sorafenib alone.

Lemieux et al. (2021) completed a systematic review and meta-analysis with the goal of assessing the efficacy and safety of Y-90 TARE to the standard of care in non-surgical HCC patients. Standard of care was based on Barcelona Clinic Liver Cancer (BCLC) staging. The meta-analysis included 8 RCTs with a total of 1439 patients. The primary outcome measured was OS. Secondary outcomes measured included the time to radiological progression (defined by PFS and time to progression at any site), disease control rate (defined as the sum of complete response, partial response, and stable disease), the incidence of severe or significant AEs, and the incidence of gastrointestinal ulcers of any severity. The patient population was noted to be mostly male (n=86%) with 59% having advanced HCC, 35.5% having intermediate HCC, and 5.5% having early HCC. Y-90 TARE was performed using resin microspheres in 5 RCTs and glass microspheres in 3 RCTs. The OS was reported in all trials. However, 2 trials only reported median survival rates or survival rates at 6- and 12-months and were not included in the analysis. There was no significant difference noted in OS between Y-90 TARE and the standard of care. PFS was reported in 4 trials and the time to progression) showed no differences between Y-90 TARE and standard of care. However, it was noted that Y-90 TARE had a significantly longer time to progression in the glass microsphere subgroup. The disease control rate was reported in 5 RCTs and



showed no significant difference between interventions. AEs were reported by all studies and analysis showed Y-90 TARE was associated with significantly lower rates of grade 3 or higher AEs when compared to the standard of care. No significant differences were noted in the rates of gastrointestinal ulcers.

Abdel-Rahman and Elsayed (2020) conducted a systematic review and meta-analysis on 6 RCTs (n = 1,340) to determine the benefits and harms of Y-90 microsphere radioembolization in comparison with placebo, no intervention, or other available interventions in patients with advanced liver cancer. The major outcomes that were measured were the overall median survival rate, the quality of life, and the occurrence of significant AEs. Cancer-related mortality, progression time, and tumor response were examined as secondary outcomes. Individuals with advanced HCC were evaluated in an RCT between radioembolization with sorafenib and sorafenib alone. Radioembolization combined with sorafenib may be associated with greater incidence of non-serious adverse events than sorafenib alone, according to evidence of very low certainty discovered by the authors. The median OS in the sorafenib group was 11.4 months and in the radioembolization plus sorafenib group it was 12.1 months. Two RCTs compared radioembolization to sorafenib in patients with locally advanced HCC and unresectable tumors. The radioembolization group had a one-year mortality rate of 62%, whereas the sorafenib group had a mortality rate of 60%. Radioembolization was associated with equivalent rates of OS and disease control when compared to sorafenib alone, according to the findings of the authors. With radioembolization, the risk of non-serious AEs was reduced. Three RCTs compared radioembolization to chemoembolization in patients with HCC in the intermediate stage. Survival rates at one year were 70% for both groups. Radioembolization and chemoembolization share a comparable risk of significant AEs, according to evidence of low certainty found by the authors.

### National and Specialty Organizations

The **National Comprehensive Cancer Network (NCCN)** clinical practice guideline for hepatocellular carcinoma (V1.2025) states:

Bridge therapy is used to decrease tumor progression and the dropout rate from the liver transplantation waiting list. It is considered for patients who meet the transplant criteria. A number of studies have investigated the role of locoregional therapies as a bridge to liver transplantation in patients on a waiting list. These studies included RFA, microwave ablation (MWA), transarterial embolization (TAE), transarterial chemoembolization (TACE), TACE with drug-eluting beads (DEB-TACE), TARE with Y-90 microspheres, conformal radiation therapy (CRT) and sorafenib as "bridge" therapies.

Limitations of these studies include size and heterogeneity of the study populations; however, the NCCN CPG states, "Nevertheless, the use of bridge therapy in this setting is increasing, and it is administered at most NCCN Member Institutions, especially in areas where there are long wait times for a transplant."

