TALVEY- talquetamab injection
Janssen Biotech, Inc.

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use TALVEY safely and effectively. See full prescribing information for TALVEY.

TALVEY™ (talquetamab-tgvs) injection, for subcutaneous use
Initial U.S. Approval: 2023

WARNING: CYTOKINE RELEASE SYNDROME and NEUROLOGIC TOXICITY, including IMMUNE EFFECTOR CELL-ASSOCIATED NEUROTOXICITY SYNDROME

See full prescribing information for complete boxed warning.

Cytokine release syndrome (CRS), including life-threatening or fatal reactions, can occur in patients receiving TALVEY. Initiate TALVEY treatment with step-up dosing to reduce the risk of CRS. Withhold TALVEY until CRS resolves or permanently discontinue based on severity. (2.2, 2.5, 5.1)
Neurologic toxicity, including immune effector cell-associated neurotoxicity syndrome (ICANS), and serious and life-threatening or fatal reactions, can occur in patients receiving TALVEY. Monitor patients for signs or symptoms of neurologic toxicity, including ICANS, during treatment. Withhold or permanently discontinue TALVEY based on severity. (2.5, 5.2)
TALVEY is available only through a restricted program called the TECVAYLI and TALVEY Risk Evaluation and Mitigation Strategy (REMS). (5.3)

INDICATIONS AND USAGE

TALVEY is a bispecific GPRC5D-directed CD3 T-cell engager indicated for the treatment of adult patients with relapsed or refractory multiple myeloma who have received at least four prior lines of therapy, including a proteasome inhibitor, an immunomodulatory agent and an anti-CD38 monoclonal antibody. This indication is approved under accelerated approval based on response rate and durability of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s). (1)

DOSAGE AND ADMINISTRATION

- For subcutaneous injection. (2.2)
- Patients should be hospitalized for 48 hours after all doses within the step-up dosing schedule. (2.1)
- Administer pretreatment medications as recommended. (2.3)
- See Full Prescribing Information for instructions on preparation and administration. (2.6)

TALVEY Weekly Dosing Schedule (2.2)			
Dosing schedule	**Day**	**Dose** *	
Step-up dosing schedule	Day 1	Step-up dose 1	0.01 mg/kg
	Day 4 †	Step-up dose 2	0.06 mg/kg
	Day 7 †	First treatment dose	0.4 mg/kg
Weekly dosing schedule	One week after first treatment dose and weekly thereafter ‡	Subsequent treatment doses	0.4 mg/kg once weekly

* Based on actual body weight.
† Dose may be administered between 2 to 4 days after the previous dose and may be given up to 7 days after the previous dose to allow for resolution of adverse reactions.
‡ Maintain a minimum of 6 days between weekly doses.

TALVEY Biweekly (Every 2 Weeks) Dosing Schedule (2.2)			
Dosing schedule	**Day**	**Dose** *	
Step-up dosing schedule	Day 1	Step-up dose 1	0.01 mg/kg
	Day 4 †	Step-up dose 2	0.06 mg/kg
	Day 7 †	Step-up dose 3	0.4 mg/kg

	Day 10 ‡	First treatment dose	0.8 mg/kg
Biweekly (every 2 weeks) dosing schedule	Two weeks after first treatment dose and every 2 weeks thereafter §	Subsequent treatment doses	0.8 mg/kg every 2 weeks

* Based on actual body weight.
† Dose may be administered between 2 to 4 days after the previous dose and may be given up to 7 days after the previous dose to allow for resolution of adverse reactions.
‡ Dose may be administered between 2 to 7 days after step-up dose 3.
§ Maintain a minimum of 12 days between biweekly (every 2 weeks) doses.

DOSAGE FORMS AND STRENGTHS

Injection

- 3 mg/1.5 mL (2 mg/mL) in a single-dose vial (3)
- 40 mg/mL in a single-dose vial (3)

CONTRAINDICATIONS

None. (4)

WARNINGS AND PRECAUTIONS

- Oral Toxicity and Weight Loss: Monitor for oral toxicity and weight loss. Withhold or permanently discontinue based on severity. (5.4)
- Infections: Can cause serious, life-threatening, or fatal infections. Monitor for signs and symptoms of infection; treat appropriately. Withhold or consider permanent discontinuation based on severity. (5.5)
- Cytopenias: Monitor complete blood counts. (5.6)
- Skin Toxicity: Monitor for skin toxicity, including rash progression, for early intervention and treat appropriately. Withhold as recommended based on severity. (5.7)
- Hepatotoxicity:Monitor liver enzymes and bilirubin at baseline and during treatment as clinically indicated. Withhold or consider permanent discontinuation based on severity. (5.8)
- Embryo-Fetal Toxicity: May cause fetal harm. Advise females of reproductive potential of the potential risk to the fetus and to use effective contraception. (5.9, 8.1, 8.3)

ADVERSE REACTIONS

The most common adverse reactions (≥20%) are pyrexia, CRS, dysgeusia, nail disorder, musculoskeletal pain, skin disorder, rash, fatigue, weight decreased, dry mouth, xerosis, dysphagia, upper respiratory tract infection, diarrhea, hypotension, and headache. (6.1)
The most common Grade 3 or 4 laboratory abnormalities (≥30%) are lymphocyte count decreased, neutrophil count decreased, white blood cell decreased, and hemoglobin decreased. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Janssen Biotech, Inc. at 1-800-JANSSEN (1-800-526-7736) or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

USE IN SPECIFIC POPULATIONS

Lactation: Advise not to breastfeed. (8.2)
See 17 for PATIENT COUNSELING INFORMATION and Medication Guide.

Revised: 8/2023

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

WARNING: CYTOKINE RELEASE SYNDROME and NEUROLOGIC TOXICITY, including IMMUNE EFFECTOR CELL-ASSOCIATED NEUROTOXICITY SYNDROME

Cytokine release syndrome (CRS), including life-threatening or fatal reactions, can occur in patients receiving TALVEY. Initiate TALVEY treatment with step-up dosing to reduce the risk of CRS. Withhold TALVEY until CRS resolves or permanently discontinue based on severity *[see Dosage and Administration (2.2, 2.5) , Warnings and Precautions (5.1)]* .

Neurologic toxicity, including immune effector cell-associated neurotoxicity syndrome (ICANS), and serious and life threatening or fatal reactions, can occur with TALVEY. Monitor patients for signs and symptoms of neurologic toxicity including ICANS during treatment and treat promptly. Withhold or permanently discontinue TALVEY based on severity *[see Dosage and Administration (2.5), Warnings and Precautions (5.2)]* .

Because of the risk of CRS and neurologic toxicity, including ICANS, TALVEY is available only through a restricted program called the TECVAYLI and TALVEY Risk Evaluation and Mitigation Strategy (REMS) *[see Warnings and Precautions (5.3)]* .

1 INDICATIONS AND USAGE

TALVEY is indicated for the treatment of adult patients with relapsed or refractory multiple myeloma who have received at least four prior lines of therapy, including a proteasome inhibitor, an immunomodulatory agent and an anti-CD38 monoclonal antibody.

This indication is approved under accelerated approval based on response rate and durability of response *[see Clinical Studies (14)].* Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).

2 DOSAGE AND ADMINISTRATION

2.1 Important Dosing Information

Administer TALVEY subcutaneously according to the step-up dosing schedule in Tables 1 and 2 to reduce the incidence and severity of cytokine release syndrome (CRS) *[see Dosage and Administration (2.2)]* .

Administer pretreatment medications prior to each dose of TALVEY in the step-up dosing schedule as recommended *[see Dosage and Administration (2.2, 2.3)].*

TALVEY should only be administered by a qualified healthcare professional with appropriate medical support to manage severe reactions such as CRS and neurologic toxicity including immune effector cell-associated neurotoxicity syndrome (ICANS) *[see Warnings and Precautions (5.1, 5.2)]* .

Due to the risk of CRS and neurologic toxicity, including ICANS, patients should be hospitalized for 48 hours after administration of all doses within the TALVEY step-up dosing schedule *[see Dosage and Administration (2.5)and Warnings and Precautions (5.1, 5.2)]* .

2.2 Recommended Dosage

For subcutaneous injection.

Administer pretreatment medications prior to each dose of TALVEY in the step-up dosing schedule *[see Dosage and Administration (2.3)]* .

Administer TALVEY subcutaneously on a weekly or biweekly (every 2 weeks) dosing schedule according to Table 1 or Table 2. Continue treatment until disease progression or unacceptable toxicity.

Table 1: TALVEY Weekly Dosing Schedule

Dosing schedule	**Day**	**Dose** *	
Step-up dosing schedule	Day 1	Step-up dose 1	0.01 mg/kg
	Day 4 †	Step-up dose 2	0.06 mg/kg
	Day 7 †	First treatment dose	0.4 mg/kg
Weekly dosing schedule	One week after first treatment dose and weekly thereafter ‡	Subsequent treatment doses	0.4 mg/kg once weekly

* Based on actual body weight.
† Dose may be administered between 2 to 4 days after the previous dose and may be given up to 7 days after the previous dose to allow for resolution of adverse reactions.
‡ Maintain a minimum of 6 days between weekly doses.

Table 2: TALVEY Biweekly (Every 2 Weeks) Dosing Schedule

Dosing schedule	**Day**	**Dose** *	
Step-up dosing schedule	Day 1	Step-up dose 1	0.01 mg/kg
	Day 4 †	Step-up dose 2	0.06 mg/kg
	Day 7 †	Step-up dose 3	0.4 mg/kg
	Day 10 ‡	First treatment dose	0.8 mg/kg
Biweekly (every 2 weeks) dosing schedule	Two weeks after first treatment dose and every 2 weeks thereafter §	Subsequent treatment doses	0.8 mg/kg every 2 weeks

* Based on actual body weight.
† Dose may be administered between 2 to 4 days after the previous dose and may be given up to 7 days after the previous dose to allow for resolution of adverse reactions.
‡ Dose may be administered between 2 to 7 days after step-up dose 3.
§ Maintain a minimum of 12 days between biweekly (every 2 weeks) doses.

2.3 Recommended Pretreatment Medications

Administer the following pretreatment medications 1 to 3 hours before each dose of TALVEY in the step-up dosing schedule to reduce the risk of CRS *[see Warnings and Precautions (5.1)]* .

- Corticosteroid (oral or intravenous dexamethasone, 16 mg or equivalent)
- Antihistamines (oral or intravenous diphenhydramine, 50 mg or equivalent)
- Antipyretics (oral or intravenous acetaminophen, 650 mg to 1,000 mg or equivalent)

Administration of pretreatment medications may be required for subsequent doses for patients who repeat doses within the TALVEY step-up dosing schedule due to dose delays (see Table 3or Table 4) or for patients who experienced CRS (see Table 5).

2.4 Dosage Delays

If a dose of TALVEY is delayed, restart therapy based on the recommendations in Table 3 and Table 4 and resume weekly or biweekly (every 2 weeks) dosing schedule accordingly *[see Dosage and Administration (2.1)]* ; if a dose is delayed by more than 28 days for an adverse reaction, evaluate the benefit-risk of restarting TALVEY. Administer pretreatment medications prior to restarting TALVEY and monitor patients following administration of TALVEY *[see Dosage and Administration (2.2)].*

Table 3: Recommendations for Restarting TALVEY after Dose Delay – Weekly Dosing Schedule

Last Dose Administered	Time from Last Dose Administered	TALVEY Recommendation *
0.01 mg/kg	More than 7 days	Restart TALVEY step-up dosing schedule at step-up dose 1 (0.01 mg/kg).
0.06 mg/kg	8 to 28 days	Repeat step-up dose 2 (0.06 mg/kg) and continue TALVEY step-up dosing schedule.
	More than 28 days	Restart TALVEY step-up dosing schedule at step-up dose 1 (0.01 mg/kg).
0.4 mg/kg	8 to 28 days	Continue TALVEY dosing schedule at treatment dose (0.4 mg/kg weekly).
	29 to 56 days	Restart TALVEY step-up dosing schedule at step-up dose 2 (0.06 mg/kg).
	More than 56 days	Consider permanent discontinuation. If restarting TALVEY, begin with the step-up dosing schedule at step-up dose 1 (0.01 mg/kg).

