FDA Approves Pepaxto for Heavily Treated Multiple Myeloma

Nearly a quarter of patients treated with the peptide-drug conjugate experienced partial remission.

December 8, 2022 By Food and Drug Administration (FDA)

UPDATE: In December 2022 the Food and Drug Administration requested withdrawal of the U.S. marketing authorization for Pepaxto.

UPDATE: In October 2021, Oncopeptides voluntarily withdrew Pepaxto from the market as a treatment for multiple myeloma after a Phase III trial showed that it had a small negative effect on survival.

FDA grants accelerated approval to melphalan flufenamide for relapsed or refractory multiple myeloma

On February 26, 2021, the Food and Drug Administration granted accelerated approval to melphalan flufenamide (Pepaxto, Oncopeptides AB) in combination with dexamethasone for adult patients with relapsed or refractory multiple myeloma who have received at least four prior lines of therapy and whose disease is refractory to at least one proteasome inhibitor, one immunomodulatory agent, and one CD-38 directed monoclonal antibody.

Efficacy was evaluated in HORIZON (NCT02963493), a multicenter, single-arm trial. Eligible patients were required to have relapsed refractory multiple myeloma. Patients received melphalan flufenamide 40 mg intravenously on day 1 and dexamethasone 40 mg orally (20 mg for patients ≥75 years of age) on day 1, 8, 15 and 22 of each 28-day cycle until disease progression or unacceptable toxicity.

Efficacy was evaluated in a subpopulation of 97 patients who received four or more prior lines of therapy and were refractory to at least one proteasome inhibitor, one immunomodulatory agent, and a CD38-directed antibody. The main efficacy outcome measure was overall response rate (ORR) and duration of response (DOR) assessed by investigators according to the International Myeloma Working Group (IMWG) Criteria. The ORR was 23.7% (95% CI: 15.7, 33.4) and median DOR 4.2 months (95% CI: 3.2, 7.6).

Safety was evaluated in the 157 patients enrolled in HORIZON. Most common adverse reactions (>

20%) are fatigue, nausea, diarrhea, pyrexia and respiratory tract infection. Most common laboratory abnormalities (≥50%) are decreased leukocytes, platelets, lymphocytes, neutrophils, and hemoglobin, and increased creatinine.

The safety and efficacy of melphalan flufenamide has not been established for use as a conditioning regimen in patients receiving transplant. The USPI includes Limitations of Use statement that melphalan flufenamide is not indicated and is not recommended for use as a conditioning regimen for transplant outside of controlled clinical trials.

The recommended dose of melphalan flufenamide is 40 mg intravenously over 30 minutes on day 1 of each 28-day treatment cycle, in combination with dexamethasone.

View full prescribing information for Pepaxto.

This indication is approved under accelerated approval based on response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trial(s).

This application was granted priority review and orphan drug designation. A description of FDA expedited programs is 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.

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