Clinical Policy: Naxitamab-gqgk (Danyelza)
Reference Number: ERX.SPA.424
Effective Date: 03.01.21
Last Review Date: 02.21
Line of Business: Commercial, Medicaid

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. Member has demonstrated a partial response, minor response, or stable disease to prior therapy (see Appendix B for examples);
      6. 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 30 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

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.

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

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) uses major prognostic factors, combined with the International Neuroblastoma Risk Group Staging System (INRGSS) stage of the disease, to place children into 3 different risk groups: low, intermediate, and high. COG risk groups in the past used certain prognostics factors along with the INSS stage of the disease, and have transitioned to INRGSS more recently. High-risk patients, per COG, are:
  - Any child who is Stage 2A or 2B, older than 1 year, whose cancer has extra copies of the MYCN gene and unfavorable histology
  - Any child who is Stage 3, not yet 1 year old, whose cancer has extra copies of the MYCN gene
o Any child who is Stage 3, older than 1 year, whose cancer has extra copies of the MYCN gene
o Any child who is Stage 3, older than 18 months, whose cancer has unfavorable histology
o Any child who is Stage 4, whose cancer has extra copies of the MYCN gene regardless of age
o Any child who is Stage 4 and older than 18 months
o Any child who is Stage 4 and between 12 and 18 months old whose cancer has extra copies of the MYCN gene, unfavorable histology, and/or normal DNA ploidy (a DNA index of 1)
• Any child who is Stage 4S (not yet 1 year old), whose cancer has extra copies of the MYCN gene
  • 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.
  o Very low risk
  o Low risk
  o Intermediate risk
  o High risk

V. Dosage and Administration

<table>
<thead>
<tr>
<th>Indication</th>
<th>Dosing Regimen</th>
<th>Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neuroblastoma</td>
<td>3 mg/kg/day IV on Days 1, 3, and 5 of each treatment cycle.</td>
<td>150 mg/day</td>
</tr>
<tr>
<td></td>
<td>Treatment cycles are repeated every 4 weeks until complete response or partial response, followed by 5 additional cycles every 4 weeks.</td>
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<tr>
<td></td>
<td>Subsequent cycles may be repeated every 8 weeks.</td>
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</tbody>
</table>

VI. Product Availability

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

VII. References


Reviews, Revisions, and Approvals

<table>
<thead>
<tr>
<th>Date</th>
<th>P&amp;T Approval Date</th>
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<tbody>
<tr>
<td>Policy created</td>
<td>01.05.21</td>
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**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.

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