Clinical Policy Title:	naxitamab-gqgk
Policy Number:	RxA.666
Drug(s) Applied:	Danyelza®
Original Policy Date:	03/09/2021
Last Review Date:	03/09/2021
Line of Business Policy Applies to:	All lines of business

Background

Danyelza® is a GD2-binding monoclonal antibody 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.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
naxitamab-gqgk (Danyelza®)	Relapsed or refractory high-risk neuroblastoma in the bone or bone marrow	3 mg/kg/day administered as an intravenous (IV) infusion after dilution on Days 1, 3, and 5 of each treatment cycle. Treatment cycles are repeated every 4 weeks until partial or complete response, followed by five additional cycles every 4 weeks. Subsequent cycles may be repeated every 8 weeks.	150 mg per day

Dosage Forms

- Injection: 40 mg/10 mL (4 mg/mL) in a single-dose vial

Clinical Policy

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

I. Initial Approval Criteria

A. Relapsed or refractory high-risk neuroblastoma (must meet all):

1. Diagnosis of relapsed or refractory high-risk neuroblastoma in the bone or bone marrow;
2. Documented partial to complete response to prior therapy;
3. Prescribed by or in consultation with an oncologist;
4. Prescribed in combination with (all below):

a. A GM-CSF;
b. A prophylactic medication for neuropathic pain (e.g. gabapentin);
c. An antihistamine, an H2 antagonist, acetaminophen, an antiemetic, with or without IV corticosteroid;

5. Patient is age 1 year or older;
6. Request meets one of the following (a or b):
   a. Dose does not exceed 150 mg per day;
   b. Dose is supported by practice guidelines 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
Commercial: 6 months
Medicaid: 6 months

II. Continued Therapy Approval

A. Relapsed or refractory high-risk neuroblastoma (must meet all):
1. Currently receiving medication that has been authorized by RxAdvance or documentation supports that member is currently receiving Danyelza® for neuroblastoma 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 per day;
   b. New dose is supported by practice guidelines 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
Commercial: 6 months
Medicaid: 6 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key
GD2: glycolipid disialoganglioside
GM-CSF: granulocyte-macrophage colony-stimulating factor
IV: intravenous
FDA: Federal Drug Administration
NCCN: National Comprehensive Cancer Network

APPENDIX B: Therapeutic Alternatives
None.

APPENDIX C: Contraindications/Boxed Warnings
- Contraindication(s):
  - History of severe hypersensitivity reaction to naxitamab-gqgk.

- Boxed Warning(s):
  - Neurotoxicity: Can cause severe neurotoxicity, including severe neuropathic pain, transverse myelitis and reversible posterior leukoencephalopathy syndrome (RPLS). Pain of any Grade occurred in 94-100% of patients of patients in clinical studies. Peripheral neuropathy, neurological disorders of the

eye, and prolonged urinary retention have also occurred. Permanently discontinue as recommended.
- Serious Infusion-Related Reactions: Can cause serious infusion reactions, including cardiac arrest, anaphylaxis, hypotension, bronchospasm, and stridor. Infusion reactions of any Grade occurred in 94-100% of patients. Severe infusion reactions occurred in 32-68% and serious infusion reactions occurred in 4 - 18% of patients in DANYELZA clinical studies. It can cause serious infusion reactions requiring urgent intervention including fluid resuscitation, administration of bronchodilators and corticosteroids, intensive care unit admission, infusion rate reduction or interruption of Danyelza® infusion. Infusion-related reactions included hypotension, bronchospasm, hypoxia, and stridor.

APPENDIX D: General Information

Additional therapy surrounding Danyelza® administration:

- Premedication: Administer an antihistamine, an H2 antagonist, acetaminophen, and an antiemetic 30 minutes prior to each naxitamab infusion. In addition, administer an IV corticosteroid such as methylprednisolone 2 mg/kg (maximum: 80 mg/dose) or equivalent corticosteroid 30 minutes to 2 hours prior to the first naxitamab infusion. The systemic corticosteroid may be administered for subsequent infusions if a severe infusion reaction occurred with the previous infusion (or during the previous cycle).
- Pain management (prior to and during naxitamab infusion): Day –4 through Day 7: Administer a 12-day course of a prophylactic medication for neuropathic pain (e.g., gabapentin); initiate 5 days prior to the first naxitamab infusion in each cycle.
- Prior to and during infusion: Administer oral opioids 45 to 60 minutes prior to initiation of each naxitamab infusion; additional IV opioids may be administered, as needed, for breakthrough pain during the infusion. If pain is not adequately controlled by opioids, may consider ketamine.
- Missed dose: If a naxitamab dose is missed, administer the missed dose the following week (by day 10 of the cycle). Administer sargramostim (GM-CSF) on the first day of the naxitamab infusion, and on the day before and on the day of the second and third infusion, respectively (for a total of 5 days of the 500 mcg/m^2/day sargramostim dose.

Warnings:

- Hypertension: Monitor blood pressure during and after infusion as recommended. Withhold, reduce infusion rate, or discontinue based on severity.
- Embryo-Fetal Toxicity: May cause fetal harm. Advise females of reproductive potential of potential risk to a fetus and to use effective contraception.

References

1. Danyelza® Prescribing Information. Y-mAbs Therapeutics, Inc., November 2020. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/761171lbl.pdf. Accessed February 6, 2021.
2. Naxitamab-gqgk, Lexi-Drug. Lexicomp. Wolters Kluwer Health, Inc. Riverwoods, IL. Accessed with subscription at: http://online.lexi.com. Accessed February 6, 2021.
3. PDQ Pediatric Treatment Editorial Board. Neuroblastoma Treatment (PDQ®): Health Professional Version. In: PDQ Cancer Information Summaries [Internet]. Bethesda (MD): National Cancer Institute (US); 2002–. PMID: 26389190. Published December 2, 2020. Accessed February 6, 2021.
4. Y-mAbs Therapeutics. A Pivotal Phase 2 Trial of Antibody Naxitamab (hu3F8) and Granulocyte-Macrophage Colony Stimulating Factor (GM-CSF) in High-Risk Neuroblastoma Patients With Primary Refractory Disease or Incomplete Response to Salvage Treatment in Bone and/or Bone Marrow. Available at: https://clinicaltrials.gov/ct2/show/NCT03363373. NLM Identifier: NCT03363373. Accessed February 6, 2021.
5. Memorial Sloan Kettering Cancer Center. Phase I/II Study of Combination Therapy of Antibody Hu3F8 With Granulocyte- Macrophage Colony Stimulating Factor (GM-CSF) in Patients With Relapsed/Refractory High-Risk Neuroblastoma. Available at: https://clinicaltrials.gov/ct2/show/NCT01757626. NLM Identifier: NCT01757626.

Accessed February 6, 2021.

Review/Revision History	Review/Revision Date	P&T Approval Date
Policy established.	03/09/2021	03/09/2021