Clinical Policy: Naxitamab-gqgk (Danyelza)

Reference Number: PA.CP.PHAR.523
Effective Date: 02/2022
Last Review Date: 01/2024

Description
Naxitamab-gqgk (Danyelza®) is a glycolipid disialoganglioside (GD2)-binding recombinant humanized monoclonal IgG1 antibody.

FDA Approved Indication(s)
Danyelza is indicated, 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.

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of PA Health & Wellness® that Danyelza is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Neuroblastoma (must meet all)**:**

1. Diagnosis of high-risk neuroblastoma;
2. Disease is relapsed or refractory, and occurring in the bone or bone marrow;
3. Prescribed by or in consultation with an oncologist;
4. Age ≥ 1 year;
5. Prescribed in combination with GM-CSF (e.g., Leukine®);*
   **Prior authorization may be required for Leukine*
6. Member has demonstrated a partial response, minor response, or stable disease to prior therapy (*see Appendix B for examples*);
7. Request meets one of the following (a or b):
   a. Dose does not exceed 150 mg (4 vials) per day for 3 days of each 4-week treatment cycle;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 6 months

B. Other diagnoses/indications

1. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

II. Continued Therapy

A. Neuroblastoma (must meet all)**:**

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;
2. Member is responding positively to therapy;
3. If request is for a dose increase, request meets one of the following (a or b):
   a. New dose does not exceed 150 mg (4 vials) per day for 3 days of each 4- or 8-week treatment cycle;
   b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.LTSS.PHAR.01) applies.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – PA.CP.PMN.53

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

COG: Children's Oncology Group
FDA: Food and Drug Administration
GD2: glycolipid disialoganglioside
INRG: International Neuroblastoma Risk Group
INRGSS: International Neuroblastoma Risk Group Staging System
INSS: International Neuroblastoma Staging System
GM-CSF: granulocyte-macrophage colony-stimulating factor

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
cisplatin, etoposide, vincristine, cyclophosphamide, doxorubicin, topotecan	Used in various combinations in variable dosing regimens	Varies
Unituxin® (dinutuximab), isotretinoin, GM-CSF	Used in various combinations in variable dosing regimens	Varies

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): history of hypersensitivity reaction to naxitamab-gqgk
- Boxed warning(s): serious infusion-related reactions and neurotoxicity

Appendix D: General Information

- Defining "high-risk" neuroblastoma: The Children's Oncology Group (COG) risk group system was initially based on the Internationl Neuroblastoma Staging System (INSS) staging system, but is now transitioning to using the International Neuroblastoma Risk Group Staging System (INRGSS), along with the major prognostic factors to place children into 3 different risk groups: low, intermediate, and high. High-risk neuroblastoma patients, per COG, are:
  - Stage 2A or 2B disease and MYCN amplification
  - Stage 3 disease and MYCN amplification
  - Stage 3 disease in children age 18 months or older, no MYCN amplification, and unfavorable histopathology
  - Stage 4 disease in children younger than 12 months and MYCN amplification
  - Stage 4 disease in children between 12 months and 18 months with MYCN amplification, and/or diploidy, and/or unfavorable histology
  - Stage 4 disease in children 18 months or older
  - Stage 4S disease and MYCN amplification
- International Neuroblastoma Risk Group (INRG) classification is a newer system that is now being used to help researchers in different countries compare results and work together to find the best treatments. This system is based on the newer INRGSS staging system, as well as many of the prognostic factors listed in the staging section, such as: the child's age, tumor histology, presence or absence of MYCN gene amplification, and presence of the 11q aberration, and DNA ploidy. The INRG classification uses these factors to put children into 16 different pre-treatment groups (lettered A through R). Each pre-treatment group falls into 1 of 4 overall risk groups listed below. This system will most likely be used in addition to the COG Risk Classification system in the United States.
  - Very low risk
  - Low risk
  - Intermediate risk
  - High risk

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Neuroblastoma	3 mg/kg/day IV on Days 1, 3, and 5 of each 28-day treatment cycle. 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 repeated every 8 weeks.	150 mg/day

VI. Product Availability

Injection solution in a single-dose vial: 40 mg/10 mL

VII. References

1. Danyelza Prescribing Information. New York, NY; November 2020. Available at: https://labeling.ymabs.com/danyelza. Accessed October 2, 2023.
2. American Cancer Society. Treating neuroblastoma. Last revised April 28, 2021. Available at: https://www.cancer.org/content/dam/CRC/PDF/Public/8761.00.pdf. Accessed November 5, 2023.
3. American Cancer Society. Neuroblastoma early detection, diagnosis, and staging. Last revised April 28, 2021. Available at: https://www.cancer.org/content/dam/CRC/PDF/Public/8760.00.pdf. Accessed November 5, 2023.
4. Cancer.net. Neuroblastoma – Childhood: Stages and Groups. Available at: https://www.cancer.net/cancer-types/neuroblastoma-childhood/stages-and-groups. AccessedNovember 5, 2023, 2022.

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J9348	Injection, naxitamab-gqgk, 1 mg

Reviews, Revisions, and Approvals	Date
Policy created	01/2022
1Q 2023 annual review: no significant changes; references reviewed and updated.	01/2023
1Q 2024 annual review: no significant changes; references reviewed and updated.	01/2024