* Administer pretreatment medications prior to restarting TALVEY. After restarting TALVEY, resume weekly dosing schedule accordingly [see Dosage and Administration (2.2)] .

Table 4: Recommendations for Restarting TALVEY after Dose Delay – Biweekly (Every 2 Weeks) Dosing Schedule

Last Dose Administered	Time from Last Dose Administered	TALVEY Recommendation *
0.01 mg/kg	More than 7 days	Restart TALVEY step-up dosing schedule at step-up dose 1 (0.01 mg/kg).
0.06 mg/kg	8 to 28 days	Repeat step-up dose 2 (0.06 mg/kg) and continue TALVEY step-up dosing schedule.
	More than 28 days	Restart TALVEY step-up dosing schedule at step-up dose 1 (0.01 mg/kg).
0.4 mg/kg	8 to 28 days	Repeat step-up dose 3 (0.4 mg/kg) and continue TALVEY step-up dosing schedule.
	29 to 56 days	Restart TALVEY step-up dosing schedule at step-up dose 2 (0.06 mg/kg).
	More than 56 days	Consider permanent discontinuation. If restarting TALVEY, begin with the step-up dosing schedule at step-up dose 1 (0.01 mg/kg).
0.8 mg/kg	15 to 28 days	Continue TALVEY dosing schedule at treatment dose (0.8 mg/kg every 2 weeks).
	29 to 56 days	Restart TALVEY step-up dosing schedule at step-up dose 3 (0.4 mg/kg).
	More than 56 days	Consider permanent discontinuation. If restarting TALVEY, begin with the step-up dosing schedule at step-up dose 1 (0.01 mg/kg).

* Administer pretreatment medications prior to restarting TALVEY. After restarting TALVEY, resume biweekly (every 2 weeks) dosing schedule accordingly [see Dosage and Administration (2.2)] .

2.5 Dosage Modifications for Adverse Reactions

Dose delays may be required to manage toxicities related to TALVEY *[see Warnings and Precautions (5)]* .

See Table 5, Table 6, and Table 7for recommended actions for the management of CRS, ICANS, and neurologic toxicity. See Table 8for recommended dose modifications for other adverse reactions.

Cytokine Release Syndrome (CRS)

Identify CRS based on clinical presentation *[see Warnings and Precautions (5.1)]* .

Evaluate and treat other causes of fever, hypoxia, and hypotension. If CRS is suspected, withhold TALVEY until CRS resolves or permanently discontinue based on severity, manage according to the recommendations in Table 5, consider further management per current practice guidelines. Administer supportive therapy for CRS, which may include intensive care for severe or life-threatening CRS. Consider laboratory testing to monitor for disseminated intravascular coagulation (DIC), hematology parameters, as well as pulmonary, cardiac, renal, and hepatic function.

Table 5: Recommendations for Management of CRS

CRS Grade *	Presenting Symptoms	Actions
Grade 1	Temperature ≥100.4°F (38°C) †	• Withhold TALVEY until CRS resolves. ‡ • Administer pretreatment medication prior to next dose.
Grade 2	Temperature ≥100.4°F (38°C) †with either: • Hypotension responsive to fluids and not requiring vasopressors, or • Oxygen requirement of low-flow nasal cannula §or blow-by.	• Withhold TALVEY until CRS resolves. • Administer pretreatment medications prior to next dose. • Patients should be hospitalized for 48 hours following the next dose. ‡
Grade 3	Temperature ≥100.4°F (38°C) †with either: • Hypotension requiring one vasopressor, with or without vasopressin, or • Oxygen requirement of high-flow nasal cannula §, facemask, non-rebreather mask, or Venturi mask	<u>Duration less than 48 hours</u> • Withhold TALVEY until CRS resolves. • Provide supportive therapy, which may include intensive care. • Administer pretreatment medications prior to the next dose. • Patients should be hospitalized for 48 hours following the next dose. ‡ <u>Recurrent or duration greater than or equal to 48 hours</u> • Permanently discontinue TALVEY. • Provide supportive therapy, which may include intensive care.
	Temperature ≥100.4°F (38°C) †with either: • Hypotension requiring	

Grade 4	multiple vasopressors (excluding vasopressin). • Or, oxygen requirement of positive pressure (e.g., continuous positive airway pressure [CPAP], bilevel positive airway pressure [BiPAP], intubation, and mechanical ventilation)	• Permanently discontinue TALVEY. • Provide supportive therapy, which may include intensive care.

* Based on American Society for Transplantation and Cellular Therapy (ASTCT) grading for CRS (Lee et al 2019).
† Attributed to CRS. Fever may not always be present concurrently with hypotension or hypoxia as it may be masked by interventions such as antipyretics or anticytokine therapy (e.g., corticosteroids).
‡ See Table 3 and Table 4 for recommendations on restarting TALVEY after dose delays for adverse reactions [see Dosage and Administration (2.4)].
§ Low-flow nasal cannula is ≤6 L/min, and high-flow nasal cannula is >6 L/min.

Neurologic Toxicity, including ICANS

At the first sign of neurologic toxicity, including ICANS, withhold TALVEY and consider neurology evaluation. Rule out other causes of neurologic symptoms. Provide supportive therapy, which may include intensive care, for severe or life-threatening neurologic toxicities, including ICANS *[see Warnings and Precautions (5.2)]* . Manage ICANS and neurologic toxicity according to the recommendations in Table 6 and Table 7 and consider further management per current practice guidelines.

Table 6: Recommendations for Management of ICANS

Grade *	**Presenting Symptoms** †	**Actions**
Grade 1	ICE score 7–9 ‡, or depressed level of consciousness §: awakens spontaneously.	• Withhold TALVEY until ICANS resolves. ¶ • Monitor neurologic symptoms, and consider consultation with neurologist and other specialists for further evaluation and management. • Consider non-sedating, anti-seizure medicines (e.g., levetiracetam) for seizure prophylaxis.
		• Withhold TALVEY until ICANS resolves. • Administer dexamethasone #10 mg intravenously every 6 hours. Continue dexamethasone use until

Grade 2	ICE score 3–6 ‡, or depressed level of consciousness §: awakens to voice.	resolution to Grade 1 or less, then taper. • Monitor neurologic symptoms and consider consultation with neurologist and other specialists for further evaluation and management. • Consider non-sedating, anti-seizure medicines (e.g., levetiracetam) for seizure prophylaxis. • Patients should be hospitalized for 48 hours following the next dose of TALVEY *[see Dosage and Administration (2.1)]* . ¶
Grade 3	ICE score 0–2 ‡, (If ICE score is 0, but the patient is arousable (e.g., awake with global aphasia) and able to perform assessment) or depressed level of consciousness §: awakens only to tactile stimulus, or seizures §, either: • any clinical seizure, focal or generalized, that resolves rapidly, or • non-convulsive seizures on electroencephalogram (EEG)	<u>First Occurrence of Grade 3 ICANS:</u> • Withhold TALVEY until ICANS resolves. • Administer dexamethasone #10 mg intravenously every 6 hours. Continue dexamethasone use until resolution to Grade 1 or less, then taper. • Monitor neurologic symptoms and consider consultation with neurologist and other specialists for further evaluation and management. • Consider non-sedating, anti-seizure medicines (e.g., levetiracetam) for seizure prophylaxis. • Provide supportive therapy, which may include intensive care. • Patients should be hospitalized for 48 hours following the next dose of TALVEY *[see Dosage and Administration (2.1)]* . ¶ <u>Recurrent Grade 3 ICANS:</u>

	that resolve with intervention, or raised intracranial pressure: focal/local edema on neuroimaging [§].	• Permanently discontinue TALVEY. • Administer dexamethasone [#]10 mg intravenously and repeat dose every 6 hours. Continue dexamethasone use until resolution to Grade 1 or less, then taper. • Monitor neurologic symptoms and consider consultation with neurologist and other specialists for further evaluation and management. • Consider non-sedating, anti-seizure medicines (e.g., levetiracetam) for seizure prophylaxis. • Provide supportive therapy, which may include intensive care.
Grade 4	ICE score 0 [‡] (Patient is unarousable and unable to perform ICE assessment) or depressed level of consciousness [§]: either: • patient is unarousable or requires vigorous or repetitive tactile stimuli to arouse, or • stupor or coma, or seizures [§], either: • life-threatening prolonged seizure (>5 minutes), or • repetitive clinical or electrical seizures without return to baseline in between, or motor findings [§]: • deep focal motor weakness such as hemiparesis or paraparesis, or raised intracranial pressure/cerebral edema [§], with signs/symptoms such as:	• Permanently discontinue TALVEY. • Administer dexamethasone [#]10 mg intravenously and repeat dose every 6 hours. Continue dexamethasone use until resolution to Grade 1 or less, then taper. • Alternatively, consider administration of methylprednisolone 1,000 mg per day intravenously and continue methylprednisolone 1,000 mg per day intravenously for 2 or more days. • Monitor neurologic symptoms and consider consultation with neurologist and other specialists for further evaluation and management. • Consider non-sedating, anti-seizure medicines (e.g.,

	• diffuse cerebral edema on neuroimaging, or • decerebrate or decorticate posturing, or • cranial nerve VI palsy, or • papilledema, or • Cushing's triad.	seizure medicines (e.g., levetiracetam) for seizure prophylaxis. • Provide supportive therapy, which may include intensive care.

* Based on ASTCT 2019 grading for ICANS.
† Management is determined by the most severe event, not attributable to any other cause.
‡ If patient is arousable and able to perform Immune Effector Cell-Associated Encephalopathy (ICE) Assessment, assess: Orientation (oriented to year, month, city, hospital = 4 points); Naming (name 3 objects, e.g., point to clock, pen, button = 3 points); Following Commands (e.g., "show me 2 fingers" or "close your eyes and stick out your tongue" = 1 point); Writing (ability to write a standard sentence = 1 point; and Attention (count backwards from 100 by ten = 1 point). If patient is unarousable and unable to perform ICE Assessment (Grade 4 ICANS) = 0 points.
§ Attributable to no other cause.
¶ See Table 3 and Table 4 for recommendations on restarting TALVEY after dose delays for adverse reactions [see Dosage and Administration (2.4)].
# All references to dexamethasone administration are dexamethasone or equivalent.

Table 7: Recommendations for Management of Neurologic Toxicity (excluding ICANS)

Adverse Reaction	**Severity** *	**Actions**
Neurologic Toxicity *(excluding ICANS)	Grade 1	• Withhold TALVEY until neurologic toxicity symptoms resolve or stabilize. †
	Grade 2 Grade 3 (First occurrence)	• Withhold TALVEY until neurologic toxicity symptoms improve to Grade 1 or less. † • Provide supportive therapy.
	Grade 3 (Recurrent) Grade 4	• Permanently discontinue TALVEY. • Provide supportive therapy, which may include intensive care.

* Based on National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE), version 4.03.
† See Table 3 and Table 4 for recommendations on restarting TALVEY after dose delays for adverse reactions [see Dosage and Administration (2.4)] .

