09-J4000-46

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Revised: 07/15/24

Subject: Teclistamab (Tecvayli) Injection

THIS MEDICAL COVERAGE GUIDELINE IS NOT AN AUTHORIZATION, CERTIFICATION, EXPLANATION OF BENEFITS, OR A GUARANTEE OF PAYMENT, NOR DOES IT SUBSTITUTE FOR OR CONSTITUTE MEDICAL ADVICE. ALL MEDICAL DECISIONS ARE SOLELY THE RESPONSIBILITY OF THE PATIENT AND PHYSICIAN. BENEFITS ARE DETERMINED BY THE GROUP CONTRACT, MEMBER BENEFIT BOOKLET, AND/OR INDIVIDUAL SUBSCRIBER CERTIFICATE IN EFFECT AT THE TIME SERVICES WERE RENDERED. THIS MEDICAL COVERAGE GUIDELINE APPLIES TO ALL LINES OF BUSINESS UNLESS OTHERWISE NOTED IN THE PROGRAM EXCEPTIONS SECTION.

DESCRIPTION:

Teclistamab (Tecvayli) is a bispecific B-cell maturation antigen (BCMA)-directed CD3 T-cell engaging antibody approved by the US Food and Drug Administration (FDA) in October 2022 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 continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trial(s). Prior to FDA approval teclistamab was granted orphan drug designation in November 2020 for the treatment of MM. Teclistamab binds to the CD3 receptor expressed on the surface of T-cells and BCMA expressed on the surface of multiple myeloma cells and some healthy B-lineage cells. In vitro, teclistamab activated T-cells, caused the release of various proinflammatory cytokines, and resulted in the lysis of multiple myeloma cells.

The National Comprehensive Cancer Network (NCCN) Guidelines for MM (Version 4.2024 – April 26, 2024) list teclistamab under “Relapse/Refractory Disease After 3 Prior Therapies” 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 “After at least four prior therapies, including an anti-CD38 monoclonal antibody, a proteasome inhibitor (PI), and an immunomodulatory agent (IMiD)”. The other treatments listed in this same “Preferred Regimens” section include the CAR-T cell therapies of idecabtagene vicleucel (Abecma) and ciltacabtagene autoleucel (Carvykti), and the bispecific antibodies of elranatamab (Elrexfio) and talquetamab (Talvey). The NCCN also includes footnotes stating “Autologous HCT should be considered in patients who are eligible and have not previously received HCT or had a prolonged response to initial HCT” and “Patients can receive more than one BCMA targeted therapy, but optimal sequencing is unclear”.

The safety and efficacy of teclistamab leading to initial FDA approval was evaluated in patients with relapsed or refractory MM in a single-arm, open-label, multicenter study (MajesTEC-1, NCT03145181 [Phase 1] and NCT04557098 [Phase 2]). The study included patients who had previously received at least three prior therapies, including a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 monoclonal antibody. The study excluded patients who had stroke, seizure, allogeneic stem cell transplantation within the past 6 months, Eastern Cooperative Oncology Group (ECOG) performance score of 2 or higher, known active CNS involvement or clinical signs of meningeal involvement of multiple myeloma, or active or documented history of autoimmune disease, with the exception of vitiligo, Type 1 diabetes, and prior autoimmune thyroiditis. Patients received step-up doses of 0.06 mg/kg and 0.3 mg/kg of teclistamab followed 1.5 mg/kg subcutaneously once weekly thereafter until disease progression or unacceptable toxicity. The efficacy population included 110 patients. The median age was 66 (range: 33 to 82) years with 16% of patients 75 years of age or older; 56% were male; 91% were White, 5% were Black, and 3% were Asian. The International Staging System (ISS) at study entry was Stage I in 50%, Stage II in 38%, and Stage III in 12% of patients. High-risk cytogenetics were present in 25% of patients. Seventeen percent of patients had extramedullary plasmacytomas. Patients with prior BCMA-targeted therapy were not included in the efficacy population. The median number of prior lines of therapy was 5 (range: 2 to 14); 78% of patients had received at least 4 prior lines of therapy. Eighty-one percent of patients received prior stem cell transplantation. All patients had received prior therapy with a proteasome inhibitor, an immunomodulatory agent and an anti-CD38 monoclonal antibody, and 76% were triple-class refractory (refractory to a proteasome inhibitor, an immunomodulatory agent and an anti-CD38 monoclonal antibody). Efficacy was established based on overall response rate (ORR) as determined by the Independent Review Committee (IRC) assessment using International Myeloma Working Group (IMWG) 2016 criteria. The median time to first response was 1.2 months (range: 0.2 to 5.5 months). With a median follow-up of 7.4 months among responders, the estimated duration of response (DOR) rate was 90.6% (95% CI: 80.3%, 95.7%) at 6 months and 66.5% (95% CI: 38.8%, 83.9%) at 9 months.

