09-J4000-63

Original Effective Date: 11/15/23

Reviewed: 06/10/26

Revised: 07/15/26

Subject: Talquetamab-tgvs (Talvey) Subcutaneous Injection

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Dosage/ Administration	Position Statement	Billing/Coding	Reimbursement	Program Exceptions	Definitions
Related Guidelines	Other	References	Updates		

DESCRIPTION:

Talquetamab (Talvey) is a bispecific GPRC5D-directed CD3 T-cell engaging antibody approved by the US Food and Drug Administration (FDA) on August 9, 2023, for the treatment of adult patients with relapsed or refractory multiple myeloma (MM) 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 was approved under accelerated approval based on response rate and durability of response, and continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s). Prior to FDA approval, talquetamab was granted orphan drug designation in May 2021 for the treatment of MM. Talquetamab was the second FDA-approved bispecific T-cell engager (BiTE) for the treatment of MM; the first being teclistamab (Tecvayli) approved in October 2022 for this same patient population; however, teclistamab targets B-cell maturation antigen (BCMA) on the surface of MM cells. A third BiTE for MM, and second BCMA-directed BiTE, elranatamab (Elrexfio), was approved 5 days after talquetamab. Talquetamab is the first BiTE to target GPRC5D (G protein-coupled receptor, class C, group 5, member D). Talquetamab binds to the CD3 receptor expressed on the surface of T-cells and GPRC5D expressed on the surface of MM cells and non-malignant plasma cells, as well as healthy tissues such as epithelial cells in keratinized tissues of the skin and tongue. In vitro, talquetamab activated T-cells caused the release of proinflammatory cytokines and resulted in the lysis of MM cells.

The National Comprehensive Cancer Network (NCCN) Guidelines for MM (Version 5.2026 - January 6, 2026) list talquetamab under “Relapse/Refractory Disease After 3 Prior Lines of Therapy” and under “Preferred Regimens” as a category 2A recommendation for the treatment of previously treated MM. Under this section, the recommendations are further categorized as either “CAR T-cell Therapy” or “After at least four prior therapies, including an anti-CD38 monoclonal antibody, a proteasome inhibitor (PI), and an immunomodulatory agent (IMiD)”. Idecabtagene vicleucel (Abecma) and ciltacabtagene autoleucel (Carvykti) are listed under the “CAR T-cell Therapy” section, and the bispecific antibodies of elranatamab (Elrexfio), linvoseltamab (Lynozyfic), talquetamab, and teclistamab (Tecvayli) are list under the “After at least four prior therapies, including an anti-CD38 monoclonal antibody, a PI, and an IMiD” section. The combination regimen of teclistamab and talquetamab is listed under “Relapse/Refractory Disease After 3 Prior Lines of Therapy” and under “Useful in Certain Circumstances” as a category 2A recommendation. The NCCN also includes footnotes stating (1) “Autologous HCT should be considered in patients who are

eligible and have not previously received HCT or had a prolonged response to initial HCT", (2) "Talquetamab-tgvs may be considered as a bridge to BCMA CAR-T therapy in relapsed and/or refractory multiple myeloma", (3) "Patients can receive more than one BCMA targeted therapy. Optimal sequencing of sequential BCMA targeted therapies is not known; however accumulated data suggests immediate follow on with second BCMA directed therapy after relapse may be associated with lower response rates", and (4) "Prophylactic tocilizumab may be considered prior to first dose to reduce the risk of CRS" (applicable to the bispecific antibodies only).

The safety and efficacy of talquetamab leading to initial FDA approval was evaluated in patients with relapsed or refractory MM in a single-arm, open-label, multicenter study, MMY1001 (MonumenTAL-1) (NCT03399799, NCT04634552). The study included patients who had previously received at least three prior systemic therapies, including a PI, an IMiD, 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 (ASCT) within the past 12 weeks, an allogeneic stem cell transplant within the past 6 months, ECOG performance score of 3 or higher, stroke or seizure within the past 6 months, CNS involvement or clinical signs of meningeal involvement of MM, and plasma cell leukemia, active or documented history of autoimmune disease (exception of vitiligo, resolved childhood atopic dermatitis, resolved Grave's Disease that is euthyroid based on clinical and laboratory testing). Patients treated with the weekly dosing schedule received step-up doses of 0.01 mg/kg and 0.06 mg/kg followed by 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 followed by 0.8 mg/kg subcutaneously biweekly, thereafter. Patients on both dosing schedules were treated until disease progression or unacceptable toxicity.

