DISABLE

This Molina Clinical Policy (MCP) is intended to facilitate the Utilization Management process. It expresses Molina's determination as to whether certain services or supplies are medically necessary, experimental, investigational, or cosmetic for purposes of determining appropriateness of payment. The conclusion that a particular service or supply is medically necessary does not constitute a representation or warranty that this service or supply is covered (i.e., will be paid for by Molina) for a particular member. The member's benefit plan determines coverage. Each benefit plan defines which services are covered, which are excluded, and which are subject to dollar caps or other limits. Members and their providers will need to consult the member's benefit plan to determine if there are any exclusion(s) or other benefit limitations applicable to this service or supply. If there is a discrepancy between this policy and a member's plan of benefits, the benefits plan will govern. In addition, coverage may be mandated by applicable legal requirements of a State, the Federal government or CMS for Medicare and Medicaid members. CMS's Coverage Database can be found on the CMS website. The coverage directive(s) and criteria from an existing National Coverage Determination (NCD) or Local Coverage Determination (LCD) will supersede the contents of this Molina Clinical Policy (MCP) document and provide the directive for all Medicare members.

DESCRIPTION OF Procedure/Service/Pharmaceutical

Transarterial chemoembolization (TACE) is a two-step procedure that involves placing a catheter in the artery that is supplying blood to a tumor to precisely infuse first, a chemotherapeutic agent and then, an embolic agent. This two-step process effectively delivers a drug and blocks blood flow to the tumor. TACE is widely used for unresectable HCC since these tumors are predominately fed by the hepatic artery, whereas the normal liver is perfused primarily via portal blood flow. This targeted delivery of a chemotherapeutic agent ensures high concentrations of drug within the tumor while sparing normal areas of the liver and reducing systemic toxicity. In addition, embolization of an artery does not affect normal liver perfusion, which prevents ischemic necrosis of healthy tissue. Chemoembolization is performed by an interventional radiologist and multiple treatments may be required to treat all lesions as well as recurrences. The treatment can be repeated every 8 to 12 weeks; however, the benefit of repetition of TACE needs to be balanced against the progressive liver damage associated with the treatment. The most common adverse effect of TACE is postembolization syndrome which consists of varying degrees of right upper quadrant pain, nausea, a moderate degree of ileus, fatigue, fever, and transient elevation of AST, ALT and bilirubin values. Symptoms are usually self-limited, lasting three to four days; full recovery is typical within 7 to 10 days.

Drug-eluting beads transarterial chemoembolization (DEB-TACE) is an adaptation of TACE and is a single-step process where beads of uniform size are loaded with a drug and delivered to the feeder artery in a single step. This procedure is easier to perform than two-step TACE. Since the drug is contained within the beads, its elution is more localized and longer lasting than in traditional TACE. Embolic beads, or microspheres, are either synthetic polymers such as ethylene vinyl acetate, or natural materials such as albumin, chitosan, gelatin,
or alginate. Doxorubicin is the most commonly used chemotherapeutic agent for DEB-TACE, however mitomycin C, cisplatin, methotrexate, and paclitaxel are also used. DEB-TACE is prescribed by an oncologist and performed in an angiography suite by an interventional radiologist. The procedure takes approximately 2 hours and patients are hospitalized for 1 to 2 days. Bilateral disease is treated in separate procedures at an interval of approximately 2 weeks. Repeat DEB-TACE procedures may be conducted, up to 4 times over a 6-month period.  

Embozene Microspheres are spherical, tightly calibrated, biocompatible, nonresorbable, hydrogel microspheres coated with an inorganic perfluorinated polymer (Polyzene-F) and are used during transarterial embolization (TAE) to decrease the blood supply of unresectable, intermediate- and advanced-stage hepatocellular carcinoma (HCC).  

