MASSACHUSETTS

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Medical Policy

Transcatheter Arterial Chemoembolization to Treat Primary or Metastatic Liver Malignancies

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Policy Number: 634

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NCD/LCD: N/A

Related Policies

- Cryosurgical Ablation of Primary or Metastatic Liver Tumors #633
- Radiofrequency Ablation of Primary or Metastatic Liver Tumors #286
- Radioembolization for Primary and Metastatic Tumors of the Liver #292

Policy

Commercial Members: Managed Care (HMO and POS), PPO, and Indemnity Medicare HMO Blue℠ and Medicare PPO Blue℠ Members

Transcatheter arterial chemoembolization of the liver, including the use of drug-eluting beads[1], may be considered **MEDICALLY NECESSARY**:

- To treat hepatocellular cancer that is unresectable but confined to the liver and not associated with portal vein thrombosis and liver function not characterized as Child-Pugh class C
- As a bridge to transplant in individuals with hepatocellular cancer where the intent is to prevent further tumor growth and to maintain a individual's candidacy for liver transplant.
- To treat liver metastasis in symptomatic individuals with metastatic neuroendocrine tumor whose symptoms persist despite systemic therapy and who are not candidates for surgical resection, or
- To treat liver metastasis in individuals with liver-dominant metastatic uveal melanoma.

Transcatheter arterial chemoembolization of the liver, including the use of drug-eluting beads[1], is considered **INVESTIGATIONAL**:

- As neoadjuvant or adjuvant therapy in hepatocellular cancer that is considered resectable.
- As part of combination therapy (with radiofrequency ablation) for resectable or unresectable hepatocellular carcinoma.
- To treat unresectable cholangiocarcinoma.

- To treat liver metastases from any other tumors or to treat hepatocellular cancer that does not meet the criteria noted above, including recurrent hepatocellular carcinoma.
- To treat hepatocellular tumors prior to liver transplantation except as noted above.

Prior Authorization Information

Inpatient

- For services described in this policy, precertification/preauthorization **IS REQUIRED** for all products if the procedure is performed **inpatient**.

Outpatient

- For services described in this policy, see below for products where prior authorization **might be required** if the procedure is performed **outpatient**.

	Outpatient
Commercial Managed Care (HMO and POS)	Prior authorization is **not required.**
Commercial PPO and Indemnity	Prior authorization is **not required.**
Medicare HMO Blue℠	Prior authorization is **not required.**
Medicare PPO Blue℠	Prior authorization is **not required.**

CPT Codes / HCPCS Codes / ICD Codes

Inclusion or exclusion of a code does not constitute or imply member coverage or provider reimbursement. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage as it applies to an individual member.

Providers should report all services using the most up-to-date industry-standard procedure, revenue, and diagnosis codes, including modifiers where applicable.

The following codes are included below for informational purposes only; this is not an all-inclusive list.

The above medical necessity criteria MUST be met for the following codes to be covered for Commercial Members: Managed Care (HMO and POS), PPO, Indemnity, Medicare HMO Blue, and Medicare PPO Blue:

CPT Codes

CPT Codes	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

Description

Transcatheter Arterial 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 include doxorubicin (36%), followed by cisplatin (31%), epirubicin (12%), mitoxantrone (8%), and mitomycin C (8%).[1]

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.

Promotion of greater diversity and inclusion in clinical research of historically marginalized groups (e.g., People of Color [African-American, Asian, Black, Latino and Native American]; LGBTQIA (Lesbian, Gay, Bisexual, Transgender, Queer, Intersex, Asexual); Women; and People with Disabilities [Physical and Invisible]) allows policy populations to be more reflective of and findings more applicable to our diverse members. While we also strive to use inclusive language related to these groups in our policies, use of gender-specific nouns (e.g., women, men, sisters, etc.) will continue when reflective of language used in publications describing study populations.

Adverse Events
Transcatheter arterial chemoembolization of the liver has been associated with potentially life-threatening toxicities and complications, including severe postembolization syndrome, hepatic insufficiency, abscess, or infarction. Transcatheter arterial chemoembolization has been investigated to treat resectable, unresectable, and recurrent hepatocellular carcinoma, cholangiocarcinoma, liver metastases, and in the liver transplant setting. Treatment alternatives include resection, when possible, other locally ablative techniques (eg, radiofrequency ablation, cryoablation), and chemotherapy administered systemically or by hepatic artery infusion. Hepatic artery infusion involves the continuous infusion of chemotherapy with an implanted pump, while TACE is administered episodically. Hepatic artery infusion does not involve the use of embolic material.

Summary

Description
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. Transcatheter arterial chemoembolization 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.