Other Adverse Reactions

The recommended dose modifications for other adverse reactions are provided in Table 8.

Table 8: Recommended Dose Modifications for Other Adverse

Reactions

Adverse Reaction	Severity	Dose Modification
Oral Toxicity and Weight Loss *[see Warnings and Precautions (5.4)]*	Grade 1–2	• Provide supportive care. • Consider withholding TALVEY if not responsive to supportive care. *
	Grade 3	• Withhold TALVEY until resolution to Grade 1 or better and provide supportive care. *
	Grade 4	• Permanently discontinue TALVEY.
Infections *[see Warnings and Precautions (5.5)]*	All Grades	• Withhold TALVEY in the step-up phase in patients until infection resolves.
	Grade 3	• Withhold TALVEY during the treatment phase until infection improves to Grade 1 or better within 28 days. †
	Grade 4	Consider permanent discontinuation of TALVEY. • If TALVEY is not permanently discontinued, withhold subsequent treatment doses of TALVEY (i.e., doses administered after TALVEY step-up dosing schedule) until adverse reaction improves to Grade 1 or better. †
Cytopenias *[see Warnings and Precautions (5.6)]*	Absolute neutrophil count less than 0.5×10^9/L	• Withhold TALVEY until absolute neutrophil count is 0.5×10^9/L or higher. *
	Febrile neutropenia	• Withhold TALVEY until absolute neutrophil count is 1.0×10^9/L or higher and fever resolves. *
	Hemoglobin less than 8 g/dL	• Withhold TALVEY until hemoglobin is 8 g/dL or higher. *
	Platelet count less than 25,000/mcL Platelet count between 25,000/mcL and 50,000/mcL with	• Withhold TALVEY until platelet count is 25,000/mcL or higher and no evidence of bleeding. *

	bleeding	
Skin Reactions *[see Warnings and Precautions (5.7)]*	Grade 3–4	• Withhold TALVEY until adverse reaction improves to Grade 1 or baseline. *
Other Non-hematologic Adverse Reactions ‡*[see Warnings and Precautions (5.8)and Adverse Reactions (6.1)]*	Grade 3	• Withhold TALVEY until adverse reaction improves to Grade 1 or baseline. *
	Grade 4	Consider permanent discontinuation of TALVEY. • If TALVEY is not permanently discontinued, withhold subsequent treatment doses of TALVEY (i.e., doses administered after TALVEY step-up dosing schedule) until adverse reaction improves to Grade 1 or less. *

* See Table 3 and Table 4 for recommendations on restarting TALVEY after dose delays for adverse reactions [see Dosage and Administration (2.4)].
† For Grade 3 or 4 infection, if TALVEY is withheld for more than 28 days, restart step-up dosing when infection improves to Grade 1 or better.
‡ Based on National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE), Version 4.03.

2.6 Preparation and Administration

Administer TALVEY via subcutaneous injection by a healthcare provider.

TALVEY should be administered by a healthcare provider with adequate medical personnel and appropriate medical equipment to manage severe reactions, including CRS and neurologic toxicity, including ICANS *[see Warnings and Precautions (5.1, 5.2)]* .

TALVEY 3 mg/1.5 mL (2 mg/mL) vial and TALVEY 40 mg/mL vial are supplied as ready-to-use solution for injection that do not need dilution prior to administration.

Do not combine TALVEY vials of different concentrations to achieve treatment dose.

Use aseptic technique to prepare and administer TALVEY.

Preparation

Refer to the following reference tables for the preparation of TALVEY.

- Use Table 9 to determine total dose, injection volume, and number of vials required based on patient's actual body weight for the 0.01 mg/kg dose using TALVEY 3 mg/1.5 mL (2 mg/mL) vial.

Table 9: 0.01 mg/kg Dose: Injection Volumes using TALVEY 3 mg/1.5 mL (2 mg/mL) Vial

	Body Weight (kg)	Total Dose (mg)	Volume of Injection	Number of Vials (1 vial = 1.5

	(kg)	(mg)	(mL)	(1 vial = 1.5 mL)
0.01 mg/kg Dose	35 to 39	0.38	0.19	1
	40 to 45	0.42	0.21	1
	46 to 55	0.5	0.25	1
	56 to 65	0.6	0.3	1
	66 to 75	0.7	0.35	1
	76 to 85	0.8	0.4	1
	86 to 95	0.9	0.45	1
	96 to 105	1	0.5	1
	106 to 115	1.1	0.55	1
	116 to 125	1.2	0.6	1
	126 to 135	1.3	0.65	1
	136 to 145	1.4	0.7	1
	146 to 155	1.5	0.75	1
	156 to 160	1.6	0.8	1

- Use Table 10 to determine total dose, injection volume, and number of vials required based on patient's actual body weight for the 0.06 mg/kg dose using TALVEY 3 mg/1.5 mL (2 mg/mL) vial.

Table 10: 0.06 mg/kg Dose: Injection Volumes using TALVEY 3 mg/1.5 mL (2 mg/mL) Vial

	Body Weight (kg)	Total Dose (mg)	Volume of Injection (mL)	Number of Vials (1 vial = 1.5 mL)
0.06 mg/kg Dose	35 to 39	2.2	1.1	1
	40 to 45	2.6	1.3	1
	46 to 55	3	1.5	1
	56 to 65	3.6	1.8	2
	66 to 75	4.2	2.1	2
	76 to 85	4.8	2.4	2
	86 to 95	5.4	2.7	2
	96 to 105	6	3	2
	106 to 115	6.6	3.3	3
	116 to 125	7.2	3.6	3
	126 to 135	7.8	3.9	3
	136 to 145	8.4	4.2	3
	146 to 155	9	4.5	3
	156 to 160	9.6	4.8	4

- Use Table 11 to determine total dose, injection volume, and number of vials required based on patient's actual body weight for the 0.4 mg/kg dose using TALVEY 40 mg/mL vial.

Table 11: 0.4 mg/kg Dose: Injection Volumes using TALVEY 40 mg/mL Vial

	Body Weight (kg)	Total Dose (mg)	Volume of Injection (mL)	Number of Vials (1 vial = 1 mL)
0.4 mg/kg Dose	35 to 39	14.8	0.37	1
	40 to 45	16	0.4	1
	46 to 55	20	0.5	1
	56 to 65	24	0.6	1
	66 to 75	28	0.7	1
	76 to 85	32	0.8	1
	86 to 95	36	0.9	1
	96 to 105	40	1	1
	106 to 115	44	1.1	2
	116 to 125	48	1.2	2
	126 to 135	52	1.3	2
	136 to 145	56	1.4	2
	146 to 155	60	1.5	2
	156 to 160	64	1.6	2

- Use Table 12 to determine total dose, injection volume, and number of vials required based on patient's actual body weight for the 0.8 mg/kg dose using TALVEY 40 mg/mL vial.

Table 12: 0.8 mg/kg Dose: Injection Volumes using TALVEY 40 mg/mL Vial

	Body Weight (kg)	Total Dose (mg)	Volume of Injection (mL)	Number of Vials (1 vial = 1 mL)
0.8 mg/kg Dose	35 to 39	29.6	0.74	1
	40 to 45	34	0.85	1
	46 to 55	40	1	1
	56 to 65	48	1.2	2
	66 to 75	56	1.4	2
	76 to 85	64	1.6	2
	86 to 95	72	1.8	2
	96 to 105	80	2	2
	106 to 115	88	2.2	3
	116 to 125	96	2.4	3
	126 to 135	104	2.6	3
	136 to 145	112	2.8	3
	146 to 155	120	3	3
	156 to 160	128	3.2	4

- Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. Check that the TALVEY solution for injection is colorless to light yellow. Do not use if the solution is discolored, cloudy, or if foreign particles are present.
- Remove the appropriate strength TALVEY vial(s) from refrigerated storage [2°C to 8°C (36°F to 46°F)] and equilibrate to ambient temperature [15°C to 30°C (59°F to 86°F)] for at least 15 minutes. Do not warm TALVEY in any other way.
- Once equilibrated, gently swirl the vial for approximately 10 seconds to mix. Do not shake.
- Withdraw the required injection volume of TALVEY from the vial(s) into an appropriately sized syringe using a transfer needle.
  - Each injection volume should not exceed 2 mL. Divide doses requiring greater than 2 mL equally into multiple syringes.
- TALVEY is compatible with stainless steel injection needles and polypropylene or polycarbonate syringe material.
- Replace the transfer needle with an appropriately sized needle for injection.

Administration

- Inject the required volume of TALVEY into the subcutaneous tissue of the abdomen (preferred injection site). Alternatively, TALVEY may be injected into the subcutaneous tissue at other sites (e.g., thigh). If multiple injections are required, TALVEY injections should be at least 2 cm apart.
- Do not inject into tattoos or scars or areas where the skin is red, bruised, tender, hard or not intact.
- Any unused medicinal product or waste material should be disposed in accordance with local requirements.

Storage

The prepared syringes should be administered immediately. If immediate administration is not possible, store the TALVEY solution refrigerated at 2°C to 8°C (36°F to 46°F) for up to 24 hours followed by at room temperature of 15°C to 30°C (59°F to 86°F) for up to 24 hours. Discard if stored for more than 24 hours refrigerated or more than 24 hours at room temperature. If stored in the refrigerator, allow the solution to come to room temperature before administration.

3 DOSAGE FORMS AND STRENGTHS

Injection

- 3 mg/1.5 mL (2 mg/mL) colorless to light yellow solution in a single-dose vial
- 40 mg/mL colorless to light yellow solution in a single-dose vial

4 CONTRAINDICATIONS

None.

5 WARNINGS AND PRECAUTIONS

5.1 Cytokine Release Syndrome (CRS)

TALVEY can cause cytokine release syndrome, including life-threatening or fatal reactions *[see Adverse Reactions (6.1)]* .

In the clinical trial, CRS occurred in 76% of patients who received TALVEY at the recommended dosages, with Grade 1 CRS occurring in 57% of patients, Grade 2 in 17%, and Grade 3 in 1.5%. Recurrent CRS occurred in 30% of patients. Most events occurred following step-up dose 1 (29%) or step-up dose 2 (44%) at the recommended dosages. CRS occurred in 33% of patients with step-up dose 3 in the biweekly dosing schedule (N=153). CRS occurred in 30% of patients with the first 0.4 mg/kg treatment dose and in 12% of patients treated with the first 0.8 mg/kg treatment dose. The CRS rate for both dosing schedules combined was less than 3% for each of the remaining doses in Cycle 1 and less than 3% cumulatively from Cycle 2 onward. The median time to onset of CRS was 27 (range: 0.1 to 167) hours from the last dose, and the median duration was 17 (range: 0 to 622) hours. Clinical signs and symptoms of CRS include but are not limited to pyrexia, hypotension, chills, hypoxia, headache, and tachycardia. Potentially life-threatening complications of CRS may include cardiac dysfunction, acute respiratory distress syndrome, neurologic toxicity, renal and/or hepatic failure, and disseminated intravascular coagulation (DIC).

Initiate TALVEY therapy with step-up dosing and administer pre-treatment medications (corticosteroids, antihistamine, and antipyretics) prior to each dose of TALVEY in the step-up dosing schedule to reduce the risk of CRS. Monitor patients following administration accordingly. In patients who experience CRS, pre-treatment medications should be administered prior to the next TALVEY dose *[see Dosage and Administration (2.2, 2.3)].*

Counsel patients to seek medical attention should signs or symptoms of CRS occur. At the first sign of CRS, immediately evaluate patient for hospitalization and institute treatment with supportive care based on severity and consider further management per current practice guidelines. Withhold TALVEY until CRS resolves or permanently discontinue based on severity *[see Dosage and Administration (2.5)]* .

