ARCHIVED (NOT ACTIVE – RETIRED)

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Next Review: ARCHIVED/NO LONGER IN USE

Subject: Belantamab Mafodotin-blmf (Blenrep®) IV Infusion

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:

Belantamab mafodotin (Blenrep) is an antibody-drug conjugate (ADC) that targets B-cell maturation antigen (BCMA), a protein expressed on normal B lymphocytes and multiple myeloma cells. It was initially approved by the Food and Drug Administration (FDA) in August 2020 for the treatment of adults with relapsed or refractory multiple myeloma (MM) who have received at least four prior therapies, including an anti-CD38 monoclonal antibody, a proteasome inhibitor, and an immunomodulatory agent. This indication was approved under accelerated approval based on response rate. In November 2022, the DREAMM-3 Phase III confirmatory trial failed to show that Blenrep was any better than on-market treatment, thus failing to meet the requirements of the FDA accelerated approval regulations. As such, the FDA requested that GSK withdraw the US marketing authorization. GSK is no longer selling Blenrep in the US. Belantamab mafodotin has 3 components consisting of an afucosylated, humanized immunoglobulin G1 (IgG1) monoclonal antibody covalently linked to a microtubule inhibitor [monomethyl auristatin F (MMAF)] via a protease-resistant maleimidocaproyl linker. Belantamab mafodotin is internalized after binding to BCMA and then MMAF is released via proteolytic cleavage which causes disruption in the microtubule network and eventually cell cycle arrest and apoptosis.

Belantamab mafodotin was the first approved therapy that targets BCMA, and provided a novel mechanism of action for the treatment of MM. The chimeric antigen receptor (CAR) T-cell therapies, idecabtagene vicleucel (Abecma) and ciltacabtagene autoleucel (Carvykti), that also target BCMA were approved in March 2021 and February 2022, respectively, for relapsed or refractory MM after four or more prior lines of therapy.

POSITION STATEMENT:

Initiation of belantamab mafodotin (Blenrep) **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 "g"):
    a. Member has received **FOUR or more** appropriate prior lines of therapy of adequate duration for the treatment of their MM
    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 belantamab mafodotin-containing treatment regimen
    d. Belantamab mafodotin will be used as single-agent therapy for the member's MM (i.e., not used in combination with other MM treatments)
    e. A baseline ophthalmic examination (visual acuity and slit lamp), within 3 weeks prior to the first dose of belantamab mafodotin, has been or will be completed
    f. The ordering provider and the infusing healthcare facility is certified with, and the treated member enrolled in, the Blenrep REMS program
    g. Dosage of belantamab mafodotin does not exceed 2.5 mg/kg (based on actual body weight) every 3 weeks
2. Member has another FDA-approved or NCCN-supported diagnosis, and **ALL** of the following are met ("a" to "e"):
    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. Belantamab mafodotin is used in a treatment regimen in accordance with the FDA-approved prescribing information or applicable NCCN guideline recommendation for the diagnosis

c. A baseline ophthalmic examination (visual acuity and slit lamp), within 3 weeks prior to the first dose of belantamab mafodotin, has been or will be completed

d. The ordering provider and the infusing healthcare facility is certified with, and the treated member enrolled in, the Blenrep REMS program

e. Dosage of belantamab mafodotin 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 belantamab mafodotin (Blenrep) **meets the definition of medical necessity** when **ALL** of the following criteria are met ("1" to "4"):

1. An authorization or reauthorization for belantamab mafodotin 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 member is receiving regularly scheduled ophthalmic examinations (visual acuity and slit lamp) occurring at least 1 week after the previous dose and within 2 weeks prior to the next dose
3. The ordering provider and the infusing healthcare facility is certified with, and the treated member enrolled in, the Blenrep REMS program
4. **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. Belantamab mafodotin 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 belantamab mafodotin does not exceed 2.5 mg/kg (based on actual body weight) every 3 weeks.
        iii. Provider attestation that the member has not had disease progression during belantamab mafodotin treatment
    b. Other FDA-approved or NCCN-supported diagnosis, and **ALL** of the following ("i", "ii", and "iii"):
        i. Dosage of belantamab mafodotin 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. Belantamab mafodotin 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 belantamab mafodotin