Summary of Evidence
Unresectable and Resectable Hepatocellular Carcinoma
For individuals who have unresectable hepatocellular carcinoma (HCC) ~~HCC~~ confined to the liver and not associated with portal vein thrombosis who receive transcatheter arterial chemoembolization (TACE) ~~TACE~~, the evidence includes several randomized controlled trials (RCTs) ~~RCTs~~, large observational studies, and systematic reviews. Relevant outcomes are overall survival (OS) ~~OS~~, disease-specific survival, quality of life, and treatment-related mortality and morbidity. Evidence from 1 RCT has suggested that survival with TACE is at least as good as with systemic chemotherapy. One systematic review has highlighted possible biases associated with RCTs that compared TACE with no therapy. The evidence is sufficient to determine 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-analyses 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-analyses 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) ~~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, 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.

Bridge to Liver Transplant
For individuals who have a single hepatocellular tumor less than 5 cm or no more than 3 tumors each less than 3 cm in size, absence of extrahepatic disease or vascular invasion, and Child-Pugh class A or B seeking to prevent further tumor growth and to maintain candidacy for liver transplant who receive pretransplant TACE, the evidence includes multiple small prospective studies. Relevant outcomes are OS, disease-specific survival, quality of life, and treatment-related mortality and morbidity. There is a lack of comparative trials on various locoregional treatments as a bridge therapy for liver transplantation. Multiple small prospective studies have demonstrated that TACE can prevent dropouts from the transplant list. Transcatheter arterial chemoembolization has become an accepted method to prevent tumor growth and progression while patients are on the liver transplant waiting list. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

Unresectable Cholangiocarcinoma
For individuals who have unresectable cholangiocarcinoma who receive TACE, the evidence includes several retrospective observational studies and systematic reviews. Relevant outcomes are OS, disease-specific survival, quality of life, and treatment-related mortality and morbidity. Randomized controlled trials evaluating the benefit of adding TACE to the standard of care for patients with unresectable cholangiocarcinoma are lacking. Results of retrospective studies have shown a survival benefit with TACE over the standard of care. These studies lacked matched patient controls. Although the observational data are consistent, the lack of randomization limits definitive conclusions. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Transcatheter Arterial Chemoembolization for Symptomatic Unresectable Neuroendocrine Tumors

For individuals who have symptomatic metastatic neuroendocrine tumors despite systemic therapy and are not candidates for surgical resection who receive TACE, the evidence includes retrospective single-cohort studies. Relevant outcomes are OS, disease-specific survival, symptoms, quality of life, and treatment-related mortality and morbidity. There is a lack of evidence from RCTs supporting the use of TACE. Uncontrolled trials have suggested that TACE reduces symptoms and tumor burden and improves hormone profiles. Generally, the response rates are over 50% and include 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 TACE to palliate the symptoms associated with hepatic neuroendocrine metastases can provide a clinically meaningful improvement in net health outcome. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

Liver-Dominant Metastatic Uveal Melanoma
For individuals who have liver-dominant metastatic uveal melanoma who receive TACE, the evidence includes observational studies and reviews. Relevant outcomes are OS, disease-specific survival, quality of life, and treatment-related mortality and morbidity. There is a lack of evidence from RCTs assessing the use of TACE. Noncomparative prospective and retrospective studies have reported improvements 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 that the technology results in an improvement in the net health outcome.

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 progression-free survival (PFS) ~~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.

Policy History

Date	Action
9/2023	Annual policy review. Reference added and guidelines updated. Policy statements unchanged.
9/2022	Annual policy review. Reference added. Minor editorial refinements to policy statements; intent unchanged.
9/2021	Annual policy review. Investigational statement clarified to be consistent with the evidence appraisal.
7/2021	Prior authorization table clarified.
12/2020	New investigational indications described for TACE as part of combination therapy (with radiofrequency ablation) for resectable or unresectable hepatocellular carcinoma. Effective 12/1/2020.
9/2019	Annual policy review. Description, summary, and references updated. Policy statements unchanged.
9/2018	Annual policy review. Description, summary, and references updated. Policy statements unchanged.
12/2017	Annual policy review. Medically necessary criteria revised. Effective 12/1/2017.

10/2016	Annual policy review. New references added.
11/2015	Annual policy review. New references added.
12/2014	Annual policy review. New references added.
8/2014	Clarified coding information.
1/2014	Annual policy review. New references added.
1/2014	Updated to remove deleted code 37204.
2/2013	Annual policy review. Changes to policy statement. Effective 2/4/2013.
11/2011-4/2012	Medical policy ICD10 remediation: Formatting, editing and coding updates. No changes to policy statements.

Information Pertaining to All Blue Cross Blue Shield Medical Policies

Click on any of the following terms to access the relevant information:

Medical Policy Terms of Use
Managed Care Guidelines
Indemnity/PPO Guidelines
Clinical Exception Process
Medical Technology Assessment Guidelines

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Endnotes

[1] Based on local expert opinion