TALVEY is available only through a restricted program under a REMS *[see Warnings and Precautions (5.3)]* .

5.2 Neurologic Toxicity including ICANS

TALVEY can cause serious, life-threatening, or fatal neurologic toxicity, including ICANS *[see Adverse Reactions (6.1)]* .

In the clinical trial, neurologic toxicity, including ICANS, occurred in 55% of patients who received TALVEY at the recommended dosages, with Grade 3 or 4 neurologic toxicity occurring in 6% of patients. The most frequent neurologic toxicities were headache (20%), encephalopathy (15%), sensory neuropathy (14%), and motor dysfunction (10%).

ICANS was reported in 9% of 265 patients where ICANS was collected and who received TALVEY at the recommended dosages *[see Adverse Reactions (6.1)]* . Recurrent ICANS occurred in 3% of patients. Most patients experienced ICANS following step-up dose 1 (3%), step-up dose 2 (3%), step-up dose 3 of the biweekly dosing schedule (1.8%), or the initial treatment dose of the weekly dosing schedule (2.6%) (N=156) or the biweekly

dosing schedule (3.7%) (N=109). The median time to onset of ICANS was 2.5 (range: 1 to 16) days after the most recent dose with a median duration of 2 (range: 1 to 22) days. The onset of ICANS can be concurrent with CRS, following resolution of CRS, or in the absence of CRS. Clinical signs and symptoms of ICANS may include but are not limited to confusional state, depressed level of consciousness, disorientation, somnolence, lethargy, and bradyphrenia.

Monitor patients for signs and symptoms of neurologic toxicity during treatment. At the first sign of neurologic toxicity, including ICANS, immediately evaluate the patient and provide supportive care based on severity; withhold or permanently discontinue TALVEY based on severity and consider further management per current practice guidelines *[see Dosage and Administration (2.5)].*

Due to the potential for neurologic toxicity, patients receiving TALVEY are at risk of depressed level of consciousness. Advise patients to refrain from driving or operating heavy or potentially dangerous machinery during the step-up dosing schedule and for 48 hours after completion of the step-up dosing schedule *[see Dosage and Administration (2.2)]* and in the event of new onset of any neurological symptoms, until symptoms resolve.

TALVEY is available only through a restricted program under a REMS *[see Warnings and Precautions (5.3)]* .

5.3 TECVAYLI and TALVEY REMS

TALVEY is available only through a restricted program under a REMS called the TECVAYLI and TALVEY REMS because of the risks of CRS and neurologic toxicity, including ICANS *[see Warnings and Precautions (5.1, 5.2)].*

Notable requirements of the TECVAYLI and TALVEY REMS include the following:

- Prescribers must be certified with the program by enrolling and completing training.
- Prescribers must counsel patients receiving TALVEY about the risk of CRS and neurologic toxicity, including ICANS and provide patients with Patient Wallet Card.
- Pharmacies and healthcare settings that dispense TALVEY must be certified with the TECVAYLI and TALVEY REMS program and must verify prescribers are certified through the TECVAYLI and TALVEY REMS program.
- Wholesalers and distributers must only distribute TALVEY to certified pharmacies.

Further information about the TECVAYLI and TALVEY REMS program is available at www.TEC-TALREMS.com or by telephone at 1-855-810-8064.

5.4 Oral Toxicity and Weight Loss

TALVEY can cause oral toxicities, including dysgeusia, dry mouth, dysphagia, and stomatitis *[see Adverse Reactions (6.1)]* .

In the clinical trial, 80% of patients had oral toxicity, with Grade 3 occurring in 2.1% of patients who received TALVEY at the recommended dosages. The most frequent oral toxicities were dysgeusia (49%), dry mouth (34%), dysphagia (23%), and ageusia (18%). The median time to onset of oral toxicity was 15 (range: 1 to 634) days, and the median time to resolution to baseline was 43 (1 to 530) days. Oral toxicity did not resolve to baseline in 65% of patients.

TALVEY can cause weight loss *[see Adverse Reactions (6.1)]* . In the clinical trial, 62% of

patients experienced weight loss, regardless of having an oral toxicity, including 29% of patients with Grade 2 (10% or greater) weight loss and 2.7% of patients with Grade 3 (20% or greater) weight loss. The median time to onset of Grade 2 or higher weight loss was 67 (range: 6 to 407) days, and the median time to resolution was 50 (range: 1 to 403) days. Weight loss did not resolve in 57% of patients who reported weight loss.

Monitor patients for signs and symptoms of oral toxicity. Counsel patients to seek medical attention should signs or symptoms of oral toxicity occur and provide supportive care as per current clinical practice including consultation with a nutritionist. Monitor weight regularly during therapy. Evaluate clinically significant weight loss further. Withhold TALVEY or permanently discontinue based on severity *[see Dosage and Administration (2.5)]* .

5.5 Infections

TALVEY can cause serious infections, including life-threatening or fatal infections *[see Adverse Reactions (6.1)]* .

In the clinical trial, serious infections occurred in 16% of patients, with fatal infections in 1.5% of patients. Grade 3 or 4 infections occurred in 17% of patients. The most common serious infections reported were bacterial infection (8%), which included sepsis, and COVID-19 (2.7%).

Monitor patients for signs and symptoms of infection prior to and during treatment with TALVEY and treat appropriately. Administer prophylactic antimicrobials according to local guidelines. Withhold or consider permanent discontinuation of TALVEY as recommended based on severity *[see Dosage and Administration (2.5)]* .

5.6 Cytopenias

TALVEY can cause cytopenias, including neutropenia and thrombocytopenia *[see Adverse Reactions (6.1)]* .

In the clinical trial, Grade 3 or 4 decreased neutrophils occurred in 35% of patients, and Grade 3 or 4 decreased platelets occurred in 22% of patients who received TALVEY. The median time to onset for Grade 3 or 4 neutropenia was 22 (range: 1 to 312) days, and the median time to resolution to Grade 2 or lower was 8 (range: 1 to 79) days. The median time to onset for Grade 3 or 4 thrombocytopenia was 12 (range: 2 to 183) days, and the median time to resolution to Grade 2 or lower was 10 (range: 1 to 64) days. Monitor complete blood counts during treatment and withhold TALVEY as recommended based on severity *[see Dosage and Administration (2.5)]* .

5.7 Skin Toxicity

TALVEY can cause serious skin reactions, including rash, maculo-papular rash, erythema, and erythematous rash *[see Adverse Reactions (6.1)]* .

In the clinical trial, skin reactions occurred in 62% of patients, with Grade 3 skin reactions in 0.3%. The median time to onset was 25 (range: 1 to 630) days. The median time to improvement to Grade 1 or less was 33 days.

Monitor for skin toxicity, including rash progression. Consider early intervention and treatment to manage skin toxicity. Withhold TALVEY as recommended based on severity *[see Dosage and Administration (2.5)]* .

5.8 Hepatotoxicity

TALVEY can cause hepatotoxicity. In the clinical trial, elevated ALT occurred in 33% of patients, with Grade 3 or 4 ALT elevation occurring in 2.7%; elevated AST occurred in 31% of patients, with Grade 3 or 4 AST elevation occurring in 3.3%. Grade 3 or 4 elevations of total bilirubin occurred in 0.3% of patients *[see Adverse Reactions (6.1)]* . Liver enzyme elevation can occur with or without concurrent CRS.

Monitor liver enzymes and bilirubin at baseline and during treatment as clinically indicated. Withhold TALVEY or consider permanent discontinuation of TALVEY based on severity *[see Dosage and Administration (2.5)]* .

5.9 Embryo-Fetal Toxicity

Based on its mechanism of action, TALVEY may cause fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to the fetus. Advise females of reproductive potential to use effective contraception during treatment with TALVEY and for 3 months after the last dose *[see Use in Specific Populations (8.1, 8.3)]* .

6 ADVERSE REACTIONS

The following adverse reactions are also described elsewhere in the labeling:

- Cytokine Release Syndrome *[see Warnings and Precautions (5.1)]*
- Neurologic Toxicity, including ICANS *[see Warnings and Precautions (5.2)]*
- Oral Toxicity and Weight Loss *[see Warnings and Precautions (5.4)]*
- Infections *[see Warnings and Precautions (5.5)]*
- Cytopenias *[see Warnings and Precautions (5.6)]*
- Skin Toxicity *[see Warnings and Precautions (5.7)]*
- Hepatotoxicity *[see Warnings and Precautions (5.8)]*

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

Relapsed/Refractory Multiple Myeloma

MonumenTAL-1

The safety of TALVEY was evaluated in 339 adult patients with relapsed or refractory multiple myeloma. Patients treated with the weekly dosing schedule received step-up doses of 0.01 mg/kg and 0.06 mg/kg of TALVEY followed by TALVEY 0.4 mg/kg subcutaneously weekly thereafter. Patients treated with the biweekly (every 2 weeks) dosing schedule received step-up doses of 0.01 mg/kg, 0.06 mg/kg, and 0.3 mg/kg (0.75 times the recommended step-up dose 3) followed by TALVEY 0.8 mg/kg subcutaneously every 2 weeks thereafter. The duration of exposure for the 0.4 mg/kg weekly regimen was 5.9 (range: 0.0 to 25.3) months (N=186) and for the 0.8 mg/kg biweekly (every 2 weeks) regimen, it was 3.7 (range: 0.0 to 17.9) months (N=153).

Serious adverse reactions occurred in 47% of patients who received TALVEY. Serious adverse reactions in ≥ 2% of patients included CRS (13%), bacterial infection (8%) including sepsis, pyrexia (4.7%), ICANS (3.8%), COVID-19 (2.7%), neutropenia (2.1%),

and upper respiratory tract infection (2.1%).

Fatal adverse reactions occurred in 3.2% of patients who received TALVEY, including COVID -19 (0.6%), dyspnea (0.6%), general physical health deterioration (0.6%), bacterial infection (0.3%) including sepsis, basilar artery occlusion (0.3%), fungal infection (0.3%), infection (0.3%), and pulmonary embolism (0.3%).

Permanent discontinuation of TALVEY due to an adverse reaction occurred in 9% of patients. Adverse reactions which resulted in permanent discontinuation of TALVEY in > 1% of patients included ICANS.

Dosage interruptions of TALVEY due to an adverse reaction occurred in 56% of patients. Adverse reactions which required dosage interruption in > 5% of patients included pyrexia (15%), CRS (12%), upper respiratory tract infection (9%), COVID-19 (9%), bacterial infection (7%) including sepsis, neutropenia (6%), and rash (6%).

The most common adverse reactions (≥ 20%) were pyrexia, CRS, dysgeusia, nail disorder, musculoskeletal pain, skin disorder, rash, fatigue, weight decreased, dry mouth, xerosis, dysphagia, upper respiratory tract infection, diarrhea, hypotension, and headache. The most common Grade 3 or 4 laboratory abnormalities (≥ 30%) were lymphocyte count decreased, neutrophil count decreased, white blood cell decreased, and hemoglobin decreased.

Table 13 summarizes the adverse reactions in MonumenTAL-1.

