Clinical Policy: Naxitamab-gqgk (Danyelza)

Reference Number: ERX.SPA.424
Effective Date: 03.01.21
Last Review Date: 02.22
Line of Business: Commercial, Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

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.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ 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 guideline or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

   **Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration: 6 months

B. Other diagnoses/indications

1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

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

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions, or documentation supports that member is currently receiving Danyelza for a covered indication and has received this medication for at least 28 days;

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 guideline or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

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 policy – ERX.PA.01 or evidence of coverage documents.

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 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: A newer risk group classification system, the INRG classification, 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: www.Danyelza.com. Accessed September 14, 2021.
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 September 14, 2021.
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 September 14, 2021.
4. Cancer.net. Neuroblastoma - Childhood: Stages and Groups. Available at: https://www.cancer.net/cancer-types/neuroblastoma-childhood/stages-and-groups. Accessed September 14, 2021.
5. Micromedex® Healthcare Series [Internet database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Accessed September 14, 2021.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	01.05.21	02.21

Reviews, Revisions, and Approvals	Date	P&T Approval Date
1Q 2022 annual review: added requirement for combination use with GM-CSF per prescribing information; updated Appendix D; reference reviewed and updated.	09.14.21	02.22

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members.