Transcatheter Arterial Chemoembolization (TACE) to Treat Primary or Metastatic Liver Malignancies

Policy # 00227
Original Effective Date: 03/19/2008
Current Effective Date: 05/15/2019

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the “Company”), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

Note: Radioembolization for Primary and Metastatic Tumors of the Liver is addressed separately in medical policy 00110.

Note: Radiofrequency Ablation of Primary or Metastatic Liver Tumors is addressed separately in medical policy 00182.

Note: Cryosurgical Ablation of Primary or Metastatic Liver Tumors is addressed separately in medical policy 00220.

When Services Are Eligible for Coverage
Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:
- Benefits are available in the member’s contract/certificate, and
- Medical necessity criteria and guidelines are met.

Based on review of available data, the Company may consider transcatheter arterial chemoembolization (TACE) of the liver to treat patients with the following conditions to be eligible for coverage:**
- Liver metastasis in symptomatic patients with metastatic neuroendocrine tumor whose symptoms persist despite systemic therapy and who are not candidates for surgical resection; and
- Liver-dominant metastatic uveal melanoma.
Transcatheter Arterial Chemoembolization (TACE) to Treat Primary or Metastatic Liver Malignancies

Policy # 00227
Original Effective Date: 03/08/2008
Current Effective Date: 05/15/2019

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- Benefits are available in the member’s contract/certificate, and
- Medical necessity criteria and guidelines are met.

Based on review of available data, the Company may consider transcatheter arterial chemoembolization (TACE) of the liver to treat hepatocellular cancer (HCC) to be eligible for coverage.**

Patient Selection Criteria

Coverage eligibility for TACE of the liver to treat HCC will be considered when all of the following criteria are met:

- Tumor is unresectable; and
- Confined to the liver; and
- Not associated with portal vein thrombosis; and
- Child-Pugh class is either A or B.

Based on review of available data, the Company may consider the use of transcatheter arterial chemoembolization (TACE) of the liver as a bridge to transplant in patients with hepatocellular cancer (HCC) where the intent is to prevent further tumor growth and to maintain a patient’s candidacy for liver transplant to be eligible for coverage.**

Patient Selection Criteria

Coverage eligibility when using TACE of the liver as a bridge to transplantation to prevent further tumor growth and to maintain a patient’s candidacy for liver transplant will be considered when all of the following criteria are met:

- A single tumor less than 5cm or no more than 3 tumors each less than 3cm in size; and
- Absence of extrahepatic disease or vascular invasion; and
- Child-Pugh class of either A or B.
Transcatheter Arterial Chemoembolization (TACE) to Treat Primary or Metastatic Liver Malignancies

Policy # 00227
Original Effective Date: 03/08/2008
Current Effective Date: 05/15/2019

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of transcatheter arterial chemoembolization (TACE) of the liver as neoadjuvant or adjuvant therapy in hepatocellular cancer (HCC) that is considered resectable to be investigational.*

Based on review of available data, the Company considers the use of transcatheter arterial chemoembolization (TACE) of the liver to treat hepatocellular tumors prior to liver transplantation, except as noted above, to be investigational.*

Based on review of available data, the Company considers the use of transcatheter arterial chemoembolization (TACE) of the liver to treat liver metastases from any other tumors or to treat hepatocellular cancer (HCC) for those conditions not listed as eligible for coverage, including recurrent HCC, to be investigational.*

Based on review of available data, the Company considers the use of transcatheter arterial chemoembolization (TACE) of the liver to treat unresectable cholangiocarcinoma to be investigational.*

The use of transcatheter arterial chemoembolization (TACE) of the liver when the patient selection criteria are not met is considered to be investigational.*

Background/Overview

Hepatocellular Carcinoma and Intrahepatic Cholangiocarcinoma

In 2015, an estimated 71,990 people in the United States live with hepatocellular carcinoma (HCC) or intrahepatic cholangiocarcinoma (ICC). Of the primary intrahepatic cancers, HCC and ICC account for 90% and 10% of cases, respectively. The number of new cases of HCC and...
ICC are estimated at 8.8 per 100,000 men and women per year. The number of deaths are estimated at 6.4 per 100000 men and women per year.