The efficacy results from the 187 patients who were not exposed to prior T cell redirection therapy and who had received at least 4 prior lines of therapy are presented in the Table below. Of these patients, the median age was 67 (range: 38 to 86) years, 57% were male, and 90% were White. Patients had received a median of 5 (range: 4 to 13) prior lines of therapy, and 78% had received prior 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 were present in 29% of patients; baseline cytogenetic data were not available in 11% of patients. Twenty-two percent (22%) of patients had extramedullary plasmacytomas. Efficacy was based on overall response rate (ORR) and duration of response (DOR) as assessed by an Independent Review Committee using IMWG criteria. The results are displayed in Table 1 below. The median duration of follow-up from first response among responders receiving talquetamab 0.4 mg/kg weekly was 13.8 (range: 0.8 to 15.4) months. The median duration of follow-up from first response among responders receiving talquetamab 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, respectively.

Table 1: Efficacy Results for MonumenTAL-1

	0.4 mg/kg Weekly (n=100)	**0.8 mg/kg Biweekly (n=87)**
Overall response rate (ORR: sCR+CR+VGPR+PR)	73 (73%)	65 (73.6%)
95% CI	(63.2%, 81.4%)	(63.0%, 82.4%)
Stringent complete response (sCR)	26%	20%
Complete response (CR)	9%	13%
Very good partial response (VGPR)	22%	25%
Partial response (PR)	16%	16%
Duration of Response (DOR) (months)		
Median DOR (95% CI) (Months):	9.5 (6.5, NE)	NE

NE = not estimable

Thirty-two (32) patients were exposed to prior T cell redirection therapy and had received at least 4 prior lines of therapy, including a PI, an IMiD, and an anti-CD38 monoclonal antibody, received talquetamab 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 (94%) 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.

The safety of talquetamab was evaluated in 339 adult patients with relapsed or refractory MM. The duration of exposure for the 0.4 mg/kg weekly regimen was 5.9 (range: 0.0 to 25.3) months (n=186) and for the 0.8 mg/kg biweekly (every 2 weeks) regimen, it was 3.7 (range: 0.0 to 17.9) months (n=153). Serious adverse reactions occurred in 47% of patients who received teclistamab. Serious adverse reactions in ≥2% of patients included CRS (13%), bacterial infection (8%) including sepsis, pyrexia (4.7%), ICANS (3.8%), COVID-19 (2.7%), neutropenia (2.1%), and upper respiratory tract infection (2.1%). Fatal adverse reactions occurred in 3.2% of patients, including COVID -19 (0.6%), dyspnea (0.6%), general physical health deterioration (0.6%), bacterial infection (0.3%) including sepsis, basilar artery occlusion (0.3%), fungal infection (0.3%), infection (0.3%), and pulmonary embolism (0.3%). Permanent discontinuation due to an adverse reaction occurred in 9% of patients. Adverse reactions which resulted in permanent discontinuation of teclistamab in >1% of patients included ICANS. Dosage interruptions due to an adverse reaction occurred in 56% of patients. Adverse reactions which required dosage interruption in >5% of patients included pyrexia (15%), CRS (12%), upper respiratory tract infection (9%), COVID-19 (9%), bacterial infection (7%) including sepsis, neutropenia (6%), and rash (6%). The most common adverse reactions (≥20%) were pyrexia, CRS, dysgeusia, nail disorder, musculoskeletal pain, skin disorder, rash, fatigue, weight decreased, dry mouth, xerosis, dysphagia, upper respiratory tract infection, diarrhea, hypotension, and headache. The most common Grade 3 or 4 laboratory abnormalities (≥30%) were lymphocyte count decreased, neutrophil count decreased, white blood cell decreased, and hemoglobin decreased. Refer to the package labeling for the specific percentages.