Table 13: Adverse Reactions (≥10%) in Patients with Relapsed or Refractory Multiple Myeloma Who Received TALVEY in MonumenTAL-1

	TALVEY N=339	
System Organ Class Adverse Reaction	**Any Grade (%)**	**Grade 3 or 4 (%)**
General disorders and administration site conditions		
Pyrexia *	83	4.7 †
Fatigue *	37	3.5 †
Chills	19	0
Pain *	18	1.8 †
Edema *	14	0
Injection site reaction *	13	0
Immune system disorders		
Cytokine release syndrome	76	1.5 †
Gastrointestinal disorders		
Dysgeusia ‡§	70	0
Dry mouth §	34	0
Dysphagia	23	0.9 †
Diarrhea †	21	0.9
Stomatitis ¶	18	1.2 †
Nausea	18	0
Constipation	16	0

Oral disorder #	12	0
Skin and subcutaneous tissue disorders		
Nail disorder Þ	50	0
Skin disorder ß	41	0.3 †
Rash à	38	3.5 †
Xerosis è	30	0
Pruritus	19	0.3 †
Musculoskeletal and connective tissue disorders		
Musculoskeletal pain *	43	3.2 †
Investigations		
Weight decreased	35	1.5 †
Infections and infestations		
Upper respiratory tract infection *	22	2.7 †
Bacterial infection including sepsis ðø	19	9
COVID-19 *ø	11	2.7
Fungal infection ýø	10	0.6
Vascular disorders		
Hypotension *	21	2.9
Nervous system disorders		
Headache *	21	0.6 †
Encephalopathy £	15	1.8 †
Sensory neuropathy ¥	14	0
Motor dysfunction Œ	10	0.6 †
Metabolism and nutrition disorders		
Decreased appetite	19	1.2 †
Respiratory, thoracic and mediastinal disorders		
Cough *	17	0
Dyspnea *ø	11	1.8
Hypoxia *	10	1.5 †
Cardiac disorders		
Tachycardia *	11	0.6 †

Adverse reactions were graded based on CTCAE Version 4.03, with the exception of CRS, which was graded per ASTCT 2019 criteria.

* Includes other related terms.
† Only grade 3 adverse reactions occurred.
‡ Dysgeusia: ageusia, dysgeusia, hypogeusia and taste disorder.
§ Per CTCAE v4.03, maximum toxicity grade for dysgeusia is 2 and maximum toxicity grade for dry mouth is 3.
¶ Stomatitis: cheilitis, glossitis, glossodynia, mouth ulceration, oral discomfort, oral mucosal erythema, oral pain, stomatitis, swollen tongue, tongue discomfort, tongue erythema, tongue edema and tongue ulceration.
# Oral disorder: oral disorder, oral dysesthesia, oral mucosal exfoliation, oral toxicity and oropharyngeal pain.
Þ Nail disorder: koilonychia, nail bed disorder, nail cuticle fissure, nail discoloration, nail disorder, nail dystrophy, nail hypertrophy, nail pitting, nail ridging, nail toxicity, onychoclasis, onycholysis and onychomadesis.

ß Skin disorder: palmar-plantar erythrodysesthesia syndrome, palmoplantar keratoderma, skin discoloration, skin exfoliation and skin fissures.
à Rash: dermatitis, dermatitis acneiform, dermatitis contact, dermatitis exfoliative, dermatitis exfoliative generalized, erythema, exfoliative rash, rash, rash erythematous, rash macular, rash maculo-papular, rash papular, rash pruritic, rash pustular, rash vesicular and stasis dermatitis.
è Xerosis: dry eye, dry skin and xerosis.
ð Bacterial infection including sepsis: bacteremia, bacterial prostatitis, carbuncle, cellulitis, citrobacter infection, clostridium difficile colitis, clostridium difficile infection, cystitis escherichia, cystitis klebsiella, diverticulitis, enterobacter bacteremia, escherichia pyelonephritis, escherichia sepsis, folliculitis, gastroenteritis escherichia coli, helicobacter gastritis, human ehrlichiosis, klebsiella bacteremia, klebsiella sepsis, moraxella infection, otitis media acute, pitted keratolysis, pneumococcal sepsis, pneumonia, pneumonia streptococcal, pseudomonal bacteremia, pyuria, renal abscess, salmonella sepsis, sepsis, septic shock, skin infection, staphylococcal bacteremia, staphylococcal infection, staphylococcal sepsis, streptococcal bacteremia, tooth abscess, tooth infection, urinary tract infection enterococcal, and urinary tract infection pseudomonal.
ø Includes fatal outcome(s): COVID-19 (N=2), dyspnea (N=2), bacterial infection including sepsis (N=1), fungal infection (N=1).
ý Fungal infection: body tinea, candida infection, ear infection fungal, esophageal candidiasis, fungal infection, fungal sepsis, fungal skin infection, genital candidiasis, onychomycosis, oral candidiasis, oral fungal infection, oropharyngeal candidiasis, tinea pedis, vulvovaginal candidiasis, and vulvovaginal mycotic infection.
£ Encephalopathy: agitation, altered state of consciousness, amnesia, aphasia, bradyphrenia, confusional state, delirium, depressed level of consciousness, disorientation, encephalopathy, hallucination, lethargy, memory impairment, mood altered, restlessness, sleep disorder and somnolence.
¥ Sensory neuropathy: dysesthesia, hyperesthesia, hypoesthesia, hypoesthesia oral, immune-mediated neuropathy, neuralgia, neuropathy peripheral, paresthesia, peripheral sensory neuropathy, polyneuropathy, sciatica and vestibular neuronitis.
Œ Motor dysfunction: dysarthria, dysgraphia, dysmetria, dysphonia, gait disturbance, muscle atrophy, muscle spasms, muscular weakness and tremor.

Clinically relevant adverse reactions reported in <10% of patients who received TALVEY included ICANS and viral infection.

Table 14 summarizes select laboratory abnormalities in MonumenTAL-1.

Table 14: Select Laboratory Abnormalities (≥30%) That Worsened from Baseline in Patients with Relapsed or Refractory Multiple Myeloma Who Received TALVEY in MonumenTAL-1

	TALVEY *	
Laboratory Abnormality	**Any Grade (%)**	**Grade 3 or 4 (%)**
Hematology		
Lymphocyte count decreased	90	80
White blood cell decreased	73	35
Hemoglobin decreased	67	30
Neutrophil count decreased	64	35
Platelet count decreased	62	22
Chemistry		
Albumin decreased	66	2.1
Alkaline phosphatase increased	49	1.5

Phosphate decreased	44	13
Gamma-glutamyl transferase increased	38	7
Alanine aminotransferase increased	33	2.7
Potassium decreased	31	4.4
Sodium decreased	31	6
Aspartate aminotransferase increased	31	3.3

Laboratory toxicity grades are derived based on the NCI CTCAE (National Cancer Institute Common Terminology Criteria for Adverse Events) Version 4.03.

* The denominator used to calculate the rate varied from 326 to 338 based on the number of patients with a baseline value and at least one post-treatment value.

7 DRUG INTERACTIONS

For certain cytochrome P450 (CYP) substrates, minimal changes in the substrate concentration may lead to serious adverse reactions. Monitor for toxicity or drug concentrations of such CYP substrates when co-administered with TALVEY.

Talquetamab-tgvs causes release of cytokines *[see Clinical Pharmacology (12.2)]* that may suppress activity of CYP enzymes, resulting in increased exposure of CYP substrates. Increased exposure of CYP substrates is more likely to occur from initiation of the TALVEY step-up dosing schedule up to 14 days after the first treatment dose and during and after CRS *[see Warnings and Precautions (5.1)]* .

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

Based on the mechanism of action, TALVEY may cause fetal harm when administered to a pregnant woman *[see Clinical Pharmacology (12.1)]* . There are no available data on the use of TALVEY in pregnant women to evaluate for a drug associated risk. No animal reproductive or developmental toxicity studies have been conducted with talquetamab-tgvs.

Talquetamab-tgvs causes T-cell activation and cytokine release; immune activation may compromise pregnancy maintenance. Human immunoglobulin G (IgG) is known to cross the placenta; therefore, TALVEY has the potential to be transmitted from the mother to the developing fetus. Advise women of the potential risk to the fetus.

In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

8.2 Lactation

Risk Summary

There is no information regarding the presence of talquetamab-tgvs in human milk, the effect on the breastfed child, or the effect on milk production. Maternal IgG is known to be present in human milk. The effects of local gastrointestinal exposure and limited

systemic exposure in the breastfed child to TALVEY are unknown. Because of the potential for serious adverse reactions in a breastfed child, advise women not to breastfeed during treatment with TALVEY and for 3 months after the last dose.

8.3 Females and Males of Reproductive Potential

TALVEY may cause fetal harm when administered to a pregnant woman *[see Use in Specific Populations (8.1)]* .

Pregnancy Testing

Verify pregnancy status of females of reproductive potential prior to initiating TALVEY.

Contraception

Females

Advise females of reproductive potential to use effective contraception during treatment with TALVEY and for 3 months after the last dose.

8.4 Pediatric Use

The safety and efficacy of TALVEY have not been established in pediatric patients.

8.5 Geriatric Use

There were 339 patients in the clinical trial for relapsed or refractory multiple myeloma. Of the total number of TALVEY-treated patients in the study, 178 (53%) patients were 65 years of age and older, while 57 (17%) patients were 75 years of age and older. No overall differences in safety or effectiveness were observed in patients 65 to less than 74 years of age compared to younger patients. There was a higher rate of fatal adverse reactions in patients 75 years of age or older compared to younger patients *[see Adverse Reactions (6.1)].* Clinical studies did not include sufficient numbers of patients 75 years of age or over to determine whether they respond differently from younger patients.

11 DESCRIPTION

Talquetamab-tgvs is a bispecific GPRC5D-directed CD3 T-cell engager. It is a humanized IgG4 proline, alanine, alanine (IgG4-PAA)-based bispecific antibody produced by Chinese hamster ovary (CHO) cells using recombinant DNA technology. Talquetamab-tgvs consists of an anti-GPRC5D heavy chain and light chain and an anti-CD3 heavy chain and light chain with two interchain disulfide bonds connecting the two arms. The molecular weight of talquetamab-tgvs is 147 kDa.

TALVEY™ (talquetamab-tgvs) injection is a sterile, preservative-free colorless to light yellow solution supplied in a single-dose vial for subcutaneous administration.

Each TALVEY 1.5 mL single-dose vial contains 3 mg of talquetamab-tgvs, edetate disodium (0.027 mg), glacial acetic acid (0.36 mg), polysorbate 20 (0.6 mg), sodium acetate (1.39 mg), sucrose (120 mg), and Water for Injection, USP. The pH is 5.2.

Each TALVEY 1 mL single-dose vial contains 40 mg of talquetamab-tgvs, edetate disodium (0.018 mg), glacial acetic acid (0.24 mg), polysorbate 20 (0.4 mg), sodium acetate (0.90 mg), sucrose (80 mg), and Water for Injection, USP. The pH is 5.2.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Talquetamab-tgvs is a bispecific T-cell engaging antibody that binds to the CD3 receptor expressed on the surface of T-cells and G protein-coupled receptor class C group 5 member D (GPRC5D) expressed on the surface of multiple myeloma cells and non-malignant plasma cells, as well as healthy tissues such as epithelial cells in keratinized tissues of the skin and tongue.

In vitro, talquetamab-tgvs activated T-cells caused the release of proinflammatory cytokines and resulted in the lysis of multiple myeloma cells. Talquetamab-tgvs had anti-tumor activity in mouse models of multiple myeloma.

12.2 Pharmacodynamics

Serum concentrations of cytokines (IL-6, IL-10, TNF-α, and IFN-γ) and IL-2R were measured before and after administration of each step-up dose, the first three treatment doses at 0.4 mg/kg once weekly, and the first two treatment doses at 0.8 mg/kg every two weeks. Increased concentrations of IL-6, IL-10, and IL-2R were observed during this period.