**Treatment**
Surgical resection represents the only form of curative therapy. However, most ICC patients are not surgical candidates due to their advanced disease at diagnosis, which is caused by the lack of symptoms until late in disease progression. The overall prognosis of ICC is far worse than for extrahepatic cholangiocarcinoma because of its late presentation. Most patients with ICC qualify for palliative therapy, including systemic chemotherapy and radiotherapy. However, such palliative options afford little to no survival benefit over supportive therapy alone, because ICC responds poorly to such existing therapies. Survival prognosis for patients with unresectable ICC is 5 to 8 months.

Transcatheter arterial chemoembolization (TACE) has been explored in various settings as a technique to prevent tumor progression in patients on the liver transplant waiting list, to downstage tumors so a patient may be considered a better candidate for liver transplantation, and to decrease the incidence of post transplant recurrence in patients with larger (T3) tumors. All uses are in part related to the United Network for Organ Sharing (UNOS) liver allocation policy, which prioritizes patients for receiving donor livers. The UNOS policy and the 3 treatment settings are discussed further in the following sections.

**Neuroendocrine Tumors**
Neuroendocrine tumors are a heterogeneous group of typically slow-growing tumors with an indolent course, with the capacity to synthesize and secrete hormones. Liver metastases may result in significant hormonal symptoms and are associated with a poor prognosis.

**Treatment**
Systemic chemotherapy for these tumors has shown modest response rates of limited duration, and although somatostatin analogues are usually effective at controlling symptoms, the disease eventually becomes refractory. Therefore, liver-directed therapies aim to reduce tumor burden, to lower hormone levels, and to palliate symptoms in patients with unresectable neuroendocrine metastases.
Transcatheter Arterial Chemoembolization (TACE) to Treat Primary or Metastatic Liver Malignancies

Policy # 00227
Original Effective Date: 03/08/2008
Current Effective Date: 05/15/2019

Uveal Melanoma
Uveal melanoma (also called ocular melanoma) is the most common primary ocular malignancy in adults and shows a strong predilection for liver metastases.

Treatment
Even with successful treatment of the primary tumor, up to 50% of patients will subsequently develop systemic metastases, with liver involvement in up to 90% of these patients. Metastatic uveal melanoma is resistant to systemic chemotherapy, leading to the evaluation of locoregional treatment modalities to control tumor progression in the liver, including TACE.

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 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 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 post treatment hepatic blood supply. With the patient under local anesthesia and mild sedation, a super selective 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.

Adverse Events
TACE of the liver has been associated with potentially life-threatening toxicities and complications, including severe post embolization syndrome, hepatic insufficiency, abscess, or infarction. TACE has been investigated to treat resectable, unresectable, and recurrent HCC, cholangiocarcinoma, liver metastases from other primary malignancies, and non-metastatic HCC.
Transcatheter Arterial Chemoembolization (TACE) to Treat Primary or Metastatic Liver Malignancies

Policy # 00227
Original Effective Date: 03/08/2008
Current Effective Date: 05/15/2019

metastases, and in the liver transplant setting. Treatment alternatives include resection when possible, chemotherapy administered systemically or by hepatic artery infusion (HAI). HAI involves the continuous infusion of chemotherapy with an implanted pump, while TACE is administered episodically. HAI does not involve the use of embolic material.

UNOS Liver Allocation Policy
In 2002, UNOS introduced the Model for End-Stage Liver Disease (MELD) system for allocating new livers to adults awaiting transplant. The MELD score is a continuous disease severity scale incorporating bilirubin, prothrombin time (ie, international normalized ratio), and creatinine into an equation, producing a number that ranges from 6 (less ill) to 40 (gravely ill). Aside from those in fulminant liver failure, donor livers are prioritized to those with the highest MELD score. This system accurately predicts the risk of dying from liver disease except for those with HCC, who often have low MELD scores, because bilirubin, international normalized ratio, and creatinine levels are near normal. Therefore, patients with HCC are assigned additional allocation points according to the size and number (T stage) of tumor nodules as follows:

- **T1:** 1 nodule greater than 1 cm and 1.9 cm or smaller
- **T2:** 1 nodule between 2.0 and 5.0 cm, or 2 or 3 nodules each 1 cm or greater and up to 3.0 cm
- **T3:** 1 nodule larger than 5.0 cm, or 2 or 3 nodules with at least 1 larger than 3.0 cm.

