Medical Policy:

Hepzato (melphalan hydrochloride)

POLICY NUMBER	LAST REVIEW	ORIGIN DATE
MG.MM.PH.428	January 30, 2025	January 30, 2025

Definitions

Melphalan is an alkylating agent of the bischloroethylamine type. As a result, its cytotoxicity appears to be related to the extent of its interstrand cross-linking with DNA, probably by binding at the N7 position of guanine. It is active against both resting and rapidly dividing tumor cells.

Hepzato for injection, as a component of the Hepzato Kit, is indicated as a liver-directed treatment for adult patients with uveal melanoma with unresectable hepatic metastases affecting less than 50% of the liver and no extrahepatic disease or extrahepatic disease limited to the bone, lymph nodes, subcutaneous tissues, or lung that is amenable to resection or radiation.

Length of Authorization

Hepzato 50 mg freeze-dried cake/powder for injection in a single-dose vial for reconstitution: 5 vials every 6 weeks for a total of 6 treatments

Dosing Limits [Medical Benefit]

250 billable units every 6 weeks for a total of 6 treatments

Guideline

I. INITIAL APPROVAL CRITERIA

Uveal Melanoma – Coverage is provided in the following conditions:

1. Patient is at least 18 years of age and weighs ≥ 35 kg ; **AND**
2. Patient has unresectable hepatic metastases; **AND**
   a. Patient has ≤ 50% histologically or cytologically-proven ocular melanoma metastases in the parenchyma of the liver AND no extrahepatic disease; **OR**
   b. Patient has limited extrahepatic disease (disease limited to the bone, lymph nodes, subcutaneous tissues, or lung that is amenable to resection or radiation) **AND**
3. Used as a single agent; **AND**
4. Patient does not have any of the following contraindications to treatment:
   a. Active intracranial metastases or brain lesions with a propensity to bleed
   b. Liver failure (i.e., Child-Pugh Class B or C cirrhosis), portal hypertension, or known varices at risk for bleeding
   c. Surgery or medical treatment of the liver in the previous 4 weeks
   d. Uncorrectable coagulopathy
   e. Inability to safely undergo general anesthesia, including active cardiac conditions including, but not limited to, unstable coronary syndromes (unstable or severe angina or myocardial infarction), worsening or new-onset congestive heart failure, significant arrhythmias, or severe valvular disease
   f. History of allergies or known hypersensitivity to a component or material utilized within the Hepzato Kit including history of allergy to natural rubber latex, history of allergy or hypersensitivity to heparin or presence of heparin-induced thrombocytopenia (HIT), or history of severe allergic reaction to iodinated contrast not controlled by premedication with antihistamines and steroids; **AND**
5. Patient does not have active hepatitis B or C infection; **AND**
6. Patient has ECOG performance status of 0 or 1; **AND**
7. Females of reproductive potential have a negative pregnancy test prior to initiating treatment and will use effective contraception during treatment and for 6 months after the last dose; **AND**
8. Males with female partners of reproductive potential will use effective contraception during treatment and for 3 months after the last dose; **AND**
9. Healthcare facility must be enrolled in and comply with the requirements of the HEPZATO KIT REMS Program; **AND**
10. Patient has the following hematological indices at baseline and subsequently, prior to each infusion:
    a. Hemoglobin ≥ 10 g/dL**; AND**
    b. Platelets ≥ 100,000/microliter**; AND**
    c. Neutrophils > 2000/microliter**; AND**
11. Patient will discontinue oral anticoagulation and drugs affecting platelet function, and ACE-inhibitors, calcium channel blockers, or alpha-1-adrenergic blockers prior to the procedure

Dosing/Administration:

<table>
<tr><th>Indication</th><th>Dose</th></tr>
<tr><td>Uveal Melanoma</td><td>Administer 3 mg/kg [based on ideal body weight (IBW)*] by infusion into the hepatic artery every 6 to 8 weeks for up to 6 total infusions, with a maximum of 220 mg during a single treatment.
Table 1: Calculation of IBW for HEPZATO Dosing
<table>
<tr><th></th><th>Height</th><th>Ideal Body Weight</th></tr>
<tr><td rowspan="2">Men</td><td>≥ 152 cm</td><td>52 kg + (0.75 kg/cm of height greater than 152 cm)</td></tr>
<tr><td>< 152 cm</td><td>52 kg – (0.75 kg/cm of height less than 152 cm)</td></tr>
<tr><td rowspan="2">Women</td><td>≥ 152 cm</td><td>49 kg + (0.67 kg/cm of height greater than 152 cm)</td></tr>
<tr><td>< 152 cm</td><td>49 kg – (0.67 kg/cm of height less than 152 cm)</td></tr>
</table></td></tr>
<tr><td colspan="2">NOTE:
• Hepzato is a component of the Hepzato Kit Hepatic Delivery System [HDS]. Refer to the Hepzato Kit Hepatic Delivery System Instructions for Use (IFU) for additional instructions including pre-infusion evaluation, hydration, premedication, anticoagulation, and supportive care.
• Reconstitute and dilute melphalan immediately prior to beginning intra-arterial infusion.
• Reconstituted and diluted solutions of Hepzato are unstable. No more than 60 minutes should elapse from reconstitution and completion of the intra-hepatic infusion of the diluted Hepzato solution.
• Do not refrigerate Hepzato once reconstituted.
• Hepzato is a hazardous drug. Follow applicable special handling and disposal procedures.</td></tr>
</table>

Applicable Procedure Codes

Code	Description
J9248	Injection, melphalan (Hepzato), 1 mg; 1 billable unit = 1 mg

Applicable NDCs

Code	Description
75833-0800-xx	Hepzato 50 mg freeze-dried cake/powder for injection in a single-dose vial for reconstitution

ICD-10 Diagnoses

Code	Description
XW053T9	Introduction of Melphalan Hydrochloride Antineoplastic into Peripheral Artery, Percutaneous Approach,

Revision History

Company(ies)	DATE	REVISION
EmblemHealth & ConnectiCare	01/30/2025	New Policy

References

1. Hepzato [package insert]. Queensbury, NY; Delcath Systems, Inc.; December 2023.