BlueCross BlueShield of Alabama

Name of Blue Advantage Policy:

Transcatheter Arterial Chemoembolization to Treat Primary or Metastatic Liver Malignancies

Policy #: 737
Latest Review Date: July 2024
Category: Surgical

BACKGROUND:

Blue Advantage *medical policy does not conflict with Local Coverage Determinations (LCDs), Local Medical Review Policies (LMRPs) or National Coverage Determinations (NCDs) or with coverage provisions in Medicare manuals, instructions or operational policy letters. In order to be covered by Blue Advantage the service shall be reasonable and necessary under Title XVIII of the Social Security Act, Section 1862(a)(1)(A). The service is considered reasonable and necessary if it is determined that the service is:*

1. *Safe and effective;*
2. *Not experimental or investigational*;*
3. *Appropriate, including duration and frequency that is considered appropriate for the service, in terms of whether it is:*
   - *Furnished in accordance with accepted standards of medical practice for the diagnosis or treatment of the patient's condition or to improve the function of a malformed body member;*
   - *Furnished in a setting appropriate to the patient's medical needs and condition;*
   - *Ordered and furnished by qualified personnel;*
   - *One that meets, but does not exceed, the patient's medical need; and*
   - *At least as beneficial as an existing and available medically appropriate alternative.*

Routine costs of qualifying clinical trial services with dates of service on or after September 19, 2000, which meet the requirements of the Clinical Trials NCD are considered reasonable and necessary by Medicare. Providers should bill* ***Original Medicare* *for covered services that are related to* ***clinical trials*** *that meet Medicare requirements (Refer to Medicare National Coverage Determinations Manual, Chapter 1, Section 310 and Medicare Claims Processing Manual Chapter 32, Sections 69.0-69.11).*

POLICY:

Effective for dates of service on or after August 17, 2020:

Blue Advantage will treat **transcatheter arterial chemoembolization (TACE)** as a **covered benefit** for individuals with one of the following indications:

- hepatocellular carcinoma (HCC)
- metastatic liver carcinoma

Blue Advantage will treat **transcatheter arterial chemoembolization of the liver** as a **non-covered benefit** and **investigational**:

- as part of combination therapy (with radiofrequency ablation) for resectable or unresectable hepatocellular carcinoma

Blue Advantage does not approve or deny procedures, services, testing, or equipment for our members. Our decisions concern coverage only. The decision of whether or not to have a certain test, treatment or procedure is one made between the physician and his/her patient. Blue Advantage administers benefits based on the members' contracts and medical policies. Physicians should always exercise their best medical judgment in providing the care they feel is most appropriate for their patients. Needed care should not be delayed or refused because of a coverage determination.

DESCRIPTION OF PROCEDURE OR SERVICE:

Transcatheter Arterial Chemoembolization (TACE)

Transcatheter arterial chemoembolization (TACE) of the liver is a proposed alternative to conventional systemic or intra-arterial chemotherapy and to various nonsurgical ablative techniques, to treat resectable and nonresectable tumors. TACE combines the infusion of chemotherapeutic drugs with particle embolization. Tumor ischemia secondary to the embolization raises the drug concentration compared with infusion alone, extending the retention of the chemotherapeutic agent and decreasing systemic toxicity. The liver is especially amenable to such an approach, given its distinct lobular anatomy, the existence of 2 independent blood supplies, and the ability of healthy hepatic tissue to grow and thus compensate for tissue mass lost during chemoembolization.

Transcatheter arterial chemoembolization (TACE) is a minimally invasive procedure performed by interventional radiologists who inject highly concentrated doses of chemotherapeutic agents into the tumor tissues and embolic agent(s) to restrict tumor blood supply. The embolic agent(s) causes ischemia and necrosis of the tumor and slows anticancer drug washout. The most common anticancer drugs used in published TACE studies for hepatocellular carcinoma (HCC) include doxorubicin (36%), followed by cisplatin (31%), epirubicin (12%), mitoxantrone (8%), and mitomycin C (8%).

The TACE procedure requires hospitalization for placement of a hepatic artery catheter and workup to establish eligibility for chemoembolization. Before the procedure, the patency of the

portal vein must be demonstrated to ensure an adequate posttreatment hepatic blood supply. With the patient under local anesthesia and mild sedation, a superselective catheter is inserted via the femoral artery and threaded into the hepatic artery. Angiography is then performed to delineate the hepatic vasculature, followed by injection of the embolic chemotherapy mixture. Embolic material varies but may include a viscous collagen agent, polyvinyl alcohol particles, or ethiodized oil. Typically, only 1 lobe of the liver is treated during a single session, with subsequent embolization procedures scheduled 5 days to 6 weeks later. In addition, because the embolized vessel recanalizes, chemoembolization can be repeated as many times as necessary.

