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

DANYELZA® Dosage Modifications for Adverse Reactions

Flashcards for quick reference

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.**

y-mAbs Therapeutics, Inc.

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

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Infusion-Related Reactions

Infusion-related reactions

Grade 2	Grade 3	Grade 4
Therapy or infusion interruption indicated but responds promptly to symptomatic treatment (e.g. antihistamines, NSAIDS, narcotics, IV fluids); prophylactic medications indicated for ≤ 24 hours	Prolonged (e.g. not rapidly responsive to symptomatic medication and/or brief interruption of infusion); recurrence of symptoms following initial improvement; hospitalization indicated for clinical sequelae	Life-threatening consequences: urgent intervention indicated or Grade 3 or 4 anaphylaxis
Reduce DANYELZA® infusion rate to 50% of previous rate and monitor closely until recovery to Grade ≤ 1	Immediately interrupt DANYELZA® infusion and monitor closely until recovery to Grade ≤ 2	Permanently discontinue DANYELZA®
Increase infusion rate gradually to rate prior to the event as tolerated	Resume infusion at 50% of the rate prior to the event and increase infusion rate gradually to infusion rate prior to the event as tolerated	Permanently discontinue DANYELZA® in patients not responding to medical intervention

Based on CTCAE v 5.0
CTCAE, Common Terminology Criteria for Adverse Events;
IV, intravenous; NSAID, nonsteroidal anti-inflammatory drug.

IMPORTANT SAFETY INFORMATION (continued)

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.

Please see additional Important Safety Information on next page.

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Reversible Posterior Leukoencephalopathy Syndrome, Transverse Myelitis, and Prolonged Urinary Retention

Reversible posterior leukoencephalopathy syndrome (RPLS)

All grades

Permanently discontinue DANYELZA®

Transverse myelitis

All grades

Permanently discontinue DANYELZA®

Prolonged urinary retention

Persisting following discontinuation of opioids

Permanently discontinue DANYELZA®

Based on CTCAE v 5.0
CTCAE, Common Terminology Criteria for Adverse Events.

IMPORTANT SAFETY INFORMATION (continued)
WARNINGS AND PRECAUTIONS

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.

Please see additional Important Safety Information on next page.

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Pain and Peripheral Neuropathy

Pain

Grade 3 unresponsive to maximum supportive measures

Permanently discontinue DANYELZA®

Peripheral neuropathy

Motor neuropathy:
Grade 2 or greater

OR

Sensory neuropathy:
Grade 3 or 4

Permanently discontinue DANYELZA®

Based on CTCAE v 5.0
CTCAE, Common Terminology Criteria for Adverse Events.

IMPORTANT SAFETY INFORMATION (continued)
WARNINGS AND PRECAUTIONS

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.

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Neurological Disorders of the Eye

Neurological disorders of the eye

Grade 2 to 4 resulting in decreased visual acuity or limiting activities of daily living

Withhold DANYELZA® until resolution

If resolved, resume DANYELZA® at 50% of the prior dose; if tolerated without recurrence of symptoms, gradually increase DANYELZA® to dose prior to onset of symptoms

Permanently discontinue DANYELZA® if not resolved within 2 weeks or upon recurrence

Subtotal or total vision loss

Permanently discontinue DANYELZA®

Based on CTCAE v 5.0
CTCAE, Common Terminology Criteria for Adverse Events.

IMPORTANT SAFETY INFORMATION (continued)

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.

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

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Hypertension

Hypertension

Grade 3

Withhold DANYELZA® or pause infusion until recovery to Grade ≤ 2

Resume infusion at 50% of prior rate; if tolerated without recurrence of symptoms, gradually increase DANYELZA® to rate prior to onset of symptoms

Permanently discontinue DANYELZA® in patients not responding to medical intervention

Grade 4

Permanently discontinue DANYELZA®

Based on CTCAE v 5.0
CTCAE, Common Terminology Criteria for Adverse Events.

IMPORTANT SAFETY INFORMATION (continued)

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.

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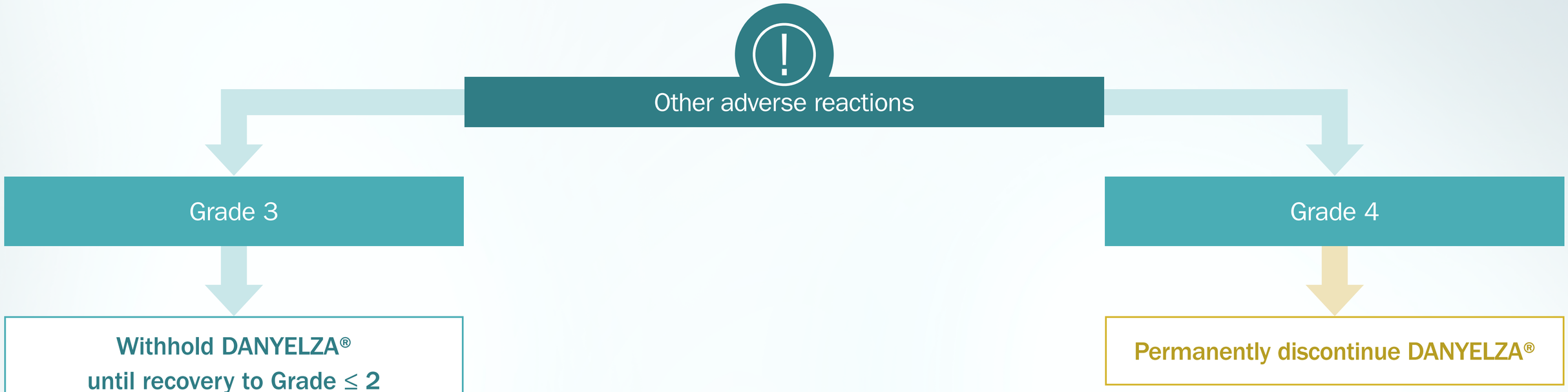
Other Adverse Reactions



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IMPORTANT SAFETY INFORMATION (continued)

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.

IMPORTANT SAFETY INFORMATION

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.

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 final 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.

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