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

A GUIDE TO TALVEY® FOR CLINICAL PHARMACISTS

What you need to know about the first-in-class GPRC5D targeting agent 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.[1,2]

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]

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 and treat promptly. Withhold or permanently 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).

CD38, cluster of differentiation 38; GPRC5D, G protein-coupled receptor class C group 5 member D.

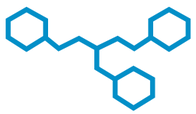
Please read full Important Safety Information on pages 8-10, and full Prescribing Information, including Boxed WARNING, for TALVEY®.

Multiple myeloma continues to evolve over time, driving the need for new therapeutic targets[3,4]

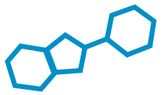
The heterogeneous nature of multiple myeloma can eventually lead to treatment resistance and disease relapse[5]

- Different targets are needed to treat the disease, including treatment-resistant clones in later lines

Multiple myeloma is currently incurable, and patients can eventually become refractory to multiple classes of treatment[4,6-8]



Proteasome inhibitors



Immunomodulatory agents

Anti-CD38 monoclonal antibodies

As patients with relapsed or refractory multiple myeloma continue to progress, the number of treatment options becomes limited, so it is essential to identify different therapeutic targets and approaches.[4,9]

What is currently known about GPRC5D expression?

GPRC5D is expressed:

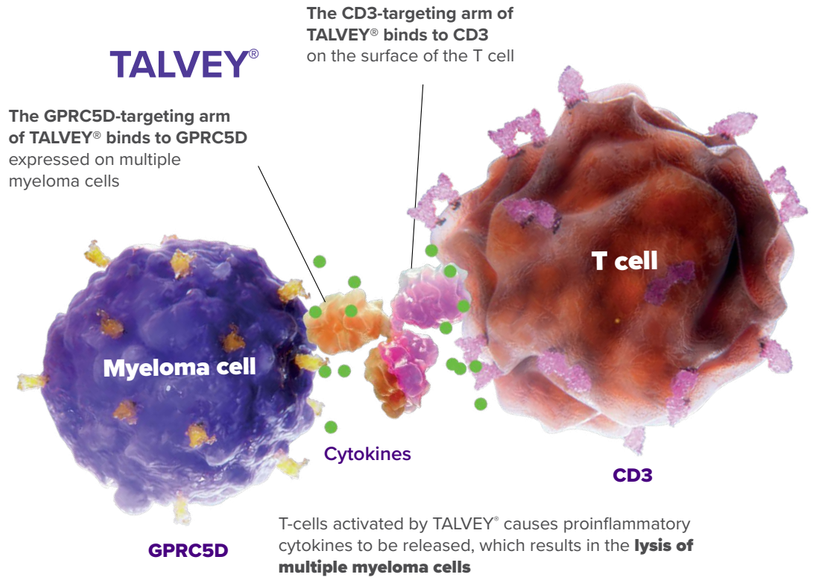
- On the surface of multiple myeloma cells and nonmalignant plasma cells, as well as healthy tissues such as epithelial cells in keratinized tissues of the skin and tongue[1,11-15]
- In a broad range of patients with multiple myeloma that varied according to disease staging, cytogenetic abnormalities, gender, and age[11]

GPRC5D expression is independent of other targets, including BCMA.[10]

TALVEY® is the first FDA-approved bispecific antibody developed to target GPRC5D[1,2]

TALVEY® induces the lysis of multiple myeloma cells by activating the immune system via GPRC5D × CD3[1]

- In research that examined GPRC5D mRNA expression in malignant cells, GPRC5D mRNA was found to be substantially expressed in multiple myeloma cell lines[10]



T-cells activated by TALVEY® causes proinflammatory cytokines to be released, which results in the **lysis of multiple myeloma cells**

BCMA, B cell maturation antigen; CD3, cluster of differentiation 3; CD38, cluster of differentiation 38; FDA, U.S. Food and Drug Administration; GPRC5D, G protein-coupled receptor class C group 5 member D; ISI, Important Safety Information; MOA, mechanism of action; mRNA, messenger ribonucleic acid; RRMM, relapsed or refractory multiple myeloma.

IMPORTANT SAFETY INFORMATION (continued)

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%. Most events occurred following step-up dose 1 (29%) or step-up dose 2 (44%) at the recommended dosages. 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).

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MonumenTAL-1 Trial Design[1]

Treatment versatility: TALVEY® was evaluated in patients naïve and exposed to T-cell redirection therapy* in the MonumenTAL-1 trial[1]

The efficacy of TALVEY® as a single agent was evaluated in 219 patients with relapsed or refractory multiple myeloma in the single-arm, open-label, multicenter, phase 1/2 MonumenTAL-1 trial[1,16,17]

Patients naïve to T-cell redirection therapy* were randomized to receive TALVEY® Q2W or QW:

(N=87)

(N=100)

Patients exposed to T-cell redirection therapy* received TALVEY® QW:

(N=32)

Key eligibility criteria[1]

- Received ≥3 prior systemic therapies, including a proteasome inhibitor, an immunomodulatory agent,and an anti-CD38 monoclonal antibody
- ECOG PS of 0-2 included
- No T-cell redirection therapy* within 3 months
- No prior Grade 3 or higher CRS related to any T-cell redirection therapy*
- No autologous stem cell transplant within the past 12 weeks
- No stroke, seizure, or allogeneic stem cell transplant within the past 6 months
- No CNS involvement or clinical signs of meningeal involvement of multiple myeloma, or plasma cell leukemia
- No active or documented history of autoimmune disease, with the exception of vitiligo, resolved childhood atopic dermatitis, resolved Graves' Disease that is euthyroid based on clinical and laboratory testing

Primary Endpoint: ORR[17]
Key Secondary Endpoints: DOR, TTR[17]

Clinical Trial dosing

Patients received TALVEY® Q2W (0.8 mg/kg) or QW (0.4mg/kg) as a subcutaneous injection until disease progression or unacceptable toxicity, after the step-up dosing schedule.