The NCCN clinical practice guidelines for HCC (V1.2025) states the following with Category 2A recommendations in the Principles of Locoregional Therapy- Arterially Directed Therapies section:

- Locoregional therapy should be considered in patients who are not candidates for surgical curative treatments, or as a part of a strategy to bridge patients for other curative therapies.
- Lesions 3 to 5 cm may be treated to prolong survival using arterially directed therapies, or with combination of an arterially directed therapy and ablation as long as tumor location is accessible for ablation.
- All tumors irrespective of location may be amenable to arterially directed therapies provided that the arterial blood supply to the tumor maybe isolated without excessive non-target treatment.
- Unresectable/inoperable lesions > 5cm should be considered for treatment using arterially directed or systemic therapy.
- Arterially directed therapies include TAE, chemoembolization (TACE and DEB-TACE) and radioembolization (RE) with Y-90 microspheres.
- All arterially directed therapies are relatively contraindicated in patients with bilirubin >3 mg/dL unless segmental injections can be performed. RE with Y-90 microspheres has an increased risk of radiation-induced liver disease in patients with bilirubin over 2 mg/dL.
- With RE, delivery of 205 Gy or more to the tumor may be associated with increased overall survival. A dose of >400 Gy to 25% of the liver or less in patients with CTP A liver function is recommended. For anatomically limited

# Molina Clinical Policy Radioembolization (Selective Internal Radiation Therapy) for Liver Tumors Policy No. 181



Policy No. 181 Last Approval: 06/11/2025 Next Review Due By: June 2026

disease, radiation segmentectomy with Y-90 or ablative dose stereotactic body radiation therapy (SBRT) should be considered.

- Arterially directed therapies in highly selected patients have been shown to be safe in the presence of limited tumor invasion of the portal vein.
- Randomized controlled trials have shown that Y-90 is not superior to sorafenib for treating advanced HCC.
- RE may be appropriate in some patients with advanced HCC, specifically patients with segmental or lobar portal vein, rather than main portal vein thrombosis.

The **European Society for Medical Oncology (ESMO)** published updated guidelines in 2022 for the management of HCC (Ducreux et al. 2022). The guidelines state the following:

- Bridging treatments are typically used if the expected waiting time for a liver transplant is > 6 months. Bridging treatments consist of TACE, DEB-TACE, TARE, and radiofrequency or microwave ablation.
- Radiofrequency or microwave ablation is typically used for patients with a BCLC score of 0 due to ablation being equivalent to surgery in terms of survival.
- TACE and DEB-TACE is the standard treatment for intermediate BCLC cases (tumor > 3cm and multinodular [≥ 4 nodules]) with an ECOG performance status of 0 or Child-Pugh score of A and without vascular invasion, extrahepatic disease, or portal thrombosis.
- TARE can be utilized in place of TACE if TACE is not available. However, evidence suggests TARE is associated with a longer time to progression compared to TACE.
- Combination treatments of sorafenib and TACE have not shown overall survival advantages when compared to either treatment alone.
- Stereotactic body radiotherapy (SBRT) has been shown to have similar outcomes to radiofrequency ablation. It has been suggested that SBRT may be useful for the treatment of tumors that are difficult to reach using radiofrequency ablation. However, SBRT is currently not widely utilized.

In 2023, the Practice Parameter for the Performance of Therapy with Radiopharmaceuticals was collaboratively revised by the American College of Radiology (ACR), the American College of Nuclear Medicine (ACNM), the American Radium Society (ARS), the American Society for Radiation Oncology (ASTRO), and the Society of Nuclear Medicine and Molecular Imaging (SNMMI). Patient selection should be based on clinical judgment and a multidisciplinary evaluation to ensure appropriate and effective use of radiopharmaceutical therapy. The document covers radiopharmaceutical therapy, including Y-90 microspheres, and outlines:

- Indications and contraindications
- Patient selection criteria
- Multidisciplinary team roles
- Procedural protocols
- Post-treatment care and follow-up

The American College of Radiology (ACR), American Brachytherapy Society (ABS), American College of Nuclear Medicine (ACNM), American Society for Radiation Oncology (ASTRO), Society of Interventional Radiology (SIR), and Society of Nuclear Medicine and Molecular Imaging (SNMMI) have published joint practice guidelines for radioembolization (also known as SIRT, TARE, and brachytherapy) with microsphere brachytherapy devices for the treatment of liver cancers. According to the parameters, radioembolization therapy aims can be palliative, curative, or a bridge to transplantation. The ultimate objective is intrahepatic tumor suppression. Patients with unresectable or inoperable primary or secondary liver cancers are the only indications for the use of radioembolization. Patients who qualify must have an ECOG performance level of 0 or 1, a Karnofsky Performance Status 70, and a survival expectancy of at least three months. For evaluation and management of eligible patients, the guidelines propose a multidisciplinary team. The disciplines of team members should include interventional radiology, radiation oncology, nuclear medicine, medical physics, radiation safety, hepatology, gastrointestinal, medical oncology, and surgical oncology. The rules specify the qualifications and responsibilities of each multidisciplinary team member, as well as the radioembolization method and post-operation care (ACR 2019).