KEY POINTS:

The most recent literature update was performed through May 21, 2024.

Summary of Evidence

Unresectable and Resectable Hepatocellular Carcinoma

For individuals who have unresectable hepatocellular carcinoma (HCC) confined to the liver and not associated with portal vein thrombosis who receive transcatheter arterial chemoembolization (TACE), the evidence includes several randomized controlled trials (RCTs), large observational studies, and systematic reviews. Relevant outcomes are overall survival (OS), disease-specific survival, quality of life, and treatment-related mortality and morbidity. Overall, studies have shown improved overall survival compared with only supportive care. There is evidence from a limited number of RCTs that TACE offers a survival advantage compared with no therapy and survival with TACE is at least as good as with systemic chemotherapy. One systematic review has highlighted possible biases associated with these studies. The evidence is sufficient to determine quantitatively that the technology results in an improvement in the net health outcome.

For individuals who have resectable HCC who receive neoadjuvant or adjuvant TACE, the evidence includes several RCTs and systematic reviews. Relevant outcomes are OS, disease-specific survival, quality of life, and treatment-related mortality and morbidity. Studies have shown little to no difference in OS rates with neoadjuvant TACE compared with surgery alone. A meta-analysis found no significant improvements in survival or recurrence with preoperative TACE for resectable HCC. While both RCTs and the meta-analysis that evaluated TACE as adjuvant therapy to hepatic resection in HCC reported positive results, the quality of individual studies and the methodologic issues related to the meta-analysis preclude certainty when interpreting the results. Well-conducted multicentric trials from the U.S. or Europe representing relevant populations with adequate randomization procedures, blinded assessments, centralized oversight, and publication in peer-reviewed journals are required. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have resectable HCC who receive TACE plus radiofrequency ablation (RFA), the evidence includes a single RCT and a systematic review. Relevant outcomes are OS, disease-specific survival, quality of life, and treatment-related mortality and morbidity.

The RCT failed to show the superiority in survival benefit with combination TACE plus RFA treatment compared with surgery for HCC lesions 3 cm or smaller. Further, an ad hoc subgroup analysis showed a significant benefit for surgery in recurrence and OS in patients with lesions larger than 3 cm. It cannot be determined from this trial whether TACE plus RFA is as effective as a surgical resection for these small tumors. The systematic review, which included mostly retrospective observational studies, did not find a survival benefit with TACE plus RFA over surgery alone. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have unresectable HCC who receive TACE plus RFA, the evidence includes multiple systematic reviews and RCTs. Relevant outcomes are OS, disease-specific survival, quality of life, and treatment-related mortality and morbidity. Multiple meta-analyses and RCTs have shown a consistent benefit in survival and RFS favoring combination TACE plus RFA over RFA alone. However, the results of these meta-analyses are difficult to interpret because the pooled data included heterogeneous patient populations and, in a few cases, data from a study retracted due to questions about data veracity. A larger well-conducted RCT has reported a relative reduction in the hazard of death by 44% and a 14% difference in 4-year survival favoring combination therapy. The major limitations of this trial were its lack of a TACE-alone arm and the generalizability of its findings to patient populations that have unmet needs such as those with multiple lesions larger than 3 cm and Child-Pugh class B or C. Further, this single-center trial was conducted in China, and until these results have been reproduced in patient populations representative of pathophysiology and clinical stage more commonly found in the U.S. or Europe, the results may not be generalizable. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Unresectable Intrahepatic Cholangiocarcinoma

For individuals who have unresectable intrahepatic cholangiocarcinoma who receive TACE, the evidence includes several retrospective observational studies and systematic reviews. Relevant outcomes are overall survival, disease-specific survival, QOL, and treatment-related mortality and morbidity. RCTs evaluating the benefit of adding TACE to the standard of care for patients with unresectable intrahepatic cholangiocarcinoma are lacking. Results of retrospective studies (noncontrolled) have shown a survival benefit with TACE over the standard of care; however, systematic reviews comparing TACE to other locoregional therapies are conflicting. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