Higher talquetamab-tgvs exposures (i.e., AUC and C_{max}) are associated with higher incidence of some adverse reactions (including oral toxicity, nail toxicity, and skin reactions). The exposure-response relationships for effectiveness and the time course of pharmacodynamic response of talquetamab-tgvs have not been fully characterized.

12.3 Pharmacokinetics

The C_{max} and AUC_{tau} of talquetamab-tgvs after subcutaneous administration increased proportionally over a dose range of 0.005 to 0.8 mg/kg weekly (0.01 to 2 times the recommended 0.4 mg/kg weekly treatment dose) and 0.8 to 1.2 mg/kg every two weeks (1 to 1.5 times the recommended 0.8 mg/kg every 2 weeks treatment dose). Ninety percent of steady state exposure was achieved 16 weeks after the first treatment dose for both regimens.

The C_{max}, C_{trough}, C_{avg}, and accumulation ratios of talquetamab-tgvs are presented in Table 15.

Table 15: Pharmacokinetic Parameters of Talquetamab-tgvs Following the Dose at 16 Weeks After the First Treatment Dose for the Approved Recommended Subcutaneous Dosages in Patients with Relapsed or Refractory Multiple Myeloma

Parameter	Talquetamab-tgvs Dosage	
	0.4 mg/kg every week	0.8 mg/kg every 2 weeks
Exposure *		
C_{max}(ng/mL)	2,940 (67%)	3,410 (63%)
C_{trough}(ng/mL)	2,410 (83%)	1,930 (103%)

C_{avg}(ng/mL)	2,730 (71%)	2,770 (72%)
Accumulation Ratio †		
C_{max}	4.4	1.8
C_{trough}	4.6	2.3
C_{avg}	5.1	2.0

C_{avg}= Average concentration over the dosing interval; :C_{max}= Maximum serum talquetamab-tgvs concentration; C_{trough}= Serum talquetamab-tgvs concentration prior to next dose

∗ Data are presented as geometric mean (coefficient of variation %).

† For the 0.4 mg/kg every week regimen, accumulation ratios are presented as the arithmetic mean of the 17 th treatment dose / the first treatment dose. For the 0.8 mg/kg every 2 weeks regimen, accumulation ratios are presented as the arithmetic mean of the 9 th treatment dose / the first treatment dose.

Absorption

The geometric mean (coefficient of variation [CV] %) bioavailability of talquetamab-tgvs was 59% (22%) when administered subcutaneously.

The median (range) $T_{max}$of talquetamab-tgvs after the first and 17 thtreatment dose of 0.4 mg/kg weekly were 3.7 (0.9 to 7) days and 2.5 (0.9 to 5.9) days, respectively.

The median (range) $T_{max}$of talquetamab-tgvs after the first and 9 thtreatment dose of 0.8 mg/kg every 2 weeks were 3.4 (0.8 to 14) days and 3.6 (1 to 7.7) days, respectively.

Distribution

The geometric mean (CV%) volume of distribution of talquetamab-tgvs was 10.1 L (25%).

Elimination

Talquetamab-tgvs clearance decreases over time, with a mean (CV%) maximal reduction from the first treatment dose to 16 weeks after the first treatment dose of 40% (56%). The geometric mean (CV%) clearance is 0.90 L/day (63%) at 16 weeks after the first treatment dose. The mean (CV%) terminal half-life was 8.4 (41%) days after the first treatment dose and 12.2 (49%) days at 16 weeks after the first treatment dose.

Metabolism

Talquetamab-tgvs is expected to be metabolized into small peptides by catabolic pathways.

Specific Populations

The volume of distribution and clearance of talquetamab-tgvs increased with increasing bodyweight (40 kg to 143 kg).

There were no clinically significant differences in the pharmacokinetics of talquetamab-tgvs based on age (33 to 86 years), sex, race (White, Black or African American), ethnicity (Not Hispanic/Latino, Hispanic/Latino), mild or moderate renal impairment (creatinine clearance [CLcr] by Cockcroft-Gault equation: 30 to 89 mL/min) or mild (total bilirubin less than or equal to upper limit of normal [ULN] with AST greater than ULN or total bilirubin greater than 1 to 1.5 times ULN with any AST) or moderate (total bilirubin greater than 1.5 to less than 3 times ULN with any AST) hepatic impairment. The effects

of severe renal impairment (CLcr less than 30 mL/min) or severe hepatic impairment (total bilirubin greater than 3 times ULN with any AST) on the pharmacokinetics of talquetamab-tgvs are unknown.

12.6 Immunogenicity

The observed incidence of anti-drug antibodies is highly dependent on the sensitivity and specificity of the assay. Differences in assay methods preclude meaningful comparisons of the incidence of anti-drug antibodies in the studies described below with the incidence of anti-drug antibodies in other studies, including those of talquetamab-tgvs or of other talquetamab products.

During treatment in MonumenTAL-1 (up to 25 months), 45/177 (25%) patients treated with subcutaneous TALVEY 0.4 mg/kg weekly (median follow-up 5.7 months) and 24/130 (18%) patients treated with subcutaneous TALVEY 0.8 mg/kg every 2 weeks (median follow-up 3.1 months) developed anti-talquetamab-tgvs antibodies. There was no identified clinically significant effect of anti-talquetamab-tgvs antibodies on the pharmacokinetics, pharmacodynamics, safety, or effectiveness of TALVEY.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

No carcinogenicity or genotoxicity studies have been conducted with talquetamab-tgvs.

No studies have been conducted to evaluate the effects of talquetamab-tgvs on fertility.

14 CLINICAL STUDIES

The efficacy of TALVEY monotherapy was evaluated in patients with relapsed or refractory multiple myeloma in a single-arm, open-label, multicenter study, MMY1001 (MonumenTAL-1) (NCT03399799, NCT04634552). The study included patients who had previously received at least three prior systemic therapies, including a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 monoclonal antibody. The study excluded patients who experienced T-cell redirection therapy within 3 months, prior Grade 3 or higher CRS related to any T-cell redirection therapy, an autologous stem cell transplant within the past 12 weeks, an allogeneic stem cell transplant within the past 6 months, Eastern Cooperative Oncology Group (ECOG) performance score of 3 or higher, stroke or seizure within the past 6 months, CNS involvement or clinical signs of meningeal involvement of multiple myeloma, and plasma cell leukemia, active or documented history of autoimmune disease (exception of vitiligo, resolved childhood atopic dermatitis, resolved Grave's Disease that is euthyroid based on clinical and laboratory testing).

Patients treated with the weekly dosing schedule received step-up doses of 0.01 mg/kg and 0.06 mg/kg of TALVEY followed by TALVEY 0.4 mg/kg subcutaneously weekly thereafter.

Patients treated with the biweekly (every 2 weeks) dosing schedule received step-up doses of 0.01 mg/kg, 0.06 mg/kg, and 0.3 mg/kg (0.75 times the recommended step-up dose 3) of TALVEY followed by TALVEY 0.8 mg/kg subcutaneously biweekly, thereafter. Patients on both dosing schedules were treated until disease progression or

unacceptable toxicity.

The efficacy results from the 187 patients treated with TALVEY who were not exposed to prior T cell redirection therapy and who had received at least 4 prior lines of therapy are presented below; of these patients, the median age was 67 (range: 38 to 86) years, 57% were male, 90% were White, 5% were Black or African American, 3% were Asian, and 8% were Hispanic. Patients had received a median of 5 (range: 4 to 13) prior lines of therapy, and 78% had received prior autologous stem cell transplantation (ASCT). Ninety-four percent (94%) of patients were refractory to their last therapy, and 73% were refractory to a proteasome inhibitor, immunomodulatory agent, and anti-CD38 antibody. The International Staging System (ISS) at study entry was Stage I in 44%, Stage II in 34%, and Stage III in 22% of patients. High-risk cytogenetic factors (presence of t(4:14), t(14:16), and/or del(17p)) were present in 29% of patients; baseline cytogenetic data were not available in 11% of patients. Twenty-two percent (22%) of patients had extramedullary plasmacytomas.

Efficacy was based on overall response rate (ORR) and duration of response (DOR) as assessed by an Independent Review Committee using IMWG criteria. The median duration of follow-up from first response among responders receiving TALVEY 0.4 mg/kg weekly was 13.8 (range: 0.8 to 15.4) months.

Table 16: Efficacy Results for MMY1001 (MonumenTAL-1) in Patients Receiving 0.4 mg/kg Weekly TALVEY

	0.4 mg/kg Weekly (N=100)
Overall response rate (ORR=sCR+CR+VGPR+PR)	73 (73%)
95% CI	(63.2%, 81.4%)
Stringent complete response (sCR)	26%
Complete response (CR)	9%
Very good partial response (VGPR)	22%
Partial response (PR)	16%
Duration of Response (DOR)	
Median DOR (95% CI) (months)	9.5 (6.5, NE)

CI=confidence interval; NE=not estimable

The median duration of follow-up from first response among responders receiving TALVEY 0.8 mg/kg biweekly was 5.9 (range: 0 to 9.5) months; an estimated 85% of responders maintained response for at least 9 months.

Table 17: Efficacy Results for MMY1001 (MonumenTAL-1) in Patients Receiving 0.8 mg/kg Biweekly (Every 2 Weeks) TALVEY

	0.8 mg/kg Biweekly (Every 2 Weeks) (N=87)
Overall response rate	65 (73.6%)

(ORR=sCR+CR+VGPR+PR)	65 (73.6%)
95% CI	(63.0%, 82.4%)
Stringent complete response (sCR)	20%
Complete response (CR)	13%
Very good partial response (VGPR)	25%
Partial response (PR)	16%
Duration of Response (DOR)	
Median DOR (95% CI) (months)	NE

CI=confidence interval; NE=not estimable

The median time to first response was 1.2 (range: 0.2 to 10.9) months and 1.3 (range: 0.2 to 9.2) months for 0.4 mg/kg weekly and 0.8 mg/kg biweekly (every 2 weeks), respectively.

Thirty-two patients were exposed to prior T cell redirection therapy and had received at least 4 prior lines of therapy, including a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 monoclonal antibody received TALVEY at the 0.4 mg/kg weekly dose. Patients had received a median of 6 (range: 4 to 15) prior therapies, with 81% exposed to CAR-T cell therapy and 25% exposed to a bispecific antibody. Ninety-four percent of patients were exposed to prior T cell redirection therapy directed at BCMA. The ORR per IRC assessment was 72% (95% CI: 53%, 86%). With a median duration of follow-up of 10.4 months, an estimated 59% of responders maintained response for at least 9 months.

16 HOW SUPPLIED/STORAGE AND HANDLING

TALVEY™ (talquetamab-tgvs) injection is a sterile, preservative-free, colorless to light yellow solution supplied as follows:

- One 3 mg/1.5 mL (2 mg/mL) single-dose vial in a carton: NDC: 57894-469-01
- One 40 mg/mL single-dose vial in a carton: NDC: 57894-470-01

Store refrigerated at 2°C to 8°C (36°F to 46°F) in original carton to protect from light.

Do not freeze.

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Medication Guide).

Cytokine Release Syndrome (CRS)

Discuss the signs and symptoms associated with CRS including, but not limited to, pyrexia, hypotension, chills, hypoxia, headache, and tachycardia. Counsel patients to seek medical attention should signs or symptoms of CRS occur. Advise patients that they should be hospitalized for 48 hours after administration of all doses within the TALVEY step-up dosing schedule *[see Dosage and Administration (2.1, 2.5), Warnings and Precautions (5.1)]* .

