Written By: Jordan Snyder, PharmD, BCOP
Institution: The University of Kansas Health System

Belantamab Mafodotin (Blenrep) for the Management of Multiple Myeloma

Description: This document provides guidance on the safe use, monitoring, and adverse event management associated with belantamab mafodotin (Blenrep) in relapsed/refractory multiple myeloma.

Background: Belantamab mafodotin (Blenrep) is an antibody drug conjugate targeting B-cell maturation antigen (BCMA) on plasma cells. Upon binding to BCMA, belantamab mafodotin is internalized and the cytotoxic moiety (cys-mcMMAF) is released, disrupting the microtubule network and leading to cell cycle arrest and apoptosis.[1]

FDA-approved Indication:

- Treatment of relapsed/refractory multiple myeloma following at least 2 prior lines of therapy including a proteasome inhibitor and an immunomodulatory agent
    - Used in combination with bortezomib and dexamethasone

Common adverse reactions (≥ 10%)[1,2]

- Boxed Warning: Ocular Toxicity
- Eye disorders: reduction in BCVA, corneal changes, blurred vision, dry eye, photophobia, foreign body sensation in eyes, eye irritation, eye pain, cataracts, visual impairment
    - Median time to onset of ophthalmic exam findings: 43 days (range: 15-611 days)
    - Median duration of ophthalmic exam findings: 85 days (range: 5-813 days)
- Infections: upper respiratory tract infection, pneumonia, COVID-19
- Laboratory changes: thrombocytopenia, neutropenia, anemia, leukopenia, increased AST/ALT, increased GGT, increased creatinine, increased creatine phosphokinase
- Other: hepatotoxicity, diarrhea, nausea, fatigue, pyrexia
    - Infusion-related reactions (< 10%; 3% in DREAMM-7 trial[2])

PQI Process:

- Dosing and Dosing Modifications[1,2]:
    - Cycles 1-8 (21-day cycles):
        - Belantamab mafodotin 2.5 mg/kg IV over 30 minutes on day 1
        - Bortezomib 1.3 mg/m^2 SQ on days 1, 4, 8, 11* *(see note below)*
        - Dexamethasone 20 mg on days 1, 2, 4, 5, 8, 9, 11, 12
    - Cycles 9+ (21-day cycles):
        - Belantamab mafodotin 2.5 mg/kg IV over 30 minutes on day 1
    - Hepatic impairment – no dose adjustment for mild impairment; effects in moderate or severe impairment are unknown
    - Renal impairment - no clinically significant pharmacokinetic differences observed

Dose adjustments for toxicity[1]:

Dose level	Belantamab Dose
Reduced Dosage Level 1	1.9 mg/kg every 3 weeks
Reduced Dosage Level 2^	1.9 mg/kg every 8 weeks

^Specific to dose reductions due to ocular toxicity based on ophthalmic exam

**In clinical practice, some institutions may administer bortezomib once weekly and dexamethasone only on bortezomib dosing days. Note: This differs from the regimen studied in DREAMM-7[2] and is not included in the Prescribing Information.*

Dose modifications for Ocular Toxicity[1]:

Severity	Recommended Dose Modification
Grade 1	Continue treatment at current dosage
Grade 2	Withhold belantamab mafodotin until improvement to grade 1 or less. Resume treatment at reduced dose level 1. If recurrent grade 2 or 3 ocular toxicity, resume treatment at reduced dosage level 2
Grade 3	
Grade 4	Consider permanent discontinuation. If continuing, withhold until improvement to grade 1 or less. For patients previously on 2.5 mg/kg every 3 weeks, resume treatment at reduced dosage level 1. For patients previously on 1.9 mg/kg every 3 weeks, resume treatment at reduced dosage level 2. If recurrent grade 4 ocular toxicity, permanently discontinue

- Supportive Care[1]:
  - Preservative-free artificial tears should be administered at least 4 times per day beginning with first infusion and continuing until end of treatment
- Monitoring[1]:
  - Monitor CBC at baseline and periodically throughout treatment as clinically indicated
  - Ophthalmic exams (including slit lamp exam and BCVA assessment) should be conducted by an eye care professional (ophthalmologist or optometrist) at baseline, before each dose, and promptly for new or worsening symptoms, and as clinically indicated
- Blenrep REMS[3-5]
  - Belantamab mafodotin is only available via the Blenrep REMS due to the risk of ocular toxicity
  - Belantamab mafodotin should not be distributed, transferred, loaned, or sold except to REMS-certified healthcare settings
  - Prescribers and healthcare settings must be certified and patients enrolled in the Blenrep REMS prior to belantamab mafodotin administration
  - Key requirements of prescribers:
    - Review Blenrep prescribing information, REMS materials, and Education program for prescribers
    - Complete and submit knowledge assessment and enrollment form
    - Counsel patients on risk of ocular toxicity and frequency of ophthalmic exams
    - Enroll patient into Blenrep REMS
    - Assess patient's ophthalmic exam prior to initiation and before each treatment to ensure appropriateness for treatment.
      - Eye exam should be completed within 28 days of the first dose and within 10 days of subsequent doses.
      - Document and submit using the Patient Status Form
    - A designee may be assigned to assist with patient enrollment and other administrative tasks