Inclusion of patients who were naïve and exposed to T-cell redirection therapy* demonstrated the versatile use of TALVEY®.

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

Patients with a range of characteristics, including those with high-risk features, were studied in MonumenTAL-1[1]

In patients naïve to T-cell redirection therapy,* 22% had ISS stage III, 29% had high-risk cytogenetics, 22% had extramedullary disease, and 73% were triple-class refractory[1]

Naïve to T-cell redirection therapy*	
Patient characteristics	**SC Q2W/QW (N=187)**
Age, median	67 years (range: 38-86)
Gender	
Male	57%
Race	
White	90%
Hispanic	8%
Black or African American	5%
Asian	3%
ISS stage	
I	44%
II	34%
III	22%
High-risk cytogenetics (presence of t[4;14], t[14;16], and/or del[17p])†	29%

Naïve to T-cell redirection therapy* (cont'd)	
Patient characteristics	**SC Q2W/QW (N=187)**
Extramedullary disease	22%
Prior lines of therapy, median	5 lines (range: 4-13)
Prior autologous stem cell transplantation	78%
Triple-class exposed (proteasome inhibitor, immunomodulatory agent, and anti-CD38 monoclonal antibody)	100%
Triple-class refractory (proteasome inhibitor, immunomodulatory agent, and anti-CD38 monoclonal antibody)	73%
Refractory to last therapy	94%

In patients exposed to T-cell redirection therapy,* 81% prior CAR-T and 25% had prior bispecific antibody treatment[1]

Exposed to T-cell redirection therapy*	
Patient characteristics	**SC QW (N=32)**
Prior lines of therapy, median	6 lines (range: 4-15)
Triple-class exposed (proteasome inhibitor, immunomodulatory agent, and anti-CD38 monoclonal antibody)	100%
Prior CAR-T	81%
Prior bispecific antibody treatment	25%
Prior BCMA-directed therapy	94%

*T-cell redirection therapy refers to both CAR-T and bispecific antibody therapy.
†Baseline cytogenic data were not available in 11% of patients.

BCMA, B-cell maturation antigen; CAR-T, chimeric antigen receptor-T cell; CD38, cluster of differentiation 38; CNS, central nervous system; CRS, cytokine release syndrome; del, deletion; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group Performance Status; ISS, International Staging System; ORR, overall response rate; SC, subcutaneous; t, translocation; TTR, time to response; Q2W, once every 2 weeks; QW, once weekly.

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

Cytokine Release Syndrome (CRS) (continued): 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.

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In patients who have been triple-class explosed, TALVEY® provided

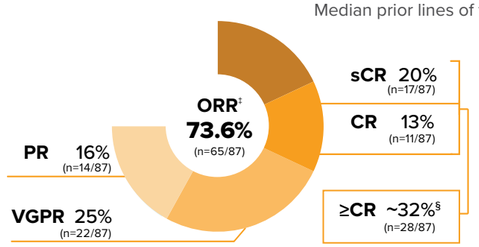
Powerful efficacy[1,16]

Efficacy was based on ORR and DOR as assessed by an IRC using IMWG criteria.*

Naïve to T-cell redirection therapy†

Response to Q2W dosing (N=87)

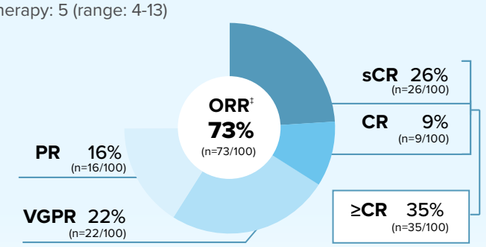
Median prior lines of therapy: 5 (range: 4-13)



(95% CI, 63.0%-82.4%)

Median follow-up of 5.9 (range: 0 to 9.5) months from first response

Response to QW dosing (N=100)



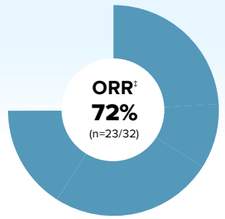
(95% CI, 63.2%-81.4%)

Median follow-up of 13.8 (range: 0.8-15.4) months from first response

Exposed to T-cell redirection therapy†

Response to QW dosing (N=32)

Median prior therapies: 6 (range: 4-15)



(95% CI, 53%-86%)

Median follow-up of 10.4 months

*Efficacy results reflect patients who received ≥4 prior lines of therapy.
†T-cell redirection therapy refers to both CAR-T and bispecific antibody therapy.
‡ORR: sCR+CR+VGPR+PR.
§Due to rounding, calculation may not be exact.

