TALVEY™
(talquetamab-tgvs) Injection for subcutaneous use
2 mg/mL and 40 mg/mL

TREATMENT MANAGEMENT GUIDE

INDICATION AND USAGE

TALVEY™ (talquetamab-tgvs) 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. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).

IMPORTANT SAFETY 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.

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. Withhold or discontinue TALVEY™ based on severity.

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).

Please see full Important Safety Information on pages 22-25. Please read full Prescribing Information, including Boxed WARNING, for TALVEY™.

TABLE OF CONTENTS

CRS, cytokine release syndrome; ICANS, immune effector cell-associated neurotoxicity syndrome.

Please see full Important Safety Information on pages 22-25. Please read full Prescribing Information, including Boxed WARNING, for TALVEY™.

MECHANISM OF ACTION

TALVEY™ is a bispecific T-cell engaging antibody that binds to the CD3 receptor expressed on the surface of T cells and to 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, TALVEY™ activated T cells caused the release of proinflammatory cytokines and resulted in the lysis of multiple myeloma cells. TALVEY™ had anti-tumor activity in mouse models of multiple myeloma.

IMPORTANT SAFETY INFORMATION (cont'd)

CONTRAINDICATIONS: None.

WARNINGS AND PRECAUTIONS

Cytokine Release Syndrome (CRS): TALVEY™ can cause cytokine release syndrome, including life-threatening or fatal reactions. 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. 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 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.

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.

CD, cluster of differentiation; GPRC5D, G-protein coupled receptor family C group 5 member D.

Please see full Important Safety Information on pages 22-25. Please read full Prescribing Information, including Boxed WARNING, for TALVEY™.

TALVEY™ (talquetamab-tgvs) Injection for subcutaneous use
2 mg/mL and 40 mg/mL

NOTES

IMPORTANT SAFETY INFORMATION (cont'd)

Neurologic Toxicity including ICANS: TALVEY™ can cause serious or life-threatening neurologic toxicity, including immune effector cell-associated neurotoxicity syndrome (ICANS), including fatal reactions. In the clinical trial, neurologic toxicity occurred in 55% of patients who received 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 the recommended dosages. 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.

Please see full Important Safety Information on pages 22-25. Please read full Prescribing Information, including Boxed WARNING, for TALVEY™.

CLINICAL STUDY DESIGN

The efficacy of TALVEY™ monotherapy was evaluated in patients with relapsed or refractory multiple myeloma in a single-arm, open-label, multicenter study, MonumenTAL-1.

- 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 Graves' 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

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.

CD, cluster of differentiation; CNS, central nervous system; CRS, cytokine release syndrome; IMWG, International Myeloma Working Group.

IMPORTANT SAFETY INFORMATION (cont'd)

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, and in the event of new onset of any neurological symptoms, until symptoms resolve.

Please see full Important Safety Information on pages 22-25. Please read full Prescribing Information, including Boxed WARNING, for TALVEY™.

TALVEY™ (talquetamab-tgvs) Injection for subcutaneous use
2 mg/mL and 40 mg/mL

PATIENT CHARACTERISTICS

Prior T-cell redirection therapy-naïve patients*

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% of patients 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

IMPORTANT SAFETY INFORMATION (cont'd)

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.

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

Please see full Important Safety Information on pages 22-25. Please read full Prescribing Information, including Boxed WARNING, for TALVEY™.

PATIENT CHARACTERISTICS (cont'd)

Prior T-cell redirection therapy-exposed patients*

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

BCMA, B-cell maturation antigen; CAR-T, chimeric antigen receptor-T cell; ORR, overall response rate.

*T-cell redirection therapy refers to both CAR-T and bispecific antibody treatment.

IMPORTANT SAFETY INFORMATION (cont'd)

Oral Toxicity and Weight Loss: TALVEY™ can cause oral toxicities, including dysgeusia, dry mouth, dysphagia, and stomatitis. In the clinical trial, 80% of patients had oral toxicity, with Grade 3 occurring in 2.1% of patients who received 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.