The safety and efficacy of teclistamab in combination talquetamab with was evaluated in a phase 1b-2 study (RedirecTT-1, NCT04586426) of patients with relapsed or refractory MM. Patients had to have previous exposure to a proteasome inhibitor, immunomodulatory drug, and anti-CD38 monoclonal antibody (i.e., at least triple-class exposure) and an ECOG performance-status score of 0 or 1. In phase 1, five dose levels were investigated in a dose-escalation study. Talquetamab 0.8 mg/kg body weight plus teclistamab 3 mg/kg every 2 weeks was selected as the recommended phase 2 regimen. Both bispecific antibodies were administered on the same day, approximately 30 minutes apart. Patients could transition to monthly administration of talquetamab and teclistamab after the occurrence of a partial response or better after cycle 4. The primary objective was to evaluate adverse events and dose-limiting toxic effects. Secondary end points included overall response (partial response or better), duration of response, time to response, pharmacokinetics, pharmacodynamics, and immunogenicity.

A total of 94 patients received treatment, with the recommended phase 2 regimen used in 44. The median follow-up was 20.3 months (range, 0.5 to 37.1) overall and 18.2 months (range, 0.7 to 27) with the recommended phase 2 regimen. Across all dose levels, the median age of the patients was 64.5 years, and patients had received a median of 4 previous lines of therapy over a median duration of 6.1 years since diagnosis. All the patients had triple-class exposure, and most patients (65%) had penta-drug exposure. Seven patients had received bispecific antibodies previously, and 4 had received CAR T-cell therapy previously. A total of 87 patients (93%) had disease that was refractory to their last line of therapy, and 81 (86%) had disease that was triple-class refractory. A total of 34 patients (36%) had extramedullary disease, and 21 of 51 patients (41%) had a high-risk cytogenetic profile. Three patients had dose-limiting toxic effects (including grade 4 thrombocytopenia in 1 patient with the recommended phase 2 regimen). Across all dose levels, the most common adverse events were CRS, neutropenia, taste changes, and non-rash skin events. Grade 3 or 4 adverse events, most commonly hematologic events, occurred in 96% of the patients. Grade 3 or 4 infections occurred in 64% of the patients. Talquetamab plus teclistamab had a similar safety profile to each agent as monotherapy, although the observed incidence of grade 3 or 4 infections was higher. With the recommended phase 2 regimen, a response occurred in 80% of the patients (including in 61% of those with extramedullary disease); across

all dose levels, a response occurred in 78%. In the phase 2 regimen, the median time to first response was 1.4 months (range, 0.3 to 5.1). A total of 34 patients (77%) had a very good partial response or better, and 23 (52%) had a complete response or better. The likelihood of continuing to have a response at 12 months and 18 months was 91% and 86%, respectively, with the recommended phase 2 regimen and 86% and 77% respectively, across all dose levels.

POSITION STATEMENT:

Drug Waste Reduction: Additional medical necessity criteria for dose optimization may apply depending on the requested dose and member's benefit. Refer to Medical Coverage Guideline Drug Waste Reduction, 09-J5000-54.

Initiation of talquetamab (Talvey) **meets the definition of medical necessity** when **EITHER** of the following criteria are met ("1" or "2"):

1. Member has a diagnosis of relapsed or refractory multiple myeloma (MM) and **ALL** of the following ("a" to "d") - *medical record documentation confirming the patient's diagnosis and complete treatment history must be submitted*:
    a. **EITHER** of the following ("i" or "ii"):
        i. **ALL** of the following ("1", "2", and "3"):
            1. Member has received **FOUR or more** appropriate prior lines of therapy of adequate duration for the treatment of their MM

               NOTE: Primary therapy, with or without subsequent hematopoietic cell transplant, followed by maintenance therapy is considered a single line of therapy
            2. Member's prior MM treatments have included **ALL** of the following ("a", "b", and "c"):
                a. An anti-CD38 monoclonal antibody [for example - daratumumab (Darzalex), daratumumab-hyaluronidase (Darzalex Faspro), or isatuximab (Sarclisa)]
                b. A proteasome inhibitor [for example - bortezomib, carfilzomib (Kyprolis), or ixazomib (Ninlaro)]
                c. An immunomodulatory agent [for example - lenalidomide (Revlimid), pomalidomide (Pomalyst), or thalidomide (Thalomid)]
            3. Talquetamab will be used as either a single-agent therapy, **OR** in combination with teclistamab (Tecvayli)
        ii. **ALL** of the following ("1", "2", and "3"):
            1. Talquetamab is being used as a bridge to B-cell maturation antigen (BCMA) CAR T-cell therapy [such as ciltacabtagene autoleucel (Carvykti) or idecabtagene vicleucel (Abecma)]
            2. Talquetamab will be used as single-agent therapy (i.e., not used in combination with other MM treatments)
            3. Member meets the following medical necessity criteria to receive BCMA CAR T-cell therapy:
                - If the planned CAR T-cell therapy is idecabtagene vicleucel (Abecma), the member meets **BOTH** of the following ("a" and "b"):
                    a. Member has received **TWO** or more appropriate prior lines of therapy of adequate duration for the treatment of their MM