Patients with T1 lesions are considered at low risk of death on the waiting list, while those with T3 lesions are at high risk of post transplant recurrence and are generally not considered transplant candidates. Patients with T2 tumors have an increased risk of dying while on the waiting list compared with those who had T1 lesions and are an acceptable risk of post transplant tumor recurrence. Therefore, UNOS criteria, which were updated in 2018, prioritize only T2 HCC patients who meet specified staging and imaging criteria by allocating additional points equivalent to a MELD score predicting a 15% probability of death within 3 months. This definition of T2 lesions is often referred to as the Milan criteria, in reference to a key study by Mazzaferro et al (1996) that examined the recurrence rate of HCC according to the size of the initial tumor. Liver transplantation for those with T3 HCC is not prohibited, but these patients do not receive priority on the waiting list. All patients with HCC awaiting transplantation are reassessed at 3-month intervals. Those whose tumors have progressed and are no longer T2 tumors lose the additional allocation points. Additionally, nodules identified through imaging of cirrhotic livers are given an Organ Procurement
Transcatheter Arterial Chemoembolization (TACE) to Treat Primary or Metastatic Liver Malignancies

Policy # 00227
Original Effective Date: 03/08/2008
Current Effective Date: 05/15/2019

and Transplantation Network class 5 designation. Class 5B and 5T nodules are eligible for automatic priority. Class 5B criteria consist of a single nodule 2 cm or larger and up to 5 cm (T2 stage) that meets specified imaging criteria. Class 5T nodules have undergone subsequent locoregional treatment after being automatically approved on initial application or extension. A single class 5A nodule (>1 cm and <2 cm) corresponds to T1 HCC and does not qualify for automatic priority. However, combinations of class 5A nodules are eligible for automatic priority if they meet stage T2 criteria. Class 5X lesions are outside of stage T2 and are not eligible for automatic exception points. Nodules less than 1 cm are considered indeterminate and are not considered for additional priority.

The UNOS allocation system provides strong incentives to use locoregional therapies to downsize tumors to T2 status and to prevent progression while on the waiting list. In a report from a national conference in the United States, Pomfret et al (2010) addressed the need to characterize better the long-term outcomes of liver transplantation for patients with HCC and to assess the justification for continuing the policy of assigning increased priority for candidates with early-stage HCC on the U.S. transplant waiting list. There was a general consensus for developing a calculated continuous HCC priority score for ranking HCC candidates on the list that would incorporate the calculated MELD score, α-fetoprotein, tumor size, and rate of tumor growth and that only candidates with at least stage T2 tumors would receive additional HCC priority points. The report addressed the role of locoregional therapy to downstage patients from T3 to T2 and stated that the results of down staging before liver transplantation are heterogeneous, with no upper limits for tumor size and number before down staging across studies, and the use of different end points for down staging before transplantation.

**FDA or Other Governmental Regulatory Approval**

**U.S. Food and Drug Administration (FDA)**

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.

**Rationale/Source**

Transcatheter arterial chemoembolization (TACE) of the liver is a proposed alternative to conventional systemic or intra-arterial chemotherapy and to various nonsurgical ablative techniques,
Transcatheter Arterial Chemoembolization (TACE) to Treat Primary or Metastatic Liver Malignancies

Policy # 00227
Original Effective Date: 03/08/2008
Current Effective Date: 05/15/2019

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.

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 TACE, the evidence includes several randomized controlled trials (RCTs), large observational studies, and systematic reviews. Relevant outcomes are overall survival, disease-specific survival, quality of life, and treatment-related mortality and morbidity. Evidence from a limited number of RCTs has suggested 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 that the technology results in a meaningful 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 overall survival, disease-specific survival, quality of life, and treatment-related mortality and morbidity. Studies have shown little to no difference in overall survival 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 United States 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 the effects of the technology on health outcomes.

