# Evolent Clinical Guideline 3224 for Danyelza™ (naxitamab-gqgk)

| Guideline Number: | Applicable Codes | |
|---|---|---|
| Evolent_CG_3224 | | |
| ***"Evolent" refers to Evolent Health LLC and Evolent Specialty Services, Inc.*** <br>  | | |
| **Original Date:** | **Last Revised Date:** | **Implementation Date:** |
| January 2021 | November 2025 | November 2025 |

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# STATEMENT

## Purpose

To define and describe the accepted indications for Danyelza (naxitamab-gqgk) usage in the treatment of cancer, including FDA approved indications, and off-label indications.

Evolent is responsible for processing all medication requests from network ordering providers. Medications not authorized by Evolent may be deemed as not approvable and therefore not reimbursable.

The use of this drug must be supported by one of the following: FDA approved product labeling, CMS-approved compendia, National Comprehensive Cancer Network (NCCN), American Society of Clinical Oncology (ASCO) clinical guidelines, or peer-reviewed literature that meets the requirements of the CMS Medicare Benefit Policy Manual Chapter 15.

# INDICATIONS

**Continuation requests for a not-approvable medication shall be exempt from this Evolent policy provided**

- The member has not experienced disease progression on the requested medication AND
- The requested medication was used within the last year without a lapse of more than 30 days of having an active authorization AND
- Additional medication(s) are not being added to the continuation request.

## Neuroblastoma

- Danyelza (naxitamab-gqgk) will be given in combination with GM-CSF for pediatric members one year of age and older and adult members with relapsed or refractory high-risk neuroblastoma in bone or bone marrow demonstrating a partial response, minor response, or stable disease to prior therapy. High risk neuroblastoma is defined as members who are older than 18 months of age and have disseminated disease, or localized disease with unfavorable markers such as MYCN amplification *(see Attachment A)*.

# CONTRAINDICATIONS/WARNINGS

- Contraindications
  - History of severe hypersensitivity (including anaphylaxis) to naxitamab-gqgk or any component of the formulation.
- US Boxed Warning
  - Serious Infusion-Related Reactions: Naxitamab-gqgk can cause serious infusion reactions, including cardiac arrest, anaphylaxis, hypotension, bronchospasm, and stridor. Premedicate prior to each naxitamab-gqgk infusion as recommended and monitor patients for at least 2 hours following completion of each infusion. Reduce the rate, interrupt infusion, or permanently discontinue naxitamab-gqgk

based on severity.

- Neurotoxicity: Naxitamab-gqgk can cause severe neurotoxicity, including severe neuropathic pain, transverse myelitis, and reversible posterior leukoencephalopathy syndrome (RPLS). Premedicate to treat neuropathic pain as recommended. Permanently discontinue naxitamab-gqgk based on the adverse reaction and severity.

# EXCLUSION CRITERIA

- Disease progression while taking Danyelza (naxitamab-gqgk)
- Dosing exceeds single dose limit of Danyelza (naxitamab-gqgk) 3 mg/kg (up to 150 mg/day).
- Investigational use of Danyelza (naxitamab-gqgk) with an off-label indication that is not sufficient in evidence or is not generally accepted by the medical community. Sufficient evidence that is not supported by CMS recognized compendia or acceptable peer reviewed literature is defined as any of the following:
  - Whether the clinical characteristics of the patient and the cancer are adequately represented in the published evidence.
  - Whether the administered chemotherapy/biologic therapy/immune therapy/targeted therapy/other oncologic therapy regimen is adequately represented in the published evidence.
  - Whether the reported study outcomes represent clinically meaningful outcomes experienced by patients. Generally, the definition of Clinically Meaningful outcomes are those recommended by ASCO, e.g., Hazard Ratio of less than 0.80 and the recommended survival benefit for OS and PFS should be at least 3 months.
  - Whether the experimental design, in light of the drugs and conditions under investigation, is appropriate to address the investigative question. (For example, in some clinical studies, it may be unnecessary or not feasible to use randomization, double blind trials, placebos, or crossover).
  - That non-randomized clinical trials with a significant number of subjects may be a basis for supportive clinical evidence for determining accepted uses of drugs.
  - That case reports are generally considered uncontrolled and anecdotal information and do not provide adequate supportive clinical evidence for determining accepted uses of drugs.
  - That abstracts (including meeting abstracts) without the full article from the approved peer-reviewed journals lack supporting clinical evidence for determining accepted uses of drugs.

