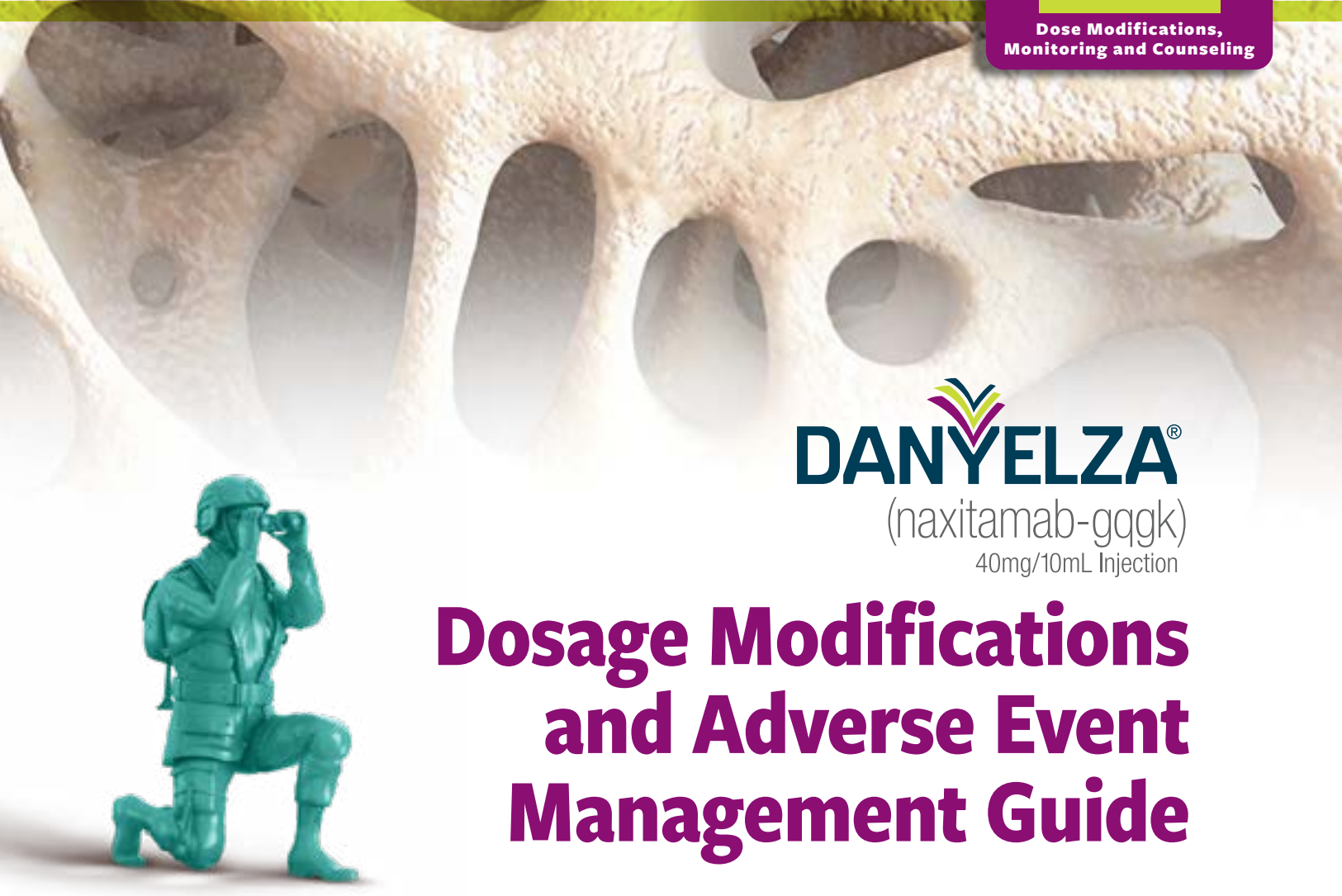

DANYELZA®
(naxitamab-gqgk)
40mg/10mL Injection

Dosage Modifications and Adverse Event Management Guide

INDICATION

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.

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).