Please see full Important Safety Information on pages 22-25. Please read full Prescribing Information, including Boxed WARNING, for TALVEY™.

TALVEY™ (talquetamab-tgvs) Injection for subcutaneous use 2 mg/mL and 40 mg/mL

WEEKLY EFFICACY RESULTS

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.

EFFICACY RESULTS FOR MONUMENTAL-1 IN PATIENTS RECEIVING TALVEY™ 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; MRD, minimal residual disease; NE, not estimable.

BIWEEKLY EFFICACY RESULTS

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.

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.

EFFICACY RESULTS FOR MONUMENTAL-1 IN PATIENTS RECEIVING TALVEY™ 0.8 mg/kg BIWEEKLY (EVERY 2 WEEKS)

	TALVEY™ 0.8 mg/kg Biweekly (Every 2 Weeks) (N=87)
Overall response rate (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.

IMPORTANT SAFETY INFORMATION (cont'd)

Infections: TALVEY™ can cause infections, including life-threatening or fatal infections. 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 permanently discontinue TALVEY™ as recommended, based on severity.

Please see full Important Safety Information on pages 22-25. Please read full Prescribing Information, including Boxed WARNING, for TALVEY™.

IMPORTANT SAFETY INFORMATION (cont'd)

Cytopenias: TALVEY™ can cause cytopenias, including neutropenia and thrombocytopenia. 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.

Please see full Important Safety Information on pages 22-25. Please read full Prescribing Information, including Boxed WARNING, for TALVEY™.

TALVEY™ (talquetamab-tgvs) Injection for subcutaneous use 2 mg/mL and 40 mg/mL

IMPORTANT DOSING INFORMATION

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

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) in the full Prescribing Information]*.

- 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 3 or Table 4 in the full Prescribing Information)* or for patients who experienced CRS *(see Table 5 in the full Prescribing Information)*.

IMPORTANT SAFETY INFORMATION (cont'd)

Skin Toxicity: TALVEY™ can cause serious skin reactions, including rash, maculo-papular rash, erythema, and erythematous rash. 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. In the clinical trial, supportive care included topical steroids (15%). Oral steroid tapers (4.4%) were typically administered for Grade 3 skin reactions. Withhold or permanently discontinue TALVEY™, based on severity.

Please see full Important Safety Information on pages 22-25. Please read full Prescribing Information, including Boxed WARNING, for TALVEY™.

IMPORTANT SAFETY INFORMATION (cont'd)

Hepatotoxicity: TALVEY™ can cause hepatotoxicity. 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. 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)].

Please see full Important Safety Information on pages 22-25. Please read full Prescribing Information, including Boxed WARNING, for TALVEY™.

TALVEY™ (talquetamab-tgvs) Injection for subcutaneous use
2 mg/mL and 40 mg/mL

WEEKLY 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) in the full Prescribing Information]*.

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

TALVEY™ WEEKLY DOSING SCHEDULE

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

[a]Based on actual body weight.

[b]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.

[c]Maintain a minimum of 6 days between weekly doses.

IMPORTANT SAFETY INFORMATION (cont'd)

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.

Please see full Important Safety Information on pages 22-25. Please read full Prescribing Information, including Boxed WARNING, for TALVEY™.

BIWEEKLY 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) in the full Prescribing Information]*.

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

TALVEY™ BIWEEKLY (EVERY 2 WEEKS) DOSING SCHEDULE

Dosing schedule	Day	Dose[a]	
Step-up dosing schedule	Day 1	Step-up dose 1	0.01 mg/kg
	Day 4[b]	Step-up dose 2	0.06 mg/kg
	Day 7[b]	Step-up dose 3	0.4 mg/kg
	Day 10[c]	First treatment dose	0.8 mg/kg
Biweekly (every 2 weeks) dosing schedule	Two weeks after first treatment dose and every 2 weeks thereafter[d]	Subsequent treatment doses	0.8 mg/kg every 2 weeks

[a]Based on actual body weight.