                       NOTE: Primary therapy, with or without subsequent hematopoietic cell transplant, followed by maintenance therapy is considered a single line of therapy

b. Member's prior MM treatments have included **ALL** of the following (i.e., triple-class exposed) ("i", "ii", and "iii"):

i. An anti-CD38 monoclonal antibody [for example - daratumumab (Darzalex), daratumumab-hyaluronidase (Darzalex Faspro), or isatuximab (Sarclisa)]

ii. A proteasome inhibitor [for example - bortezomib, carfilzomib (Kyprolis), or ixazomib (Ninlaro)]

iii. An immunomodulatory agent [for example - lenalidomide (Revlimid), pomalidomide (Pomalyst), or thalidomide (Thalomid)]

- If the planned CAR T-cell therapy is ciltacabtagene autoleucel (Carvykti), the member meets **EITHER** of the following ("a" or "b"):

a. **ALL** of the following ("i", "ii", and "iii"):

i. Member has received at least **ONE** appropriate prior line of therapy of adequate duration for the treatment of their MM

NOTE: Primary therapy, with or without subsequent hematopoietic cell transplant, followed by maintenance therapy is considered a single line of therapy

ii. Member's prior MM treatment has included **BOTH** of the following ("1" and "2"):

1. A proteasome inhibitor [for example - bortezomib, carfilzomib (Kyprolis), or ixazomib (Ninlaro)]

2. An immunomodulatory agent [for example - lenalidomide (Revlimid), pomalidomide (Pomalyst), or thalidomide (Thalomid)]

iii. Member is refractory to lenalidomide (i.e., disease progression on treatment or progression within 60 days of the last dose of therapy; this includes disease progression during primary therapy or low-dose maintenance therapy)

b. **BOTH** of the following ("i" and "ii"):

i. Member has received **THREE** or more appropriate prior lines of therapy of adequate duration for the treatment of their MM

NOTE: Primary therapy, with or without subsequent hematopoietic cell transplant, followed by maintenance therapy is considered a single line of therapy

ii. Member's prior MM treatments have included **ALL** of the following (i.e., triple-class exposed):

- An anti-CD38 monoclonal antibody [for example - daratumumab (Darzalex), daratumumab-hyaluronidase (Darzalex Faspro), or isatuximab (Sarclisa)]
- A proteasome inhibitor [for example - bortezomib, carfilzomib (Kyprolis), or ixazomib (Ninlaro)]
- An immunomodulatory agent [for example - lenalidomide (Revlimid), pomalidomide (Pomalyst), or thalidomide (Thalomid)]

b. Member's MM was **NOT** previously refractory (i.e., disease progression on treatment or progression within 60 days after the last dose of a given therapy) to a talquetamab-containing treatment regimen

c. The ordering provider and the infusing healthcare facility is certified in the TECVAYLI and TALVEY REMS program

d. Dosage of talquetamab does not exceed the following depending on the dosage schedule selected:

- Weekly Dosing Schedule [for talquetamab monotherapy only]
  - Day 1 (Step-up dose 1) – 0.01 mg/kg (based on actual body weight)
  - Day 4 (Step-up dose 2) – 0.06 mg/kg (based on actual body weight)
  - Day 7 (First treatment dose) – 0.4 mg/kg (based on actual body weight)
  - One week after first treatment dose – 0.4 mg/kg once weekly (based on actual body weight)
- Biweekly (Every 2 Weeks) Dosing Schedule
  - Day 1 (Step-up dose 1) – 0.01 mg/kg (based on actual body weight)
  - Day 4 (Step-up dose 2) – 0.06 mg/kg (based on actual body weight)
  - Day 7 (Step-up dose 3) – 0.4 mg/kg (based on actual body weight)
  - Day 10 (First treatment dose) – 0.8 mg/kg (based on actual body weight)
  - Two weeks after first treatment dose– 0.8 mg/kg every 2 weeks (based on actual body weight)