Table 1: Efficacy Results for MajesTEC-1

	N=110
Overall response rate (ORR: sCR+CR+VGPR+PR)	68 (61.8%)
95% CI	(52.1%, 70.9%)
Complete response (CR) or better*	31 (28.2%)
Very good partial response (VGPR)	32 (29.1%)
Partial response (PR)	5 (4.5%)
Duration of Response (DOR) (months)	
DOR (Months): Median (95% CI)	NE (9.0, NE)

NE = not estimable

* Complete response or better = Stringent complete response (sCR) + complete response (CR)

The safety of teclistamab from MajesTEC-1 was assessed in 165 drug-exposed patients. Serious adverse reactions occurred in 54% of patients who received teclistamab. Serious adverse reactions in >2% of patients included pneumonia (15%), cytokine release syndrome (8%), sepsis (6%), general physical health deterioration (6%), COVID-19 (6%), acute kidney injury (4.8%), pyrexia (4.8%), musculoskeletal

pain (2.4%), and encephalopathy (2.4%). Fatal adverse reactions occurred in 5% of patients who received teclistamab, including COVID-19 (1.8%), pneumonia (1.8%), septic shock (0.6%), acute renal failure (0.6%), and hemoperitoneum (0.6%). Permanent discontinuation of teclistamab due to adverse reactions occurred in 1.2% of patients. Adverse reactions resulting in permanent discontinuation of teclistamab included pneumonia (adenoviral and pneumocystis jirovecii pneumonia in the same patient) and hypercalcemia. Dosage interruptions of teclistamab due to an adverse reaction occurred in 73% of patients. Adverse reactions which required dosage interruption in >5% of patients included neutropenia, pneumonia, pyrexia, cytokine release syndrome, upper respiratory tract infection, and COVID-19. The most common adverse reactions (≥20%) were pyrexia, CRS, musculoskeletal pain, injection site reaction, fatigue, upper respiratory tract infection, nausea, headache, pneumonia, and diarrhea. The most common Grade 3 to 4 laboratory abnormalities (≥20%) were decreased lymphocytes, decreased neutrophils, decreased white blood cells, decreased hemoglobin, and decreased platelets. Refer to the product labeling for the specific percentages.

POSITION STATEMENT:

Initiation of teclistamab (Tecvayli) **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 "f") - *medical record documentation confirming the patient's diagnosis and complete treatment history must be submitted*:
    a. 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

    b. Member's prior MM treatments have included **ALL** of the following ("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)]
    c. 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 teclistamab-containing treatment regimen
    d. Teclistamab will be used as single-agent therapy for the member's MM (i.e., not used in combination with other MM treatments)
    e. The ordering provider and the infusing healthcare facility is certified in the TECVAYLI REMS program
    f. Dosage of teclistamab does not exceed the following:
        - Day 1 (Step-up dose 1) - 0.06 mg/kg

- Day 4 (Step-up dose 2) - 0.3 mg/kg
- Day 7 (First treatment dose) – 1.5 mg/kg
- One week after first treatment dose and weekly thereafter - 1.5 mg/kg once weekly

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. Teclistamab 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 REMS program
   d. Dosage of teclistamab 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: 9 months

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

1. An authorization or reauthorization for teclistamab has been previously approved by Florida Blue or another health plan in the past 2 years for the treatment of multiple myeloma, or other FDA-approved or NCCN-supported diagnosis; **OR** the member previously met **ALL** indication-specific initiation criteria
2. The ordering provider and the infusing healthcare facility is certified in the TECVAYLI 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. Teclistamab is being used as single-agent therapy for the member's MM (i.e., not used in combination with other MM treatments)
      ii. Dosage of teclistamab does not exceed one of the following:
         - 1.5 mg/kg once weekly, **AND EITHER** of the following:
            - Member has not achieved a complete response (CR) to therapy
            - Member has not maintained a CR to therapy for a minimum of 6 months
         - 1.5 mg/kg once every two weeks

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

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

i. Dosage of teclistamab 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. Teclistamab 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 teclistamab

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. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trial(s).
- The recommended dosing schedule is as follows:
  - Step-up dosing schedule:
    - Day 1 (Step-up dose 1) - 0.06 mg/kg
    - Day 4* (Step-up dose 2) - 0.3 mg/kg
    - Day 7* (First treatment dose) – 1.5 mg/kg
  - Weekly dosing schedule:
    - One week after first treatment dose and weekly thereafter - 1.5 mg/kg once weekly
  - Every 2 weeks dosing schedule:
    - In patients who have achieved and maintained a complete response or better for a minimum of 6 months, the dosing frequency may be decreased to 1.5 mg/kg every two weeks until disease progression or unacceptable toxicity

  **The second and third doses may be given between 2 to 4 days after the prior dose and may be given up to 7 days after the prior dose to allow for resolution of adverse reaction.*

- Teclistamab is intended for subcutaneous use by a healthcare provider only and be administered by a healthcare provider with adequate medical personnel and appropriate medical equipment to manage severe reactions, including CRS and 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 (i.e., Day 1, 4, and 7).
- Teclistamab 30 mg/3 mL (10 mg/mL) and 153 mg/1.7 mL (90 mg/mL) vial are supplied as ready-to-use solution that do not need dilution prior to administration. Do NOT combine vials of different concentrations to achieve treatment dose.
- Administer the following pretreatment medications 1 to 3 hours before each dose of the teclistamab step-up dosing schedule, which includes step-up dose 1, step-up dose 2, and the first treatment dose, to reduce the risk of CRS:
    - Corticosteroid (oral or intravenous dexamethasone 16 mg)
    - Histamine-1 (H1) receptor antagonist (oral or intravenous diphenhydramine 50 mg or equivalent)
    - Antipyretics (oral or intravenous acetaminophen 650 mg to 1,000 mg or equivalent)
- Some patients may require pretreatment medications for subsequent doses – refer to the product labeling.
- Prior to starting treatment with teclistamab, consider initiation of antiviral prophylaxis to prevent herpes zoster reactivation per guidelines.
- If a dose of teclistamab is delayed outside of the recommended dosing schedule, a new treatment schedule is required - refer to the product labeling.