For individuals who have resectable HCC who receive TACE plus radiofrequency ablation (RFA), the evidence includes a single RCT. Relevant outcomes are overall survival, disease-specific survival, quality of life, and treatment-related mortality and morbidity. The RCT failed to show the
Transcatheter Arterial Chemoembolization (TACE) to Treat Primary or Metastatic Liver Malignancies

Policy # 00227
Original Effective Date: 03/08/2008
Current Effective Date: 05/15/2019

superiority in survival benefit with combination TACE plus RFA treatment compared with surgery for HCC lesions 3.0 cm or smaller. Further, an ad hoc subgroup analysis showed a significant benefit for surgery in recurrence and overall survival in patients with lesions larger than 3 cm. It cannot be determined from this trial whether TACE plus RFA is as effective as surgical resection for these small tumors. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have unresectable HCC who receive TACE plus RFA, the evidence includes multiple systematic reviews and RCTs. Relevant outcomes are overall survival, 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 recurrence-free survival 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 United States or Europe, the results may not be generalizable. The evidence is insufficient to determine the effects of the technology on health outcomes.

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 patient candidacy for liver transplant who receive pre-transplant TACE, the evidence includes multiple small prospective studies. Relevant outcomes are overall survival, 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. TACE has become an accepted method to prevent tumor growth and progression while patients are on the liver
Transcatheter Arterial Chemoembolization (TACE) to Treat Primary or Metastatic Liver Malignancies

Policy # 00227  
Original Effective Date: 03/08/2008  
Current Effective Date: 05/15/2019

transplant waiting list. The evidence is sufficient to determine that the technology results in a meaningful 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 overall survival, disease-specific survival, quality of life, and treatment-related mortality and morbidity. RCT evaluating the benefit of adding TACE to the standard of care for patients with unresectable cholangiocarcinoma are lacking. Results of 3 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 the effects of the technology on health outcomes.

**TACE 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 overall survival, disease-specific survival, 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 a meaningful 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 overall survival, 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. No comparative 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 a meaningful 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 overall survival, 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. 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 the effects of the technology on health outcomes.

Supplemental Information
Clinical Input from Physician Specialty Societies and Academic Medical Centers
While the various physician specialty societies and academic medical centers may collaborate with and make recommendations during this process, through the provision of appropriate reviewers, input received does not represent an endorsement or position statement by the physician specialty societies or academic medical centers, unless otherwise noted.

In response to requests, input was received from 1 specialty medical society (2 reviewers) and 3 academic medical centers while this policy was under review in 2012. There was general agreement that use of transcatheter arterial chemoembolization (TACE) was medically necessary for indications in the policy; however, reviewers were split for its use as a bridge to transplant. There was general
Transcatheter Arterial Chemoembolization (TACE) to Treat Primary or Metastatic Liver Malignancies

Policy # 00227  
Original Effective Date: 03/08/2008  
Current Effective Date: 05/15/2019

support for the investigational policy statement for the use of TACE as neoadjuvant or adjuvant therapy in resectable hepatocellular carcinoma. Reviewers were split over the investigational policy statement to treat other liver metastases or for recurrent hepatocellular carcinoma. Four reviewers provided input on the use of TACE in unresectable cholangiocarcinoma; 2 reviewers considered it investigational and 2 others considered it investigational but also medically necessary, the latter citing data showing a survival benefit of TACE compared with supportive therapy.

Practice Guidelines and Position Statements

National Comprehensive Cancer Network Guidelines

**Hepatocellular Carcinoma**
National Comprehensive Cancer Network (NCCN) guidelines on hepatocellular carcinoma (v.2.2018) list transcatheter arterial chemoembolization (TACE) as an option for patients, not candidates for surgically curative treatments or as a part of a strategy to bridge patients for other curative therapies (category 2A). The guidelines also recommend that patients with tumors size between 3 and 5 cm can be considered for combination therapy with ablation and arterial embolization and those with unresectable or inoperable tumors greater than 5 cm be treated using arterial embolic approaches or systemic therapies. Additionally, TACE in highly selected patients has been shown to be safe in the presence of limited tumor invasion of the portal vein.

**Intrahepatic Cholangiocarcinoma**
NCCN guidelines on intrahepatic cholangiocarcinoma (v.2.2018) consider arterially directed therapies, including TACE, to be treatment options for unresectable and metastatic intrahepatic cholangiocarcinoma.