2. Member has another FDA-approved or NCCN-supported diagnosis, and **ALL** of the following are met ("a" to "d"):
   a. **EITHER** of the following ("i" or "ii"):
      i. Member is diagnosed with a condition that is consistent with an indication listed in the product's FDA-approved prescribing information (or package insert) **AND** member meets any additional requirements listed in the "Indications and Usage" section of the FDA-approved prescribing information (or package insert)
      ii. Indication **AND** usage are recognized in NCCN Drugs and Biologics Compendium as a Category 1 or 2A recommendation
   b. Talquetamab is used in a treatment regimen in accordance with the FDA-approved prescribing information or applicable NCCN guideline recommendation for the diagnosis
   c. The ordering provider and the infusing healthcare facility is certified in the TECVAYLI and TALVEY REMS program
   d. Dosage of talquetamab does not exceed the maximum recommended in the FDA-approved prescribing information or the maximum recommended by the applicable NCCN guidelines for the diagnosis

Approval duration: 6 months

Continuation* of talquetamab (Talvey) meets the definition of medical necessity when **ALL** of the following criteria are met ("1" to "3"):

1. An authorization or reauthorization for talquetamab has been previously approved by Florida Blue or another health plan in the past 2 years for the treatment of multiple myeloma (excluding when used as CAR T-cell bridge therapy – see initiation criteria), or other FDA-approved or NCCN-supported diagnosis (if another health plan, documentation of a health plan-paid claim for talquetamab during the 90 days immediately before the authorization request must be provided); **OR** the member previously met **ALL** indication-specific initiation criteria
2. The ordering provider and the infusing healthcare facility is certified in the TECVAYLI and TALVEY REMS program
3. **EITHER** of the following based on the member's diagnosis ("a" or "b"):

a. Multiple myeloma, and **ALL** of the following ("i", "ii", and "iii"):

   i. Talquetamab is being used as either single-agent therapy **OR** in combination with teclistamab (Tecvayli)

   ii. Dosage of talquetamab does not exceed the following based on the regimen used:

   - Weekly Dosing Schedule (one week after first treatment dose and weekly thereafter) – 0.4 mg/kg once weekly (based on actual body weight) [for talquetamab monotherapy only]
   - Biweekly Dosing Schedule (two weeks after first treatment dose and every 2 weeks thereafter) – 0.8 mg/kg every 2 weeks (based on actual body weight)

   iii. Provider attestation that the member has not had disease progression during talquetamab treatment

b. Other FDA-approved or NCCN-supported diagnosis, and **ALL** of the following ("i", "ii", and "iii"):

   i. Dosage of talquetamab does not exceed the maximum recommended in the FDA-approved prescribing information or the maximum recommended by the applicable NCCN guideline for the specific diagnosis

   ii. Talquetamab is used in a treatment regimen in accordance with the FDA-approved prescribing information or applicable NCCN guideline recommendation for the diagnosis

   iii. Member has had a beneficial response to treatment with talquetamab

Approval duration: 1 year

**For members that may have only completed the initial step-up dosing schedule during an inpatient admission, please refer to the initiation criteria*

DOSAGE/ADMINISTRATION:

THIS INFORMATION IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY AND SHOULD NOT BE USED AS A SOURCE FOR MAKING PRESCRIBING OR OTHER MEDICAL DETERMINATIONS. PROVIDERS SHOULD REFER TO THE MANUFACTURER'S FULL PRESCRIBING INFORMATION FOR DOSAGE GUIDELINES AND OTHER INFORMATION RELATED TO THIS MEDICATION BEFORE MAKING ANY CLINICAL DECISIONS REGARDING ITS USAGE.

