

## Medical Policy:

### Hepzato (melphalan hydrochloride)

POLICY NUMBER	LAST REVIEW	ORIGIN DATE
<b>MG.MM.PH.428</b>	<b>January 30, 2025</b>	<b>January 30, 2025</b>

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The treating physician or primary care provider must submit to EmblemHealth, or ConnectiCare, as applicable (hereinafter jointly referred to as “EmblemHealth”), the clinical evidence that the member meets the criteria for the treatment or surgical procedure. Without this documentation and information, EmblemHealth will not be able to properly review the request preauthorization or post-payment review. The clinical review criteria expressed below reflects how EmblemHealth determines whether certain services or supplies are medically necessary. This clinical policy is not intended to pre-empt the judgment of the reviewing medical director or dictate to health care providers how to practice medicine. Health care providers are expected to exercise their medical judgment in rendering appropriate care. Health care providers are expected to exercise their medical judgment in rendering appropriate care.

EmblemHealth established the clinical review criteria based upon a review of currently available clinical information (including clinical outcome studies in the peer reviewed published medical literature, regulatory status of the technology, evidence-based guidelines of public health and health research agencies, evidence-based guidelines and positions of leading national health professional organizations, views of physicians practicing in relevant clinical areas, and other relevant factors). EmblemHealth expressly reserves the right to revise these conclusions as clinical information changes and welcomes further relevant information. Each benefit program defines which services are covered. 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 and/or paid for by EmblemHealth, as some programs exclude coverage for services or supplies that EmblemHealth considers medically necessary.

If there is a discrepancy between this guideline and a member's benefits program, the benefits program will govern. Identification of selected brand names of devices, tests and procedures in a medical coverage policy is for reference only and is not an endorsement of any one device, test or procedure over another. In addition, coverage may be mandated by applicable legal requirements of a state, the Federal Government or the Centers for Medicare & Medicaid Services (CMS) for Medicare and Medicaid members. All coding and web site links are accurate at time of publication.

EmblemHealth may also use tools developed by third parties, such as the MCG™ Care Guidelines, to assist us in administering health benefits. The MCG™ Care Guidelines are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice. EmblemHealth Services Company, LLC, has adopted this policy in providing management, administrative and other services to EmblemHealth Plan, Inc., EmblemHealth Insurance Company, EmblemHealth Services Company, LLC, and Health Insurance Plan of Greater New York (HIP) related to health benefit plans offered by these entities. ConnectiCare, an EmblemHealth company, has also adopted this policy. All of the aforementioned entities are affiliated companies under common control of EmblemHealth Inc.

## 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  $\geq 35$  kg ; **AND**
2. Patient has unresectable hepatic metastases; **AND**
  - a. Patient has  $\leq 50\%$  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  $\geq 10$  g/dL; **AND**
  - b. Platelets  $\geq 100,000$ /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:

Indication	Dose													
Uveal Melanoma	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.  <b>Table 1: Calculation of IBW for HEPZATO Dosing</b> <table border="1"><thead><tr><th></th><th>Height</th><th>Ideal Body Weight</th></tr></thead><tbody><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>&lt; 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>&lt; 152 cm</td><td>49 kg – (0.67 kg/cm of height less than 152 cm)</td></tr></tbody></table>		Height	Ideal Body Weight	Men	≥ 152 cm	52 kg + (0.75 kg/cm of height greater than 152 cm)	< 152 cm	52 kg – (0.75 kg/cm of height less than 152 cm)	Women	≥ 152 cm	49 kg + (0.67 kg/cm of height greater than 152 cm)	< 152 cm	49 kg – (0.67 kg/cm of height less than 152 cm)
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<b>NOTE:</b> <ul style="list-style-type: none"><li>• 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.</li><li>• Reconstitute and dilute melphalan immediately prior to beginning intra-arterial infusion.</li><li>• 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.</li><li>• Do not refrigerate Hepzato once reconstituted.</li><li>• Hepzato is a hazardous drug. Follow applicable special handling and disposal procedures.</li></ul>														

## 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.