Patients who received TALVEY® achieved durable responses[1,16]

Naïve to T-cell redirection therapy*

Response to Q2W dosing (N=87)

mDOR: NE

mTTR: 1.3 months

(range: 0.2-9.2 months)

Median duration of follow-up from first response among responders was 5.9 months; an estimated

85% of patients continued to respond for at least 9 months

Response to QW dosing (N=100)

mDOR: 9.5 months

(95% CI, 6.5-NE months)

mTTR: 1.2 months

(range: 0.2-10.9 months)

Exposed to T-cell redirection therapy*

Response to QW dosing (N=32)

With a median duration of follow-up of 10.4 months, an estimated

59% of patients continued to respond for at least 9 months

*T-cell redirection therapy refers to both CAR-T and bispecific antibody therapy.
CI, confidence interval; CR, complete response; IMWG, International Myeloma Working Group; IRC, Independent Review Committee; mDOR, median duration of response; mTTR, median time to response; NE, not estimable; PR, partial response; sCR, stringent complete response; VGPR, very good partial response.

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

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.

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

INDICATION AND IMPORTANT SAFETY INFORMATION

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

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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.

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).

CONTRADICTIONS: 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%. Most events occurred following step-up dose 1 (29%) or step-up dose 2 (44%) at the recommended dosages. 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.

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%).

WARNINGS AND PRECAUTIONS (continued)

Neurologic Toxicity including ICANS (continued) - 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 and treat promptly. 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.

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 consider permanent discontinuation of TALVEY® as recommended, based on severity.

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IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

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) time to improvement to grade 1 or less was 33 days.

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. Withhold TALVEY® as recommended 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.

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.

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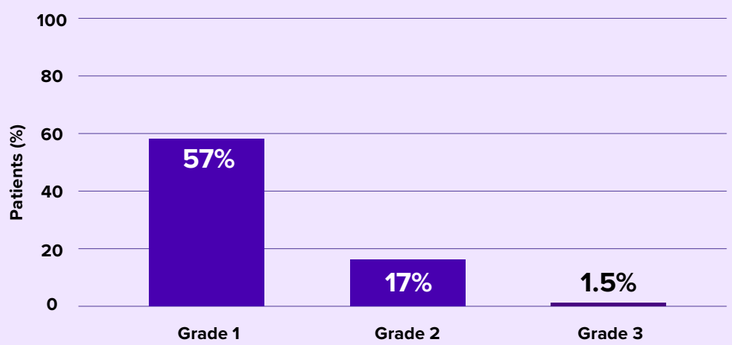
CRS, including life-threatening or fatal reactions, can occur in patients receiving TALVEY®[1]

In the clinical trial, CRS primarily occurred in 76% of patients (N=339) who received TALVEY® at the recommended dosages

- CRS was primarily Grade 1/2, with Grade 3 events occurring in 1.5% of patients
- Recurrent CRS occurred in 30% of patients

Median time to onset: 27 hours (range 0.1-167) from the last dose
Median duration: 17 hours (range: 0-622)

Incidence of CRS



CRS experienced after each dose of TALVEY® (N=339)

Q2W	QW
Step-up dosing schedule	
Step-up dose 1 **29%**	
Step-up dose 2 **44%**	
Step-up dose 3 (N=153) **33%**	First treatment dose **30%**
First treatment dose **12%**	N/A
Dosing after step-up schedule	
Each remaining dose in Cycle 1 **<3%**	
Cumulatively from Cycle 2 onwards **<3%**	

CRS, including life-threatening or fatal reactions, can occur in patients receiving TALVEY®[1] (continued)

Signs and symptoms of CRS may include but are not limited to:

- Pyrexia
- Hypotension
- Chills
- Hypoxia
- Headache
- Tachycardia

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. Advise patients to immediately contact their healthcare provider if they experience any signs or symptoms of CRS.

Manage CRS according to the recommendations in Table 5 in the full Prescribing Information and consider further management per current practice guidelines.

TALVEY® is available only through a restricted program called the TECVAYLI® and TALVEY® Risk Evaluation and Mitigation Strategy (REMS) Program. Visit **TEC-TALREMS.COM**

N/A, not available; REMS, Risk Evaluation and Mitigation Strategy. Q2W, once every 2 weeks; QW, once weekly.

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

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%. Most events occurred following step-up dose 1 (29%) or step-up dose 2 (44%) at the recommended dosages. 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 read full Important Safety Information on pages 8-10, and full Prescribing Information, including Boxed WARNING, for TALVEY®.

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

Neurologic toxicity, including ICANS, and serious and life-threatening or fatal reactions, can occur with TALVEY®[1]

Neurologic toxicity, including ICANS, occurred in 55% of patients at the recommended dosages

- Grade 3/4 events occurred in 6% of patients
- Most frequent neurologic toxicities were headache (20%), encephalopathy (15%), sensory neuropathy (14%), motor dysfunction (10%)

ICANS was reported in 9% of 265 patients where ICANS was collected and who received TALVEY® at the recommended dosages

- Recurrent ICANS occurred in 3% of patients
- ICANS can occur concurrently 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
- 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

Median time to onset: 2.5 days (range: 1-16) from the last dose
Median duration: 2 days (range: 1-22)

ICANS experienced after each dose of TALVEY® (N=265)	
Q2W	**QW**
Step-up dosing schedule	
Step-up dose 1 **3%**	
Step-up dose 2 **3%**	
Step-up dose 3 **1.8%**	First treatment dose (N=156) **2.6%**
First treatment dose (N=109) **3.7%**	N/A

Neurologic toxicity, including ICANS, and serious and life-threatening or fatal reactions, can occur with TALVEY®[1] (continued)

Signs and symptoms associated with neurologic toxicity, including ICANS, may include but are not limited to:

- Confusional state
- Depressed level of consciousness
- Disorientation
- Somnolence
- Lethargy
- Bradyphrenia

Monitor patients for signs and symptoms of neurologic toxicity during treatment. At first sign of neurologic toxicity, including ICANS, immediately evaluate patient and provide supportive therapy based on severity.