IMPORTANT SAFETY INFORMATION

WARNING: SERIOUS INFUSION-RELATED REACTIONS and NEUROTOXICITY

Serious Infusion-Related Reactions

- **DANYELZA 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.**
- **Premedicate prior to each DANYELZA infusion as recommended and monitor patients for at least 2 hours following completion of each infusion. Reduce the rate, interrupt infusion, or permanently discontinue DANYELZA based on severity.**

Neurotoxicity

- **DANYELZA 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 in DANYELZA clinical studies.**
- **Premedicate to treat neuropathic pain as recommended. Permanently discontinue DANYELZA based on the adverse reaction and severity.**

Please see additional Important Safety Information throughout. Please see full Prescribing Information and Patient Information for DANYELZA including Boxed Warning on serious infusion-related reactions and neurotoxicity.

Monitor patients during and after the DANYELZA infusion.

See back page for definitions/descriptions of Common Terminology Criteria for Adverse Events (CTCAE) severity scale.

Dose modifications for managing adverse reactions[1]

Adverse Reaction	Severity	Action
Infusion-related reactions	**Grade 2** ■ Responds promptly to symptomatic treatment	🟡 Reduce infusion rate to 50%, monitor until Grade ≤1 🟢 Gradually increase infusion rate
	Grade 3 ■ Prolonged, recurrent, or hospitalization indicated	🟡 Interrupt and monitor until Grade ≤2 🟢 Resume at 50% rate, increase gradually
	Grade 3 ■ Not responding to medical intervention	🔴 Permanently discontinue
	Grade 4 ■ Life-threatening	🔴 Permanently discontinue
Anaphylaxis	**Grade 3 or 4**	🔴 Permanently discontinue
Pain	**Grade 3** unresponsive to maximum supportive measures	🔴 Permanently discontinue
RPLS	**All grades**	🔴 Permanently discontinue
Transverse myelitis	**All grades**	🔴 Permanently discontinue
Peripheral neuropathy	**Grade ≥2** motor neuropathy or **Grade 3-4** sensory neuropathy	🔴 Permanently discontinue
Neurological disorders of the eye	**Grade 2-4** resulting in decreased visual acuity or limiting ADL	🟡 Withhold until resolved 🟢 Resume at 50% dose; gradually increase to prior dose
	Grade 2-4 not resolved in ≤2 weeks	🔴 Permanently discontinue
	Subtotal or total vision loss	🔴 Permanently discontinue
Prolonged urinary retention	**Persisting** after opioid discontinuation	🔴 Permanently discontinue

Adverse reactions were graded and defined using Common Terminology Criteria for Adverse Events version 5.0.[2]
ADL=activities of daily life; RPLS=reversible posterior leukoencephalopathy syndrome.

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Monitor patients during and after the DANYELZA infusion.

See back page for definitions/descriptions of Common Terminology Criteria for Adverse Events (CTCAE) severity scale.

Dose modifications for managing adverse reactions[1] (cont)

Adverse Reaction	Severity	Action
Myocarditis	**Grade 2 or 3**	Withhold, reduce dose, or permanently discontinue based on severity and duration
	Grade 4	Permanently discontinue
Hypertension Do not initiate DANYELZA in patients with uncontrolled hypertension	**Grade 3** ■ Pediatric and adolescent: systolic and/or diastolic BP >5 mmHg above the 99th percentile[2] ■ Adult: medical intervention indicated (systolic BP ≥160 mmHg or diastolic ≥100 mmHg)[2]	Withhold until recovery to Grade ≤2 Resume infusion at 50% prior rate; gradually increase rate
	Grade 3 ■ Not responding to medical intervention	Permanently discontinue
	Grade 4 ■ Life-threatening	Permanently discontinue
Orthostatic hypotension	**All grades**	Withhold DANYELZA until recovery to Grade ≤1 If resolved in ≤1 week, restart at 50% prior dose Subsequent cycles: resume at recommended dose
	Any grade not resolved in ≤1 week	Permanently discontinue
Other adverse reactions	**Grade 3** ■ Severe or medically significant but not immediately life-threatening ■ Hospitalization or prolongation of hospitalization indicated; disabling; limiting self-care ADL	Withhold DANYELZA until recovery to Grade ≤2 If resolved to Grade ≤2, resume DANYELZA at same rate Permanently discontinue if not resolved to Grade ≤2 within 2 weeks
	Grade 4 ■ Life-threatening	Permanently discontinue

Adverse reactions were graded and defined using Common Terminology Criteria for Adverse Events version 5.0.[2]
ADL=activities of daily life; BP=blood pressure.

