Prior Authorization Review Panel

CHC-MCO Policy Submission

A separate copy of this form must accompany each policy submitted for review.
Policies submitted without this form will not be considered for review.

Plan: PA Health & Wellness	**Submission Date: 11/01/2025**
Policy Number: PA.CP.PHAR.653	**Effective Date: 12/2023** **Revision Date: 10/2025**
Policy Name: Melphalan (Hepzato)	

Type of Submission – Check all that apply:

- ☐ **New Policy**
- ✓ **Revised Policy***
- ☐ **Annual Review - No Revisions**
- ☐ **Statewide PDL -** *Select this box when submitting policies for Statewide PDL implementation and when submitting policies for drug classes included on the Statewide PDL.*

***All revisions to the policy must be highlighted using track changes throughout the document.**

Please provide any changes or clarifying information for the policy below:

4Q 2025 annual review: extended initial approval duration from 6 months to 12 months for this maintenance medication for a chronic condition; references reviewed and updated.

Name of Authorized Individual (Please type or print): **Craig A. Butler, MD MBA**	**Signature of Authorized Individual:**

Clinical Policy: Melphalan for hepatic Delivery (Hepzato)

Reference Number: PA.CP.PHAR.653
Effective Date: 12/2023
Last Review Date: 10/2025

Description
Melphalan for hepatic delivery (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: 12 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.PHARM.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.PHARM.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.

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; up to 6 total infusions</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: www.hepzatokit.com. Accessed July 17, 2025.
2. National Comprehensive Cancer Network. Melanoma: Uveal Version 1.2025. Available at: https://www.nccn.org/professionals/physician_gls/pdf/uveal.pdf. Accessed July 17, 2025.
3. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at www.nccn.org. Accessed July 17, 2025.

4. Zager JS, Orloff M, Ferrucci PF, et al. Efficacy and safety of the melphalan/hepatic delivery system in patients with unresectable metastatic uveal melanoma: results from an open-label, single-arm, multicenter phase 3 study. *Ann Surg Oncol*. 2024 Aug;31(8):5340-5351. doi: 10.1245/s10434-024-15293-x.

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J9248	Injection, melphalan (hepzato), 1 mg

Reviews, Revisions, and Approvals	Date
Policy created	10/2023
4Q 2024 annual review: no significant changes; added HCPC code [J9248]; references reviewed and updated.	10/2024
4Q 2025 annual review: extended initial approval duration from 6 months to 12 months for this maintenance medication for a chronic condition; references reviewed and updated.	10/2025