[b]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.

[c]Dose may be administered between 2 to 7 days after step-up dose 3.

[d]Maintain a minimum of 12 days between biweekly (every 2 weeks) doses.

IMPORTANT SAFETY INFORMATION (cont'd)

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.

The most common Grade 3 or 4 laboratory abnormalities (≥30%) are lymphocyte count decreased, neutrophil count decreased, white blood cell decreased, and hemoglobin decreased.

Please see full Important Safety Information on pages 22-25. Please read full Prescribing Information, including Boxed WARNING, for TALVEY™.

TALVEY™ (talquetamab-tgvs) Injection for subcutaneous use 2 mg/mL and 40 mg/mL

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) in the full Prescribing information]*.

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™.

IMPORTANT SAFETY INFORMATION (cont'd)

CONTRAINDICATIONS: None.

WARNINGS AND PRECAUTIONS

Cytokine Release Syndrome (CRS): TALVEY™ can cause cytokine release syndrome, including life-threatening or fatal reactions. 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. 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).

Please see full Important Safety Information on pages 22-25. Please read full Prescribing Information, including Boxed WARNING, for TALVEY™.

PREPARATION AND ADMINISTRATION (cont'd)

Preparation

- Use Table 9 in the full Prescribing Information 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

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 (mL)	Number of Vials (1 vial=1.5 mL)
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

CRS, cytokine release syndrome; ICANS, immune effector cell-associated neurotoxicity syndrome.

IMPORTANT SAFETY INFORMATION (cont'd)

Initiate 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.

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.

Please see full Important Safety Information on pages 22-25. Please read full Prescribing Information, including Boxed WARNING, for TALVEY™.

TALVEY™ (talquetamab-tgvs) Injection for subcutaneous use
2 mg/mL and 40 mg/mL

PREPARATION AND ADMINISTRATION (cont'd)

- Use Table 10 in the full Prescribing Information 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

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)
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

IMPORTANT SAFETY INFORMATION (cont'd)

Neurologic Toxicity including ICANS: TALVEY™ can cause serious or life-threatening neurologic toxicity, including immune effector cell-associated neurotoxicity syndrome (ICANS), including fatal reactions. In the clinical trial, neurologic toxicity occurred in 55% of patients who received 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 the recommended dosages. 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.

Please see full Important Safety Information on pages 22-25. Please read full Prescribing Information, including Boxed WARNING, for TALVEY™.

PREPARATION AND ADMINISTRATION (cont'd)

- Use Table 11 in the full Prescribing Information 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

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)
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

IMPORTANT SAFETY INFORMATION (cont'd)

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, and in the event of new onset of any neurological symptoms, until symptoms resolve.

Please see full Important Safety Information on pages 22-25. Please read full Prescribing Information, including Boxed WARNING, for TALVEY™.

TALVEY™ (talquetamab-tgvs) Injection for subcutaneous use 2 mg/mL and 40 mg/mL

PREPARATION AND ADMINISTRATION (cont'd)

- Use Table 12 in the full Prescribing Information 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

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)
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

IMPORTANT SAFETY INFORMATION (cont'd)

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.

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

PREPARATION AND ADMINISTRATION (cont'd)

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 (eg, 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 of 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.

- 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

RESTARTING TALVEY™ AFTER DOSAGE DELAY

If a dose of TALVEY™ is delayed, restart therapy based on the recommendations in Table 3 and Table 4 in the full Prescribing Information and resume weekly or biweekly (every 2 weeks) dosing schedule accordingly *[see Dosage and Administration (2.1) in the full Prescribing Information]*; 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) in the full Prescribing Information]*.

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) in the full Prescribing Information]*.

RESTARTING TALVEY™ AFTER DOSAGE DELAY (cont'd)

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) in the full Prescribing Information]*.