Approval duration: 1 year

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

- Treatment of adults with relapsed or refractory multiple myeloma who have received at least 4 prior therapies, including an anti-CD38 monoclonal antibody, a proteasome inhibitor, and an immunomodulatory agent. This indication is approved under accelerated approval based on response rate, and continued approval may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).
- The recommended dosage is 2.5 mg/kg of actual body weight given as an intravenous infusion over approximately 30 minutes once every 3 weeks until disease progression or unacceptable toxicity.

Dose Adjustments

- Adverse Drug Reactions - the recommended dose reduction for adverse reactions is 1.9 mg/kg once every 3 weeks. Discontinue in patients who are unable to tolerate a dose of 1.9 mg/kg. Refer to the product labeling for the specific recommendations for the different adverse reactions.
- Hepatic Impairment – No dosage adjustment is necessary in patients with mild hepatic impairment (total bilirubin level of the upper limit of normal (ULN) or less and an AST level greater than the ULN OR total bilirubin level of 1 to 1.5 times the ULN and any AST level). Specific guidelines for dosage adjustments in moderate to severe hepatic impairment (total bilirubin level greater than 1.5 times the ULN and any AST level) are not available; it appears that no dosage adjustments are needed.
- Renal Impairment - No dosage adjustment is necessary in patients with mild or moderate renal impairment (estimated glomerular filtration rate (eGFR) of 30 to 89 mL/min/1.73 m^2). Specific guidelines for dosage adjustments in severe renal impairment (eGFR of 15 to 29 mL/min/1.73 m^2) or end-stage renal disease (eGFR of less than 15 mL/min/1.73 m^2) with or without dialysis are not available; it appears that no dosage adjustments are needed.

Drug Availability

- 100-mg single-dose vial as a sterile, preservative-free, white to yellow lyophilized powder for reconstitution.
- Store vials refrigerated at 36ºF to 46ºF (2ºC to 8ºC).

PRECAUTIONS:

Boxed Warning

- WARNING: OCULAR TOXICITY
    - 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.

- Conduct ophthalmic exams at baseline, prior to each dose, and promptly for worsening symptoms. Withhold Blenrep until improvement and resume, or permanently discontinue, based on severity.
- Because of the risk of ocular toxicity, Blenrep is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the BLENREP REMS.

Contraindications

- None

Precautions/Warnings

- **Ocular Toxicity:** Ocular adverse reactions occurred in 77% of the 218 patients in the pooled safety population. Ocular adverse reactions included keratopathy (76%), changes in visual acuity (55%), blurred vision (27%), and dry eye (19%). Among patients with keratopathy (n = 165), 49% had ocular symptoms, 65% had clinically relevant visual acuity changes (decline of 2 or more lines on Snellen Visual Acuity in any eye), and 34% had both ocular symptoms and visual acuity changes. Conduct ophthalmic examinations (visual acuity and slit lamp) at baseline, prior to each dose, and promptly for worsening symptoms. Perform baseline examinations within 3 weeks prior to the first dose. Perform each follow-up examination at least 1 week after the previous dose and within 2 weeks prior to the next dose. Withhold belantamab mafodotin until improvement and resume at same or reduced dose, or consider permanently discontinuing based on severity. Advise patients to use preservative-free lubricant eye drops at least 4 times a day starting with the first infusion and continuing until end of treatment. Avoid use of contact lenses unless directed by an ophthalmologist. Changes in visual acuity may be associated with difficulty for driving and reading. Advise patients to use caution when driving or operating machinery.
- **Blenrep REMS**: Blenrep is available only through a restricted program under a REMS called the BLENREP REMS because of the risks of ocular toxicity. Notable requirements of the BLENREP REMS include the following:
  - Prescribers must be certified with the program by enrolling and completing training in the BLENREP REMS.
  - Prescribers must counsel patients receiving belantamab mafodotin about the risk of ocular toxicity and the need for ophthalmic examinations prior to each dose.
  - Patients must be enrolled in the BLENREP REMS and comply with monitoring.
  - Healthcare facilities must be certified with the program and verify that patients are authorized to receive belantamab mafodotin.
  - Wholesalers and distributers must only distribute belantamab mafodotin to certified healthcare facilities.

