Medical Policy

Healthcare Services Department

Policy Name	Policy Number	Scope
Naxitamab-gqgk (Danyelza®)	MP-RX-FP-129-24	☒ MMM MA ☒ MMM Multihealth

Service Category

☐ Anesthesia
☐ Surgery
☐ Radiology Procedures
☐ Pathology and Laboratory Procedures
☐ Medicine Services and Procedures
☐ Evaluation and Management Services
☐ DME/Prosthetics or Supplies
☒ Part B Drugs

Service Description

This document addresses the use of *Naxitamab-gqgk (Danyelza®),* a GD2-binding monoclonal antibody approved by the Food and Drug Administration (FDA), 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.

Background Information

Danyelza is a glycolipid disialoganglioside (GD2)- binding recombinant humanized IgG1 antibody that induces cytotoxicity in GD2-overexpressing neuroblastoma cells.

Neuroblastomas are a clinically heterogeneous group of tumors that arise from primitive sympathetic ganglion cells. The pathology varies according to the degree of differentiation reached by cancerous cells as they develop. Prognosis largely depends on the extent of metastatic spread and age at diagnosis. Neuroblastoma can be classified into risk categories (low, intermediate, and high) based on various characteristics. High-risk individuals may include those with *MYCN*- amplified disease stage 2 or greater, or *MYCN*- nonamplified stage 4 in patients over the age of 18 months. Treatment for high-risk individuals is multimodal including chemotherapy, surgical resection, stem cell transplant, and radiation therapy.

Danyelza has a black box warning for serious infusion-related reactions and neurotoxicity. Serious infusion reactions including cardiac arrest, anaphylaxis, hypotension, bronchospasm, and stridor can occur. Premedicate as recommended and based on severity, reduce rate, interrupt, or discontinue infusion. Danyelza can also cause severe neurotoxicity including neuropathic pain, transverse myelitis, and reversible posterior leukoencephalopathy syndrome (RPLS). Premedicate as recommended and permanently discontinue Danyelza based on adverse reaction and severity.

Definitions and Measures

- Autologous hematopoietic stem cell transplantation: Infusion of previously harvested hematopoietic stem cells to the same individual from whom they were harvested.
- Complete Response (CR): The disappearance of all signs of cancer as a result of treatment; also called complete remission; does not indicate the cancer has been cured.

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- Partial response (PR): A decrease in the size of a tumor, or in the amount of cancer in the body, resulting from treatment; also called partial remission.
- Primary refractory disease: Cancer that does not respond at the beginning of treatment; may also be called resistant disease.
- Primary treatment: The first treatment given for a disease. It is often part of a standard set of treatments, such as surgery followed by chemotherapy and radiation. Also called first-line therapy, induction therapy, and primary therapy.
- Progressive Disease (PD): Cancer that is growing, spreading, or getting worse.
- Refractory Disease: Illness or disease that does not respond to treatment.
- Relapse or recurrence: After a period of improvement, during which time a disease (for example, cancer) could not be detected, the return of signs and symptoms of illness or disease. For cancer, it may come back to the same place as the original (primary) tumor or to another place in the body.
- Stable disease: Cancer that is not decreasing or increasing in extent or severity.

Approved Indications

A. 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).

Other Uses

i. None

Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

HCPCS	Description
J9348	Injection, naxitamab-gqgk, 1 mg [Danyelza]
ICD-10	**Description**

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C74.00-C74.92	Malignant neoplasm of adrenal gland

Medical Necessity Guidelines

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

Naxitamab-gqgk (Danyelza®)

A. Criteria For Initial Approval (*Provider must submit documentation [such as office chart notes, lab results, pathology reports, imaging studies, and any other pertinent clinical information] supporting the patient's diagnosis for the drug and confirming that the patient has met **all** approval criteria.)*

i. Individual has a diagnosis of relapsed or refractory high-risk neuroblastoma; **AND**
ii. Individual has disease in the bone or bone marrow; **AND**
iii. Individual has demonstrated a partial response, minor response, or stable disease to prior therapy; **AND**
iv. Individual is using in combination with GM-CSF (sargramostim).

B. Criteria For Continuation of Therapy

i. MMM considers continuation of Naxitamab-gqgk (Danyelza®) therapy medically necessary in members requesting reauthorization for an indication listed in Section A above (Criteria for Initial Approval) when there is no evidence of unacceptable toxicity or disease progression while on the current regimen and the maximum duration of treatment has not been exceeded. The following information should be submitted for reauthorization:
   A. A current oncology note documenting the patient's response to treatment showing no progression of disease.
   B. Current imaging studies and other objective measures, as appropriate, showing no progression of disease when compared with previous results.

C. Authorization Duration

i. Initial Approval Duration: Up to 6 months
ii. Reauthorization Approval Duration: Up to 6 months

D. Conditions Not Covered

Any other use is considered experimental, investigational, or unproven, including the following (this list may not be all inclusive):

i. Requests for Danyelza (naxitamab-gqgk) may not be approved if the above criteria (Section A: Criteria for Initial Approval) are not met and for all other indications.

Limits or Restrictions

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A. Therapeutic Alternatives

The list below includes preferred alternative therapies recommended in the approval criteria and may be subject to prior authorization.

i. N/A

B. Quantity Limitations

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines. The chart below includes dosing recommendations as per the FDA-approved prescribing information.

Drug	Recommended Dosing Schedule
Subcutaneous GM-CSF (granulocyte-macrophage colony-stimulating factor)	- Days -4 to 0: 250 µg/m^2/day by subcutaneous injection, beginning 5 days prior to DANYELZA infusion. - Days 1 to 5: 500 µg/m^2/day by subcutaneous injection. Administer at least 1 hour prior to DANYELZA administration on Days 1, 3, and 5.
Naxitamab-gqgk (Danyelza®) 40 mg/10 mL (4 mg/mL) SDV	- Days, 1, 3, and 5: administer DANYELZA 3 mg/kg/day (up to 150 mg/day) by intravenous infusion.
Exceptions	
• 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. • Discontinue DANYELZA and GM-CSF for disease progression or unacceptable toxicity.	

Reference Information

1. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.: 2023. URL: http://www.clinicalpharmacology.com. Updated periodically.
2. DailyMed. Package inserts. U.S. National Library of Medicine, National Institutes of Health website. http://dailymed.nlm.nih.gov/dailymed/about.cfm. Accessed: October 11, 2023.
3. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.
4. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc.; 2023; Updated periodically.

Federal and state laws or requirements, contract language, and Plan utilization management programs or polices may take precedence over the application of this clinical criteria.

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Policy History

Revision Type	Summary of Changes	P&T Approval Date	UM/CMPC Approval Date
Annual Review 12/29/2024	Updated background information to remove duplicities. Updated quantity limit table to add dosage forms and strengths and include recommended dosage regimen for GM-CSF. Wording and formatting changes. Coding Reviewed: no changes.	3/20/2025	4/2/2025
Policy Inception 01/31/2024	New Medical Policy creation	4/18/2024	6/28/2024