TACE for Symptomatic Unresectable Neuroendocrine Tumors

For individuals who have symptomatic metastatic neuroendocrine tumors despite systemic therapy who are not candidates for surgical resection who receive TACE, the evidence includes retrospective single cohort studies. Relevant outcomes are overall survival, disease-specific survival, symptoms, quality of life, and treatment-related mortality and morbidity. There is a lack of evidence from RCTs supporting use of TACE. Uncontrolled trials have reported that TACE reduces symptoms and tumor burden, and improves hormone profiles. Generally, the response rates are over 50% including patients with massive hepatic tumor burden. While many studies

have demonstrated symptom control, survival benefits are less clear. Despite the uncertain benefit on survival, the use of transcatheter arterial chemoembolization to palliate the symptoms associated with hepatic neuroendocrine metastases can provide a clinically meaningful improvement in net health outcomes. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

TACE for Liver Dominant Metastatic Uveal Melanoma

For individuals who have metastatic uveal melanoma who receive TACE, the evidence includes observational studies and reviews. Relevant outcomes are overall survival, disease-specific survival, quality of life, and treatment-related mortality and morbidity. There is a lack of evidence from RCTs assessing use of TACE. Noncomparative prospective and retrospective studies have reported improvement in tumor response and survival compared with historical controls. Given the very limited treatment response from systemic therapy and the rarity of this condition, the existing evidence may support conclusions that TACE meaningfully improves outcomes for patients with hepatic metastases from uveal melanoma. The evidence is sufficient to determine qualitatively that the technology results in an improvement in net health outcomes.

TACE for other Unresectable Hepatic Metastases

For individuals who have unresectable hepatic metastases from any other types of primary tumors (eg, colorectal or breast cancer) who receive TACE, the evidence includes multiple RCTs, observational studies, and systematic reviews. Relevant outcomes are OS, disease-specific survival, quality of life, and treatment-related mortality and morbidity. Multiple RCTs and numerous nonrandomized studies have compared TACE with alternatives in patients who have colorectal cancer and metastases to the liver. Nonrandomized studies have reported that TACE can stabilize disease in 40% to 60% of treated patients but whether this translates into a prolonged survival benefit relative to systemic chemotherapy alone is uncertain. Two small RCTs have reported that TACE with drug-eluting beads has resulted in statistically significant improvements in response rate and PFS. Whether this translates into a prolonged survival benefit relative to systemic chemotherapy alone is uncertain. For cancers other than colorectal, the evidence is extremely limited and no conclusions can be made. Studies have assessed small numbers of patients and the results have varied due to differences in patient selection criteria and treatment regimens used. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Practice Guidelines and Position Statements

Hepatocellular Carcinoma

The National Comprehensive Cancer Network (NCCN) (v.1.2024) guidelines on hepatocellular carcinoma list TACE as an option for patients who are not candidates for surgically curative treatments or as a part of a strategy to bridge patients for other curative therapies. Arterially directed therapies, including TACE, are appropriate for patients with unresectable or inoperable tumors that are not amenable to ablation therapy. Additionally, TACE in highly selected patients has been shown to be safe in the presence of limited tumor invasion of the portal vein. The American Association for the Study of Liver Diseases 2023 guideline on hepatocellular

carcinoma state that patients with Barcelona Clinic Liver Cancer Stage B HCC should receive TACE (Level 1, strong recommendation).118, Both conventional TACE and drug-eluting bead TACE are mentioned, with no preference noted between these 2 modalities. The guideline also suggests using neoadjuvant locoregional therapies (which may include TACE) for bridging to liver transplant in patients with T2 lesions, in order to prevent disease progression and prevent dropouts from the waiting list. The guidelines recommend the use of locoregional therapies, including TACE, in patients with cirrhosis and T2 or T3 disease that is not amenable to resection or transplantation. The American Society of Clinical Oncology (ASCO) 2024 guideline on advanced HCC states that patients with locally advanced disease may be candidates for liver-directed therapies (including TACE); however, the guideline is focused on systemic therapy so there are no recommendations regarding TACE.

Intrahepatic Cholangiocarcinoma

The NCCN (v.2.2024) guidelines on biliary tract cancers including intrahepatic cholangiocarcinoma consider arterially directed therapies, including TACE, to be treatment options for unresectable and metastatic intrahepatic cholangiocarcinoma.