**Hepatocellular Carcinoma General Information**

The incidence of hepatocellular carcinoma (HCC), or primary liver cancer is increasing due to the spread of hepatitis virus infection. In the majority of patients, HCC is associated with cirrhosis of the liver, and survival rates for HCC are poor. Patients with primary liver cancer are broadly classified into those with localized resectable, localized unresectable and advanced disease. Surgery is the only potentially curative treatment but only in patients with localized resectable disease, where the tumor is confined to a solitary mass in a portion of the liver that allows its complete surgical removal with a margin of normal liver, and in the absence of cirrhosis and chronic hepatitis. In patients with localized unresectable disease, although the cancer appears to be confined to the liver, surgical resection of the entire tumor is not possible due to its location within the liver or the presence of concomitant medical conditions such as cirrhosis. While some of these patients may be candidates for liver transplantation, limited availability of donor livers remains a problem. In advanced liver cancer, the cancer is present in both lobes of the liver or has metastasized to distant sites.

**RECOMMENDATION**  

1. Transarterial chemoembolization (TACE) is considered medically necessary for the treatment of primary hepatocellular liver carcinoma (HCC) when ALL of the following criteria are met:  
   - Localized unresectable or multifocal tumor with all of the following: [ALL]  
     - No vascular invasion  
     - No extrahepatic spread  
     - Tumor burden involving < 50 percent of the liver  
     - Tumor size > 5 cm  
   - No portal vein thrombus  
   - No encephalopathy  
   - No biliary obstruction  
   - Serum bilirubin < 2 mg/dL  
   - Liver function preserved: [ANY]  
     - Child-Turcotte-Pugh (CPT) score A (<7); OR  
     - Child-Turcotte-Pugh (CPT) score B (7-9)
The Child-Turcote-Pugh (CPT) score determines short-term prognosis among groups of patients awaiting liver transplantation and has been widely adopted for risk-stratifying patients before transplantation.

### Child-Turcote-Pugh Score of Severity of Liver Disease

<table>
<thead>
<tr>
<th>Points</th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Encephalopathy</td>
<td>None</td>
<td>1 – 2</td>
<td>3 – 4</td>
</tr>
<tr>
<td>Ascites</td>
<td>Absent</td>
<td>Slight</td>
<td>Moderate</td>
</tr>
<tr>
<td>Bilirubin (mg/dL)</td>
<td>&lt; 2</td>
<td>2 – 3</td>
<td>&gt; 3</td>
</tr>
<tr>
<td>For PBC/PSC, Bilirubin</td>
<td>&lt; 4</td>
<td>4 – 10</td>
<td>&gt; 10</td>
</tr>
<tr>
<td>Albumin (g/dL)</td>
<td>&gt; 3.5</td>
<td>2.8 – 3.5</td>
<td>&lt; 2.8</td>
</tr>
<tr>
<td>INR*</td>
<td>&lt; 1.7</td>
<td>1.7 – 2.3</td>
<td>&gt; 2.3</td>
</tr>
<tr>
<td>PT (seconds prolonged)</td>
<td>&lt; 4</td>
<td>4 - 6</td>
<td>&gt; 6</td>
</tr>
</tbody>
</table>

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

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

*INR = International Normalized Ratio; PT = prothrombin time.

### CONTINUATION OF THERAPY

The TACE procedure may be repeated every 8-12 weeks if there is clear evidence of progressive tumor growth in the treated areas.

**Note:**

- **Multiple courses of TACE, especially if spaced too closely together, can increase deaths from liver failure despite successful tumor shrinkage, and these excess deaths from deterioration of liver function may counterbalance any prolongation of survival that results from enhanced tumor control.**
- **TACE may cause hepatic artery damage, the likelihood of which is higher in patients with impaired liver function.**
- **Hepatic artery interruption by repeated TACE or arterial dissection also leads to the development of extrahepatic collateralization, which may create an alternative blood supply to the tumor, and contribute to treatment failure.**

### COVERAGE EXCLUSIONS

1. TACE utilizing chemotherapy-loaded microspheres (i.e. drug-loaded microspheres, drug-eluting beads, and doxorubicin drug-eluting bead transarterial chemoembolization [DEB-TACE] and Embozene Microspheres are considered experimental, investigational and unproven for all liver-related conditions.