Advise patients to immediately contact their healthcare provider if they experience any signs or symptoms of neurologic toxicity, including ICANS.

Manage both neurotoxicity and ICANS according to the recommendations in Tables 6 and 7 in the full Prescribing Information and consider further management per current practice guidelines.

TALVEY® is available only through a restricted program called the TECVAYLI® and TALVEY® Risk Evaluation and Mitigation Strategy (REMS) Program. Visit **TEC-TALREMS.COM**

CRS, cytokine release syndrome; ICANS, immune effector cell-associated neurotoxicity syndrome; Q2W, once every 2 weeks; QW, once weekly; REMS, Risk Evaluation and Mitigation Strategy

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

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.

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.

Please read full Important Safety Information on pages 8-10, and full Prescribing Information, including Boxed WARNING, for TALVEY®.

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

Safety profile of TALVEY®[1]

Adverse reactions (≥10%) in patients with relapsed or refractory multiple myeloma who received TALVEY® in MonumenTAL-1

System organ class Adverse reaction	TALVEY® (N=339)	
	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**	50	0
Skin disorder††	41	0.3‡
Rash‡‡	38	3.5‡
Xerosis§§	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†‖‖	19	9
COVID-19*†	11	2.7
Fungal infection†¶¶	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†††	10	0.6‡
Metabolism and nutrition disorders		
Decreased appetite	19	1.2‡
Respiratory, thoracic and mediastinal disorders		
Cough*	17	0
Dyspnea*†	11	1.8
Hypoxia*	10	1.5‡
Cardiac disorders		
Tachycardia*	11	0.6‡

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

Serious adverse reactions occurred in 47% of patients who received TALVEY®. Serious adverse reactions reported 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%).

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%).

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

Safety profile of TALVEY®[1]

Most common adverse reactions

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.

Laboratory abnormalities

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

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.

Duration of exposure for Q2W was 3.7 months (range: 0.0-17.9) (N=153) and for QW was 5.9 months (range: 0.0-25.3) (N=186).

* Includes other related terms.
† Includes fatal outcome(s): COVID-19 (N=2), dyspnea (N=2), bacterial infection including sepsis (N=1), fungal infection (N=1).
‡ Only grade 3 adverse reactions occurred.
§ Per CTCAE version 4.03, maximum toxicity grade for dysgeusia is 2 and maximum toxicity grade for dry mouth is 3.
‖ Dysgeusia: ageusia, dysgeusia, hypogeusia and taste disorder.
¶ 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.
** 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.
†† Skin disorder: palmar-plantar erythrodysesthesia syndrome, palmoplantar keratoderma, skin discoloration, skin exfoliation and skin fissures.
‡‡ 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.
§§ Xerosis: dry eye, dry skin and xerosis.
‖‖ 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.
¶¶ 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.
††† Motor dysfunction: dysarthria, dysgraphia, dysmetria, dysphonia, gait disturbance, muscle atrophy, muscle spasms, muscular weakness and tremor.

ASTCT, American Society for Transplantation and Cellular Therapy; COVID, coronavirus disease (COVID-19); CRS, cytokine release syndrome; CTCAE, Common Terminology Criteria for Adverse Events; ICANS, immune effector cell-associated neurotoxicity syndrome; Q2W, once every 2 weeks; QW, once weekly.

Please read full Important Safety Information on pages 8-10, and full Prescribing Information, including Boxed WARNING, for TALVEY®.

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

Incidence and management of adverse reactions: Oral Toxicity[1]

TALVEY® can cause oral toxicities

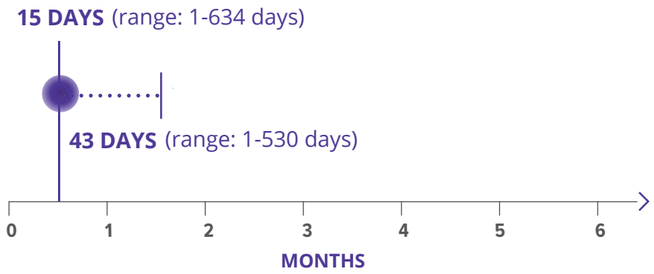
- These may include a change in taste, dry mouth, difficulty swallowing, or sores in the mouth

80% **of patients experienced oral toxicity**

Grade 3 occurred 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%).

Median time to onset and resolution based on clinical trial data



Median time to onset in the clinical trial: 15 days (range: 1-634 days)
Median time to resolution in the clinical trial: 43 days (range: 1-530 days)

65% **of patients**
had oral toxicity that did not resolve to baseline

Tips for managing oral toxicities

- Monitor for signs and symptoms of oral toxicity
- Advise 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
- Withhold or permanently discontinue TALVEY® based on severity

Incidence and management of adverse reactions: Weight Loss[1]

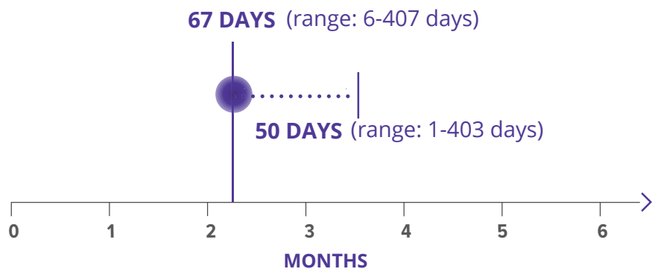
TALVEY® can cause weight loss

- Notable weight loss may occur over time and clinically significant weight loss should be further evaluated

62% **of patients experienced weight loss***

With 29% of patients experiencing Grade 2 (>10%) weight loss and 2.7% of patients experiencing Grade 3 (>20%) weight loss.

