# Clinical Policy: Melphalan (Hepzato)

Reference Number: PA.CP.PHAR.653
Effective Date: 12/2023
Last Review Date: 10/2023

**Description**
Melphalan (Hepzato™) is an alkylating drug.

**FDA Approved Indication(s)**
Hepzato 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.

**Policy/Criteria**
*Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.*

It is the policy of PA Health & Wellness® that Hepzato is **medically necessary** when the following criteria are met:

**I. Initial Approval Criteria**

**A. Uveal Melanoma** (must meet all)**:**

1. Diagnosis of unresectable or metastatic uveal melanoma;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Weight ≥ 35 kg;
5. Histologically or cytologically-proven ocular melanoma metastases affecting 50% or less of the parenchyma of the liver;
6. Member has one of the following (a or b):
   a. No extrahepatic disease;
   b. Extrahepatic disease limited to the bone, lymph nodes, subcutaneous tissues, or lung that is amenable to resection or radiation;
7. Recent (within the last 30 days) hematologic testing demonstrating all the following (a, b, and c):
   a. Platelet count ≥ 100,000/µL;
   b. Hemoglobin ≥ 10 g/dL;
   c. Neutrophils > 2,000/µL;
8. Member does not have Child-Pugh Class B or C cirrhosis;
9. Request meets one of the following (a or b):
   a. Dose does not exceed both of the following (i and ii):
      i. 3 mg/kg based on ideal body weight (*see Section V*) every 6 weeks for up to 6 total infusions;
      ii. 220 mg per infusion;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Approval duration: 6 months**

**B. Other diagnoses/indications**
1. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

## II. Continued Therapy

**A. Uveal Melanoma** (must meet all)**:**
1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;
2. Member is responding positively to therapy;
3. Member has not received ≥ 6 total Hepzato infusions;
4. If request is for a dose increase, request meets one of the following (a or b):
   a. New dose does not exceed both of the following (i and ii):
      i. 3 mg/kg based on ideal body weight (*see Section V*) every 6 weeks for up to 6 total infusions;
      ii. 220 mg per infusion;
   b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Approval duration: 12 months (up to 6 total infusions)**

**B. Other diagnoses/indications** (must meet 1 or 2)**:**
1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.LTSS.PHAR.01) applies.
   **Approval duration: Duration of request or 12 months (whichever is less)**; or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

## III. Diagnoses/Indications for which coverage is NOT authorized:

**A.** Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off-label use policies – PA.CP.PMN.53

## IV. Appendices/General Information

*Appendix A: Abbreviation/Acronym Key*
FDA: Food and Drug Administration

*Appendix B: Therapeutic Alternatives*
Not applicable.

*Appendix C: Contraindications/Boxed Warnings*
- Contraindication(s):
  - Active intracranial metastases or brain lesions with a propensity to bleed.

- Liver failure, portal hypertension, or known varices at risk for bleeding.
- Surgery or medical treatment of the liver in the previous 4 weeks
- Uncorrectable coagulopathy
- 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.
- History of allergies or known hypersensitivity to melphalan or a component or material utilized within the Hepzato Kit including natural rubber latex, heparin, and severe hypersensitivity to iodinated contrast not controlled by antihistamines and steroids.

- Boxed warning(s): severe peri-procedural complications, myelosuppression

## V. Dosage and Administration

<table>
<tr><th>Indication</th><th>Dosing Regimen</th><th>Maximum Dose</th></tr>
<tr><td>Uveal melanoma</td><td>3 mg/kg based on ideal body weight administered by intraarterial infusion into the hepatic artery infused over 30 minutes followed by a 30 minute washout period. Treatments should be administered every 6 to 8 weeks but can be delayed until recovery from toxicities.<br><br>Calculation of ideal body weight:
<table>
<tr><td></td><td>Height</td><td>Ideal</td></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><td>220 mg per treatment</td></tr>
</table>

## VI. Product Availability

Injection: 50 mg lyophilized powder per vial in 5 single dose vials

## VII. References

1. Hepzato Prescribing Information. Queensbury, NY: Delcath Systems, Inc.; August 2023. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/201848s000lbl.pdf. Accessed August 31, 2023.
2. National Comprehensive Cancer Network. Melanoma: Uveal Version 1.2023 Available at: https://www.nccn.org/professionals/physician_gls/pdf/uveal.pdf. Accessed August 31, 2023.

3. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at www.nccn.org. Accessed August 31, 2023.
4. ClinicalTrails.gov. NCT02678572: Percutaneous Hepatic Perfusion in Patients With Hepatic-dominant Ocular Melanoma (FOCUS). Available at: https://clinicaltrials.gov/study/NCT02678572. Accessed August 31, 2023.

| Reviews, Revisions, and Approvals | Date | P&T Approval Date |
|---|---|---|
| Policy created | 10/2023 | |