**Neuroendocrine Tumors, Carcinoid, and Islet Cell Tumors**
NCCN guidelines on neuroendocrine tumors, carcinoid, and islet cell tumors (v.2.2018) consider chemoembolization as an effective approach for patients with hepatic-predominant metastatic disease (category 2A).
Transcatheter Arterial Chemoembolization (TACE) to Treat Primary or Metastatic Liver Malignancies

Policy #  00227  
Original Effective Date:  03/08/2008  
Current Effective Date:  05/15/2019

**Uveal Cancer**  
No NCCN guidelines were identified for uveal malignancies.

**Colon Cancer**  
NCCN guidelines on colon cancer (v.2.2018) recommend that, for highly selected patients with chemotherapy-resistant and -refractory disease and with predominant hepatic metastases, arterially directed catheter therapy and, in particular, yttrium-90 microsphere selective internal radiation is an option.

**Breast Cancer**  
NCCN guidelines on breast cancer (v.1.2018) do not address TACE as a treatment option for breast cancer metastatic to the liver.

**U.S. Preventive Services Task Force Recommendations**  
Not applicable.

**Medicare National Coverage**  
There is no national coverage determination. In the absence of a national coverage determination, coverage decisions are left to the discretion of local Medicare carriers.

**Ongoing and Unpublished Clinical Trials**  
Some currently unpublished trials that might influence this review are listed in Table 1.

<table>
<thead>
<tr>
<th>NCT No.</th>
<th>Trial Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ongoing</td>
<td></td>
</tr>
<tr>
<td>NCT01869088</td>
<td>Phase III Trial of Transcatheter Arterial Chemoembolization(TACE) Plus Recombinant Human Adenovirus Type 5 Injection for Unresectable Hepatocellular Carcinoma (HCC)</td>
</tr>
<tr>
<td>NCT01004978</td>
<td>A Phase III Randomized, Double-Blind Trial of Chemoembolization With or Without Sorafenib in Unresectable Hepatocellular Carcinoma (HCC) in Patients With and Without Vascular Invasion</td>
</tr>
</tbody>
</table>

©2019 Blue Cross and Blue Shield of Louisiana

Blue Cross and Blue Shield of Louisiana is an independent licensee of the Blue Cross and Blue Shield Association and incorporated as Louisiana Health Service & Indemnity Company.

No part of this publication may be reproduced, stored in a retrieval system, or transmitted, in any form or by any means, electronic, mechanical, photocopying, or otherwise, without permission from Blue Cross and Blue Shield of Louisiana.

Page 13 of 25
Transcatheter Arterial Chemoembolization (TACE) to Treat Primary or Metastatic Liver Malignancies

Policy # 00227
Original Effective Date: 03/08/2008
Current Effective Date: 05/15/2019

<table>
<thead>
<tr>
<th>NCT No.</th>
<th>Trial Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>NCT02936388</td>
<td>Transarterial Radioembolisation in Comparison to Transarterial Chemoembolisation in Uveal Melanoma Liver Metastasis (SirTac)</td>
</tr>
<tr>
<td>NCT01906216</td>
<td>Sorafenib With or Without Transarterial Chemoembolization (TACE) in Advanced Hepatocellular Carcinoma: A Multicenter, Randomized, Controlled Trial</td>
</tr>
<tr>
<td>NCT01833286</td>
<td>Radiofrequency Ablation Combined With Transcatheter Arterial Chemoembolization Versus Re-resection for Recurrent Hepatocellular Carcinoma</td>
</tr>
<tr>
<td>Unpublished</td>
<td>Efficacy of Transarterial Chemoembolization With DC-BeadsR Prior to Liver Transplantation for Hepatocellular Carcinoma on Patient Survival: A Prospective Multicentre and Randomized Study</td>
</tr>
<tr>
<td>NCT01512407</td>
<td>Randomised Controlled Trial on Adjuvant Transarterial Chemoembolisation After Curative Hepatectomy for Hepatocellular Carcinoma</td>
</tr>
<tr>
<td>NCT00908752</td>
<td>A Randomized, Double-blind, Multicenter Phase III Study of Brivanib Versus Placebo as Adjuvant Therapy to Trans-Arterial Chemo-Embolization (TACE) in Patients With Unresectable Hepatocellular Carcinoma (The BRISK TA Study)</td>
</tr>
</tbody>
</table>

NCT: national clinical trial.

a Denotes industry-sponsored or cosponsored trial.