  Further information is available, at www.BLENREPREMS.com and 1-855-209-9188.
- **Thrombocytopenia**: Thrombocytopenia occurred in 69% of 218 patients in the pooled safety population, including Grade 2 in 13%, Grade 3 in 10%, and Grade 4 in 17%. The median time to onset of the first thrombocytopenic event was 26.5 days. Thrombocytopenia resulted in dose reduction, dose interruption, or discontinuation in 9%, 2.8%, and 0.5% of patients, respectively. Grade 3 to 4 bleeding events occurred in 6% of patients, including Grade 4 in 1 patient. Fatal adverse reactions included cerebral hemorrhage in 2 patients. Perform complete blood cell counts at baseline and during treatment as clinically indicated. Consider withholding and/or reducing the dose based on severity.

- **Infusion-Related Reactions**: Infusion-related reactions occurred in 18% of 218 patients in the pooled safety population, including Grade 3 in 1.8%. Monitor patients for infusion-related reactions. For Grade 2 or 3 reactions, interrupt the infusion and provide supportive treatment. Once symptoms resolve, resume at a lower infusion rate. Administer premedication for all subsequent infusions. Discontinue belantamab mafodotin for life-threatening infusion-related reactions and provide appropriate emergency care.
- **Embryo-Fetal Toxicity**: Based on its mechanism of action, belantamab mafodotin can cause fetal harm when administered to a pregnant woman because it contains a genotoxic compound (the microtubule inhibitor, monomethyl auristatin F [MMAF]) and it targets actively dividing cells. Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with belantamab mafodotin and for 4 months after the last dose. Advise males with female partners of reproductive potential to use effective contraception during treatment with belantamab mafodotin and for 6 months after the last dose.

BILLING/CODING INFORMATION:

The following codes may be used to describe:

HCPCS Coding

J9037	Injection, belantamab mafodontin-blmf, 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: BCBSF 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 guideline creation.

DEFINITIONS:

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
Bortezomib Injection, 09-J0000-92
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
Isatuximab (Sarclisa) Injection, 09-J3000-67
Ixazomib (Ninlaro), 09-J2000-51
Oral Oncology Medications, 09-J3000-65
Thalidomide (Thalomid) Capsules, 09-J1000-56

OTHER:

None

REFERENCES:

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4. GSK.Press Releases. GSK provides an update on Blenrep (belantamab mafodotin-blmf) US marketing authorization. Accessed 5/8/23 at: https://www.gsk.com/en-gb/media/press-releases/gsk-provides-update-on-blenrep-us-marketing-authorisation/.
5. 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 Oncol 2020;21(2):207-221.
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8. National Comprehensive Cancer Network. Cancer Guidelines. Cancer Guidelines and Drugs and Biologics Compendium. Accessed 5/16/22.
9. National Comprehensive Cancer Network. Clinical Practice Guidelines in Oncology. Version 5.2022 – March 9, 2022. Multiple Myeloma. Available at http://www.nccn.org/professionals/physician_gls/PDF/myeloma.pdf. Accessed 5/16/22.

COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 06/14/23.

GUIDELINE UPDATE INFORMATION:

11/15/20	New Medical Coverage Guideline.
01/01/21	Revision: Added HCPCS code C9069.
04/01/21	Revision: Added HCPCS code J9037 and deleted codes C9069 and J9999.
07/15/21	Review and revision including updates to the description section, position statement, related guidelines, and references.
07/15/22	Review and revision of guideline including updates to the description section and references.
07/15/23	MCG retired as Blenrep is no longer available in the US.