Clinical Policy: Teclistamab-cqyv (Tecvayli)

Reference Number: PA.CP.PHAR.611
Effective Date: 01/2023
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Revision Log

Description
Teclistamab-cqyv (Tecvayli™) is a humanized recombinant immunoglobulin G4-proline, alanine, alanine (IgG4-PAA) antibody, and a bispecific B-cell maturation antigen (BCMA)-directed CD3 T-cell engager.

FDA Approved Indication(s)
Tecvayli 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 (PI), an immunomodulatory agent (IMiD), 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).

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of PA Health & Wellness® that Tecvayli is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Multiple Myeloma (must meet all)**:**

1. Diagnosis of relapsed or refractory multiple myeloma (RRMM);
2. Prescribed by or in consultation with a hematologist or an oncologist;
3. Age ≥ 18 years;
4. Tecvayli is prescribed as monotherapy;
5. Member has measurable disease as evidenced by one of the following assessed within the last 28 days (a, b, or c):
   a. Serum M-protein ≥ 1 g/dL;
   b. Urine M-protein ≥ 200 mg/24 h;
   c. Serum free light chain (FLC) assay: involved FLC level ≥ 10 mg/dL (100 mg/L) provided serum kappa lambda FLC ratio is abnormal;
6. Member has received or has documented intolerance to ≥ 4 prior lines of therapy (*see Appendix B for examples*) that include all of the following (a, b, and c):
   a. One proteasome inhibitor (e.g., bortezomib, Kyprolis®, Ninlaro®);
   b. One immunomodulatory agent (e.g., Revlimid®, pomalidomide, Thalomid®);
   c. One anti-CD38 antibody (e.g., Darzalex®/Darzalex Faspro™, Sarclisa®);
   **Prior authorization may be required*

7. Member does not have a known active central nervous system (CNS) involvement (e.g., seizure, cerebrovascular ischemia) or exhibits clinical signs of meningeal involvement of multiple myeloma;
8. Member has not previously received treatment with anti-BCMA targeted therapy (e.g., Blenrep™, Abecma®, or Carvykti™);
9. Dose does not exceed all of the following (a, b, c, d, and e):
    a. Day 1: 0.06 mg/kg;
    b. Day 4: 0.3 mg/kg;
    c. Day 7: 1.5 mg/kg;
    d. Day 8 and thereafter: 1.5 mg/kg per week;
    e. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label dose use (*prescriber must submit supporting evidence*).

Approval duration: 6 months

B. Other diagnoses/indications

1. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

II. Continued Therapy

A. Multiple Myeloma (must meet all)**:**

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;
2. Member is responding positively to therapy;
3. If request is for a dose increase, request meets one of the following (a or b):
    a. New dose does not exceed 1.5 mg/kg per week;
    b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label dose use (*prescriber must submit supporting evidence*)

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.LTSS.PHAR.01) applies.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – PA.CP.PMN.53.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

BCMA: B-cell maturation antigen CNS: central nervous system

CRS: cytokine release syndrome
FDA: Food and Drug Administration
ICANS: immune effector cell-associated neurotoxicity syndrome
IMiD: immunomodulatory drug
MM: multiple myeloma
PI: proteasome inhibitor
RRMM: relapsed or refractory multiple myeloma