Median time to onset and resolution based on clinical trial data



Median time to onset of Grade 2 or higher in the clinical trial: 67 days (~2.2 months; range: 6-407 days)
Median time to resolution in the clinical trial: 50 days (~1.6 months; range: 1-403 days)

57% **of patients**
continued to experience weight loss

Tips for managing weight loss

- Monitor for signs and symptoms of oral toxicity
- Monitor weight regularly during therapy
- Evaluate clinically significant weight loss further
- Withhold or permanently discontinue TALVEY® based on severity

*62% of patients experienced weight loss, regardless of having an oral toxicity.

Please read full Important Safety Information on pages 8-10, and full Prescribing Information, including Boxed WARNING, for TALVEY®.

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

Incidence and management of adverse reactions: Skin Reactions and Nail Changes[1]

Skin reactions

- Skin changes may include skin problems, itchy or red skin or raised rash, abnormally dry skin that may affect the mouth and eyes, skin discoloration, peeling, dried and cracked skin, rash with acne-like bumps or blisters, or itchy skin

TALVEY® can cause serious skin reactions

62% **of patients experienced skin reactions**

Skin reactions included rash, maculo-papular rash, erythema, and erythematous rash.

Grade 3 skin reactions occurred in 0.3% of patients.

Median time to onset and resolution based on clinical trial data

Median time to onset in the clinical trial: 25 days (range: 1-630 days)
Median time to improvement to Grade 1 or less in the clinical trial: 33 days

Tips for managing skin reactions

- Monitor for skin toxicity, including rash progression
- Consider early intervention and treatment to manage skin toxicity
- Withhold TALVEY® as recommended based on severity

Nail changes

- Nail changes may include a change in the appearance of the nail, nail bed, nail cuticle fissure, pitting or ridging of the nail, nail toxicity, or nail loss
- Any grade nail disorder occurred in 50% of patients

*The median time to improvement to Grade 1 or less was 33 days.

Please read full Important Safety Information on pages 8-10, and full Prescribing Information, including Boxed WARNING, for TALVEY®.

Additional considerations for select adverse reactions[18]

You are now viewing additional considerations related to the management of TALVEY® ARs, including supportive measures based on the experiences from clinical sites that participated in the MonumenTAL-1 study. The considerations are purely descriptive and there is no clinical correlation or clinical analysis demonstrating that these steps mitigate oral, skin, and nail ARs. This information is not included in the current Prescribing Information and has not been evaluated by the FDA. No conclusions should be drawn. The information should be understood in context of the methodology.

Methodology[18]

- Advanced practice providers and nurses from 4 clinical sites collaborated on a data presentation to provide considerations for monitoring and management of talquetamab-tgvs ARs based on their experience in the MonumenTAL-1 trial
- These supportive measures are based on clinical experience, and were influenced in part by clinical practice guidelines (eg, ASCO, ESMO) and approaches to managing similar toxicities related to other anticancer agents
- The supportive measures described were contained within a poster presentation at the 20th International Myeloma Society Annual Meeting Nurse Symposium; September 27–30, 2023; Athens, Greece
- In the MonumenTAL-1 trial, sites were permitted to provide supportive care as per clinical practice[18]

Oral toxicity supportive measures[18]

- Food texture and flavor experimentation
- Increased hydration
- Salivary substitutes (salt mouth rinse, artificial saliva spray)
- Local corticosteroids (dexamethasone mouthwash for dry mouth)
- Anti-infection agents
- Vitamin and nutritional support
- Dose modification may be an effective management strategy

Skin-related ARs supportive measures[18]

- Heavy moisturizers and hydration
- While topical corticosteroids can be used to control inflammation, irritation and redness, oral corticosteroids may be considered for severe events

Nail toxicity supportive measures[18]

- Education to avoid irritants
- Use of comfortable shoes
- Good hygiene
- Soft shoes/socks
- Treatment with moisturizers and/or topical corticosteroids

Conclusions[18]

- Educating patients about what to expect is key to managing ARs appropriately
- Dermatologists, dentists, and nutritionists can be consulted to provide additional guidance on managing ARs

AR, adverse reaction; ASCO, American Society of Clinical Oncology; ESMO, European Society for Medical Oncology; FDA, U.S. Food and Drug Administration.

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

Flexibility from the start: Q2W and QW dosing available[1]

TALVEY® is administered via subcutaneous injection by a healthcare provider Q2W or QW following the step-up dosing schedule

2 weeks after first treatment dose and every 2 weeks thereafter. **Maintain a minimum of 12 days between Q2W doses**

1 week after first treatment dose and weekly thereafter. **Maintain a minimum of 6 days between QW doses**

Step-up doses 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.

TALVEY® is given until disease progression or unacceptable toxicity.