2. TACE is contraindicated for any of the following conditions:
   - Thrombus in the main portal vein and portal vein obstruction
   - Encephalopathy
   - Biliary obstruction
   - Child-Turcote-Pugh C cirrhosis
3. Relative contraindications include any of the following: 34

- Serum bilirubin >2 mg/dL
- Lactate dehydrogenase >425 units/L
- Aspartate aminotransferase >100 units/L
- Tumor burden involving >50 percent of the liver
- Cardiac or renal insufficiency
- Ascites, recent variceal bleed, or significant thrombocytopenia
- Transjugular intrahepatic portosystemic shunt (TIPS)

### SUMMARY OF MEDICAL EVIDENCE

The available evidence on the efficacy and safety of DEB-TACE with doxorubicin for unresectable HCC is conflicting and consists of RCTs (n=30-201), that compared the efficacy and safety of treatment with DEB-TACE with conventional TACE or compared it with bland embolization with inert beads. Additional published evidence consists of controlled retrospective, uncontrolled, and prospective trials (n=62-71). The overall quality of the evidence is low because of study size, limitations of the uncontrolled studies, and the lack of RCTs. The available evidence suggests that DEB-TACE with doxorubicin is a safe and efficacious treatment for unresectable HCC, however there is insufficient evidence to draw conclusions regarding superiority of DEB-TACE over conventional TACE. Additional trials are necessary to compare the efficacy and safety of DEB-TACE with conventional TACE, assess quality of life and assess a consistent imaging method to monitor the tumor response to DEB-TACE. 16-23

The available evidence on the efficacy and safety of TACE to treat unresectable HCC is from limited RCT’s, (n=40-400) systematic reviews, retrospective reviews, and prospective studies (n=120-1293). Overall survival rates for chemoembolization as palliative treatment of unresectable disease ranged from 42% to 93% at 1 year, 22% to 87% at 2 years, and 3% to 43% at 3 years. Although the data is limited it does demonstrate that TACE provides a survival benefit for the treatment of unresectable primary hepatocellular carcinoma (HCC) when compared with supportive care only or when added as an additional therapy versus supportive care or systemic chemotherapy alone in the management of unresectable HCC. 2-15 Consensus opinion from professional organizations suggests that TACE may be a treatment option for unresectable HCC. 27-33

### CODING INFORMATION

THE CODES LISTED IN THIS POLICY ARE FOR REFERENCE PURPOSES ONLY. LISTING OF A SERVICE OR DEVICE CODE IN THIS POLICY DOES NOT IMPLY THAT THE SERVICE DESCRIBED BY THIS CODE IS COVERED OR NON-COVERED. COVERAGE IS DETERMINED BY THE BENEFIT DOCUMENT. THIS LIST OF CODES MAY NOT BE ALL INCLUSIVE.

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<thead>
<tr>
<th>CPT</th>
<th>Description</th>
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<tr>
<td>37243</td>
<td>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</td>
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### ICD-9 | Description: [For dates of service prior to 10/01/2015]

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<td>155.0</td>
<td>Malignant neoplasm of liver, primary</td>
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<tr>
<td>155.2</td>
<td>Malignant neoplasm of liver, not specified as primary or secondary</td>
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<tr>
<td>197.7</td>
<td>Secondary malignant neoplasm of respiratory and digestive systems; liver, specified as secondary</td>
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</table>

### ICD-10 | Description: [For dates of service on or after 10/01/2015]

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<td>C22.0</td>
<td>Carcinoma malignant, hepatocellular</td>
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<tr>
<td>C22.9</td>
<td>Malignant neoplasm of liver, not specified as primary or secondary</td>
</tr>
<tr>
<td>C78.7</td>
<td>Secondary malignant neoplasm of liver and intrahepatic bile duct</td>
</tr>
</tbody>
</table>

### Resource References

#### Government Agencies

#### Peer Reviewed Literature

Hayes
25. Hayes Health Technology Brief. Doxorubicin Drug-Eluting Bead Transarterial Chemoembolization (DEB-TACE) for Patients with Hepatocellular Carcinoma (HCC). April, 2014
Professional Society Guidelines


Other Resources


36. MD Consult [website]: Hepatocellular Carcinoma. April 15, 2010

37. Advanced Medical Review (AMR): Policy reviewed by MD board certified in Internal Medicine, Oncology, Hematology. October 15, 2012