Neuroendocrine and Adrenal Tumors

The NCCN (v.1.2023) guidelines on neuroendocrine and adrenal tumors recommend hepatic regional therapy, including arterial embolization, chemoembolization, or radioembolization, for unresectable liver metastases (category 2B).

Uveal Melanoma Cancer

The NCCN (v.1.2023) guidelines on uveal melanoma state that in patients with disease that is confined to the liver, regional liver-directed therapies such as chemoembolization, radioembolization, or immunoembolization should be considered.

Colon Cancer

The NCCN (v.2.2024) guidelines on colon cancer recommend TACE only for clinical trials. The ASCO-2020 resource-stratified guidelines on late-stage colorectal cancer state that patients with unresectable liver metastases may receive TACE (weak recommendation). However, this recommendation should only be implemented in centers with expertise in the technique, after multidisciplinary review, or in the context of a clinical trial. The 2022 guidelines for metastatic colorectal cancer from ASCO do not address TACE.

Breast Cancer

The NCCN (v.2.2024) guidelines on breast cancer do not address TACE as a treatment option for breast cancer metastatic to the liver.

U.S. Preventive Services Task Force Recommendations

TACE is not a Preventive Service.

KEY WORDS:

Transcatheter Arterial Chemoembolization (TACE)

APPROVED BY GOVERNING BODIES:

Chemoembolization for hepatic tumors is a medical procedure and, as such, is not subject to regulation by the U.S. Food and Drug Administration. However, the embolizing agents and drugs are subject to Food and Drug Administration approval.

BENEFIT APPLICATION:

Coverage is subject to member's specific benefits. Group-specific policy will supersede this policy when applicable.

CURRENT CODING:

CPT Codes:

37243	Vascular embolization or occlusion, inclusive of all radiological supervision and interpretation, intraprocedural road mapping, and imaging guidance necessary to complete the intervention; for tumors, organ ischemia, or infarction
75894	Transcatheter therapy, embolization, any method, radiological supervision and interpretation (this code cannot be reported with code 37243 in the same surgical field)

REFERENCES:

1. Ako S, Nakamura S, Nouso K, et al. Transcatheter Arterial Chemoembolization to Reduce Size of Hepatocellular Carcinoma before Radiofrequency Ablation. Acta Med Okayama. Feb 2018; 72(1): 47-52.
2. Aliberti C, Fiorentini G, Muzzio PC, et al. Trans-arterial chemoembolization of metastatic colorectal carcinoma to the liver adopting DC Bead(R), drug-eluting bead loaded with irinotecan: results of a phase II clinical study. Anticancer Res. Dec 2011; 31(12): 4581-7.
3. Bholee AK, Peng K, Zhou Z, et al. Radiofrequency ablation combined with transarterial chemoembolization versus hepatectomy for patients with hepatocellular carcinoma within Milan criteria: a retrospective case-control study. Clin Transl Oncol. Jul 2017; 19(7): 844-852.