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 teclistamab 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, clear to slightly opalescent, colorless to light yellow solution supplied as follows:
    - One 30 mg/3 mL (10 mg/mL) single-dose vial in a carton
    - One 153 mg/1.7 mL (90 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 Tecvayli. Initiate treatment with Tecvayli step-up dosing schedule to reduce risk of CRS. Withhold Tecvayli 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 Tecvayli. Monitor patients for signs or symptoms of neurologic toxicity, including ICANS, during treatment. Withhold Tecvayli until neurologic toxicity resolves or permanently discontinue based on severity.

Because of risk of CRS and neurologic toxicity, including ICANS, Tecvayli is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the TECVAYLI REMS.

Contraindications

- None

Precautions/Warnings

- **Cytokine Release Syndrome** – see Boxed Warning
- **Neurologic Toxicity including ICAN** – see Boxed Warning
- **TECVAYLI REMS** – see Boxed Warning
- **Hepatotoxicity**: Can cause hepatotoxicity, including fatalities. Monitor liver enzymes and bilirubin at baseline and during treatment as clinically indicated.
- **Infections**: Can cause severe, life-threatening, or fatal infections. Monitor patients for signs and symptoms of infection and treat appropriately. Withhold in patients with active infection during the step-up dosing schedule.
- **Neutropenia**: Monitor complete blood cell counts at baseline and periodically during treatment.
- **Hypersensitivity and Other Administration Reactions**: Systemic administration-related reactions and local injection site reactions can occur. 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

J9380	Injection, teclistamab-cqyv, 0.5 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.

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
Ixazomib (Ninlaro), 09-J2000-51
Oral Oncology Medications, 09-J3000-65
Teclistamab (Tecvayli) Injection, 09-J4000-46
Thalidomide (Thalomid) Capsules, 09-J1000-56

OTHER:

None

REFERENCES:

1. Clinical Pharmacology powered by ClinicalKey [Internet]. Tampa, FL: Elsevier.; 2024. Available at: https://www.clinicalkey.com/pharmacology/. Accessed 05/24/24.
2. Micromedex Healthcare Series [Internet Database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Accessed 05/24/24.
3. Moreau P, Garfall AL, van de Donk NWCJ, et al. Teclistamab in Relapsed or Refractory Multiple Myeloma. N Engl J Med. 2022 Aug 11;387(6):495-505. Epub 2022 Jun 5.
4. National Comprehensive Cancer Network. NCCN clinical practice guidelines in oncology (NCCN Guidelines). Multiple Myeloma (Version 4.2024 - April 26, 2024) [cited 2024 May 24]. Available at http://www.nccn.org/professionals/physician_gls/PDF/myeloma.pdf.
5. NCCN Drugs & Biologics Compendium [Internet]. Fort Washington (PA): National Comprehensive Cancer Network; 2024 [cited 2024 May 24]. Available at: http://www.nccn.org/professionals/drug_compendium/content/contents.asp/.
6. Orphan Drug Designations and Approval [Internet]. Silver Spring (MD): US Food and Drug Administration; 2024 [cited 2024 May 24]. Available from: http://www.accessdata.fda.gov/scripts/opdlisting/oopd/index.cfm/.
7. Tecvayli (teclistamab injection) [package insert]. Janssen Biotech, Inc..; Horsham, PA. February 2024.
8. Usmani SZ, Garfall AL, van de Donk NWCJ, et al. Teclistamab, a B-cell maturation antigen × CD3 bispecific antibody, in patients with relapsed or refractory multiple myeloma (MajesTEC-1): a multicentre, open-label, single-arm, phase 1 study. Lancet. 2021;398(10301):665-674.

9. Verkleij CPM, Frerichs KA, Broekmans M, et al. T-cell redirecting bispecific antibodies targeting BCMA for the treatment of multiple myeloma. Oncotarget. 2020 Nov 10;11(45):4076-4081.

COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 06/12/24.

GUIDELINE UPDATE INFORMATION:

03/15/23	New Medical Coverage Guideline.
04/01/23	Revision: Added HCPCS code C9148.
07/01/23	Revision: Added HCPCS code J9380 and deleted codes C9148 and J9999.
07/15/24	Review and revision to guideline consisting of updating the position statement, related guidelines, and references. For continuation, added a requirement that the dosage be optimized to a frequency of every 2 weeks for members who have achieved and maintained a CR for a minimum of 6 months.