Danyelza® (naxitamab-gqgk) – New orphan drug approval

- On November 25, 2020, Y-mAbs Therapeutics announced the FDA approval of Danyelza (naxitamab-gqgk), in combination with granulocyte-macrophage colony-stimulating factor (GM-CSF), for the treatment of pediatric patients 1 year of age and older and adult patients with relapsed or refractory high-risk neuroblastoma in the bone or bone marrow who have demonstrated a partial response, minor response, or stable disease to prior therapy.

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

- Neuroblastoma is a solid tumor of childhood that arises in the nervous system, outside of the brain. All patients are staged based on the International Neuroblastoma Staging System Committee system, ranging from stage 1 through stage 4S. All patients with stage 4 disease diagnosed after one year of age are classified in the high-risk category, where the neuroblastoma tumor cells have already metastasized to other sites in the body, such as the bone or bone marrow.

- Danyelza binds to the glycolipid GD2. GD2 is overexpressed on neuroblastoma cells and other cells of neuroectodermal origin, including the central nervous system and peripheral nerves. *In vitro*, Danyelza was able to bind to cell surface GD2 and induce complement dependent cytotoxicity and antibody dependent cell-mediated cytotoxicity.

- The efficacy of Danyelza was established in two open-label, single arm studies in patients with high-risk neuroblastoma with refractory or relapsed disease in the bone or bone marrow (study 201 and study 12-230). Study 201 included 22 patients in the efficacy analysis. Study 12-230 included 38 patients in the efficacy analysis. The major efficacy outcome measures were overall response rate (ORR) and duration of response (DOR).

    — In study 201, the ORR was 45% (95% CI: 24, 68). The median duration of response was 6.2 months (95% CI: 4.9, not estimable) and 30% of responders had a DOR ≥ 6 months.
    — In study 12-230, the ORR was 34% (95% CI: 20, 51) and 23% of responders had a DOR ≥ 6 months.

- Danyelza carries a boxed warning for serious infusion-related reactions and neurotoxicity.

- Additional warnings and precautions for Danyelza include hypertension and embryo-fetal toxicity.

- The most common adverse reactions (≥ 25%) with Danyelza use were infusion-related reaction, 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%) with Danyelza use 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 dosage of Danyelza is 3 mg/kg/day (up to 150 mg/day) on days 1, 3, and 5 of each treatment cycle, administered as an intravenous infusion after dilution in combination with GM-CSF subcutaneously. Treatment cycles are repeated every 4 weeks until complete response or partial response, followed by 5 additional cycles every 4 weeks. Subsequent cycles may be

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repeated every 8 weeks. Danyelza and GM-CSF should be discontinued for disease progression or unacceptable toxicity.

  - — Pre-infusion medications and supportive treatment should be administered, as appropriate, during infusion.
  - — Refer to the Danyelza and GM-CSF drug labels for additional dosing and administration recommendations.

- Y-mAbs Therapeutics plans to launch Danyelza in the coming weeks. Danyelza will be available as 40 mg/10 mL (4 mg/mL) in a single-dose vial.