IMPORTANT SAFETY 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.

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. Withhold or discontinue TALVEY™ based on severity.

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).

CONTRAINDICATIONS: None.

WARNINGS AND PRECAUTIONS

Cytokine Release Syndrome (CRS): TALVEY™ can cause cytokine release syndrome, including life-threatening or fatal reactions. 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. 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 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.

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.

Please see full Important Safety Information on pages 22-25. Please read full Prescribing Information, including Boxed WARNING, for TALVEY™.

IMPORTANT SAFETY INFORMATION (cont'd)

Neurologic Toxicity including ICANS: TALVEY™ can cause serious or life-threatening neurologic toxicity, including immune effector cell-associated neurotoxicity syndrome (ICANS), including fatal reactions. In the clinical trial, neurologic toxicity occurred in 55% of patients who received 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 the recommended dosages. 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, and in the event of new onset of any neurological symptoms, until symptoms resolve.

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.

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

Oral Toxicity and Weight Loss: TALVEY™ can cause oral toxicities, including dysgeusia, dry mouth, dysphagia, and stomatitis. In the clinical trial, 80% of patients had oral toxicity, with Grade 3 occurring in 2.1% of patients who received 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.

Please see full Important Safety Information on pages 22-25. Please read full Prescribing Information, including Boxed WARNING, for TALVEY™.

TALVEY™ (talquetamab-tgvs) Injection for subcutaneous use 2 mg/mL and 40 mg/mL

IMPORTANT SAFETY INFORMATION (cont'd)

TALVEY™ can cause weight loss. In the clinical trial, 62% of patients experienced weight loss of 5% or greater, regardless of having an oral toxicity, including 28% 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.

Infections: TALVEY™ can cause infections, including life-threatening or fatal infections. 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 permanently discontinue TALVEY™ as recommended, based on severity.

Cytopenias: TALVEY™ can cause cytopenias, including neutropenia and thrombocytopenia. 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.

Skin Toxicity: TALVEY™ can cause serious skin reactions, including rash, maculo-papular rash, erythema, and erythematous rash. 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. In the clinical trial, supportive care included topical steroids (15%). Oral steroid tapers (4.4%) were typically administered for Grade 3 skin reactions. Withhold or permanently discontinue TALVEY™, based on severity.

Hepatotoxicity: TALVEY™ can cause hepatotoxicity. 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. Liver enzyme elevation can occur with or without concurrent CRS.

IMPORTANT SAFETY INFORMATION (cont'd)

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)].

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.

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.

The most common Grade 3 or 4 laboratory abnormalities (≥30%) are lymphocyte count decreased, neutrophil count decreased, white blood cell decreased, and hemoglobin decreased.

Please read full Prescribing Information, including Boxed WARNING, for TALVEY™.

cp-394174v2

DOSAGE MODIFICATIONS FOR ADVERSE REACTIONS

Dose delays may be required to manage toxicities related to TALVEY™ *[see Warnings and Precautions (5) in the full Prescribing Information]*.

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

RECOMMENDATIONS FOR MANAGEMENT OF CRS

CRS Grade[a]	Presenting Symptoms	Actions
Grade 1	Temperature ≥100.4°F (38°C)[b]	• Withhold TALVEY™ until CRS resolves.[c] • Administer pretreatment medication prior to next dose.
Grade 2	Temperature ≥100.4°F (38°C)[b] with either: • Hypotension responsive to fluids and not requiring vasopressors, or • Oxygen requirement of low-flow nasal cannula[d] 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.[c]
Grade 3	Temperature ≥100.4°F (38°C)[b] with either: • Hypotension requiring one vasopressor, with or without vasopressin, or • Oxygen requirement of high-flow nasal cannula[d], facemask, non-rebreather mask, or Venturi mask	Duration less than 48 hours • 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.[c] Recurrent or duration greater than or equal to 48 hours • Permanently discontinue TALVEY™. • Provide supportive therapy, which may include intensive care.
Grade 4	Temperature ≥100.4°F (38°C)[b] with either: • Hypotension requiring 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.

