8.01.11 Transcatheter Arterial Chemoembolization to Treat Primary or Metastatic Liver Malignancies

**Summary**
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.

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

**POLICY STATEMENT**
Transcatheter hepatic arterial chemoembolization may be considered medically necessary to treat hepatocellular cancer that is unresectable but confined to the liver and not associated with portal vein thrombosis.

Transcatheter hepatic arterial chemoembolization may be considered medically necessary as a bridge to transplant in patients with hepatocellular cancer where the intent is to prevent further tumor growth and to maintain a patient's candidacy for liver transplant (see Policy Guidelines section).

Transcatheter hepatic arterial chemoembolization may be considered medically necessary to treat liver metastasis in symptomatic patients with metastatic neuroendocrine tumor whose symptoms persist despite systemic therapy and who are not candidates for surgical resection.

Transcatheter hepatic arterial chemoembolization may be considered medically necessary to treat liver metastasis in patients with liver-dominant metastatic uveal melanoma.
Transcatheter hepatic arterial chemoembolization is considered **investigational** as neoadjuvant or adjuvant therapy in hepatocellular cancer that is considered resectable.

Transcatheter hepatic arterial chemoembolization is considered **investigational** to treat unresectable cholangiocarcinoma.

Transcatheter hepatic arterial chemoembolization is considered **investigational** 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.

Transcatheter hepatic arterial chemoembolization is considered **investigational** to treat hepatocellular tumors prior to liver transplantation except as noted above.

**POLICY GUIDELINES (IF NEEDED)**

When using transcatheter hepatic arterial chemoembolization as a bridge to transplantation to prevent further tumor growth, the patient candidate should have the following characteristics: a single 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 of either A or B.

**BENEFIT APPLICATION**

Experimental or investigational procedures, treatments, drugs, or devices are not covered (See General Exclusion Section of brochure).

**RATIONALE**

**Summary of Evidence**

**TACE for Unresectable 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, disease-specific survival, quality of life, and treatment-related mortality and morbidity. Studies of TACE have shown improved overall survival compared with only supportive care. One systematic review highlighted some of the possible biases associated with these studies. The evidence is sufficient to determine quantitatively that the technology results in a meaningful improvement in the net health outcome.

**TACE for Resectable HCC as Neoadjuvant or Adjuvant Therapy**

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 or adjuvant TACE compared with surgery alone. A meta-analysis found no significant improvements in survival or recurrence with preoperative TACE for resectable HCC. The evidence is insufficient to determine the effects of the technology on health outcomes.

**TACE as a 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 TACE, the evidence includes many observational studies. Relevant outcomes are overall survival, disease-specific survival, quality of life, and treatment-related mortality and morbidity. TACE 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 qualitatively that the technology results in a meaningful improvement in the net health outcome.
TACE for 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. Most data on TACE are for unresectable intrahepatic cholangiocarcinoma. Although the data have suggested an overall survival advantage with TACE versus supportive care or systemic chemotherapy alone, the data consist mostly of retrospective reviews without matched patient controls. 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 tumor despite systemic therapy who are not candidates for surgical resection 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. Several studies have shown reduced tumor burden, reduced hormone levels, and palliation of symptoms with TACE. The evidence is sufficient to determine qualitatively that the technology results in a meaningful improvement in the net health outcome.

TACE for 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. Several studies have shown a survival advantage using locoregional treatment modalities, including TACE, in patients who have liver-dominant metastases from uveal melanoma. The evidence is sufficient to determine qualitatively that the technology results in a meaningful improvement in the net health outcome.

TACE for Other Unresectable Hepatic Metastases
For individuals who have unresectable hepatic metastases from any other type of primary tumor (eg, colorectal or breast cancer) who receive TACE, the evidence includes RCTs, numerous observational studies, and systematic reviews. Relevant outcomes are overall survival, disease-specific survival, quality of life, and treatment-related mortality and morbidity. Studies have small numbers of patients and the results have varied across studies 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

Practice Guidelines and Position Statements

National Comprehensive Cancer Network Guidelines
Hepatocellular Carcinoma
The National Comprehensive Cancer Network (NCCN) guidelines on hepatocellular carcinoma (v.2.2016) list chemoembolization as an option for patients with hepatocellular tumors not amenable to ablation therapy only and, in absent large-volume extrahepatic disease (category 2A), with the additional recommendation that tumor lesions larger than 5 cm be treated using arterial embolic approaches, whereas tumors 3 to 5 cm can be considered for combination therapy with ablation and arterial embolization. Additionally, TACE is relatively contraindicated in patients with portal vein thrombosis and bilirubin levels greater than 3 mg/dL and is absolutely contraindicated with Child-Pugh class C liver function.
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**Intrahepatic Cholangiocarcinoma**

NCCN guidelines on intrahepatic cholangiocarcinoma (v.2.2016) do not address the use of TACE in intrahepatic cholangiocarcinoma.

**Neuroendocrine Tumors, Carcinoid, and Islet Cell Tumors**

NCCN guidelines on neuroendocrine tumors, carcinoid, and islet cell tumors (v.2.2016) recommend chemoembolization for patients with unresectable liver metastases (category 2B).

**Uveal Cancer**

No NCCN guidelines were identified for uveal malignancies.

**Colon Cancer**

NCCN guidelines on colon cancer (v.2.2016) recommend the use of arterially directed embolic therapy for metastatic colon cancer to the liver (category 3 recommendation; based on any level of evidence. There is major NCCN disagreement about whether the intervention is appropriate.

**Breast Cancer**

NCCN guidelines on breast cancer (v.2.2016) 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 (NCD). In the absence of an NCD, coverage decisions are left to the discretion of local Medicare carriers.

**REFERENCES**

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42. Sato T. Locoregional management of hepatic metastasis from primary uveal melanoma. Semin Oncol. Apr 2010;37(2):127-138. PMID 20494705
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**POLICY HISTORY**

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<td>December 2016</td>
<td>Update Policy</td>
<td>Policy updated with literature review through June 14, 2016; references 6-7, 10, 16 and 47 added. Policy statements unchanged.</td>
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*Signature on File*

**Deborah M. Smith, MD, MPH**