Clinical Policy: Belantamab Mafodotin-blmf (Blenrep)

Reference Number: CP.PHAR.469
Effective Date: 08.05.20
Last Review Date: 05.24
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

Belantamab mafodotin-blmf (Blenrep™) is an anti-B-cell maturation antigen (BCMA) monoclonal antibody and microtubule inhibitor conjugate.

FDA Approved Indication(s)*

Blenrep is indicated for the treatment of adult patients with relapsed or refractory multiple myeloma who have received at least 4 prior lines of therapy, including an anti-CD38 antibody, a proteasome inhibitor, and an immunomodulatory agent.

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).

***GlaxoSmithKline (GSK), the manufacturer of Blenrep, voluntarily withdrew Blenrep after post-market data from the DREAMM-3 Phase 3 trial revealed Blenrep did not meet the requirements of the FDA Accelerated Approval regulation. The FDA withdrew its approval for the product (*see Appendix D*).**

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 Blenrep is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

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

1. Provider attestation of acknowledgement of FDA's request for withdrawal of product due to failure to demonstrate superior progression-free survival (PFS) compared to placebo;
2. Diagnosis of multiple myeloma;
3. Prescribed by or in consultation with an oncologist or hematologist;
4. Age ≥ 18 years;
5. Blenrep is prescribed as monotherapy;
6. Member has received ≥ 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. Request meets one of the following (a or b):*
   a. Dose does not exceed 2.5 mg/kg every 3 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: 6 months

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. Provider attestation of acknowledgement of FDA's request for withdrawal of product due to failure to demonstrate superior PFS compared to placebo;
2. Currently receiving medication via Centene benefit, or documentation supports that member is currently receiving Blenrep for a covered indication and has received this medication for at least 30 days;
3. Member is responding positively to therapy;
4. Dose is ≥ 1.9 mg/kg every 3 weeks;
5. If request is for a dose increase, request meets one of the following (a or b):*
   a. New dose does not exceed 2.5 mg/kg every 3 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: 12 months

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
GSK: GlaxoSmithKline
PFS: progression free survival

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/lenalidomide/dexamethasone	Varies	Varies
bortezomib/cyclophosphamide/dexamethasone	Varies	Varies
bortezomib/doxorubicin (or liposomal doxorubicin)/ dexamethasone	Varies	Varies
Kyprolis® (carfilzomib)/lenalidomide/ dexamethasone	Varies	Varies
Kyprolis® (carfilzomib)/cyclophosphamide/ dexamethasone	Varies	Varies
Kyprolis® (carfilzomib – weekly or twice weekly)/ dexamethasone	Varies	Varies
Ninlaro® (ixazomib)/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/lenalidomide/ dexamethasone	Varies	Varies

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
lenalidomide/dexamethasone	Varies	Varies
VTD-PACE (dexamethasone/Thalomid® (thalidomide)/ cisplatin/doxorubicin/cyclophosphamide/etoposide/ bortezomib)	Varies	Varies
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)/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)/lenalidomide/dexamethasone	Varies	Varies
Empliciti® (elotuzumab)/bortezomib/dexamethasone	Varies	Varies
Empliciti® (elotuzumab)/pomalidomide/dexamethasone	Varies	Varies
bendamustine/bortezomib/dexamethasone	Varies	Varies
bendamustine/lenalidomide/dexamethasone	Varies	Varies
panobinostat/bortezomib/dexamethasone	Varies	Varies
panobinostat/Kyprolis® (carfilzomib)	Varies	Varies
panobinostat/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): ocular toxicity
  - In clinical studies, Blenrep caused changes in the corneal epithelium resulting in changes in vision, including severe vision loss and corneal ulcer, and symptoms, such as blurred vision and dry eyes. Because of these risks, Blenrep is only available through a restricted program, called the Blenrep REMS.

Appendix D: Withdrawal from Market

- GSK, the manufacture of Blenrep, voluntarily withdrew Blenrep after post-market data from the DREAMM-3 Phase 3 trial revealed Blenrep did not meet the requirements of the FDA Accelerated Approval regulation.
  - Blenrep did not meet its primary endpoint of superior PFS compared to pomalidomide and dexamethasone (PomDex) for relapsed or refractory multiple myeloma.
  - The hazard ratio for PFS was 1.03 (95% CI: 0.72, 1.47). However, the observed median PFS was longer for Blenrep vs PomDex (11.2 vs 7 months).
- GSK has stopped new patient enrollment (as of November 22, 2022) into the Blenrep REMS.
- GSK recommends prescribers discuss the individual risk vs benefits to decide ongoing care.
- For enrolled patients deriving clinical benefits, Blenrep will continue to be available until GSK launces compassionate use program.
  - Details on compassionate use program will be provided directly to REMS enrolled prescriber.
- GSK recommends patients currently being treated with Blenrep should consult their healthcare providers.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Multiple myeloma	2.5 mg/kg* IV infusion every 3 weeks until disease progression or unacceptable toxicity	2.5 mg/kg/dose

**If dose reduction to < 1.9 mg/kg is required, discontinue therapy.*

VI. Product Availability

Lyophilized powder in a single-dose vial for reconstitution and further dilution for injection: 100 mg

VII. References

1. Blenrep Prescribing Information. Research Triangle Park, NC: GlaxoSmithKline; February 2022. Available at: https://www.blenrephcp.com/. Accessed February 2, 2024
2. Lonial S, Lee HC, Badros A, et al. Belantamab mafodotin for relapsed or refractory multiple myeloma (DREAMM-2): a two-arm, randomised, open-label, phase 2 study. Lancet Oncology. 2020; 21(2): 207-221.
3. National Comprehensive Cancer Network. Multiple Myeloma Version 2.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf. Accessed February 2, 2024.
4. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed Accessed February 2, 2024.
5. GSK provides an update on Blenrep (belantamab mafodotin-blmf) US marketing authorisation. November 22, 2022. Available at https://www.gsk.com/en-gb/media/press-releases/gsk-provides-update-on-blenrep-us-marketing-authorisation/. Accessed February 2, 2024.

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
J9037	Injection, belantamab mafodontin-blmf, 0.5 mg

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created pre-emptively	03.03.20	05.20
Drug is now FDA approved - criteria updated per FDA labeling: revised from 3 to 4 prior lines of therapy; modified to the actual FDA max dose; on re-auth, added requirement that dose is at least 1.9 mg/kg; references reviewed and updated.	08.18.20	11.20
2Q 2021 annual review: no significant changes; references to HIM.PHAR.21 revised to HIM.PA.154; added non-specific HCPCS code as no drug-specific codes are currently available; references reviewed and updated.	01.15.21	05.21
2Q 2022 annual review: no significant changes; updated HCPCS codes; references reviewed and updated.	01.25.22	05.22
Template changes applied to other diagnoses/indications.	09.28.22	
RT4: added disclaimer about FDA and manufacturer withdrawal; added requirement for prescriber attestation to all criteria sets; added Appendix D.	12.14.22	
2Q 2023 annual review: no significant changes, removed inactive HCPCS code C9069; references reviewed and updated.	01.13.23	05.23
2Q 2024 annual review: no significant changes; references reviewed and updated.	02.02.24	05.24

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.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members, and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members 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.