CRS, cytokine release syndrome; ICANS, immune effector cell-associated neurotoxicity syndrome.

[a]Based on American Society for Transplantation and Cellular Therapy (ASTCT) grading for CRS (Lee et al 2019).

[b]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).

[c]See Table 3 and Table 4 in the full Prescribing Information for recommendations on restarting TALVEY™ after dose delays for adverse reactions *[see Dosage and Administration (2.4) in the full Prescribing Information]*.

[d]Low-flow nasal cannula is ≤6 L/min, and high-flow nasal cannula is >6 L/min.

RECOMMENDATIONS FOR MANAGEMENT OF NEUROLOGIC TOXICITY (EXCLUDING ICANS)

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

ICANS, immune effector cell-associated neurotoxicity syndrome.

[a]Based on National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE), version 4.03.

[b]See Table 3 and Table 4 in the full Prescribing Information for recommendations on restarting TALVEY™ after dose delays for adverse reactions *[see Dosage and Administration (2.4) in the full Prescribing Information]*.

RECOMMENDATIONS FOR MANAGEMENT OF ICANS

Grade[a]	Presenting Symptoms[b]	Actions
Grade 1	ICE score 7-9[c], or depressed level of consciousness[d]: awakens spontaneously.	• Withhold TALVEY™ until ICANS resolves.[e] • 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.
Grade 2	ICE score 3-6[c], or depressed level of consciousness[d]: awakens to voice.	• Withhold TALVEY™ until ICANS resolves. • Administer dexamethasone[f] 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. • Patients should be hospitalized for 48 hours following the next dose of TALVEY™ *[see Dosage and Administration (2.1) in the full Prescribing Information]*.[e]
Grade 3	ICE score 0-2[c], (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[d]: awakens only to tactile stimulus, or seizures[d], either: • any clinical seizure, focal or generalized, that resolves rapidly, or • non-convulsive seizures on EEG that resolve with intervention, or raised intracranial pressure: focal/local edema on neuroimaging.[d]	<u>First Occurrence of Grade 3 ICANS:</u> • Withhold TALVEY™ until ICANS resolves. • Administer dexamethasone[f] 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) in the full Prescribing Information]*.[e] <u>Recurrent Grade 3 ICANS:</u> • Permanently discontinue TALVEY™ . • Administer dexamethasone[f] 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.

RECOMMENDATIONS FOR MANAGEMENT OF ICANS (cont'd)

Grade[a]	Presenting Symptoms[b]	Actions
Grade 4	ICE score 0[c], (Patient is unarousable and unable to perform ICE assessment) or depressed level of consciousness[d] either: • patient is unarousable or requires vigorous or repetitive tactile stimuli to arouse, or • stupor or coma, or seizures[d], either: • life-threatening prolonged seizure (>5 minutes), or • repetitive clinical or electrical seizures without return to baseline in between, or motor findings[d]: • deep focal motor weakness such as hemiparesis or paraparesis, or raised intracranial pressure/ cerebral edema[d], with signs/ symptoms such as: • diffuse cerebral edema on neuroimaging, or • decerebrate or decorticate posturing, or • cranial nerve VI palsy, or • papilledema, or • Cushing's triad	• Permanently discontinue TALVEY™. • Administer dexamethasone[f] 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., levetiracetam) for seizure prophylaxis. • Provide supportive therapy, which may include intensive care.

[a]Based on ASTCT 2019 grading for ICANS.
[b]Management is determined by the most severe event, not attributable to any other cause.
[c]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.
[d]Attributable to no other cause.
[e]See Table 3 and Table 4 in the full Prescribing Information for recommendations on restarting TALVEY™ after dose delays for adverse reactions *[see Dosage and Administration (2.4) in the full Prescribing Information]*.
[f]All references to dexamethasone administration are dexamethasone or equivalent.