Because DANYELZA can cause serious drug- and infusion-related reactions that require immediate medical attention, it is important that you and your patients' caregivers remain vigilant and observant.

Post-infusion monitoring[1]

Observation is required for at least 2 hours after the DANYELZA infusion in a setting where cardiopulmonary resuscitation medication and equipment are available

Serious infusion-related reactions (IRRs)

- Symptoms of serious IRRs include hypotension, bronchospasm, hypoxia, and stridor
- In clinical trials, onset was generally within 24 hours of infusion, most often within 30 minutes of initiating infusion, and most frequent during the first infusion of DANYELZA in each cycle
- Serious IRRs may require urgent intervention, including fluid resuscitation, administration of bronchodilators and corticosteroids, intensive care unit admission, infusion rate reduction, or interruption of DANYELZA infusion

Actor portrayals

Hypertension and neurologic symptoms: Monitor blood pressure during the infusion, and at least daily on Days 1 through 8 of each cycle to assess for complications of hypertension, including neurologic RPLS

Myocarditis: Monitor for symptoms such as chest pain, shortness of breath, or abnormal heart rhythms

Myocarditis has occurred in adolescent patients within days of receiving DANYELZA

Orthostatic hypotension: Monitor blood pressure and assess for signs and symptoms, including dizziness, lightheadedness, or fainting

Lab abnormalities: Monitor for lab abnormalities, including cytopenia, changes in glucose, liver, and cardiac abnormalities

IRRs=infusion-related reactions; RPLS=reversible posterior leukoencephalopathy syndrome.

Because DANYELZA can cause serious drug- and infusion-related reactions that require immediate medical attention, it is important that you and your patients' caregivers remain vigilant and observant.

Patient counseling[1]

Advise patients and caregivers to immediately contact their HCP for any new or worsening adverse reactions that occur during or after the DANYELZA infusions, including the following:

- **IRRs:** Facial or lip swelling, itching, rash, trouble breathing, cough/wheezing, dizziness
- **Severe pain:** Including pain in the belly, bone, neck, legs, or arms, weakness in arms or legs
- **Inflammation of the spinal cord:** Including weakness in arms or legs, bladder and bowel problems, pain in back, legs, or stomach, numbness, tingling, burning sensation

Actor portrayals

- **RPLS:** Severe headache, vision changes, confusion or disorientation, decreased alertness, difficulty speaking, weakness in arms or legs, seizures
- **Neurological eye disorders:** Unequal pupil size, blurred vision, mydriasis, visual impairment, photophobia
- **Prolonged urinary retention:** Problems urinating or emptying the bladder
- **Myocarditis:** Chest pain, shortness of breath, or abnormal heart rhythms
- **Orthostatic hypotension:** Dizziness, lightheadedness or fainting, especially when standing after sitting or lying down

Indication and Important Safety Information

INDICATION

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.

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IMPORTANT SAFETY INFORMATION

WARNING: SERIOUS INFUSION-RELATED REACTIONS and NEUROTOXICITY

Serious Infusion-Related Reactions

- **DANYELZA 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.**
- **Premedicate prior to each DANYELZA infusion as recommended and monitor patients for at least 2 hours following completion of each infusion. Reduce the rate, interrupt infusion, or permanently discontinue DANYELZA based on severity.**

Neurotoxicity

- **DANYELZA 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 in DANYELZA clinical studies.**
- **Premedicate to treat neuropathic pain as recommended. Permanently discontinue DANYELZA based on the adverse reaction and severity.**

CONTRAINDICATION

DANYELZA is contraindicated in patients with a history of severe hypersensitivity reaction to naxitamab-gqgk. Reactions have included anaphylaxis.

WARNINGS AND PRECAUTIONS

Serious Infusion-Related Reactions

DANYELZA 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.

Serious infusion-related reactions occurred in 4% of patients in Study 201 and in 18% of patients in Study 12-230. Infusion-related reactions of any Grade occurred in 100% of patients in Study 201 and 94% of patients in Study 12-230. Hypotension of any grade occurred in 100% of patients in Study 201 and 89% of patients in Study 12-230.