Neurologic Toxicity, including ICANS

Discuss the signs and symptoms associated with neurologic toxicity, including ICANS

including headache, encephalopathy, sensory neuropathy, motor dysfunction, ICANS, confusional state, depressed level of consciousness, disorientation, somnolence, lethargy, and bradyphrenia. Counsel patients to seek medical attention should signs or symptoms of ICANS occur. Advise patients to refrain from driving or operating heavy or potentially dangerous machinery during the step-up dosing schedule and for 48 hours after completion of the step-up dosing schedule and in the event of new onset of any neurologic toxicity symptoms, until symptoms resolve *[see Dosage and Administration (2.2, 2.5), Warnings and Precautions (5.2)].*

TECVAYLI and TALVEY REMS

TALVEY is available only through a restricted program called the TECVAYLI and TALVEY REMS. Inform patients that they will be given a Patient Wallet Card that they should carry with them at all times and show to all of their healthcare providers. This card describes signs and symptoms of CRS and neurologic toxicity, including ICANS which, if experienced, should prompt the patient to immediately seek medical attention *[see Warnings and Precautions (5.3)].*

Oral Toxicity and Weight Loss

Discuss the signs and symptoms of oral toxicities including dysgeusia, dry mouth, dysphagia, and stomatitis. Counsel patients to seek medical attention should signs or symptoms of oral toxicity occur. Advise patients that they may experience weight loss and to report weight loss. Advise patients that they may be referred to a nutritionist for consultation *[see Dosage and Administration (2.5), Warnings and Precautions (5.4)]* .

Infections

Discuss the signs and symptoms of serious infections *[see Dosage and Administration (2.5), Warnings and Precautions (5.5)]* .

Cytopenias

Discuss the signs and symptoms associated with neutropenia and thrombocytopenia *[see Dosage and Administration (2.5)*, *Warnings and Precautions (5.6)]* .

Skin Toxicity

Discuss the signs and symptoms of skin reactions *[see Dosage and Administration (2.5), Warnings and Precautions (5.7)]* .

Hepatotoxicity

Advise patients that liver enzyme elevations may occur and that they should report symptoms that may indicate liver toxicity, including fatigue, anorexia, right upper abdominal discomfort, dark urine, or jaundice *[see Warnings and Precautions (5.8)].*

Embryo-Fetal Toxicity

Advise pregnant women and females of reproductive potential of the potential risk to a fetus. Advise females of reproductive potential to inform their healthcare provider if they are pregnant or become pregnant. Advise females of reproductive potential to use effective contraception during treatment with TALVEY and for 3 months after the last dose *[see Warnings and Precautions (5.9), Use in Specific Populations (8.1, 8.3)]* .

Lactation

Advise women not to breastfeed during treatment with TALVEY and for 3 months after

the last dose *[see Use in Specific Populations (8.2)]* .

Manufactured by:
Janssen Biotech, Inc.
Horsham, PA 19044, USA
U.S. License Number 1864

For patent information: www.janssenpatents.com

MEDICATION GUIDE
TALVEY™ [tal vay]
(talquetamab-tgvs) injection, for subcutaneous use

What is the most important information I should know about TALVEY?
TALVEY may cause side effects that are serious, life-threatening, or lead to death, including Cytokine Release Syndrome (CRS) and neurologic problems.
Call your healthcare provider or get medical help right away if you develop any of the signs or symptoms of CRS or neurologic problems listed below at any time during your treatment with TALVEY:
Cytokine Release Syndrome (CRS).CRS is common during treatment with TALVEY and can also be serious or life-threatening. Signs and symptoms of CRS may include:

- fever (100.4°F or higher)
- dizziness or lightheadedness
- chills
- difficulty breathing
- feeling anxious
- headache
- fast heartbeat

Neurologic problems. Symptoms of neurologic problems with TALVEY may include:

- headache
- feeling confused
- being less alert or aware
- feeling disoriented
- trouble speaking or writing
- shaking (tremors)
- numbness and tingling (feeling like "pins and needles")
- feeling sleepy
- feeling very sleepy with low energy
- slow or difficulty thinking
- seizures
- muscle weakness
- memory loss
- burning, throbbing, or stabbing pain

- Due to the risk of CRS and neurologic problems, you should be hospitalized for 48 hours after all doses of TALVEY that are part of the "step-up dosing schedule". The "step-up dosing schedule" is when you receive the first 2 or 3 doses of TALVEY, which are smaller "step-up" doses, and also the first full "treatment dose" of TALVEY.
- TALVEY is given weekly or every 2 weeks. Your healthcare provider will decide the number of days to wait between your doses of TALVEY as well as how many treatments you will receive.
  - If you receive TALVEY weekly, "Step-up dose 1" is given on day 1 of treatment. "Step-up dose 2" is usually given on day 4 of treatment. The first "treatment dose" is usually given on day 7 of treatment.
  - If you receive TALVEY every 2 weeks, "Step-up dose 1" is given on day 1 of treatment. "Step-up dose 2" is usually given on day 4 of treatment. "Step-up dose

3" is usually given on day 7 of treatment. The first "treatment dose" is usually given on day 10 of treatment.

- If your dose of TALVEY is delayed for any reason, you may need to repeat the "step-up dosing schedule" to receive TALVEY.
- Before each "step up" dose of TALVEY, you will receive medicines to help reduce your risk of CRS. Your healthcare provider will decide if you need to receive medicines to help reduce your risk of CRS with future doses.
- Your healthcare provider will monitor you for signs and symptoms of CRS, neurologic problems, as well as other side effects and treat you as needed.

TALVEY is available only through the TECVAYLI and TALVEY Risk Evaluation and Mitigation Strategy (REMS) due to the risk of CRS and neurologic problems.
You will receive a Patient Wallet Card from your healthcare provider. **Carry the Patient Wallet Card with you at all times and show it to all of your healthcare providers.**The Patient Wallet Card lists signs and symptoms of CRS and neurologic problems.
Get medical help right away if you develop any of the signs and symptoms listed on the Patient Wallet Card. You may need to be treated in a hospital.

- If you have any questions about TALVEY, ask your healthcare provider.
- Your healthcare provider may temporarily stop or completely stop your treatment with TALVEY if you develop CRS, neurologic problems or any other side effects that are severe.

See " **What are the possible side effects of TALVEY?"** for more information about side effects.

What is TALVEY?
TALVEY is a prescription medicine used to treat adults with multiple myeloma who:

- have already received at least 4 treatment regimens, including a proteasome inhibitor, an immunomodulatory agent and an anti-CD38 monoclonal antibody to treat their multiple myeloma, **and**
- their cancer has come back or did not respond to prior treatment.

It is not known if TALVEY is safe and effective in children.

Before you receive TALVEY, tell your healthcare provider about all of your medical conditions, including if you:

- have an infection
- are pregnant or plan to become pregnant. TALVEY may harm your unborn baby. Tell your healthcare provider if you become pregnant or think that you may be pregnant during treatment with TALVEY.
  Females who are able to become pregnant:
  - Your healthcare provider should do a pregnancy test before you start treatment with TALVEY.
  - You should use effective birth control (contraception) during treatment and for 3 months after your last dose of TALVEY.
- are breastfeeding or plan to breastfeed. It is not known if TALVEY passes into your breast milk. Do not breastfeed during treatment and for 3 months after your last dose of TALVEY.

Tell your healthcare provider about all the medicines you take,including prescription and over-the-counter medicines, vitamins, and herbal supplements.

How will I receive TALVEY?

- TALVEY will be given to you by your healthcare provider as an injection under your skin (subcutaneous injection), usually in the stomach area (abdomen). TALVEY may also be injected into your thigh or another area of your body.
- **See " What is the most important information I should know about TALVEY?" at the beginning of this Medication Guide for information about how you will receive TALVEY.**
- If you miss any appointments, call your healthcare provider as soon as possible to reschedule your appointment.

What should I avoid while receiving TALVEY?

Do notdrive, operate heavy machinery, or do other dangerous activities during and for 48 hours after your TALVEY "step-up dose" is completed or at any time during treatment with TALVEY, if you develop dizziness, confusion, tremors, sleepiness, or any other symptoms that impair consciousness until your signs and symptoms go away. These may be signs and symptoms of CRS or neurologic problems.
See "**What is the most important information I should know about TALVEY**?" for more information about signs and symptoms of CRS and neurologic problems.

What are the possible side effects of TALVEY?

TALVEY may cause serious side effects, including:

- **See " What is the most important information I should know about TALVEY?"**
- **Mouth problems and weight loss.**Tell your healthcare provider or get medical help right away if you develop any of the following symptoms of mouth problems:

  - changes in sense of taste
  - dry mouth
  - trouble swallowing
  - mouth sores

Your healthcare provider will monitor you for these symptoms and will monitor your weight during treatment with TALVEY. Tell your healthcare provider if you lose weight during treatment with TALVEY.

- **Infections**. TALVEY can cause serious infections that can be life-threatening and may lead to death. Your healthcare provider will monitor you for signs and symptoms of infection before and during treatment with TALVEY. Tell your healthcare provider right away if you get develop any signs or symptoms of infection during treatment with TALVEY, including:

  - fever of 100.4°F (38°C) or higher
  - chills
  - cough
  - chest pain
  - tiredness
  - shortness of breath
  - painful rash
  - sore throat
  - pain during urination
  - feeling weak or generally unwell

- **Decreased blood cell counts.**Decreased blood cell counts are common during treatment with TALVEY and can also be severe. Your healthcare provider will check your blood cell counts during treatment with TALVEY.

- **Skin problems**. Skin problems are common during treatment with TALVEY and can also be serious. Tell your healthcare provider if you get skin problems such as skin rash, raised red bumps, or redness of the skin.
- **Liver problems.**Abnormal liver tests can happen during treatment with TALVEY. Your healthcare provider will do blood tests before and during treatment with TALVEY to check your liver. Tell your healthcare provider if you develop any of the following symptoms of liver problems:
  - tiredness
  - loss of appetite
  - pain in your right upper stomach-area (abdomen)
  - dark urine
  - yellowing of your skin or the white part of your eyes

The most common side effects of TALVEY include:

- changes in your sense of taste
- nail problems
- muscle and joint pain
- feeling very tired
- weight loss
- dry mouth
- fever
- very dry skin that may affect the mucous membranes (such as the mouth and eyes)
- difficulty swallowing
- infected nose, sinuses or throat (cold)
- diarrhea

The most common severe abnormal lab test results with TALVEY include: decreased white blood cells and red blood cells. These are not all the possible side effects of TALVEY.
Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

General Information about the safe and effective use of TALVEY.
Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. You can ask your pharmacist or healthcare provider for information about TALVEY that is written for health professionals.

What are the ingredients of TALVEY?
Active ingredient: talquetamab-tgvs
Inactive ingredients: edetate disodium, glacial acetic acid, polysorbate 20, sodium acetate, sucrose, and Water for Injection, USP.
Manufactured by: Janssen Biotech, Inc., Horsham, PA 19044, USA
U.S. License Number 1864

For patent information: www.janssenpatents.com
For more information, go to www.TALVEY.com or call 1-800-526-7736.

