FDA Grants Accelerated Approval to Elrexfio for Multiple Myeloma

The new bispecific T-cell engager is approved for people who have received at least four prior lines of treatment.

August 16, 2023 By Food and Drug Administration (FDA)

On August 14, 2023, the Food and Drug Administration granted accelerated approval to elranatamab-bcmm (Elrexfio, Pfizer, Inc.), a bispecific B-cell maturation antigen (BCMA)-directed CD3 T-cell engager, for adults with relapsed or refractory multiple myeloma who have received at least four prior lines of therapy, including a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 monoclonal antibody.

View full prescribing information for Elrexfio.

Efficacy was evaluated in MagnetisMM-3 (NCT04649359), an open-label, single-arm, multi-center study that included patients with relapsed/refractory MM who are refractory to at least one proteasome inhibitor, one immunomodulatory drug, and one anti-CD38 antibody. Patients had measurable disease by International Myeloma Working Group (IMWG) criteria at enrollment.

The main efficacy outcome measures were objective response rate (ORR) and duration of response (DOR), as assessed by a blinded independent central review based on IMWG criteria. The primary efficacy population consisted of 97 patients naïve to prior BCMA-directed therapy and who had previously received at least four prior lines of therapy, including a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 monoclonal antibody.

The ORR in the 97 patients receiving the recommended dose was 57.7% (95% CI: 47.3%, 67.7%). With a median follow-up of 11.1 months among responders, the median DOR was not reached (95% CI: 12 months, not reached). The DOR rate at 6 months was 90.4% (95% CI: 78.4%, 95.9%) and at 9 months was 82.3% (95% CI: 67.1%, 90.9%).

The prescribing information for elranatamab-bcmm has a Boxed Warning for life threatening or fatal cytokine release syndrome (CRS) and neurologic toxicity, including immune effector cell-associated neurotoxicity (ICANS). Among patients who received elranatamab-bcmm at the recommended dose, CRS occurred in 58% of patients, neurologic toxicity in 59%, and ICANS in 3.3%. Grade 3 CRS occurred in 0.5% of patients and Grade 3 or 4 neurologic toxicity occurred in 7%.

Because of the risks of CRS and neurologic toxicity, including ICANS, elranatamab-bcmm is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS), called the ELREXFIO REMS.

The most common adverse reactions (≥20%) were CRS, fatigue, injection site reaction, diarrhea, upper respiratory tract infection, musculoskeletal pain, pneumonia, decreased appetite, rash, cough, nausea, and pyrexia. The most common Grade 3 to 4 laboratory abnormalities (≥20%) were decreased lymphocytes, decreased neutrophils, decreased hemoglobin, decreased white blood cells, and decreased platelets.

The recommended elranatamab-bcmm dosages include the following: “step-up dose 1” of 12 mg on Day 1, “step-up dose 2” of 32 mg on Day 4, followed by the first treatment dose of 76 mg on Day 8, and then 76 mg weekly, thereafter, through week 24. For patients who have received at least 24 weeks of elranatamab-bcmm and have achieved partial responses or better and maintained responses for at least 2 months, the dose interval should transition to an every two-week schedule. Elranatamab-bcmm may be continued until disease progression or unacceptable toxicity.

This review was conducted under Project Orbis, an initiative of the FDA Oncology Center of Excellence. Project Orbis provides a framework for concurrent submission and review of oncology drugs among international partners. For this review, FDA collaborated with the Australian Therapeutic Goods Administration (TGA), the Brazilian Health Regulatory Agency (ANVISA), Health Canada, and Switzerland’s Swissmedic. The application reviews are ongoing at the other regulatory agencies.

This review used the Assessment Aid, a voluntary submission from the applicant to facilitate the FDA’s assessment. This application was granted priority review, breakthrough designation and 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.