ASTCT, American Society for Transplantation and Cellular Therapy; EEG, electroencephalogram; ICANS, immune effector cell-associated neurotoxicity syndrome; ICE, immune effector cell-associated encephalopathy.

Please see full Important Safety Information on pages 22-25. Please read full Prescribing Information, including Boxed WARNING, for TALVEY™.

TALVEY™ (talquetamab-tgvs) Injection for subcutaneous use
2 mg/mL and 40 mg/mL

OTHER ADVERSE REACTIONS

RECOMMENDED DOSE MODIFICATIONS FOR OTHER ADVERSE REACTIONS

Adverse Reaction	Severity	Dose Modification
Oral Toxicity and Weight Loss *[see Warnings and Precautions (5.4) in the full Prescribing Information]*	Grade 1-2	• Provide supportive care. • Consider withholding TALVEY™ if not responsive to supportive care.[a]
	Grade 3	• Withhold TALVEY™ until resolution to Grade 1 or better and provide supportive care.[a]
	Grade 4	• Permanently discontinue TALVEY™.
Infections *[see Warnings and Precautions (5.5) in the full Prescribing Information]*	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.[b]
	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.[b]
Cytopenias *[see Warnings and Precautions (5.6) in the full Prescribing Information]*	Absolute neutrophil count less than 0.5×10^9/L	• Withhold TALVEY™ until absolute neutrophil count is 0.5×10^9/L or higher.[a]
	Febrile neutropenia	• Withhold TALVEY™ until absolute neutrophil count is 1.0×10^9/L or higher and fever resolves.[a]
	Hemoglobin less than 8 g/dL	• Withhold TALVEY™ until hemoglobin is 8 g/dL or higher.[a]
	Platelet count less than 25,000/mcL Platelet count between 25,000/mcL and 50,000/mcL with bleeding	• Withhold TALVEY™ until platelet count is 25,000/mcL or higher and no evidence of bleeding.[a]
Skin Reactions *[see Warnings and Precautions (5.7) in the full Prescribing Information]*	Grade 3-4	• Withhold TALVEY™ until adverse reaction improves to Grade 1 or baseline.[a]
Other Non-hematologic Adverse Reactions[c] *[see Warnings and Precautions (5.8) and Adverse Reactions (6.1) in the full Prescribing Information]*	Grade 3	• Withhold TALVEY™ until adverse reaction improves to Grade 1 or baseline.[a]
	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.[a]

[a]See Table 3 and Table 4 in the full Prescribing Information for recommendations on restarting TALVEY™ after dose delays for adverse reactions *[see Dosage and Administration (2.4) in the full Prescribing Information]*.
[b]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.
[c]Based on National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE), Version 4.03.

NOTES

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) in the full Prescribing Information]*.

Neurologic Toxicity, including ICANS

Discuss the signs and symptoms 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) in the full Prescribing Information]*.

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) in the full Prescribing Information]*.

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) in the full Prescribing Information]*.

Infections

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

PATIENT COUNSELING INFORMATION (cont'd)

Cytopenias

Discuss the signs and symptoms associated with neutropenia and thrombocytopenia

[see Dosage and Administration (2.5), Warnings and Precautions (5.6) in the full Prescribing Information].

Skin Toxicity

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

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) in the full Prescribing Information]*.

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) in the full Prescribing Information]*.

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) in the full Prescribing Information]*.

TALVEY™

(talquetamab-tgvs) Injection for subcutaneous use

2 mg/mL and 40 mg/mL

Visit TALVEYHCP.com

Please see full Important Safety Information on pages 22-25. Please read accompanying full Prescribing Information, including Boxed WARNING, for TALVEY™.

janssen Oncology

PHARMACEUTICAL COMPANIES OF Johnson & Johnson

 08/23 cp-389950v1