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
bortezomib/Revlimid® (lenalidomide)/dexamethasone	Varies	Varies
bortezomib/cyclophosphamide/dexamethasone	Varies	Varies
bortezomib/doxorubicin (or liposomal doxorubicin)/ dexamethasone	Varies	Varies
Kyprolis® (carfilzomib) Revlimid® (lenalidomide)/ dexamethasone	Varies	Varies
Kyprolis® (carfilzomib)/cyclophosphamide/ dexamethasone	Varies	Varies
Kyprolis® (carfilzomib – weekly or twice weekly)/ dexamethasone	Varies	Varies
Ninlaro® (ixazomib)/Revlimid® (lenalidomide)/ dexamethasone	Varies	Varies
Ninlaro® (ixazomib)/dexamethasone	Varies	Varies
Ninlaro® (ixazomib)/pomalidomide/dexamethasone	Varies	Varies
bortezomib/dexamethasone	Varies	Varies
bortezomib/Thalomid® (thalidomide)/dexamethasone	Varies	Varies
cyclophosphamide/Revlimid® (lenalidomide)/ dexamethasone	Varies	Varies
Revlimid® (lenalidomide)/dexamethasone	Varies	Varies
VTD-PACE (dexamethasone/Thalomid®(thalidomide) /cisplatin/doxorubicin/cyclophosphamide/etoposide/ bortezomib)	Varies	Varies
Revlimid® (lenalidomide)/low-dose dexamethasone	Varies	Varies
Darzalex® (daratumumab) or Darzalex Faspro™ (daratumumab/hyaluronidase-fihj)/bortezomib/ melphan/prednisone	Varies	Varies
Darzalex® (daratumumab) or Darzalex Faspro™ (daratumumab/hyaluronidase-fihj)/ bortezomib/dexamethasone	Varies	Varies
Darzalex® (daratumumab) or Darzalex Faspro™ (daratumumab/hyaluronidase-fihj)/Revlimid® (lenalidomide)/dexamethasone	Varies	Varies

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Darzalex® (daratumumab) or Darzalex Faspro™ (daratumumab/hyaluronidase-fihj)	Varies	Varies
Darzalex® (daratumumab) or Darzalex Faspro™ (daratumumab/hyaluronidase-fihj)/pomalidomide/ dexamethasone	Varies	Varies
Empliciti® (elotuzumab)/Revlimid® (lenalidomide)/ dexamethasone	Varies	Varies
Empliciti® (elotuzumab)/bortezomib/dexamethasone	Varies	Varies
Empliciti®(elotuzumab)/pomalidomide/dexamethasone	Varies	Varies
bendamustine/bortezomib/dexamethasone	Varies	Varies
bendamustine/Revlimid® (lenalidomide)/dexamethasone	Varies	Varies
panobinostat/bortezomib/dexamethasone	Varies	Varies
panobinostat/Kyprolis® (carfilzomib)	Varies	Varies
panobinostat/Revlimid® (lenalidomide)/dexamethasone	Varies	Varies
pomalidomide/cyclophosphamide/dexamethasone	Varies	Varies
pomalidomide/dexamethasone	Varies	Varies
pomalidomide/bortezomib/dexamethasone	Varies	Varies
pomalidomide/Kyprolis® (carfilzomib)/dexamethasone	Varies	Varies
Sarclisa® (isatuximab-irfc)/pomalidomide/dexamethasone	Varies	Varies

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): None
- Boxed warning(s): Cytokine release syndrome (CRS) with life-threatening and/or fatal reactions, and neurologic toxicity, including immune effector cell-associated neurotoxicity syndrome (ICANS)

Appendix D: General Information

- Due to the risks of cytokine release syndrome, patients should be hospitalized for 48 hours after administration of all doses within the step-up dosing schedule including the first maintenance dose. Subsequent weekly maintenance doses are managed on outpatient basis according to the Tecvayli REMS program (*see appendix E for more details on REMS Program*).
- In the MajesTEC-1 trial, 100% of enrolled patients reported having an adverse event, of which 94.5% were grade 3 or 4. The most common hematologic adverse events were neutropenia (70.9%), anemia (52.1%), and thrombocytopenia (44.0%). The most common non-hematologic adverse events were diarrhea (28.5%), fatigue (27.9%), and nausea (27.3%).
- In the MajesTEC-1 trial, 72.1% of participants experienced any grade cytokine release syndrome (CRS), and 14.5% of participants experienced any grade immune effector cell-associated neurotoxicity syndrome (ICANS). Both toxicities were managed with supportive measures that included administration of tocilizumab (in 60/119 patients with CRS, and 3/24

patients with ICANS), low-flow oxygen by nasal cannula, glucocorticoids, levetiracetam, and gabapentin.
- In the MajesTEC-1 trial, five deaths were considered to have been related to Tecvayli treatment including one death resulting from progressive multifocal leukoencephalopathy, two deaths related to Covid-19, one death related to hepatic failure, and one death related to streptococcal pneumonia. Subjects positive for hepatitis B, hepatitis C, and/or HIV were excluded from the trial. Prior to treatment with Tecvayli initiation of antiviral prophylaxis to prevent herpes zoster reactivation is recommended.

