Clinical Policy: Melphalan for Hepatic Delivery (Hepzato)

Reference Number: LA.PHAR.653
Effective Date: 06.06.24
Last Review Date: 12.22.25~~01.15.25~~
Line of Business: Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

****Please note: This policy is for medical benefit****

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.

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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 Louisiana Healthcare Connections 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*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration: ~~6~~12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to LA.PMN.255;
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to ~~LA.PMN.53~~ off-label use policy LA.PMN.53.

II. Continued Therapy

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

1. Currently receiving medication via Louisiana Healthcare Connections benefit, or documentation supports that member is currently receiving Hepzato for a covered indication and has received this medication for at least 30 days;
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*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

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

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to LA.PMN.255;
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to ~~LA~~the off-label use policy LA.PMN.53~~ for Medicaid~~.

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 policyies – LA.PMN.53 for Medicaid or evidence of coverage documents.

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

Indication	Dosing Regimen	Maximum Dose
Uveal melanoma	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: Men, ≥ 152 cm: 52 kg + (0.75 kg/cm of height greater than 152 cm) Men, < 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) Women, < 152 cm: 49 kg – (0.67 kg/cm of height less than 152 cm)	220 mg per treatment; up to 6 total infusions

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.~~hepzatokit.com. Accessed ~~August 1, 2024~~July 17, 2025.
2. National Comprehensive Cancer Network. Melanoma: Uveal Version 1.~~2024~~2025 Available at: https://www.nccn.org/professionals/physician_gls/pdf/uveal.pdf. Accessed ~~August 1, 2024~~July 17, 2025.
3. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at www.nccn.org. Accessed ~~August 1, 2024~~July 17, 2025.
~~4. ClinicalTrails.gov. NCT02678572: Percutaneous Hepatic Perfusion in Patients With Hepatic-dominant Ocular Melanoma (FOCUS). Available at: https://clinicaltrials.gov/study/NCT02678572. Accessed August 1, 2024.~~
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

CLINICAL POLICY
Melphalan for Hepatic Delivery

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	LDH Approval Date
Converted corporate to local policy.	01.04.24	05.06.24
Annual review: no significant changes; added HCPC code [J9248]; references reviewed and updated.	01.15.25	04.07.25
Annual review: extended initial approval duration from 6 months to 12 months for this maintenance medication for a chronic condition; references reviewed and updated	12.22.25	

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. LHCC makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable LHCC administrative policies and procedures.

This clinical policy is effective as of the date determined by LHCC. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. LHCC retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

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