- Key requirements of patients:
  - Review the Patient Guide and enroll in the Blenrep REMS
  - Receive counseling on risk of ocular toxicity and the need for eye exams prior to each dose
  - Inform healthcare provider right away of any new or worsening eye symptoms or vision changes
- Key requirements of the healthcare system:
  - Designate an authorized representative to carry out certification process and oversee implementation/compliance
    - Authorized representative may be a: pharmacist, physician, nurse, nurse practitioner, director of healthcare setting, physician assistant, or any responsible individual in the healthcare setting
  - Complete enrollment for the healthcare system
  - Train all relevant staff involved in dispensing of belantamab
  - Report the healthcare setting, prescriber, and patient information (that is, number of vials to be dispensed, dosage to be administered, and date of infusion) to the REMS
  - Obtain authorization to dispense each dose by contacting the REMS to verify the prescriber is certified, the healthcare setting is setting is certified, and the patient is enrolled and authorized to receive the drug by using the online REMS portal or by calling the REMS at 1-855-690-9572
  - Comply with audits to ensure that all training, processes and procedures are in place and being followed
- Eye care professionals (ECP) within the area can be identified via the ECP Locator Tool on the Blenrep patient website
  - GSK Eyecare Education Specialists are available to educate local ophthalmologists and optometrists on the required eye exams. Clinicians may contact their GSK representative to request this support.

Patient-Centered Activities[1,6]**:**

- Counsel on risks of ocular toxicities and need for routine ophthalmic exams.
- Patients should promptly alert the healthcare provider for any new or worsening ocular symptoms
- Patients should use preservative-free artificial tears at least 4 times daily beginning with the first infusion and continuing until the end of treatment
  - Preservative-free artificial tears may be available at no cost through Together with Blenrep patient assistance program
- Avoid wearing contact lenses for the duration of therapy. Bandage contact lenses may be used under the direction of an eye care professional
- Counsel to use caution while driving or operating machinery, as decreased visual acuity may be associated with difficulty driving or reading
- Monitor for infusion-related reactions throughout the infusion. Report any side effects to the healthcare team
- Verify pregnancy status before initiation. Use effective contraception throughout treatment and for 4 months after the last dose in females of reproductive potential. In males with female partners of reproductive potential, use effective contraception during treatment and for 6 months after the last dose
  - Locating trained eye care professionals, co-pay assistance, and other patient resources are available through Together with Blenrep Patient assistance program

References:
1. Blenrep (Belantamab Mafodotin). Package Insert. GlaxoSmithKline LLC; 2025.
2. Hungria V, Robak P, Hus M, et al. Belantamab Mafodotin, Bortezomib, and Dexamethasone for Multiple Myeloma. *N Engl J Med* 2024'391:393-407. DOI: 10.1056/NEJMoa2405090.
3. BLENREP REMS. https://www.blenreprems.com/. Accessed 2/16/2026.
4. BLENREP Risk Evaluation and Mitigation Strategy (REMS) Program Overview. Accessed 2/16/2026.
5. BLENREP Risk Evaluation and Mitigation Strategy (REMS) Education Program for Healthcare Settings. Accessed 2/16/2026.
6. Together with BLENREP. https://www.togetherwithgsk.com/blenrep/patient/. Accessed 2/16/2026.

Supplemental Information:

Ophthalmic Exam Grading:

Severity	Ophthalmic Exam Findings
Grade 1	Corneal Exam Findings: Mild superficial punctate keratopathy and/or Change in BCVA: Decline from baseline of 1 line on Snellen Equivalent BCVA
Grade 2	Corneal Exam Findings: Moderate superficial punctate keratopathy, patchy microcyst-like deposits, peripheral sub-epithelial haze, or a new peripheral stromal opacity and/or Change in BCVA: Decline from baseline of 2 lines on Snellen Equivalent BCVA and not worse that 20/200
Grade 3	Corneal Exam Findings: Severe superficial punctate keratopathy, diffuse microcyst-like deposits involving the central cornea, central sub-epithelial haze, or new central stromal opacity and/or Change in BCVA: Decline from baseline of 3 or more lines on Snellen Equivalent BCVA and not worse than 20/200
Grade 4	Corneal Exam Findings: Corneal epithelial defect or corneal ulcer, with or without infection and/or Change in BCVA: Decline to Snellen Equivalent BCVA of worse than 20/200

Dose Adjustments for Other Adverse Reactions:

Adverse Reaction	Severity	Recommended Dose Modification
Thrombocytopenia	Platelet count between 25,000/mcL and 50,000/mcL without bleeding	• For patients on 2.5 mg/kg, reduce to reduced dosage level 1 • For patients on 1.9 mg/kg continue at same dosage
	Platelet count between 25,000/mcL and 50,000/mcL with bleeding	• Withhold until bleeding resolves • For patients on 2.5 mg/kg, reduce to reduced dosage level 1 • For patients on 1.9 mg/kg continue at same dosage
	Platelet count less than 25,000/mcL	• Withhold until platelet count recovers to 25,000/mcL or higher • For patients on 2.5 mg/kg, reduce to reduced dosage level 1 • For patients on 1.9 mg/kg continue at same dosage
Infusion-Related Reactions	Grade 2	• Interrupt infusion and provide supportive care. Once symptoms resolve to grade 1 or less, resume infusion at 50% of initial rate. Consider pre-medication with subsequent infusions.

	Grade 3	• Interrupt infusion and provide supportive care. Once symptoms resolve to grade 1 or less, resume infusion at 50% of initial rate. Administer pre-medication with subsequent infusions.
	Grade 4	• Permanently discontinue. If anaphylactic or life-threatening, institute appropriate emergency care.
Other Adverse Reactions	Grade 3	• Withhold until adverse reaction resolves to grade 1 or less • For patients on 2.5 mg/kg, reduce to reduced dosage level 1 • For patients on 1.9 mg/kg continue at same dosage

	Grade 4	• Consider permanent discontinuation
		• If continuing, withhold until adverse reaction resolves to grade 1 or less
		  ○ For patients on 2.5 mg/kg, reduce to reduced dosage level 1
		  ○ For patients on 1.9 mg/kg continue at same dosage