4. Biederman DM, Titano JJ, Korff RA, et al. Radiation Segmentectomy versus Selective Chemoembolization in the Treatment of Early-Stage Hepatocellular Carcinoma. J Vasc Interv Radiol. Jan 2018; 29(1): 30-37.e2.
5. Blue Cross and Blue Shield Association Technology Evaluation Center (TEC). Transcatheter arterial chemoembolization ofhepatic tumors. TEC Assessments. 2000;Volume 15;Tab 22.
6. Boehm LM, Jayakrishnan TT, Miura JT, et al. Comparative effectiveness of hepatic artery based therapies for unresectable intrahepatic cholangiocarcinoma. J Surg Oncol. Feb 2015; 111(2): 213-20.
7. Bruix J, Llovet JM, Castells A, et al. Transarterial embolization versus symptomatic treatment in patients with advanced hepatocellular carcinoma: results of a randomized, controlled trial in a single institution. Hepatology. Jun 1998; 27(6): 1578-83.
8. Bush DA, Smith JC, Slater JD, et al. Randomized Clinical Trial Comparing Proton Beam Radiation Therapy with Transarterial Chemoembolization for Hepatocellular Carcinoma: Results of an Interim Analysis. Int J Radiat Oncol Biol Phys. May 01 2016; 95(1): 477-482.
9. Butcher DA, Brandis KJ, Wang H, et al. Long-term survival and postoperative complications of pre-liver transplantation transarterial chemoembolisation in hepatocellular carcinoma: A systematic review and meta-analysis. Eur J Surg Oncol. Mar 2022; 48(3): 621-631.
10. Carr BI, Kondragunta V, Buch SC, et al. Therapeutic equivalence in survival for hepatic arterial chemoembolization and yttrium 90 microsphere treatments in unresectable hepatocellular carcinoma: a two-cohort study. Cancer. Mar 01 2010;116(5): 1305-14.
11. Chan KS, Tay WX, Cheo FY, et al. Preoperative transarterial chemoembolization (TACE) + liver resection versus upfront liver resection for large hepatocellular carcinoma (≥5 cm): a systematic review and meta-analysis. Acta Chir Belg. Dec 2023; 123(6): 601-617.
12. Chiorean EG, Nandakumar G, Fadelu T, et al. Treatment of Patients With Late-Stage Colorectal Cancer: ASCO Resource-Stratified Guideline. JCO Glob Oncol. Mar 2020; 6: 414-438.
13. Chua TC, Liauw W, Saxena A, et al. Systematic review of neoadjuvant transarterial chemoembolization for resectable hepatocellular carcinoma. Liver Int. Feb 2010; 30(2): 166-74.
14. Edeline J, Lamarca A, McNamara MG, et al. Locoregional therapies in patients with intrahepatic cholangiocarcinoma: A systematic review and pooled analysis. Cancer Treat Rev. Sep 2021; 99: 102258.
15. Eichler K, Zangos S, Mack MG, et al. First human study in treatment of unresectable liver metastases from colorectal cancer with irinotecan-loaded beads (DEBIRI). Int J Oncol. Oct 2012; 41(4): 1213-20.
16. Fiorentini G, Aliberti C, Tilli M, et al. Intra-arterial infusion of irinotecan-loaded drug-eluting beads (DEBIRI) versus intravenous therapy (FOLFIRI) for hepatic metastases

from colorectal cancer: final results of a phase III study. Anticancer Res. Apr 2012; 32(4): 1387-95.

17. Gabr A, Abouchaleh N, Ali R, et al. Comparative study of post-transplant outcomes in hepatocellular carcinoma patients treated with chemoembolization or radioembolization. Eur J Radiol. Aug 2017; 93: 100-106.
18. Gordan JD, Kennedy EB, Abou-Alfa GK, et al. Systemic Therapy for Advanced Hepatocellular Carcinoma: ASCO Guideline Update. J Clin Oncol. May 20 2024; 42(15): 1830-1850
19. Gui CH, Baey S, D'cruz RT, et al. Trans-arterial chemoembolization + radiofrequency ablation versus surgical resection in hepatocellular carcinoma - A meta-analysis. Eur J Surg Oncol. May 2020; 46(5): 763-771.
20. Haochen W, Jian W, Li S, et al. Transarterial chemoembolization plus multi-imaging-guided radiofrequency ablation for elimination of hepatocellular carcinoma nodules measuring 3.1 to 5.0 cm: a single-center study. J Int Med Res. Jul 2018; 46(7): 2650-2657.
21. Heimbach JK, Kulik LM, Finn RS, et al. AASLD guidelines for the treatment of hepatocellular carcinoma. Hepatology. Jan 2018; 67(1): 358-380.
22. Huppert PE, Fierlbeck G, Pereira P, et al. Transarterial chemoembolization of liver metastases in patients with uvealmelanoma. Eur J Radiol. Jun 2010; 74(3): e38-44.
23. IOM (Institute of Medicine). 2011. Clinical Practice Guidelines We Can Trust. Washington, DC: The National Academies Press.
24. Kaibori M, Tanigawa N, Kariya S, et al. A prospective randomized controlled trial of preoperative whole-liver chemolipiodolization for hepatocellular carcinoma. Dig Dis Sci. May 2012; 57(5): 1404-12.
25. Knuppel M, Kubicka S, Vogel A, et al. Combination of conservative and interventional therapy strategies for intra- and extrahepatic cholangiocellular carcinoma: a retrospective survival analysis. Gastroenterol Res Pract. 2012; 2012: 190708.
26. Lan T, Chang L, Rahmathullah MN, et al. Comparative Efficacy of Interventional Therapies for Early-stage Hepatocellular Carcinoma: A PRISMA-compliant Systematic Review and Network Meta-analysis. Medicine (Baltimore). Apr 2016; 95(15): e3185.
27. Li L, Tian J, Liu P, et al. Transarterial chemoembolization combination therapy vs monotherapy in unresectable hepatocellular carcinoma: a meta-analysis. Tumori. Jun 02 2016; 2016(3): 301-10.
28. Liang L, Li C, Diao YK, et al. Survival benefits from adjuvant transcatheter arterial chemoembolization in patients undergoing liver resection for hepatocellular carcinoma: a systematic review and meta-analysis. Therap Adv Gastroenterol. 2020; 13: 1756284820977693.
29. Liao M, Zhu Z, Wang H, et al. Adjuvant transarterial chemoembolization for patients after curative resection of hepatocellular carcinoma: a meta-analysis. Scand J Gastroenterol. Jun 2017; 52(6-7): 624-634.