Appendix E: Tecvayli REMS Program Information
- Tecvayli is available only through a restricted REMS program due to the risk of cytokine release syndrome and neurologic toxicity, including ICANS.
- Prescribers are required to:
  1) obtain certification with the program by enrolling and completing training,
  2) counsel patients about the risks associated with Tecvayli therapy,
  3) provide patients with patient wallet card.
- Dispensers are required to:
  1) obtain certification with the program,
  2) verify prescriber certification status with the program prior to dispensing the product.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Multiple Myeloma	Step-up Dosing Schedule[a]: • Day 1: 0.06 mg/kg subcutaneously (step-up dose 1) • Day 4[b]: 0.3 mg/kg subcutaneously (step-up dose 2) • Day 7[c]: 1.5 mg/kg subcutaneously (first treatment dose) Weekly Dosing Schedule[a]: 1.5 mg/kg subcutaneously once weekly (one week after first treatment dose and weekly thereafter)	1.5 mg/kg per week subcutaneously

[a] *Refer to prescribing information Table 2 for recommendations on restarting therapy due to dose delays.*
[b] *Step-up dose 2 may be given between 2 to 4 days after step-up dose 1 and may be given up to 7 days after step-up dose 1 to allow for resolution of adverse reactions.*
[c] *First treatment dose may be given between 2 to 4 days after step-up dose 2 and may be given up to 7 days after step-up dose 2 to allow for resolution of adverse reactions.*

VI. Product Availability

Solution for subcutaneous injection in a single-dose vial:
- 30 mg/3 mL (10 mg/mL) used for step-up doses 1 and 2
- 153 mg/1.7 mL (90 mg/mL) used for treatment doses

VII. References

1. Tecvayli Prescribing Information. Horsham, PA: Janssen Biotech, Inc.; October 2022. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/761291s000lbl.pdf. Accessed November 10, 2022.
2. ClinicalTrials.gov. A phase 1, first-in-human, open-label, dose escalation study of teclistamab, a humanized BCMA x CD3 bispecific antibody in subjects with relapsed or refractory multiple myeloma. Available at: https://www.clinicaltrials.gov/ct2/show/NCT03145181. Accessed November 10, 2022.
3. ClinicalTrials.gov. A phase 1/2, first-in-human, open-label, dose escalation study of teclistamab, a humanized BCMA x CD3 bispecific antibody, in subjects with relapsed or refractory multiple myeloma. Available at: https://clinicaltrials.gov/ct2/show/NCT04557098. Accessed November 10, 2022.
4. Girgis S, Lin SXW, Pillarisetti K, et al. Translational modeling predicts efficacious therapeutic dosing range of teclistamab for multiple myeloma. Target Oncol. 2022;17(4):433-439.
5. Moreau P, Garfall AL, van de Donk NWCJ, et al. Teclistamab in relapsed or refractory multiple myeloma. N Engl J Med. 2022;387(6):495-505.
6. National Comprehensive Cancer Network. Multiple Myeloma Version 2.2023. Available at: https://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf. Accessed November 10, 2022.
7. Pillarisetti K, Powers G, Luistro L, et al. Teclistamab is an active T cell-redirecting bispecific antibody against B-cell maturation antigen for multiple myeloma. Blood Adv. 2020;4(18):4538-4549.
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.

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J3590	Unclassified biologics
J9999	Not otherwise classified antineoplastic drugs
C9399	Unclassified drugs or biologicals

Reviews, Revisions, and Approvals	Date	P&T Approval Date
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