Dosing Considerations

- Initiate TALVEY® treatment with step-up dosing to reduce the risk of CRS
- Dose delays may be required to manage toxicities.

Preparation and administration considerations

- 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.
- Rapid subcutaneous injection: TALVEY® does not require the wait time associated with infusions.[19†]
- Do not combine TALVEY® vials of different concentrations to achieve treatment dose.
- 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.

*Based on actual body weight.
†Supplied as ready-to-use solution for injection that does not require dilution prior to administration.

Personalized weight-based dosing

Please refer to tables 9-12 in the full Prescribing Information to determine total dose, injection volume, and number of vials required.

Dosing schedule and administration[1]

Pretreatment medications

1 to 3 hours before each step-up dose

Administer the following pretreatment medications before each dose in the step-up dosing schedule to reduce the risk of CRS

- Corticosteriod (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 equivalent)

Subsequent doses

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 or for patients who experience CRS.

kg, kilograms; mg, milligrams; SUD, step-up dose

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

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 consider permanent discontinuation of 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.

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

Please read full Important Safety Information on pages 8-10, and full Prescribing Information, including Boxed WARNING, for TALVEY®.

Dosing schedule and administration[1] (continued)

Restarting TALVEY® after dosage delay

- Dose delays may be required to manage toxicities
- Administer pretreatment medications prior to restarting TALVEY® and monitor patients following administration
- If a dose of TALVEY® is delayed, restart therapy based on the recommendations in Table 3 and Table 4 in the full Prescribing Information

Recommendations for restarting therapy with TALVEY® after dose delay

Dosing Schedule	Last Dose Administered	Time From Last Dose Administered	TALVEY® Recommendation*
Q2W Dosing Schedule	0.01 mg/kg	More than 7 days	Restart at 0.01 mg/kg
	0.06 mg/kg	8 to 28 days	Repeat at 0.06 mg/kg
		More than 28 days	Restart at 0.01 mg/kg
	0.4 mg/kg	8 to 28 days	Repeat at 0.4 mg/kg
		29 to 56 days	Restart at 0.06 mg/kg
		More than 56 days	Consider permanent discontinuation. If restarting TALVEY®, begin at 0.01 mg/kg
	0.8 mg/kg	15 to 28 days	Continue at 0.8 mg/kg
		29 to 56 days	Restart at 0.4 mg/kg
		More than 56 days	Consider permanent discontinuation. If restarting TALVEY®, begin at 0.01 mg/kg

Dosing Schedule	Last Dose Administered	Time From Last Dose Administered	TALVEY® Recommendation*
QW Dosing Schedule	0.01 mg/kg	More than 7 days	Restart at 0.01 mg/kg
	0.06 mg/kg	8 to 28 days	Repeat at 0.06 mg/kg
		More than 28 days	Restart at 0.01 mg/kg
	0.4 mg/kg	8 to 28 days	Repeat at 0.4 mg/kg
		29 to 56 days	Restart at 0.06 mg/kg
		More than 56 days	Consider permanent discontinuation. If restarting TALVEY®, begin at 0.01 mg/kg

*Administer pretreatment medications prior to restarting TALVEY®. After restarting TALVEY®, resume dosing schedule accordingly.

Storage of TALVEY®

TALVEY® injection is a sterile, preservative-free, colorless to light yellow solution supplied in a single-dose vial for subcutaneous administration.

3 mg/1.5 mL (2 mg/mL)
single-dose **step-up vial**

No dilution required

40 mg/mL (40 mg/mL)
single-dose **treatment vial**

No dilution required

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.

Preparation and administration[1]

Preparation of TALVEY®

1. 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.
2. Once equilibrated, gently swirl the vial for approximately 10 seconds to mix. Do not shake.
3. Withdraw the required injection volume of TALVEY® from the vial(s) into an appropriately sized syringe using a transfer needle.
4. Replace the transfer needle with an appropriately sized needle for injection.

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.

Administration of TALVEY®

- 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 in accordance with local requirements

CRS, cytokine release syndrome; cm, centimeter; mg, milligram; mL, milliliter; Q2W, once every 2 weeks; QW, once weekly

IMPORTANT SAFETY INFORMATION (continued)

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. Withhold TALVEY® as recommended based on severity.