References


©2019 Blue Cross and Blue Shield of Louisiana

Blue Cross and Blue Shield of Louisiana is an independent licensee of the Blue Cross and Blue Shield Association and incorporated as Louisiana Health Service & Indemnity Company.

No part of this publication may be reproduced, stored in a retrieval system, or transmitted, in any form or by any means, electronic, mechanical, photocopying, or otherwise, without permission from Blue Cross and Blue Shield of Louisiana.
Transcatheter Arterial Chemoembolization (TACE) to Treat Primary or Metastatic Liver Malignancies

Policy # 00227
Original Effective Date: 03/08/2008
Current Effective Date: 05/15/2019

7. Blue Cross and Blue Shield Association Technology Evaluation Center (TEC). Transcatheter arterial chemoembolization of hepatic tumors. TEC Assessments. 2000;Volume 15;Tab 22. PMID
Transcatheter Arterial Chemoembolization (TACE) to Treat Primary or Metastatic Liver Malignancies

Policy #  00227
Original Effective Date:  03/08/2008
Current Effective Date:  05/15/2019


©2019 Blue Cross and Blue Shield of Louisiana

Blue Cross and Blue Shield of Louisiana is an independent licensee of the Blue Cross and Blue Shield Association and incorporated as Louisiana Health Service & Indemnity Company.

No part of this publication may be reproduced, stored in a retrieval system, or transmitted, in any form or by any means, electronic, mechanical, photocopying, or otherwise, without permission from Blue Cross and Blue Shield of Louisiana.
Transcatheter Arterial Chemoembolization (TACE) to Treat Primary or Metastatic Liver Malignancies

Policy # 00227
Original Effective Date: 03/08/2008
Current Effective Date: 05/15/2019


©2019 Blue Cross and Blue Shield of Louisiana

Blue Cross and Blue Shield of Louisiana is an independent licensee of the Blue Cross and Blue Shield Association and incorporated as Louisiana Health Service & Indemnity Company.

No part of this publication may be reproduced, stored in a retrieval system, or transmitted, in any form or by any means, electronic, mechanical, photocopying, or otherwise, without permission from Blue Cross and Blue Shield of Louisiana.
Transcatheter Arterial Chemoembolization (TACE) to Treat Primary or Metastatic Liver Malignancies

Policy # 00227
Original Effective Date: 03/08/2008
Current Effective Date: 05/15/2019


©2019 Blue Cross and Blue Shield of Louisiana

Blue Cross and Blue Shield of Louisiana is an independent licensee of the Blue Cross and Blue Shield Association and incorporated as Louisiana Health Service & Indemnity Company.

No part of this publication may be reproduced, stored in a retrieval system, or transmitted, in any form or by any means, electronic, mechanical, photocopying, or otherwise, without permission from Blue Cross and Blue Shield of Louisiana.
Transcatheter Arterial Chemoembolization (TACE) to Treat Primary or Metastatic Liver Malignancies

Policy # 00227
Original Effective Date: 03/08/2008
Current Effective Date: 05/15/2019

Transcatheter Arterial Chemoembolization (TACE) to Treat Primary or Metastatic Liver Malignancies

Policy #  00227
Original Effective Date:  03/08/2008
Current Effective Date:  05/15/2019


Policy History
Original Effective Date:  03/19/2008
Current Effective Date:  05/15/2019
03/12/2008     Medical Director review
03/19/2008     Medical Policy Committee approval.
03/04/2009     Medical Director review
03/18/2009     Medical Policy Committee approval. No change to coverage.
06/03/2010     Medical Policy Committee approval
06/16/2010     Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
05/05/2011     Medical Policy Committee review
05/18/2011     Medical Policy Implementation Committee approval. Added that the use of transcatheter hepatic arterial chemoembolization as neoadjuvant or adjuvant therapy in hepatocellular cancer that is considered resectable is considered to be investigational.
05/03/2012     Medical Policy Committee review

©2019 Blue Cross and Blue Shield of Louisiana

Blue Cross and Blue Shield of Louisiana is an independent licensee of the Blue Cross and Blue Shield Association and incorporated as Louisiana Health Service & Indemnity Company.

No part of this publication may be reproduced, stored in a retrieval system, or transmitted, in any form or by any means, electronic, mechanical, photocopying, or otherwise, without permission from Blue Cross and Blue Shield of Louisiana.

