FDA Approves Melphalan as a Liver-Directed Treatment for Uveal Melanoma

Hepato Kit was approved for patients with uveal melanoma that has spread to the liver.

August 15, 2023 By Food and Drug Administration (FDA)

On August 14, 2023, the Food and Drug Administration approved Hepzato Kit (melphalan for injection/hepatic helivery system) containing melphalan (Hepzato, Delcath Systems, Inc.) 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.

View full prescribing information for the Hepzato Kit.

Efficacy was evaluated in the FOCUS study (NCT02678572), a single-arm, multicenter, open-label trial in 91 patients with uveal melanoma with unresectable hepatic metastases. Limited extrahepatic disease in the bone, subcutaneous sites, lymph nodes, or lung was permitted if the life-threatening component of the uveal melanoma was in the liver and the extrahepatic disease was amenable to resection or radiation. Key exclusion criteria were metastases in ≥50% of the liver parenchyma, Child-Pugh Class B or C cirrhosis, or hepatitis B or C infection.

The main efficacy outcome measures were objective response rate (ORR) and duration of response (DoR) as assessed by an independent central review committee using RECIST v1.1. ORR was 36.3% (95% CI: 26.4, 47) and median DoR was 14 months (95% CI: 8.3, 17.7).

Melphalan (Hepzato) is administered via the device constituent part, Hepatic Delivery System (HDS), by infusion into the hepatic artery every 6 to 8 weeks for up to 6 total infusions. The recommended melphalan dose is 3 mg/kg based on ideal body weight, with a maximum dose of 220 mg during a single treatment.

The prescribing information for the Hepzato Kit has a Boxed Warning for severe peri-procedural complications including hemorrhage, hepatocellular injury, and thromboembolic events. The prescribing information also has a Boxed Warning for myelosuppression with resulting severe infection, bleeding, or symptomatic anemia.

Because of the risk of severe peri-procedural complications including hemorrhage, hepatocellular injury, and thromboembolic events, Hepzato Kit is available only through a restricted program under a Risk Evaluation and Mitigation Strategy called the Hepzato Kit REMS.

The most common (≥20%) adverse reactions or laboratory abnormalities were thrombocytopenia, fatigue, anemia, nausea, musculoskeletal pain, leukopenia, abdominal pain, neutropenia, vomiting, increased alanine aminotransferase, prolonged activated partial thromboplastin time, increased aspartate aminotransferase increased blood alkaline phosphatase, and dyspnea.

Hepzato and the Hepzato Kit are contraindicated in patients with 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; 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); and history of severe allergic reaction to iodinated contrast not controlled by premedication with antihistamines and steroids.

This review used the Assessment Aid, a voluntary submission from the applicant to facilitate the FDA’s assessment.

This application was granted orphan drug designation. FDA expedited programs are described in the Guidance for Industry: Expedited Programs for Serious Conditions-Drugs and Biologics.

Healthcare professionals should report all serious adverse events suspected to be associated with the use of any medicine and device to FDA’s MedWatch Reporting System or by calling 1-800-FDA-1088.

This announcement was published by the Food and Drug Administration on August 14, 2023.