# CODING AND STANDARDS

## Codes

- J9348 - Injection, naxitamab-gqgk, 1 mg

## Applicable Lines of Business

| | |
|---|---|
| ☐ | CHIP (Children's Health Insurance Program) |
| ☒ | Commercial |
| ☒ | Exchange/Marketplace |
| ☒ | Medicaid |
| ☐ | Medicare Advantage |

# POLICY HISTORY

| Date | Summary |
|---|---|
| November 2025 | • Converted to new Evolent guideline template<br>• This guideline replaces UM ONC_1419 Danyelza (naxitamab-gqgk)<br>• Updated references |
| November 2024 | • Updated NCH verbiage to Evolent<br>• Added new references |

# LEGAL AND COMPLIANCE

## Guideline Approval

### *Committee*

**Reviewed / Approved by Evolent Specialty Services Clinical Guideline Review Committee**

## Disclaimer

*Evolent Clinical Guidelines do not constitute medical advice. Treating health care professionals are solely responsible for diagnosis, treatment, and medical advice. Evolent uses Clinical Guidelines in accordance with its contractual obligations to provide utilization management. Coverage for services varies for individual members according to the terms of their health care coverage or government program. Individual members' health care coverage may not utilize some Evolent Clinical Guidelines. Evolent clinical guidelines contain guidance that requires prior authorization and service limitations. A list of procedure codes, services or drugs may not be all inclusive and does not imply that a service or drug is a covered or non-covered service or drug. Evolent reserves the right to review and update this Clinical Guideline in its sole discretion. Notice of any changes shall be provided as*

*required by applicable provider agreements and laws or regulations. Members should contact their Plan customer service representative for specific coverage information.*

# REFERENCES


1. Mora J, et al. Outpatient administration of naxitamab in combination with granulocyte-macrophage colony-stimulating factor in patients with refractory and/or relapsed high-risk neuroblastoma: Management of adverse events. *Cancer Rep (Hoboken)*. 2023 Jan;6(1):e1627. doi: 10.1002/cnr2.1627.
2. Kushner BH, et al. Humanized 3F8 Anti-GD2 Monoclonal Antibody Dosing With Granulocyte-Macrophage Colony-Stimulating Factor in Patients With Resistant Neuroblastoma: A Phase 1 Clinical Trial. *JAMA Oncol*. 2018 Dec 1;4(12):1729-1735. doi: 10.1001/jamaoncol.2018.4005.
3. Danyelza prescribing information. Y-mAbs Therapeutics, Inc. Princeton, NJ 2025.
4. Clinical Pharmacology Elsevier Gold Standard 2025.
5. Micromedex® Healthcare Series: Micromedex Drugdex Ann Arbor, Michigan 2025.
6. National Comprehensive Cancer Network. Cancer Guidelines and Drugs and Biologics Compendium 2025.
7. AHFS Drug Information. American Society of Health-Systems Pharmacists or Wolters Kluwer Lexi-Drugs. Bethesda, MD 2025.
8. Ellis LM, et al. American Society of Clinical Oncology perspective: Raising the bar for clinical trials by defining clinically meaningful outcomes. *J Clin Oncol*. 2014 Apr 20;32(12):1277-80.
9. Medicare Benefit Policy Manual Chapter 15 Covered Medical and Other Health Services: **https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/Downloads/bp102c15.pdf**.
10. Current and Resolved Drug Shortages and Discontinuations Reported to the FDA: **http://www.accessdata.fda.gov/scripts/drugshortages/default.cfm**.

# ATTACHMENT A: CHILDREN'S ONCOLOGY GROUP NEUROBLASTOMA RISK STRATA

**Children's Oncology Group neuroblastoma risk strata**

| Risk | Stage | Age | MYCN status | DNA ploidy | INPC | Other |
|---|---|---|---|---|---|---|
| **Low*** | 1 | Any | Any | Any | Any | |
| | 2a/2b | Any | Not amp | Any | Any | Resection ≥50 percent |
| | 4s | <365 days | Not amp | DI >1 | FH | Asymptomatic |
| **Intermediate¶** | 2a/2b | 0-12 years | Not amp | Any | Any | Biopsy or resection <50 percent |
| | 3 | <547 days | Not amp | Any | Any | |
| | 3 | ≥547 days - 12 years | Not amp | Any | FH | |
| | 4 | <365 days | Not amp | Any | Any | |
| | 4 | 365 - <547 days | Not amp | DI >1 | FH | |
| | 4s | <365 days | Not amp | Any | Any | Symptomatic |
| | 4s | <365 days | Not amp | DI = 1 | Any | Asymptomatic or symptomatic |
| | 4s | <365 days | Not amp | Any | UH | Asymptomatic or symptomatic |
| | 4s | <365 days | Missing | Missing | Missing | Too sick for biopsy |
| **High△** | 2a/2b | Any | Amp | Any | Any | Any degree of resection |
| | 3 | Any | Amp | Any | Any | |
| | 3 | ≥547 days | Not amp | Any | UH | |
| | 4 | <365 days | Amp | Any | Any | |
| | 4 | 365 - <547 days | Amp | Any | Any | |
| | 4 | 365 - <547 days | Any | DI = 1 | Any | |
| | 4 | 365 - <547 days | Any | Any | UH | |
| | 4 | ≥547 days | Any | Any | Any | |
| | 4s | <365 days | Amp | Any | Any | Asymptomatic or symptomatic |

INPC: International Neuroblastoma Pathology Classification; FH: favorable histology; UH: unfavorable histology; Amp: amplified; DI: DNA Index.
* Low risk groups as defined in Children's Oncology Group trial ANBL00B1.
¶ Intermediate risk group as defined in Children's Oncology Group trial ANBL0531.
△ High risk group as defined in the Children's Oncology Group trial ANBL0532.

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