Page 21 of 25
Transcatheter Arterial Chemoembolization (TACE) to Treat Primary or Metastatic Liver Malignancies

Policy # 00227
Original Effective Date: 03/08/2008
Current Effective Date: 05/15/2019

05/16/2012 Medical Policy Implementation Committee approval. Added that TACE for unresectable cholangio-carcinoma is considered investigational. Revised the format of the remaining investigational statements while preserving their intent.

05/02/2013 Medical Policy Committee review
05/22/2013 Medical Policy Implementation Committee approval. Format Coverage eligibility unchanged.

05/01/2014 Medical Policy Committee review
05/21/2014 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.

05/07/2015 Medical Policy Committee review
05/20/2015 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.

08/03/2015 Coding update: ICD10 Diagnosis code section added; ICD9 Procedure code section removed.

05/05/2016 Medical Policy Committee review
05/18/2016 Medical Policy Implementation Committee approval. Coverage eligibility unchanged

01/01/2017 Coding update: Removing ICD-9 Diagnosis Codes
05/04/2017 Medical Policy Committee review
05/17/2017 Medical Policy Implementation Committee approval. Coverage eligibility unchanged

05/03/2018 Medical Policy Committee review
05/16/2018 Medical Policy Implementation Committee approval. Changed formatting from one statement to bulleted conditions in the “When Services Are Eligible for Coverage” section. Changed formatting by grouping individual coverage statements into 2 separate coverage statements for TACE with criteria by adding a “When Services May Be Eligible for Coverage” section. Added “Child-Pugh class is either A or B” as criteria for TACE to treat HCC. Replaced “hepatic” with “of the liver” in all statements in the coverage section. Added a link for the Child-Pugh Score calculator in the coverage section.

05/02/2019 Medical Policy Committee review
05/15/2019 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
Transcatheter Arterial Chemoembolization (TACE) to Treat Primary or Metastatic Liver Malignancies

Policy # 00227
Original Effective Date: 03/08/2008
Current Effective Date: 05/15/2019

Next Scheduled Review Date: 05/2020

Coding
The five character codes included in the Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology (CPT®), copyright 2018 by the American Medical Association (AMA). CPT is developed by the AMA as a listing of descriptive terms and five character identifying codes and modifiers for reporting medical services and procedures performed by physician.

The responsibility for the content of Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines is with Blue Cross and Blue Shield of Louisiana and no endorsement by the AMA is intended or should be implied. The AMA disclaims responsibility for any consequences or liability attributable or related to any use, nonuse or interpretation of information contained in Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines. Fee schedules, relative value units, conversion factors and/or related components are not assigned by the AMA, are not part of CPT, and the AMA is not recommending their use. The AMA does not directly or indirectly practice medicine or dispense medical services. The AMA assumes no liability for data contained or not contained herein. Any use of CPT outside of Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines should refer to the most current Current Procedural Terminology which contains the complete and most current listing of CPT codes and descriptive terms. Applicable FARS/DFARS apply.

CPT is a registered trademark of the American Medical Association.

Codes used to identify services associated with this policy may include (but may not be limited to) the following:

<table>
<thead>
<tr>
<th>Code Type</th>
<th>Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPT</td>
<td>37243, 75894</td>
</tr>
<tr>
<td>HCPCS</td>
<td>Q0083</td>
</tr>
<tr>
<td>ICD-10 Diagnosis</td>
<td>C22.0-C22.9, C78.7</td>
</tr>
</tbody>
</table>
Transcatheter Arterial Chemoembolization (TACE) to Treat Primary or Metastatic Liver Malignancies

Policy # 00227
Original Effective Date: 03/08/2008
Current Effective Date: 05/15/2019

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or

B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
   1. Consultation with the Blue Cross and Blue Shield Association technology assessment program (TEC) or other nonaffiliated technology evaluation center(s);
   2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
   3. Reference to federal regulations.

**Medically Necessary (or “Medical Necessity”) - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and 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.

For these purposes, “nationally accepted standards of medical practice” means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally valid.
Transcatheter Arterial Chemoembolization (TACE) to Treat Primary or Metastatic Liver Malignancies

Policy # 00227
Original Effective Date: 03/08/2008
Current Effective Date: 05/15/2019

recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.