30. Liu H, Wang ZG, Fu SY, et al. Randomized clinical trial of chemoembolization plus radiofrequency ablation versus partial hepatectomy for hepatocellular carcinoma within the Milan criteria. Br J Surg. Mar 2016; 103(4): 348-56.
31. Lu Z, Wen F, Guo Q, et al. Radiofrequency ablation plus chemoembolization versus radiofrequency ablation alone for hepatocellular carcinoma: a meta-analysis of randomized-controlled trials. Eur J Gastroenterol Hepatol. Feb 2013; 25(2): 187-94.
32. Lv TR, Hu HJ, Liu F, et al. The effect of trans arterial chemoembolization in the management of intrahepatic cholangiocarcinoma. A systematic review and meta-analysis. Eur J Surg Oncol. May 2022; 48(5): 956-966.
33. Martin RC, Joshi J, Robbins K, et al. Hepatic intra-arterial injection of drug-eluting bead, irinotecan (DEBIRI) in unresectable colorectal liver metastases refractory to systemic chemotherapy: results of multi-institutional study. Ann Surg Oncol. Jan 2011;18(1): 192-8.
34. Martin RC, Scoggins CR, Schreeder M, et al. Randomized controlled trial of irinotecan drug-eluting beads with simultaneous FOLFOX and bevacizumab for patients with unresectable colorectal liver-limited metastasis. Cancer. Oct 15 2015; 121(20): 3649-58.
35. Martin RC, Scoggins CR, Tomalty D, et al. Irinotecan drug-eluting beads in the treatment of chemo-naive unresectable colorectal liver metastasis with concomitant systemic fluorouracil and oxaliplatin: results of pharmacokinetics and phase I trial. J Gastrointest Surg. Aug 2012; 16(8): 1531-8.
36. Morimoto M, Numata K, Kondou M, et al. Midterm outcomes in patients with intermediate-sized hepatocellular carcinoma:a randomized controlled trial for determining the efficacy of radiofrequency ablation combined with transcatheter arterialchemoembolization. Cancer. Dec 01 2010; 116(23): 5452-60.
37. Morris VK, Kennedy EB, Baxter NN, et al. Treatment of Metastatic Colorectal Cancer: ASCO Guideline. J Clin Oncol. Jan20 2023; 41(3): 678-700.
38. Mosconi C, Solaini L, Vara G, et al. Transarterial Chemoembolization and Radioembolization for Unresectable Intrahepatic Cholangiocarcinoma-a Systemic Review and Meta-Analysis. Cardiovasc Intervent Radiol. May 2021; 44(5): 728-738.
39. National Cancer Institute, Surveillance Epidemiology and End Results Program. Cancer Stat Facts: Liver and Intrahepatic Bile Duct Cancer. 2024; seer.cancer.gov/statfacts/html/livibd.html.
40. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines): Biliary Tract Cancers, Version 2.2024. Updated April 19, 2024. www.nccn.org/professionals/physician_gls/pdf/btc.pdf.
41. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines): Neuroendocrine and Adrenal Tumors, Version 2.2022. Updated August 2, 2023. www.nccn.org/professionals/physician_gls/pdf/neuroendocrine.pdf.
42. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines): Hepatobiliary Cancers, Version 1.2022. Updated March 29, 2022. www.nccn.org/professionals/physician_gls/pdf/hepatobiliary.pdf.

43. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines): Melanoma: Uveal, Version 1.2023. Updated May 4, 2023. www.nccn.org/professionals/physician_gls/pdf/uveal.pdf.
44. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines): Colon Cancer, Version 2.2024. Updated April 30, 2024. www.nccn.org/professionals/physician_gls/pdf/colon.pdf
45. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines): Breast Cancer, Version 4.2024. Updated March 11, 2024. www.nccn.org/professionals/physician_gls/pdf/breast.pdf.
46. Oliveri RS, Wetterslev J, Gluud C. Transarterial (chemo)embolisation for unresectable hepatocellular carcinoma. Cochrane Database Syst Rev. Mar 16 2011; (3): CD004787.
47. Organ Procurement and Transplantation Network (OPTN). OPTN Policies. Updated May 2, 2024; optn.transplant.hrsa.gov/media/1200/optn_policies.pdf.
48. Park SY, Kim JH, Yoon HJ, et al. Transarterial chemoembolization versus supportive therapy in the palliative treatment of unresectable intrahepatic cholangiocarcinoma. Clin Radiol. Apr 2011; 66(4): 322-8.
49. Peng ZW, Zhang YJ, Chen MS, et al. Radiofrequency ablation with or without transcatheter arterial chemoembolization in the treatment of hepatocellular carcinoma: a prospective randomized trial. J Clin Oncol. Feb 01 2013; 31(4): 426-32.
50. Peng ZW, Zhang YJ, Liang HH, et al. Recurrent hepatocellular carcinoma treated with sequential transcatheter arterial chemoembolization and RF ablation versus RF ablation alone: a prospective randomized trial. Radiology. Feb 2012; 262(2): 689-700.
51. Qi X, Wang D, Su C, et al. Hepatic resection versus transarterial chemoembolization for the initial treatment of hepatocellular carcinoma: A systematic review and meta-analysis. Oncotarget. Jul 30 2015; 6(21): 18715-33.
52. Richardson AJ, Laurence JM, Lam VW. Transarterial chemoembolization with irinotecan beads in the treatment of colorectal liver metastases: systematic review. J Vasc Interv Radiol. Aug 2013; 24(8): 1209-17.
53. Rivera K, Jeyarajah DR, Washington K. Hepatectomy, RFA, and Other Liver Directed Therapies for Treatment of Breast Cancer Liver Metastasis: A Systematic Review. Front Oncol. 2021; 11: 643383.
54. Rowcroft A, Loveday BPT, Thomson BNJ, et al. Systematic review of liver directed therapy for uveal melanoma hepatic metastases. HPB (Oxford). Apr 2020; 22(4): 497-505.
55. 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. Feb 2011; 140(2): 497-507.e2.
56. Seidensticker R, Seidensticker M, Doegen K, et al. Extensive Use of Interventional Therapies Improves Survival in Unresectable or Recurrent Intrahepatic Cholangiocarcinoma. Gastroenterol Res Pract. 2016; 2016: 8732521.

57. Shen PC, Chang WC, Lo CH, et al. Comparison of Stereotactic Body Radiation Therapy and Transarterial Chemoembolization for Unresectable Medium-Sized Hepatocellular Carcinoma. Int J Radiat Oncol Biol Phys. Oct 01 2019; 105(2): 307-318.
58. Si T, Chen Y, Ma D, et al. Preoperative transarterial chemoembolization for resectable hepatocellular carcinoma in Asia area: a meta-analysis of random controlled trials. Scand J Gastroenterol. Dec 2016; 51(12): 1512-1519.
59. Si T, Chen Y, Ma D, et al. Transarterial chemoembolization prior to liver transplantation for patients with hepatocellular carcinoma: A meta-analysis. J Gastroenterol Hepatol. Jul 2017; 32(7): 1286-1294.
60. Singal AG, Llovet JM, Yarchoan M, et al. AASLD Practice Guidance on prevention, diagnosis, and treatment of hepatocellular carcinoma. Hepatology. Dec 01 2023; 78(6): 1922-1965.
61. Sugumar K, Stitzel H, Wu V, et al. Outcomes of Hepatic Artery-Based Therapies and Systemic Multiagent Chemotherapy in Unresectable Colorectal Liver Metastases: A Systematic Review and Meta-analysis. Ann Surg Oncol. Jul 2024; 31(7): 4413-4426.
62. Swierz MJ, Storman D, Riemsma RP, et al. Transarterial (chemo)embolisation versus no intervention or placebo for liver metastases. Cochrane Database Syst Rev. Mar 12 2020; 3(3): CD009498.
63. Tai E, Kennedy S, Farrell A, et al. Comparison of transarterial bland and chemoembolization for neuroendocrine tumours: a systematic review and meta-analysis. Curr Oncol. Dec 2020; 27(6): e537-e546.
64. Tian X, Dai Y, Wang DQ, et al. Transarterial chemoembolization versus hepatic resection in hepatocellular carcinoma treatment: a meta-analysis. Drug Des Devel Ther. 2015; 9: 4431-40.
65. Vogl TJ, Jost A, Nour-Eldin NA, et al. Repeated transarterial chemoembolisation using different chemotherapeutic drug combinations followed by MR-guided laser-induced thermotherapy in patients with liver metastases of colorectal carcinoma. Br J Cancer. Mar 27 2012; 106(7): 1274-9.
66. Wang X, Hu Y, Ren M, et al. Efficacy and Safety of Radiofrequency Ablation Combined with Transcatheter Arterial Chemoembolization for Hepatocellular Carcinomas Compared with Radiofrequency Ablation Alone: A Time-to-Event Meta-Analysis. Korean J Radiol. Jan-Feb 2016; 17(1): 93-102.
67. Xie F, Zang J, Guo X, et al. Comparison of transcatheter arterial chemoembolization and microsphere embolization for treatment of unresectable hepatocellular carcinoma: a meta-analysis. J Cancer Res Clin Oncol. Mar 2012; 138(3): 455-62.
68. Yeh ML, Huang CI, Huang CF, et al. Neoadjuvant transcatheter arterial chemoembolization does not provide survival benefit compared to curative therapy alone in single hepatocellular carcinoma. Kaohsiung J Med Sci. Feb 2015; 31(2): 77-82.
69. Yi Y, Zhang Y, Wei Q, et al. Radiofrequency ablation or microwave ablation combined with transcatheter arterial chemoembolization in treatment of hepatocellular carcinoma by comparing with radiofrequency ablation alone. Chin J Cancer Res. Feb 2014; 26(1): 112-8.