The **European Association for the Study of the Liver (EASL)** guidelines provide updated recommendations on the use of Y-90 microspheres (TARE) in hepatocellular carcinoma (HCC). TARE is considered a safe and effective locoregional therapy with strong local tumor control, particularly in patients with BCLC stage A who are unsuitable for



resection or ablation, and in BCLC B patients when TACE is not feasible. While randomized trials have not shown an overall survival benefit over sorafenib or TACE, newer evidence supports the use of personalized dosimetry and radiation segmentectomy to improve outcomes. TARE is also recognized as a bridging or downstaging option to liver transplantation, especially when time to transplant exceeds 6 months. However, TARE is not recommended as a replacement for systemic therapy in BCLC C patients, except in select cases with segmental or lobar portal vein invasion and no extrahepatic spread. All decisions regarding TARE should be made by a multidisciplinary team with expertise in dosimetry and patient selection (EASL 2025).

The **National Institute for Health and Care Excellence (NICE)** notes that SIR-Spheres are indicated for treating advanced inoperable liver tumors, while TheraSphere is indicated for treating hepatic neoplasia. The appraisal committee considered SIR-Spheres and TheraSphere to be a cost-effective use of resources and recommended both as options for treating advanced HCC for people with Child–Pugh grade A liver impairment for whom conventional transarterial therapy is inappropriate (NICE 2024).

# SUPPLEMENTAL INFORMATION

The **Eastern Cooperative Oncology Group** (ECOG, Zubrod, WHO) performance scale definition:

- 0 = Fully active; no performance restrictions
- 1 = Strenuous physical activity restricted; fully ambulatory and able to carry out light work
- 2 = Capable of all self-care but unable to carry out any work activities. Up and about >50 percent of waking hours
- 3 = Capable of only limited self-care; confined to bed or chair >50 percent of waking hours
- 4 = Completely disabled; cannot carry out any self-care; totally confined to bed or chair

The **Child-Turcotte-Pugh** score determines short-term prognosis among groups of patients awaiting liver transplantation and has been widely adopted for risk-stratifying patients before transplantation.

Child-Turcotte-Pugh Score of Severity of Liver Disease				
Points	1	2	3	
Encephalopathy	None	1 – 2	3 – 4	
Ascites	Absent	Slight	Moderate	
Bilirubin (mg/dL)	< 2	2 – 3	> 3	
For PBC/PSC, Bilirubin	< 4	4 – 10	> 10	
Albumin (g/dL)	> 3.5	2.8 – 3.5	< 2.8	
INR: International Normalized Ratio	< 1.7	1.7 – 2.3	> 2.3	
PT = prothrombin time (seconds prolonged)	< 4	4 – 6	> 6	

The individual scores are summed and then grouped as a classification:

- < 7 = A
- 7-9 = B
- > 9 = C (forecasts a survival of less than 12 months)

# CODING & BILLING INFORMATION

#### **CPT (Current Procedural Terminology)**

Code	Description
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
75894	Transcatheter therapy, embolization, any method, radiological supervision and interpretation
79445	Radiopharmaceutical therapy, by intra-arterial particulate administration



Policy No. 181 Last Approval: 06/11/2025 Next Review Due By: June 2026

#### HCPCS (Healthcare Common Procedure Coding System)

Code	Description
C2616	Brachytherapy source, non-stranded, yttrium-90, per source
C9797	Vascular embolization or occlusion procedure with use of a pressure-generating catheter (e.g., one- way valve, intermittently occluding), inclusive of all radiological supervision and interpretation, intraprocedural roadmapping, and imaging guidance necessary to complete the intervention; for tumors, organ ischemia, or infarction
S2095	Transcatheter occlusion or embolization for tumor destruction, percutaneous, any method, using yttrium-90 microspheres
Q3001	Radioelements for brachytherapy, any type, each

**CODING DISCLAIMER.** Codes listed in this policy are for reference purposes only and may not be all-inclusive. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement. Listing of a service or device code in this policy does not guarantee coverage. Coverage is determined by the benefit document. Molina adheres to Current Procedural Terminology (CPT®), a registered trademark of the American Medical Association (AMA). All CPT codes and descriptions are copyrighted by the AMA; this information is included for informational purposes only. Providers and facilities are expected to utilize industry standard coding practices for all submissions. When improper billing and coding is not followed, Molina has the right to reject/deny the claim and recover claim payment(s). Due to changing industry practices, Molina reserves the right to revise this policy as needed.

