FDA Grants Accelerated Approval of Danyelza For Neuroblastoma in the Bones

The drug is approved for adults and children with relapsed or refractory neuroblastoma in the bone or bone marrow.

November 27, 2020 By Food and Drug Administration (FDA)

FDA grants accelerated approval to naxitamab for high-risk neuroblastoma in bone or bone marrow

On November 25, 2020, the Food and Drug Administration granted accelerated approval to naxitamab (DANYELZA, Y-mAbs Therapeutics, Inc.) in combination with granulocyte-macrophage colony-stimulating factor (GM-CSF) for pediatric patients one year of age and older and adult patients with relapsed or refractory high-risk neuroblastoma in the bone or bone marrow demonstrating a partial response, minor response, or stable disease to prior therapy.

Efficacy was evaluated in patients with relapsed or refractory neuroblastoma in the bone or bone marrow enrolled in two single-arm, open-label trials: Study 201 (NCT 03363373) and Study 12-230 (NCT 01757626). Patients with progressive disease following their most recent therapy were excluded.

Patients received 3 mg/kg naxitamab administered as an intravenous infusion on days 1, 3, and 5 of each 4-week cycle in combination with GM-CSF subcutaneously at 250 µg/m^2/day on days -4 to 0 and at 500 µg/m^2/day on days 1 to 5. At the investigator's discretion, patients were permitted to receive pre-planned radiation to the primary disease site in Study 201 and radiation therapy to non-target bony lesions or soft tissue disease in Study 12-230.

The main efficacy outcome measures were confirmed overall response rate (ORR) per the revised International Neuroblastoma Response Criteria (INRC) and duration of response (DOR). Among 22 patients treated in the multicenter Study 201, the ORR was 45% (95% CI: 24%, 68%) and 30% of responders had a DOR greater or equal to 6 months. Among 38 patients treated in the single-center Study 12-230, the ORR was 34% (95% CI: 20%, 51%) with 23% of patients having a DOR greater or equal to 6 months. For both trials, responses were observed in either the bone, bone marrow or both.

The prescribing information contains a Boxed Warning stating that naxitamab can cause serious infusion-related reactions and neurotoxicity, including severe neuropathic pain, transverse myelitis and reversible posterior leukoencephalopathy syndrome (RPLS). To mitigate these risks, patients should receive premedication prior to each naxitamab infusion and be closely monitored during and for at least two hours following completion of each infusion.

The most common adverse reactions (incidence ≥25% in either trial) in patients receiving naxitamab were infusion-related reactions, pain, tachycardia, vomiting, cough, nausea, diarrhea, decreased appetite, hypertension, fatigue, erythema multiforme, peripheral neuropathy, urticaria, pyrexia, headache, injection site reaction, edema, anxiety, localized edema, and irritability. The most common Grade 3 or 4 laboratory abnormalities (≥5% in either trial) were decreased lymphocytes, decreased neutrophils, decreased hemoglobin, decreased platelet count, decreased potassium, increased alanine aminotransferase, decreased glucose, decreased calcium, decreased albumin, decreased sodium and decreased phosphate.

The recommended naxitamab dose is 3 mg/kg/day (up to 150 mg/day) on days 1, 3, and 5 of each treatment cycle, administered after dilution as an intravenous infusion in combination with GM-CSF, subcutaneously at 250 µg/m^2/day on days -4 to 0 and at 500 µg/m^2/day on days 1 to 5. Treatment cycles are repeated every 4 to 8 weeks.

View full prescribing information for Danyelza.

This review used the Real-Time Oncology Review (RTOR) pilot program and the Assessment Aid, a voluntary submission from the applicant to facilitate the FDA's assessment.

This application was granted accelerated approval based on overall response rate and duration of response. Continued approval may be contingent upon verification and description of clinical benefit in confirmatory trials. This application was granted priority review, breakthrough therapy, and orphan drug designation. A priority review voucher was issued for this rare pediatric disease product application. 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.

For assistance with single-patient INDs for investigational oncology products, healthcare professionals may contact OCE's Project Facilitate at 240-402-0004 or email OncProjectFacilitate@fda.hhs.gov.

This announcement was originally published on the Food and Drug Administration website on November 25, 2020.