FDA-approved

- 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 of clinical benefit in a confirmatory trial(s).
- The recommended dosing schedules are as follows:
  - Weekly Dosing Schedule:
    - Step-up dosing schedule:
      - Day 1 (Step-up dose 1) – 0.01 mg/kg (based on actual body weight)
      - Day 4* (Step-up dose 2) – 0.06 mg/kg (based on actual body weight)
      - Day 7* (First treatment dose) – 0.4 mg/kg (based on actual body weight)
    - Weekly dosing schedule†:

- One week after first treatment dose and weekly thereafter – 0.4 mg/kg once weekly (based on actual body weight)

**Dose may be administered between 2 to 4 days after the previous dose and may be given up to 7 days after the previous dose to allow for resolution of adverse reactions*

†*Maintain a minimum of 6 days between weekly doses*

- Biweekly (Every 2 Weeks) Dosing Schedule:
  - Step-up dosing schedule:
    - Day 1 (Step-up dose 1) – 0.01 mg/kg (based on actual body weight)
    - Day 4* (Step-up dose 2) – 0.06 mg/kg (based on actual body weight)
    - Day 7* (Step-up dose 3) – 0.4 mg/kg (based on actual body weight)
    - Day 10 (First treatment dose) - 0.8 mg/kg (based on actual body weight)
  - Biweekly (every 2 weeks) dosing schedule†:
    - Two weeks after first treatment dose and every 2 weeks thereafter – 0.8 mg/kg every 2 weeks (based on actual body weight)

**Dose may be administered between 2 to 4 days after the previous dose and may be given up to 7 days after the previous dose to allow for resolution of adverse reactions*

#*Dose may be administered between 2 to 7 days after step-up dose 3*

†*Maintain a minimum of 12 days between biweekly (every 2 weeks) doses*

- Talquetamab should only be administered by a qualified healthcare professional with appropriate medical support to manage severe reactions such as CRS and neurologic toxicity, including ICANS.
- 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 step-up dosing schedule
- Talquetamab 3 mg/1.5 mL (2 mg/mL) vial and 40 mg/mL vial are supplied as ready-to-use solution for injection that do not need dilution prior to administration. Do not combine vials of different concentrations to achieve treatment dose.
- Administer the following pre-treatment medications 1 to 3 hours before each dose of talquetamab in the step-up dosing schedule to reduce the risk of CRS:
  - 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 step-up dosing schedule due to dose delays or for patients who experienced CRS

Dose Adjustments

- Hepatic Impairment - Specific guidelines for dosage adjustments in hepatic impairment are not available; it appears that no initial dosage adjustments are needed. Therapy interruption or permanent discontinuation may be necessary in patients who develop severe hepatotoxicity.
- Renal Impairment - Specific guidelines for dosage adjustments in renal impairment are not available; it appears that no initial dosage adjustments are needed.
- Adverse Effects - Dosage reductions of talquetamab are not recommended. However, dosage delays may be required to manage toxicities related such as CRS, neurologic toxicity, and ICANS. Refer to the product labeling for the specific recommendations.

Drug Availability

- Sterile, preservative-free, colorless to light yellow solution supplied as follows:
  - One 3 mg/1.5 mL (2 mg/mL) single-dose vial in a carton [used for step-up doses 1 and 2 only]
  - One 40 mg/mL single-dose vial in a carton
- Store refrigerated at 2°C to 8°C (36°F to 46°F) in the original carton to protect from light. Do not freeze.

PRECAUTIONS:

Boxed Warning

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 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 reactions, can occur with Talvey. Monitor patients for signs or symptoms of neurologic toxicity including ICANS during treatment and treat promptly. Withhold or permanently discontinue Talvey based on severity.
- Because of 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

Precautions/Warnings

- **Cytokine Release Syndrome** – see Boxed Warning
- **Neurologic Toxicity including ICAN** – see Boxed Warning
- **TECVAYLI and TALVEY REMS** – see Boxed Warning
- **Oral Toxicity and Weight Loss** - Monitor for oral toxicity and weight loss. Withhold or permanently discontinue based on severity.
- **Infections**: Can cause severe, life-threatening, or fatal infections. Monitor for signs and symptoms of infection; treat appropriately. Withhold or consider permanent discontinuation based on severity.
- **Cytopenia**: Monitor complete blood counts.
- **Hepatotoxicity**: Monitor liver enzymes and bilirubin at baseline and during treatment as clinically indicated. Withhold or consider permanent discontinuation based on severity.
- **Embryo-Fetal Toxicity**: May cause fetal harm. Advise females of reproductive potential of the potential risk to the fetus and to use effective contraception.