This Medication Guide has been approved by the U.S. Food and Drug Administration. Issued: August 2023

PRINCIPAL DISPLAY PANEL - 3 mg Vial Carton

NDC 57894-469-01

One Vial
Rx only

Talvey™
(talquetamab-tgvs)
Injection

3 mg/1.5 mL
(2 mg/mL)

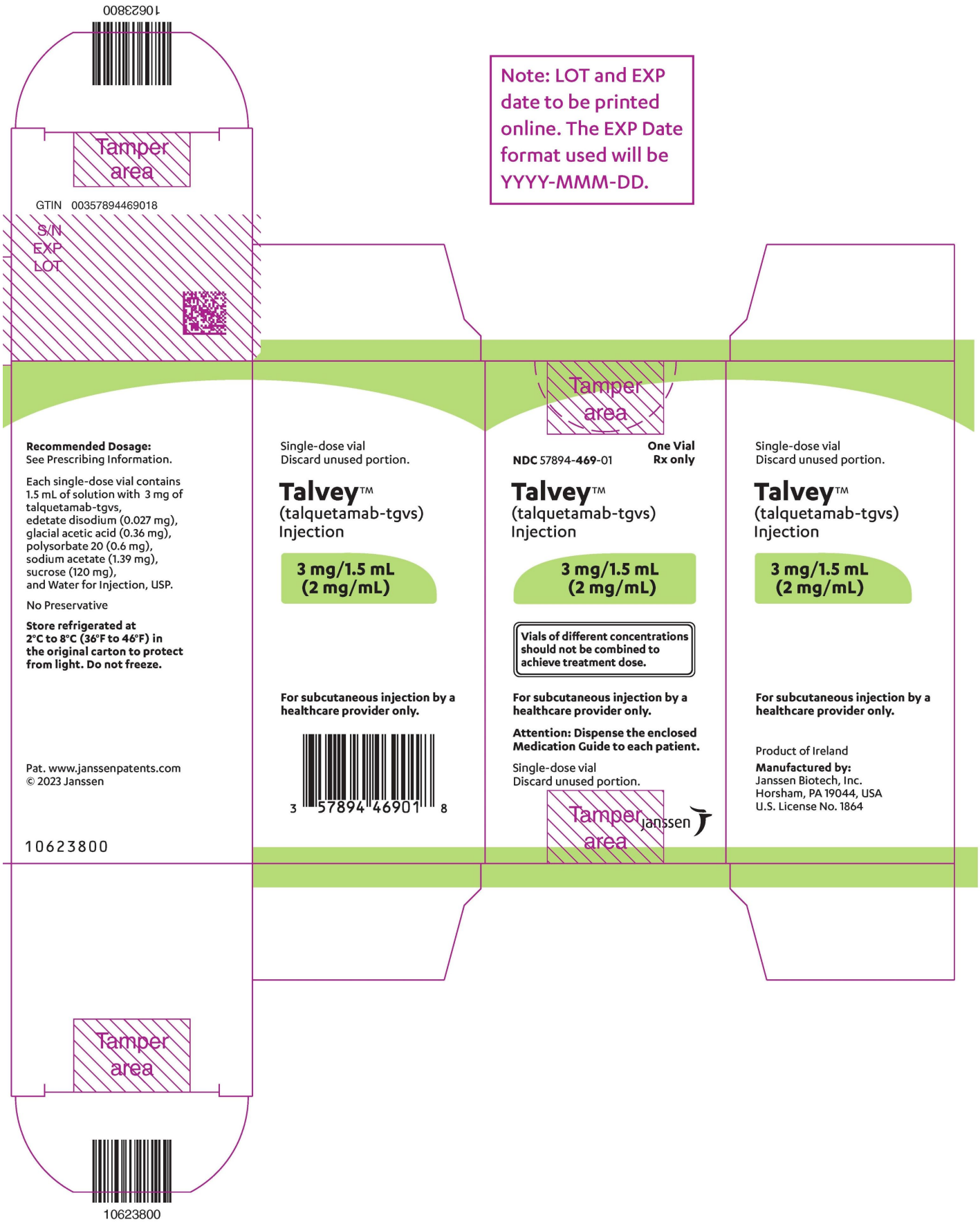
Vials of different concentrations should not be combined to achieve treatment dose.

For subcutaneous injection by a healthcare provider only.

Attention: Dispense the enclosed Medication Guide to each patient.

Single-dose vial
Discard unused portion.

janssen



PRINCIPAL DISPLAY PANEL - 40 mg Vial Carton

NDC 57894-470-01

One Vial
Rx only

Talvey™
(talquetamab-tgvs)
Injection

40 mg/mL

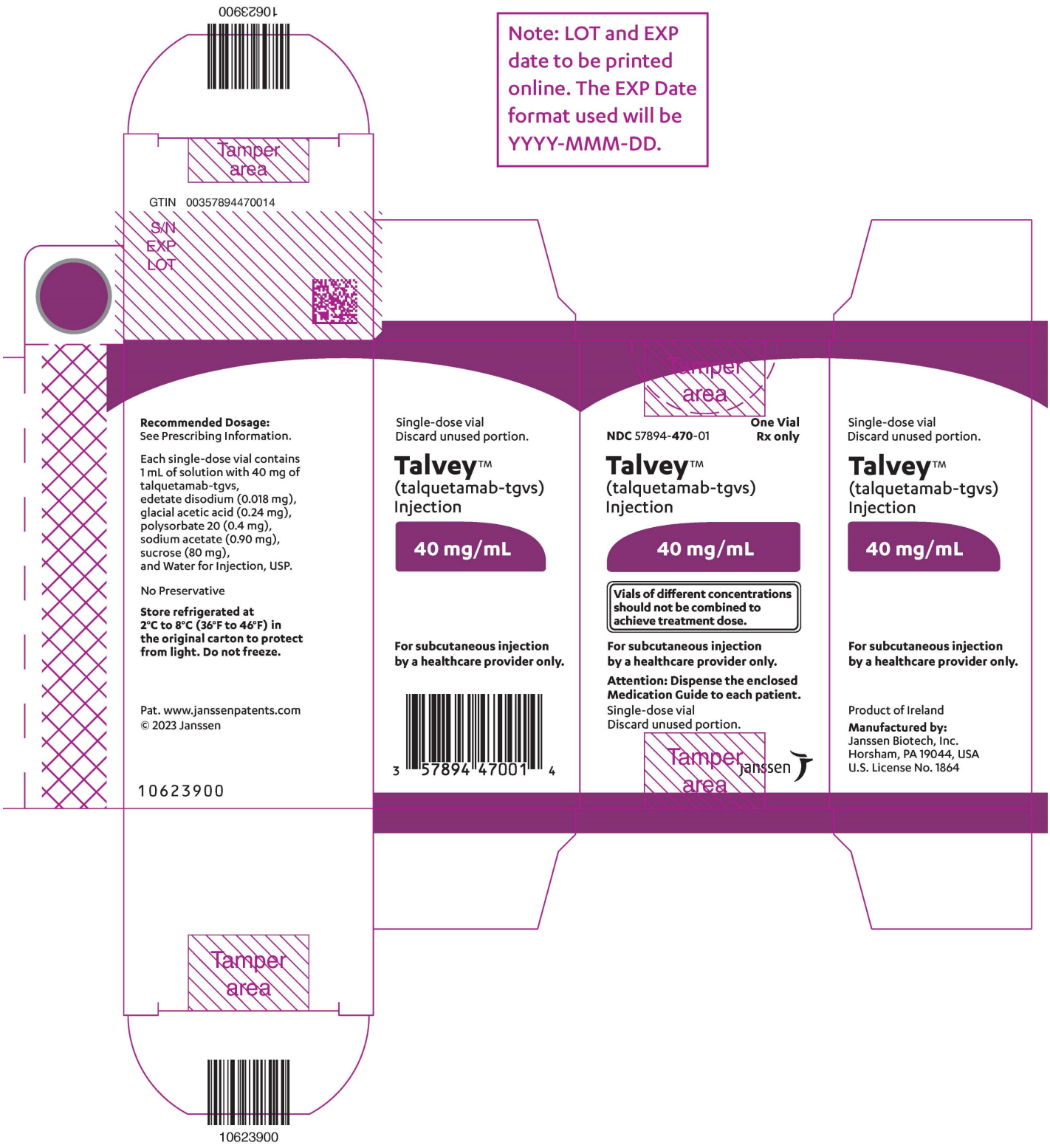
Vials of different concentrations
should not be combined to
achieve treatment dose.

For subcutaneous injection
by a healthcare provider only.

Attention: Dispense the enclosed
Medication Guide to each patient.

Single-dose vial
Discard unused portion.

janssen



Note: LOT and EXP date to be printed online. The EXP Date format used will be YYYY-MMM-DD.

TALVEY

talquetamab injection

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:57894-469
Route of Administration	SUBCUTANEOUS		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
TALQUETAMAB (UNII: 4W3KFI3TN3) (TALQUETAMAB - UNII:4W3KFI3TN3)	TALQUETAMAB	3 mg in 1.5 mL

Inactive Ingredients

Ingredient Name	Strength
EDETATE DISODIUM (UNII: 7FLD91C86K)	
ACETIC ACID (UNII: Q40Q9N063P)	
SUCROSE (UNII: C151H8M554)	
POLYSORBATE 20 (UNII: 7T1F30V5YH)	
SODIUM ACETATE (UNII: 4550K0SC9B)	
WATER (UNII: 059QF0KO0R)	

Product Characteristics

Color	yellow (Colorless to light yellow)	**Score**	
Shape		**Size**	
Flavor		**Imprint Code**	
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:57894-469-01	1 in 1 CARTON	08/09/2023	
1		1.5 mL in 1 VIAL, SINGLE-DOSE; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
BLA	BLA761342	08/09/2023	

TALVEY

talquetamab injection

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:57894-470
Route of Administration	SUBCUTANEOUS		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
TALQUETAMAB (UNII: 4W3KFI3TN3) (TALQUETAMAB - UNII:4W3KFI3TN3)	TALQUETAMAB	40 mg in 1 mL

Inactive Ingredients

Ingredient Name	Strength
EDETATE DISODIUM (UNII: 7FLD91C86K)	
ACETIC ACID (UNII: Q40Q9N063P)	
SUCROSE (UNII: C151H8M554)	
POLYSORBATE 20 (UNII: 7T1F30V5YH)	
SODIUM ACETATE (UNII: 4550K0SC9B)	
WATER (UNII: 059QF0KO0R)	

Product Characteristics

Color	yellow (Colorless to light yellow)	**Score**	
Shape		**Size**	
Flavor		**Imprint Code**	
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:57894-470-01	1 in 1 CARTON	08/09/2023	
1		1 mL in 1 VIAL, SINGLE-DOSE; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
BLA	BLA761342	08/09/2023	

Labeler - Janssen Biotech, Inc. (099091753)

Establishment

Name	Address	ID/FEI	Business Operations
Janssen Biotech, Inc.		038978363	api manufacture(57894-469, 57894-470)

Establishment

Name	Address	ID/FEI	Business Operations
AndersonBrecon, Inc.		053217022	pack(57894-469, 57894-470) , label(57894-469, 57894-470)

Establishment

Name	Address	ID/FEI	Business Operations
Patheon Manufacturing Services LLC		079415560	analysis(57894-469, 57894-470) , manufacture(57894-469, 57894-470) , label(57894-469, 57894-470) , pack(57894-469, 57894-470)

Establishment

Name	Address	ID/FEI	Business Operations
BioReliance Corporation		147227730	analysis(57894-470, 57894-469)

Establishment

Name	Address	ID/FEI	Business Operations
Janssen Biologics B.V.		409612918	analysis(57894-469, 57894-470)

Establishment

Name	Address	ID/FEI	Business Operations
Cilag AG		483237103	analysis(57894-469, 57894-470)

Establishment

Name	Address	ID/FEI	Business Operations
Biogen MA, Inc.		841087823	api manufacture(57894-469, 57894-470) , analysis(57894-469, 57894-470)

Establishment

Name	Address	ID/FEI	Business Operations
Janssen Sciences Ireland Unlimited Company		986030167	api manufacture(57894-469, 57894-470) , analysis(57894-469, 57894-470)