References: 1. TALVEY® [Prescribing Information]. Horsham, PA: Janssen Biotech, Inc. **2.** U.S. FDA approves TALVEY™ (talquetamab-tgvs), a first-in-class bispecific therapy for the treatment of patients with heavily pretreated multiple myeloma. News release. Janssen Biotech, Inc.; August 10, 2023. Accessed April 19, 2024. https://www.janssen.com/fda-approves-talveytm-talquetamab-tgvs-first-class-bispecific-therapy-treatment-patients-heavily **3.** Barwick BG, et al. *Front Immunol.* 2019;10:1121. **4.** Mikhael J. *Clin Lymphoma Myeloma Leuk.* 2019;20(1):1-7. **5.** Kurtin S. *J Adv Pract Oncol.* 2013;4(6):1-14. **6.** Minnie SA, Hill GR. *J Clin Invest.* 2020;130(4):1565-1575. **7.** Mateos MV, et al. *Leukemia.* 2022;36;1371-1376. **8.** Franssen LE, et al. *Ther Adv Hematol.* 2019;10:1-19. **9.** Usmani S, et al. *The Oncologist.* 2016;21:1355-1361. **10.** Smith EL, et al. *Sci Transl Med.* 2019;11:1-14. **11.** Atamaniuk J, et al. *Eur J Clin Invest.* 2012;42(9):953-960. **12.** Lancman G, et al. *Blood Cancer Discov.* 2021;2(5):423-433. **13.** Kodama T, et al. *Mol Cancer Ther.* 2019;18(9):1555-1564. **14.** Verkeij CPM, et al. *Blood Adv.* 2021;5(8):2196-2215. **15.** Inoue S, Nambu T, Shimomura T. *J Invest Dermatol.* 2004;122:565-573. **16.** Data on file. Janssen Biotech, Inc. **17.** A Study of talquetamab in participants with relapsed or refractory multiple myeloma. ClinicalTrials.gov identifier: NCT04634552. Updated March 27, 2024. Accessed April 19, 2024. https://clinicaltrials.gov/study/NCT04634552 **18.** Catamero D, Purcell K, Ray C, et al. Practical management of patients with relapsed/refractory multiple myeloma receiving talquetamab, a GPRC5DxCD3 bispecific antibody: experience in MonumenTAL-1. Poster presented at International Myeloma Society (IMS) Annual Meeting: September 27-30, 2023; Athens, Greece. **19.** Kim H, Park H, Lee SJ. Effective method for drug injection into subcutaneous tissue. *Sci Rep.* 2017;7(1):9613.

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

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The following section provides information and considerations based on various sources and the experiences of various professionals and is intended to help you achieve RRMM bispecific operational readiness in your organization.

This information, sample milestones, and suggestions to help you achieve operational readiness in your facility are recommendations but they are not mandatory items for operationalizing bispecific treatment for RRMM. It is recommended that you review this information and adapt based on your own facility.

Three states of readiness can help establish a framework for the journey to operationalize a bispecifics treatment program

Ensuring operational readiness for each of 3 stakeholder groups—facility, provider and care team, and patient and care partner—are key to your RRMM bispecific treatment program.

Facility Readiness

Operational considerations, including identification of an operational champion, facilitating multidisciplinary engagement, SOP development, REMS certification, and financial considerations.

Provider & Care Team Readiness

Staff education, dosing considerations, organizational and provider preparation for care transitions, site of care coordination, and adverse reaction screening, monitoring, and management.

Patient & Care Partner Readiness

Logistical preparedness including travel and transportation and access and affordability, care partner support, and education and expectations for treatment.

REMS, risk evaluation and mitigation strategy; RRMM, relapsed or refractory multiple myeloma; SOP, standard operating procedure.

Bispecific RRMM therapies require a dedicated operational framework[1]

A designated operational champion can facilitate key activities for a multidisciplinary team[2]

The operational champion is a volunteer or appointed healthcare provider who can orchestrate multidisciplinary coordination and facilitate implementation of a bispecific treatment program.

The responsibilities of the operational champion often coincide with the responsibilities of pharmacy staff members.

Some key responsibilities of the operational champion may include:

- Team coordination
- Ownership of the REMS process
- Oversight of SOP development and staff training curriculum
- Design of approaches to transitions of care
- Operationalization of the dosing strategy

The operational champion should be supported by a multidisciplinary team to successfully operationalize a bispecific therapy

Multidisciplinary coordination is required for a multi-phase treatment journey

Core bispecific therapy stakeholders[3,4]

- ✓ Hematologists
- ✓ Medical oncologists
- ✓ APPs
- ✓ Nurses
- ✓ Pharmacists

Ancillary support[3,5]

- ✓ Care coordinators/navigators
- ✓ Emergency department
- ✓ Critical care
- ✓ Infectious disease
- ✓ Dieticians
- ✓ Neurologists
- ✓ Social workers
- ✓ Psychologists
- ✓ Hospitalists
- ✓ Dermatologists

Mandatory REMS requirements for a bispecific therapy require staff training and provider and pharmacy certification[1,4,6]

- Prescribers must be REMS-certified to prescribe
- Both pharmacies and healthcare settings must be certified in REMS to dispense to patients

One additional thing to consider is understanding what may be required of your organization during a REMS audit. **Establishing standardized documentation processes which align with those requirements can help ensure preparedness for a potential audit.**

Bispecific RRMM therapies require a dedicated operational framework[1] (continued)

SOPs and treatment protocols can help facilitate consistency of care[1,3-5]

Consider establishing SOPs for bispecific therapy. Below are several examples of components.

Education and training plans

- Relevant stakeholders
- Training frequency
- Curriculum refresh

Transition of care coordination, roles, and responsibilities

- Internal collaboration
- Treatment initiation partnerships
- Memorandum of understanding

Adverse reaction (AR) management

- AR signs and symptoms
  - CRS/ICANS, infections, drug-specific ARs, etc.
- Management algorithms
- Additional drug-specific AR protocols*
- Drug availability for supportive care
- Reaction notification protocol
- Admission criteria
- Hospitalization procedure
- Local AR management team†

A memorandum of understanding (MOU) may be used to create a shared agreement between different sites of care[7]

Publically available MOU templates may be found online for reference

Key business considerations when onboarding a bispecific therapy

- **Clinical & Economic**
- **Coverage**
- **Coding**

Informational resources may be available from the bispecific therapy manufacturers to help address questions related to these financial considerations.