BILLING/CODING INFORMATION:

HCPCS Coding

J3055	Injection, talquetamab-tgvs, 0.25 mg

ICD-10 Diagnosis Codes That Support Medical Necessity

C90.00	Multiple myeloma not having achieved remission
C90.02	Multiple myeloma in relapse
C90.10	Plasma cell leukemia not having achieved remission
C90.12	Plasma cell leukemia in relapse
C90.20	Extramedullary plasmacytoma not having achieved remission
C90.22	Extramedullary plasmacytoma in relapse
C90.30	Solitary plasmacytoma not having achieved remission
C90.32	Solitary plasmacytoma in relapse

REIMBURSEMENT INFORMATION:

Refer to section entitled **POSITION STATEMENT**.

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Part D: Florida Blue has delegated to Prime Therapeutics authority to make coverage determinations for the Medicare Part D services referenced in this guideline.

Medicare Advantage: No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) were found at the time of the last guideline review date.

If this Medical Coverage Guideline contains a step therapy requirement, in compliance with Florida law 627.42393, members or providers may request a step therapy protocol exemption to this requirement if based on medical necessity. The process for requesting a protocol exemption can be found at Coverage Protocol Exemption Request

DEFINITIONS:

Autologous - cells or tissues obtained from the same individual (as opposed to from a different person).

Heavy chain - the larger component of an immunoglobulin. There are five types: IgG, IgA, IgM, IgD, and IgE.

Immunoglobulins (a.k.a., antibodies) - proteins made by normal plasma cells that have an important role in fighting infection as part of the humoral immune response. Antibodies are composed of two heavy chains and two light chains that form a larger complex. Each plasma cell produces only one type of heavy chain and one type of light chain.

Light chain - the smaller component of an immunoglobulin. There are two types: kappa and lambda.

Myeloma Protein (M-Protein) - a nonfunctional immunoglobulin protein or protein fragment produced by malignant plasma cells (or myeloma cells). Since myeloma cells are monoclonal, the M-proteins for a given patient are structurally identical. Both portions of an immunoglobulin (the heavy chain and light chain) can be found in the serum, while only light chains can be found in the urine.

Plasma cell - a fully differentiated B lymphocyte (a type of white blood cell) that is specialized for immunoglobulin production and is found primarily in bone marrow.

Primary refractory MM - patients who never achieve at least a MR to initial induction therapy and progress while on therapy.

Progressive MM - at least a 25% increase from nadir in the serum M-protein (absolute increase must be ≥0.5 g/dL) or urine M-protein (absolute increase must be ≥200mg/24 hours), or in the difference between

involved and uninvolved serum-free light-chain (FLC) levels (with an abnormal FLC ratio and FLC difference >100 mg/L).

Relapsed and refractory MM - patients who never achieve at least a MR or who progress within 60 days of their last therapy.

RELATED GUIDELINES:

Allogeneic Bone Marrow and Stem Cell Transplantation, 02-38240-01
Carfilzomib (Kyprolis) IV, 09-J1000-81
Chimeric Antigen Receptor (CAR) T-Cell Therapies, 09-J3000-94
Daratumumab (Darzalex) Infusion and Daratumumab-Hyaluronidase-fihj (Darzalex Faspro), 09-J2000-49
Doxorubicin HCl Liposome (Doxil) IV, 09-J0000-91
Elotuzumab (Empliciti) IV, 09-J2000-50
Elranatamab-bcmm (Elrexfio) Injection, 09-4000-64
Isatuximab (Sarclisa) Injection, 09-J3000-67
Linvoseltamab (Lynozyfic) IV Infusion, 09-J5000-27
Oncology Self-Administered Medications, 09-J3000-65
Teclistamab (Tecvayli) Injection, 09-J4000-46
Thalidomide (Thalomid) Capsules, 09-J1000-56

OTHER:

None

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COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 06/10/26.

GUIDELINE UPDATE INFORMATION:

11/15/23	New Medical Coverage Guideline.
01/01/24	Revision: Added HCPCS code C9163.
04/01/24	Revision: Added HCPCS code J3055 and deleted codes C9163 and J9999.
07/15/24	Review and revision to guideline consisting of updating the references.
07/15/25	Review and revision to guideline consisting of updating the description section, position statement and references. Added an allowance for the combination regimen of teclistamab and talquetamab based on inclusion in the NCCN recommendations for MM.
06/01/26	Revision: Added Drug Waste Reduction statement to the Position Statement.
07/15/26	Review and revisions of guidelines consisting of updates to the description, position statement, related guidelines and references. New use as monotherapy as a bridge to BCMA CAR T-cell therapy per NCCN.