In Study 201, 68% of patients experienced Grade 3 or 4 infusion reactions; and in Study 12-230, 32% of patients experienced Grade 3 or 4 infusion reactions. Anaphylaxis occurred in 12% of patients and two patients (8%) permanently discontinued DANYELZA due to anaphylaxis in Study 201. One patient in Study 12-230 (1.4%) experienced a Grade 4 cardiac arrest 1.5 hours following completion of DANYELZA infusion.

In Study 201, infusion reactions generally occurred within 24 hours of completing a DANYELZA infusion, most often within 30 minutes of initiation. Infusion reactions were most frequent during the first infusion of DANYELZA in each cycle. Eighty percent of patients required reduction in infusion rate and 80% of patients had an infusion interrupted for at least one infusion-related reaction.

Caution is advised in patients with pre-existing cardiac disease, as this may exacerbate the risk of severe hypotension.

Premedicate with an antihistamine, acetaminophen, an H2 antagonist and corticosteroid as recommended. Monitor patients closely for signs and symptoms of infusion reactions during and for at least 2 hours following completion of each DANYELZA infusion in a setting where cardiopulmonary resuscitation medication and equipment are available.

Reduce the rate, interrupt infusion, or permanently discontinue DANYELZA based on severity and institute appropriate medical management as needed.

Neurotoxicity

DANYELZA can cause severe neurotoxicity, including severe neuropathic pain, transverse myelitis, and reversible posterior leukoencephalopathy syndrome.

Pain

Pain, including abdominal pain, bone pain, neck pain, and extremity pain, occurred in 100% of patients in Study 201 and 94% of patients in Study 12-230. Grade 3 pain occurred in 72% of patients in Study 201. One patient in Study 201 (4%) required interruption of an infusion due to pain. Pain typically began during the infusion of DANYELZA and lasted a median of less than one day in Study 201 (range less than one day and up to 62 days).

Premedicate with drugs that treat neuropathic pain (e.g., gabapentin) and oral opioids. Administer intravenous opioids as needed for breakthrough pain. Permanently discontinue DANYELZA based on severity.

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DANYELZA® (naxitamab-gqgk) 40mg/10mL Injection

Important Safety Information (cont)

WARNINGS AND PRECAUTIONS

Neurotoxicity (cont)

Transverse Myelitis

Transverse myelitis has occurred with DANYELZA. Permanently discontinue DANYELZA in patients who develop transverse myelitis.

Reversible Posterior Leukoencephalopathy Syndrome (RPLS)

Reversible posterior leukoencephalopathy syndrome (RPLS) (also known as posterior reversible encephalopathy syndrome or PRES) occurred in 2 (2.8%) patients in Study 12-230. Events occurred 2 and 7 days following completion of the first cycle of DANYELZA. Monitor blood pressure during and following DANYELZA infusion and assess for neurologic symptoms. Permanently discontinue DANYELZA in case of symptomatic RPLS.

Peripheral Neuropathy

Peripheral neuropathy, including peripheral sensory neuropathy, peripheral motor neuropathy, paresthesia, and neuralgia, occurred in 32% of patients in Study 201 and in 25% of patients in Study 12-230. Most signs and symptoms of neuropathy began on the day of the infusion and neuropathy lasted a median of 5.5 days (range 0 to 22 days) in Study 201 and 0 days (range 0 to 22 days) in Study 12-230.

Permanently discontinue DANYELZA based on severity.

Neurological Disorders of the Eye

Neurological disorders of the eye including unequal pupils, blurred vision, accommodation disorder, mydriasis, visual impairment, and photophobia occurred in 24% of patients in Study 201 and 19% of patients in Study 12-230. Neurological disorders of the eye lasted a median of 17 days (range 0 to 84 days) in Study 201 with two patients (8%) experiencing an event that had not resolved at the time of data cutoff, and a median of 1 day (range less than one day to 21 days) in Study 12-230. Permanently discontinue DANYELZA based on severity.