*May include infectious disease prophylaxis and management of immune deficiencies.
†Emergency department, critical care, infectious disease, hospitalist teams, nursing, pharmacy, neurology, etc.
APP, advanced practice provider; CRS, cytokine release syndrome; ICANS, immune effector cell-associated neurotoxicity syndrome; REMS, risk evaluation and mitigation strategy; RRMM, relapsed or refractory multiple myeloma; SOP, standard operating procedures.

HCP and care team readiness for RRMM treatment with a bispecific therapy[4,5]

Staff education is a key component of the operational plan. Potential educational topics include[4]:

Clinical
Efficacy and safety of the therapy, its preparation, dosing, and administration, infection prophylaxis and AR pretreatment, and clinical pearls.

Operational
SOPs and treatment protocols, including AR management, and transitions of care and care coordination.

Ensure organizational and provider preparation for care transitions that may occur as part of the multi-phase bispecific treatment journey[5]

	Diagnosis & treatment choice	Step-up dosing	Treatment dosing
1 center	1 care center for diagnosis, step-up dosing, and treatment dosing		
2 centers	Local oncologist refers patient for step-up dosing (T)	(T)	Patient returns for treatment dosing
Multi-center	Local oncologist refers patient for step-up dosing (T)	(T)	Patient goes to another center for treatment dosing

(T) =transition site of care.

Assess your organization's current infrastructure and ability to support patients through step-up and/or treatment dosing; then consider which model to operationalize.

Site of care coordination between departments and institutions:

- **Ensure site of care preparation:** REMS certification, service line training, treatment and AR management protocols.[4]
- **Align processes and define responsibilities for each care center**[4,5]
- **Coordinate information transfer approaches:** Determine what information needs to be transferred, who is responsible for transferring the information, how receipt of information will be confirmed, EHR system compatibility, and how information will be shared if not compatible.[4]

HCP and care team readiness for RRMM treatment with a bispecific therapy[4,5] (continued)

The following are the roles/responsibilities of the care centers[4,5]:

- Conduct BI/PA
- Develop treatment plan
- Inform patient of estimated costs
- Review patient care plan*
- Schedule patient
- Connect patient with a care navigator
- Follow-up care/ rehospitalization
- Provide patient wallet cards
- Provide social work support
- Care partner support and education

*Ensure patient understands potential toxicities and complications of treatment.

Select adverse reaction screening, monitoring, and management is a key factor in operationalizing an RRMM bispecific treatment[5]

Bispecific therapies may be associated with a distinct adverse reaction profile, including a risk of developing[5]:

CRS (cytokine release syndrome)

Neurologic toxicity, including ICANS (immune effector cell-associated neurotoxicity syndrome)

Considerations in the management of CRS and neurologic toxicity, including ICANS

- Establish on-call physician to help manage CRS and neurotoxicity, including ICANS
- Ensure ED/hospitalists are aware of on-call physician
- Deploy training program to all stakeholders
- Develop centralized repository of treatment protocols and algorithms for toxicity management

Management

Please consult current practice guidelines and the protocols of your own institution for further information about managing ARs, including CRS and neurologic toxicities, including ICANS.

AR, adverse reaction; BI, benefits investigation; ED, emergency department; EHR, electronic health record; HCP, healthcare professional; PA, prior authorization; REMS, risk evaluation and mitigation strategy; RRMM, relapsed or refractory multiple myeloma; SOP, standard operating procedure.

Enabling patient and care partner readiness for RRMM bispecific therapy

Logistical preparedness can help patients prepare for their bispecific treatment journey

Travel and transportation[4,5]

- Patients may need help considering all aspects of travel and transportation over the course of therapy (as needed). This can include transportation to and from the treatment center, food, lodging, frequency of visits, and length of visits
- If care is being transitioned, determine whether there is a treatment center that is more convenient for the patient. Geographic convenience can also factor into patient expenses

Access and Affordability[4,7]

- Provide patients with estimates for the cost of therapy, taking insurance coverage into consideration
- Provide estimates of additional costs, including care partner support, visiting nurse services, loss of work

Education for care partners is critical to ensure the ability to confidently care for a patient on bispecific therapy

Considerations for a committed care partner[5]

- Awareness of the commitment and availability for the duration of the treatment
- Familiarity with the signs and symptoms of ARs and ability to monitor for them
- Planning times of absence (home visiting nurse)
- Training on monitoring devices
- Knowing what to do and who to call in the event of an emergency

Patients and care partners should be educated on expectations for treatment[1,4,5]

- Patients and care partners should know how the therapy works and its clinical results, the differences between the discrete phases of treatment, potential side effects, the unique dosing schedule, and the overall patient care plan
- Consider developing an informational package for patients and care partners

Additional resources are available to assist with the 3 states of readiness

Facility Readiness

EHR Order Set Guides
- Cerner Guide
- EHR System-Agnostic
- Epic®
- iKnowMed®
- OncoEMR®

Access and Reimbursement Guide

Billing and Coding Flashcard

Provider & Care Team Readiness

Transition of Care Checklist for Initiating Treatment Centers

Transition of Care Checklist for Ongoing Treatment Centers

Treatment Locator Tool on HCP website

Patient & Care Partner Readiness

TALVEY® Patient Brochure English/Spanish

Patient Starter Kit

My Journey with TALVEY® Brochure

TALVEY® Care Partner Brochure

Scan the QR code to connect with a local Johnson & Johnson representative for more information and to learn more about these resources.

AR, adverse reaction; EHR, electronic health record; HCP, healthcare provider; QR, quick response; RRMM, relapsed or refractory multiple myeloma

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