# APPROVAL HISTORY

06/11/2025	Policy revised. Title changed. Removed sub criteria under bridge therapy criteria. Applied failure of systemic therapy to neuroendocrine tumors only. Updated contraindications. Updated Summary of Medical Evidence and References. IRO Peer
	Review on June 9, 2025, by a practicing physician board certified in Radiation Oncology.
08/14/2024	Policy reviewed, no changes to coverage criteria. Overview, Summary of Medical Evidence, and References sections updated.
08/09/2023	Policy reviewed, no changes to coverage criteria. Overview, Summary of Medical Evidence, and References sections updated. Added code Q3001 and replaced code 75854 with 75894.
08/10/2022	Policy reviewed and updated. Title updated to 'Radioembolization for Primary and Metastatic Tumors of the Liver' (previously Radioactive Microspheres for Liver Cancer.' Clarifications to coverage criteria with no change in intent. Added 'Related Policies' section. Updated references. IRO review June 2022 by practicing board certified diagnostic radiologist.
08/11/2021	Policy reviewed, no changes, updated references.
06/17/2020	Policy reviewed, no changes, updated references.
06/19/2019	Policy reviewed, no changes, updated references.
07/10/2018	Policy reviewed, no changes, updated references.
05/09/2017	Policy reviewed, no changes. Sections updated: Exclusions, Summary of Medical Evidence, references.
06/15/2016	Policy reviewed, no changes.
12/16/2015	Policy reviewed, no changes.
07/10/2014	New policy.

# REFERENCES

- 1. Abdalla EK, Stuart KE, Singal AG. Overview of treatment approaches for hepatocellular carcinoma. Updated May 7, 2025. Accessed May 23, 2025. www.uptodate.com.
- American College of Radiology (ACR), American College of Nuclear Medicine (ACNM), American Radium Society (ARS), American Society for Radiation Oncology (ASTRO), Society of Nuclear Medicine and Molecular Imaging (SNMMI). ACR–ACNM–ARS–ASTRO–SNMMI practice parameter for the performance of therapy with radiopharmaceuticals. 2023. Available from: https://gravitas.acr.org/PPTS/DownloadPreviewDocument?DocId=21
- American College of Radiology (ACR). ACR-ABS-ACNM-ASTRO-SIR-SNMMI practice parameter for radioembolization with microsphere brachytherapy device (RMBD) for treatment of liver malignancies (Resolution 21). Published 2014. Updated 2019. https://www.acr.org/-/media/ACR/Files/Practice-Parameters/rmbd.pdf.
- 4. Curley SA, Stuart KE, Schwartz JM, et al. Localized hepatocellular carcinoma: Liver-directed therapies for nonsurgical candidates not eligible for local thermal ablation. Updated April 23, 2025. Accessed May 23, 2025. www.uptodate.com.
- Ducreux M, Abou-Alfa GK, Bekaii-Saab T, et al. The management of hepatocellular carcinoma. Current expert opinion and recommendations derived from the 24th ESMO/World Congress on Gastrointestinal Cancer, Barcelona, 2022. ESMO Open. 2023 Jun;8(3):101567. doi: 10.1016/j.esmoop.2023.101567. Epub 2023 May 31. PMID: 37263081; PMCID: PMC10245111.
- 6. Eastern Cooperative Oncology Group. ECOG performance status scale [Internet]. Philadelphia (PA): ECOG-ACRIN Cancer Research Group. Accessed May 29, 2025. Available from: https://ecog-acrin.org/resources/ecog-performance-status/
- European Association for the Study of the Liver. EASL Clinical Practice Guidelines on the management of hepatocellular carcinoma. J Hepatol. 2025 Feb;82(2):315-374. doi: 10.1016/j.jhep.2024.08.028. Epub 2024 Dec 17. PMID: 39690085.
- Garin E, Tselikas L, Guiu B, et al. DOSISPHERE-01 Study Group. Personalised versus standard dosimetry approach of selective internal radiation therapy in patients with locally advanced hepatocellular carcinoma (DOSISPHERE-01): A randomised, multicentre, open-label phase 2 trial. Lancet Gastroenterol Hepatol. 2021 Jan;6(1):17-29. doi: 10.1016/S2468-1253(20)30290-9. Epub 2020 Nov 7. PMID: 33166497.