70. 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): e0139940.
71. Zhou Y, Zhang X, Wu L, et al. Meta-analysis: preoperative transcatheter arterial chemoembolization does not improve prognosis of patients with resectable hepatocellular carcinoma. BMC Gastroenterol. Mar 19 2013; 13: 51.

POLICY HISTORY:

Medical Policy Group, August 2020: New policy. Available for comment August 24, 2020, through October 8, 2020.
Medical Policy Group, July 2021
Medical Policy Group, July 2022
Medical Policy Group, July 2023
UM Committee, December 2023: Policy approved by UM Committee for use for Blue Advantage business.
Medical Policy Group, July 2024

This medical policy is not an authorization, certification, explanation of benefits, or a contract. Eligibility and benefits are determined on a case-by-case basis according to the terms of the member's plan in effect as of the date services are rendered. All medical policies are based on (i) research of current medical literature and (ii) review of common medical practices in the treatment and diagnosis of disease as of the date hereof. Physicians and other providers are solely responsible for all aspects of medical care and treatment, including the type, quality, and levels of care and treatment.

This policy is intended to be used for adjudication of claims (including pre-admission certification, pre-determinations, and pre-procedure review) in Blue Cross and Blue Shield's administration of plan contracts.

The plan does not approve or deny procedures, services, testing, or equipment for our members. Our decisions concern coverage only. The decision of whether or not to have a certain test, treatment or procedure is one made between the physician and his/her patient. The plan administers benefits based on the member's contract and corporate medical policies. Physicians should always exercise their best medical judgment in providing the care they feel is most appropriate for their patients. Needed care should not be delayed or refused because of a coverage determination.
As a general rule, benefits are payable under health plans only in cases of medical necessity and only if services or supplies are not investigational, provided the customer group contracts have such coverage.

The following Association Technology Evaluation Criteria must be met for a service/supply to be considered for coverage:

1. *The technology must have final approval from the appropriate government regulatory bodies;*
2. *The scientific evidence must permit conclusions concerning the effect of the technology on health outcomes;*
3. *The technology must improve the net health outcome;*
4. *The technology must be as beneficial as any established alternatives;*
5. *The improvement must be attainable outside the investigational setting.*

Medical Necessity means that health care services (e.g., procedures, treatments, supplies, devices, equipment, facilities or drugs) that a physician, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury or disease or its symptoms, and that are:

1. *In accordance with generally accepted standards of medical practice; and*

2. Clinically appropriate in terms of type, frequency, extent, site and duration and considered effective for the patient's illness, injury or disease; and
3. Not primarily for the convenience of the patient, physician or other health care provider; and
4. Not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.