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IN BRIEF

Melphalan (*Hepzato*) for Uveal Melanoma

The alkylating agent melphalan (*Hepzato* – Delcath) has been approved by the FDA for treatment of uveal melanoma in adults with unresectable hepatic metastases that affects <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. Melphalan is available in a kit (*Hepzato Kit*) that contains a hepatic delivery system for infusion into the hepatic artery. The drug has been available for years in a tablet formulation for treatment of multiple myeloma and palliative treatment of nonresectable epithelial ovarian cancer and in an IV solution for treatment of multiple myeloma.

MECHANISM OF ACTION – Melphalan is an alkylating agent that binds to the N7 position of guanine, resulting in inter- and intrastrand links of DNA and cytotoxicity.

CLINICAL STUDIES – FDA approval of *Hepzato* was based on the results of a single-arm, open-label trial (FOCUS) in 91 patients with uveal melanoma with unresectable hepatic metastases or limited extrahepatic disease in the bone, subcutaneous tissues, lymph nodes, or lung amenable to resection or radiation. Patients received melphalan 3 mg/kg every 6-8 weeks for up to 6 doses. The overall response rate was 35.2% and the median duration of response was 14 months.¹

ADVERSE EFFECTS – In the FOCUS trial, cytopenias, fatigue, nausea, musculoskeletal pain, dyspnea, and

abdominal pain were reported with use of melphalan. The label of *Hepzato* contains a boxed warning about the risks of severe periprocedural complications, including hemorrhage, hepatocellular injury, and thromboembolic events, and myelosuppression; patients should be monitored for 72 hours after receiving the drug.

Melphalan is contraindicated for use in patients with active intracranial metastases or brain lesions that are likely to bleed, liver failure, portal hypertension, known varices at risk for bleeding, or active cardiac conditions or in those who had surgery or medical treatment of the liver within the previous 4 weeks.

DOSAGE, ADMINISTRATION, AND COST – The recommended dosage of *Hepzato* is 3 mg/kg (max 220 mg) infused into the hepatic artery over 30 minutes once every 6-8 weeks for up to 6 infusions. The drug should not be used in patients who weigh <35 kg. The label contains dosage adjustments that should be made if adverse effects occur. Because of the risk of severe periprocedural complications, *Hepzato* is only available through a Risk Evaluation and Mitigation Strategy (REMS) program. The wholesale acquisition cost (WAC) for one dose of *Hepzato* for a 70-kg patient is \$182,500.² ■

1. JS Zager et al. Focus phase 3 trial results: percutaneous hepatic perfusion (PHP) with melphalan for patients with ocular melanoma liver metastases (PHP-OCM-301/301A). *J Clin Oncol* 2022; 40(16_Suppl):9510.
2. Approximate WAC or manufacturer's published price to wholesalers; WAC represents a published catalogue or list price and may not represent an actual transactional price. Source: AnalySource® Monthly. November 5, 2024. Reprinted with permission by First Databank, Inc. All rights reserved. ©2024. www.fdbhealth.com/policies/drug-pricing-policy.

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