Clinical Policy: Linvoseltamab-gcpt (Lynozyfic)

Reference Number: CP.PHAR.743
Effective Date: 10.01.25
Last Review Date: 08.25
Line of Business: Commercial, HIM, Medicaid

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Linvoseltamab-gcpt (Lynozyfic™) a bispecific B-cell maturation antigen (BCMA)-directed CD3 T-cell engager.

FDA Approved Indication(s)

Lynozyfic is indicated 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 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 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 health plans affiliated with Centene Corporation® that Lynozyfic is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

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

1. Diagnosis of MM;
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age ≥ 18 years;
4. Disease is relapsed or refractory;
5. One of the following (a or b):
   a. Member has measurable disease as evidenced by one of the following assessed within the last 28 days (i, ii, or iii):
      i. Serum M-protein ≥ 0.5 g/dL;
      ii. Urine M-protein ≥ 200 mg/24 h;
      iii. Serum free light chain (FLC) assay: involved FLC level ≥ 10 mg/dL (100 mg/L) provided serum kappa lambda FLC ratio is abnormal;
   b. Member has progressive disease, as defined by the International Myeloma Working Group (IMWG) response criteria (see *Appendix D*), assessed within 60 days following the last dose of the last anti-myeloma drug regimen received;

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®, Pomalyst®, Thalomid®);
   c. One anti-CD38 monoclonal antibody (e.g., Darzalex®/Darzalex Faspro™, Sarclisa®);

   **Prior authorization may be required*
7. Member does not have known multiple myeloma brain lesions or meningeal involvement;
8. Request meets one of the following (a or b):*
   a. Dose does not exceed all of the following (i – v):
      i. Day 1: 5 mg;
      ii. Day 8: 25 mg;
      iii. Day 15: 200 mg;
      iv. One week after Day 15 treatment dose and once weekly from week 4 to week 13 for 10 treatment doses: 200 mg per week;
      v. Week 14 and every 2 weeks thereafter: 200 mg every 2 weeks;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

   **Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Medicaid/HIM – 6 months
Commercial –6 months or to the member's renewal date, whichever is longer

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Multiple Myeloma (must meet all)**:**
1. Currently receiving medication via Centene benefit, or documentation supports that member is currently receiving Lynozyfic for a covered indication and has received this medication for at least 30 days;

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 one of the following (i or ii):
      i. 200 mg every 2 weeks;
      ii. For members that have achieved and maintained very good partial response (VGPR) or better at or after week 24 and received at least 17 doses of 200 mg: 200 mg every 4 weeks;
   b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Medicaid/HIM – 12 months
Commercial – 6 months or to the member's renewal date, whichever is longer

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

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

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 – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

BCMA: B-cell maturation antigen
FDA: Food and Drug Administration
FLC: free light chain
IMWG: International Myeloma Working Group
MM: multiple myeloma
VGPR: very good partial response
NCCN: National Comprehensive Cancer Network

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)/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/dexamethasone	Varies	Varies
Darzalex® (daratumumab) or Darzalex Faspro™ (daratumumab/hyaluronidase-fihj)/Revlimid® (lenalidomide)/dexamethasone	Varies	Varies
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

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
bendamustine/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 reported
- Boxed warning(s): cytokine release syndrome and neurologic toxicity, including immune effector cell-associated neurotoxicity syndrome

Appendix D: General Information

- Patients with MM brain lesions or meningeal involvement were excluded from the pivotal LINKER-MM1 trial.
- The IMWG response criteria for MM definition of progressive disease requires only one of the following:
  - Increase of 25% from lowest response value in any of the following:
    - Serum M-component (absolute increase must be ≥ 0.5 g/dL), and/or
    - Urine M-component (absolute increase must be ≥ 200 mg/24 h), and/or
    - Only in patients without measurable serum and urine M-protein levels: the difference between involved and uninvolved FLC levels (absolute increase must be > 10 mg/dL)
    - Only in patients without measurable serum and urine M protein levels and without measurable disease by FLC levels, bone marrow plasma cell percentage irrespective of baseline status (absolute increase must be ≥ 10%)

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
MM	Step-up dosing schedule: Day 1: 5 mg IV (Step-up dose 1) Day 8: 25 mg IV (Step-up dose 2) Day 15: 200 mg IV (first treatment dose) Weekly dosing schedule: Week 4 to Week 13: 200 mg IV once weekly (one week after Day 15 treatment dose and once weekly from week 4 to week 13 for 10 treatment doses)	Maintenance dosing: 200 mg every 2 weeks (200 mg every 4 weeks for patients who have achieved and maintained VGPR or better at or after week 24 and received at least 17 doses of 200 mg)

Indication	Dosing Regimen	Maximum Dose
	Biweekly dosing schedule: Week 14 and every 2 weeks thereafter: 200 mg IV every 2 weeks Patients who have achieved and maintained VGPR or better at or after week 24 and received at least 17 doses of 200 mg: 200 mg IV every 4 weeks	

VI. Product Availability

Single-dose vials for intravenous infusion: 5 mg/2.5 mL, 200 mg/10 mL

VII. References

1. Lynozyfic Prescriber Information. Tarrytown, NY. Regeneron Pharmaceuticals, Inc. July 2025. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/761400s000lbl.pdf. Accessed July 15, 2025.
2. National Comprehensive Cancer Network. Multiple Myeloma Version 2.2026. Available at: https://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf. Accessed July 17, 2025.
3. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed July 17, 2025.
4. ClinicalTrials.gov. Phase 1/2 Study of REGN5458 in Adult Patients with Relapsed or Refractory Multiple Myeloma (LINKER-MM1). Available at: https://clinicaltrials.gov/study/NCT03761108. Accessed July 15, 2025.
5. International Myeloma Foundation. International Myeloma Working Group (IMWG) Uniform Response Criteria for Multiple Myeloma. 2025. Available at: https://www.myeloma.org/resource-library/international-myeloma-working-group-imwg-uniform-response-criteria-multiple. Accessed July 17, 2025.

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
C9307	Injection, linvoseltamab-gcpt, 1 mg
J9999	Not otherwise classified, antineoplastic drugs

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	07.17.25	08.25
Updated effective date to 10.01.25. HCPCS code added [J9999] and removed [J3590, C9399].	09.11.25	
HCPCS code added [C9307].	01.06.26	

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

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and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

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