Prolonged Urinary Retention

Urinary retention occurred in 1 (4%) patient in Study 201 and in 3 patients (4%) in Study 12-230. All events in both studies occurred on the day of an infusion of DANYELZA and lasted between 0 and 24 days. Permanently discontinue DANYELZA in patients with urinary retention that does not resolve following discontinuation of opioids.

Myocarditis

Myocarditis has occurred in adolescent patients receiving DANYELZA in clinical trials and expanded access programs. Myocarditis occurred within days of receiving DANYELZA requiring drug interruption. Monitor for signs and symptoms of myocarditis during treatment with DANYELZA. Withhold, reduce the dose, or permanently discontinue DANYELZA based on severity.

Hypertension

Hypertension occurred in 44% of patients in Study 201 and 28% of patients in Study 12-230 who received DANYELZA. Grade 3 or 4 hypertension occurred in 4% of patients in Study 201 and 7% of patients in Study 12-230. Four patients (6%) in Study 12-230 permanently discontinued DANYELZA due to hypertension. In both studies, most events occurred on the day of DANYELZA infusion and occurred up to 9 days following an infusion of DANYELZA.

Do not initiate DANYELZA in patients with uncontrolled hypertension. Monitor blood pressure during infusion, and at least daily on Days 1 to 8 of each cycle of DANYELZA and evaluate for complications of hypertension including RPLS. Interrupt DANYELZA infusion and resume at a reduced rate, or permanently discontinue DANYELZA based on the severity.

Orthostatic Hypotension

Orthostatic hypotension has occurred in patients receiving DANYELZA in clinical trials and expanded access programs. Severe orthostatic hypotension, including cases requiring hospitalization, have occurred. Cases occurred within hours to 6 days of DANYELZA infusions in any cycle.

In patients with symptoms of orthostatic hypotension, monitor postural blood pressure prior to initiating treatment with DANYELZA and as clinically indicated with subsequent dosing. Withhold, reduce dose, or permanently discontinue DANYELZA based on severity.

Embryo-Fetal Toxicity

Based on its mechanism of action, DANYELZA may cause fetal harm when administered to a pregnant woman. Advise females of reproductive potential, including pregnant women, of the potential risk to a fetus. Advise females of reproductive potential to use effective contraceptive during treatment with DANYELZA and for two months after the last dose.

ADVERSE REACTIONS

The most common adverse reactions in Studies 201 and 12-230 (≥25% in either study) were infusion-related reaction, pain, tachycardia, vomiting, cough, nausea, diarrhea, decreased appetite, hypertension, fatigue, erythema multiforme, peripheral neuropathy, urticaria, pyrexia, headache, injection site reaction, edema, anxiety, localized edema and irritability. The most common Grade 3 or 4 laboratory abnormalities (≥5% in either study) were decreased lymphocytes, decreased neutrophils, decreased hemoglobin, decreased platelet count, decreased potassium, increased alanine aminotransferase, decreased glucose, decreased calcium, decreased albumin, decreased sodium and decreased phosphate.

To review important state-specific disclosure information for licensed healthcare practitioners, please visit https://www.ymabs.com/information-for-prescribers

References: 1. DANYELZA® [package insert]. New York, NY: Y-mAbs Therapeutics, Inc.; 2024. Available online at https://labeling.ymabs.com/danyelza.
2. Common terminology criteria for adverse events (CTCAE). Version 5.0. Published 11/27/2017.

Common terminology criteria for adverse events (CTCAE)[2]

The CTCAE system, a product of the US National Cancer Institute (NCI), allows standardized classification of severity of adverse events associated with drugs and treatment used in cancer therapy. Use this grade scale to determine appropriate dose modifications as prescribed on pages 2-3 of this booklet.

Grade	Severity	Description
Grade 1	Mild	■ Asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated
Grade 2	Moderate	■ Minimal, local, or noninvasive intervention indicated
Grade 3	Severe	■ Severe or medically significant but not immediately life-threatening ■ Hospitalization or prolongation of hospitalization indicated
Grade 4	Life-threatening	■ Life-threatening consequences ■ Urgent intervention indicated
Grade 5	Death related to adverse events	■ Grade 5 is not appropriate for some adverse events and is therefore not an option

Access valuable clinical resources, from expert videos to a variety of downloadable materials, on managing DANYELZA infusion-related reactions.

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Learn more at danyelzahcp.com

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