Hepzato Kit™ (melphalan/hepatic delivery system) – New drug approval

- On August 14, 2023, Delcath announced the FDA approval of Hepzato Kit (melphalan/hepatic delivery system [HDS]), 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.

- Metastatic uveal melanoma is a rare and aggressive form of cancer with a U.S. incidence of approximately 1,000 cases per year; 90% of cases involve the liver, and liver failure is often the cause of death.

- Hepzato Kit is a combination product that administers melphalan, a chemotherapeutic agent, directly to the liver through Delcath's delivery system, the HDS, which permits higher drug exposure in target tissues.

    — The use of the HDS allows a healthcare provider team to surgically isolate the liver while the hepatic venous blood is filtered during melphalan infusion and subsequent washout during a Percutaneous Hepatic Perfusion (PHP) procedure.

- The efficacy of Hepzato Kit was established in an open-label study in 91 patients with hepatic-dominant metastatic uveal melanoma. Patients received Hepzato every 6 to 8 weeks for up to 6 infusions. The major outcome measures were objective response rate (ORR) and duration of response (DOR).

    — The ORR was 36.3% (95% CI: 26.4, 47.0).
    — The median DOR was 14.0 months (95% CI: 8.3, 17.7).

- Hepzato Kit carries a boxed warning for peri-procedural complications and myelosuppression.

    — Hepzato is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the Hepzato Kit REMS.

- Hepzato Kit is 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, 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

- Additional warnings and precautions for Hepzato Kit include hypersensitivity reactions; gastrointestinal adverse reactions; secondary malignancies; embryo-fetal toxicity; and infertility.

- The most common adverse reactions or laboratory abnormalities (≥ 20%) with Hepzato Kit use were thrombocytopenia, fatigue, anemia, nausea, musculoskeletal pain, leukopenia, abdominal pain,

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neutropenia, vomiting, increased alanine aminotransferase, prolonged activated partial thromboplastin time, increased aspartate aminotransferase, increased alkaline phosphatase, and dyspnea.

- Hepzato is administered via the Hepzato Kit HDS only to patients weighing 35 kg or greater due to potential size limitations with respect to percutaneous catheterization.
    - Hepzato is administered by infusion into the hepatic artery every 6 to 8 weeks for up to 6 total infusions.
    - The recommended Hepzato dose is 3 mg/kg based on ideal body weight, with a maximum of 220 mg during a single treatment.
    - Refer to the Hepzato Kit drug label for complete dosing and administration recommendations.
- Delcath plans to launch Hepzato Kit in the fourth quarter of 2023. Hepzato will be available in the Hepzato Kit, which will include:
    - 5 single dose vials containing 50 mg melphalan for reconstitution with the supplied diluents.

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