# Molina Clinical Policy Radioembolization (Selective Internal Radiation Therapy) for Liver Tumors Policy No. 181



#### Last Approval: 06/11/2025 Next Review Due By: June 2026

- Hayes. Health technology assessment: Radioactive yttrium-90 microspheres for the treatment of primary unresectable liver cancer for downstaging or as a bridge to transplantation or surgery. Published September 11, 2019. Updated September 29, 2022. Accessed May 23, 2025. https://evidence.hayesinc.com.
- Lemieux S, Buies A, F Turgeon A, Hallet J, Daigle G, Côté F, Provencher S. Effect of Yttrium-90 transarterial radioembolization in patients with non-surgical hepatocellular carcinoma: A systematic review and meta-analysis. PLoS One. 2021 Mar 4;16(3):e0247958. doi: 10.1371/journal.pone.0247958. PMID: 33662011; PMCID: PMC7932100.National Cancer Institute (NCI). Adult primary liver cancer treatment (PDQ®). Published 2021.
- 11. <sup>1</sup>National Comprehensive Cancer Network (NCCN). Biliary tract cancers (V1. 2025). Updated March 20, 2025. Accessed May 23, 2025. https://www.nccn.org/professionals/physician\_gls/pdf/btc.pdf
- 12. <sup>2</sup>National Comprehensive Cancer Network (NCCN). Hepatocellular carcinoma (V1.2025). Updated March 20, 2025. Accessed May 23, 2025. https://www.nccn.org/professionals/physician\_gls/pdf/hcc.pdf
- National Institute for Health and Care Excellence (NICE). Selective internal radiation therapies for treating hepatocellular carcinoma [TA688]. Published March 31, 2021. Updated July 3, 2024. Accessed May 23, 2025. https://www.nice.org.uk/guidance/ ta688.
- 14. Schwartz JM, Carithers RL. Epidemiology and risk factors for hepatocellular carcinoma. Updated April 10, 2025. Accessed May 23, 2025. www.uptodate.com.
- 15. Tsoulfas G, Curley SA, Abdalla EK, et al. Liver transplantation for hepatocellular carcinoma. Updated December 15, 2023. Accessed May 23, 2025. www.uptodate.com.
- 16. United States Food and Drug Administration (FDA). Humanitarian device exemption (HDE): TheraSphere (HDE no. H980006). Published December 10, 1999. Accessed May 22, 2025. https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfhde/hde.cfm/.
- 17. United States Food and Drug Administration (FDA). Humanitarian device exemption (HDE): TheraSphere (HDE no. H980006/S011). Published November 14, 2006. Accessed May 22, 2025. https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfhde/hde.cfm/.
- 18. United States Food and Drug Administration (FDA). Premarket approval (PMA) for the SIR-Spheres (PMA no. P990065) Published March 5, 2002. Accessed May 22, 2025. https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMA/pma.cfm/.
- 19. United States Food and Drug Administration (FDA). Premarket approval (PMA) for the SIR-Spheres (PMA no. P200029) Published March 17, 2021. Accessed May 22, 2025. https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMA/pma.cfm/.
- United States Nuclear Regulatory Commission (NRC). Yttrium-90 Microsphere Brachytherapy Sources and Devices TheraSphere® and SIR-20. Guidance Revision 10.2 Revised April 20, Spheres® Licensing 2021. Accessed May 23 2025 https://www.nrc.gov/docs/ML2108/ML21089A364.pdf
- Zeng H, Zhou C, Chen X, et al. Comparison of the efficacy and safety of selective internal radiotherapy and sorafenib alone or combined for hepatocellular carcinoma: a systematic review and Bayesian network meta-analysis. Clin Exp Med. 2023 Feb 3. doi: 10.1007/s10238-023-00997-3. Epub ahead of print. PMID: 36737488.