

# **BLNREP- belantamab mafodotin injection, powder, for solution**

## **GlaxoSmithKline LLC**

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### **HIGHLIGHTS OF PRESCRIBING INFORMATION**

These highlights do not include all the information needed to use BLNREP safely and effectively. See full prescribing information for BLNREP.

**BLNREP (belantamab mafodotin-blmf) for injection, for intravenous use**

Initial U.S. Approval: 2020

#### **WARNING: OCULAR TOXICITY**

*See full prescribing information for complete boxed warning.*

- **BLNREP causes changes in the corneal epithelium resulting in changes in vision, including severe visual impairment, and symptoms such as blurred vision and dry eyes. In the clinical study, corneal ulcers, including cases with infection, also occurred. (5.1)**
- **Conduct ophthalmic exams at baseline, before each dose, promptly for new or worsening symptoms, and as clinically indicated. In the clinical study, 83% of patients required a dosage modification due to ocular toxicity. Withhold BLNREP until improvement and resume or permanently discontinue, based on severity. (2.3, 5.1)**
- **BLNREP is available only through a restricted program, called the BLNREP Risk Evaluation and Mitigation Strategy (REMS). (5.2)**

#### **INDICATIONS AND USAGE**

BLNREP, a B-cell maturation antigen (BCMA)-directed antibody and microtubule inhibitor conjugate, is indicated in combination with bortezomib and dexamethasone for the treatment of adult patients with relapsed or refractory multiple myeloma who have received at least two prior lines of therapy, including a proteasome inhibitor and an immunomodulatory agent. (1)

#### **DOSAGE AND ADMINISTRATION**

- The recommended dosage of BLNREP, in combination with bortezomib and dexamethasone, is 2.5 mg/kg as an intravenous infusion over 30 minutes once every 3 weeks for 8 cycles, followed by BLNREP 2.5 mg/kg every 3 weeks as a single agent. (2.2)
- See Full Prescribing Information for instructions on preparation and administration. (2.4)

#### **DOSAGE FORMS AND STRENGTHS**

For injection: 70 mg as a lyophilized powder in a single-dose vial for reconstitution and further dilution. (3)

#### **CONTRAINDICATIONS**

None. (4)

#### **WARNINGS AND PRECAUTIONS**

- **Thrombocytopenia:** Monitor complete blood counts at baseline and periodically during treatment. Withhold or reduce the dosage based on severity. (2.3, 5.3)
- **Embryo-fetal Toxicity:** Can cause fetal harm. Advise patients of the potential risk to fetus and to use effective contraception. (5.4, 8.1, 8.3)

#### **ADVERSE REACTIONS**

The most common adverse reactions ( $\geq 20\%$ ) with BLNREP in combination with bortezomib and dexamethasone are reduction in best-corrected visual acuity (BCVA), corneal exam findings, blurred vision, dry eye, photophobia, foreign body sensation in eyes, eye irritation, upper respiratory tract infection, hepatotoxicity, eye pain, diarrhea, fatigue, pneumonia, cataract, and COVID-19. The most common Grade 3 or 4 ( $\geq 10\%$ ) laboratory abnormalities are decreased platelets, decreased lymphocytes, decreased neutrophils, increased gamma-glutamyl transferase, decreased white blood cells, and decreased hemoglobin. (6.1)

**To report SUSPECTED ADVERSE REACTIONS, contact GlaxoSmithKline at 1-888-825-5249 or**

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**FULL PRESCRIBING INFORMATION: CONTENTS\***

**WARNING: OCULAR TOXICITY**

**1 INDICATIONS AND USAGE**

**2 DOSAGE AND ADMINISTRATION**

- 2.1 Important Safety Information
- 2.2 Recommended Dosage
- 2.3 Dosage Modifications for Adverse Reactions
- 2.4 Preparation and Administration

**3 DOSAGE FORMS AND STRENGTHS**

**4 CONTRAINDICATIONS**

**5 WARNINGS AND PRECAUTIONS**

- 5.1 Ocular Toxicity
- 5.2 BLENREP Risk Evaluation and Mitigation Strategy (REMS)
- 5.3 Thrombocytopenia
- 5.4 Embryo-fetal Toxicity

**6 ADVERSE REACTIONS**

- 6.1 Clinical Trials Experience

**8 USE IN SPECIFIC POPULATIONS**

- 8.1 Pregnancy
- 8.2 Lactation
- 8.3 Females and Males of Reproductive Potential
- 8.4 Pediatric Use
- 8.5 Geriatric Use
- 8.6 Hepatic Impairment

**11 DESCRIPTION**

**12 CLINICAL PHARMACOLOGY**

- 12.1 Mechanism of Action
- 12.2 Pharmacodynamics
- 12.3 Pharmacokinetics
- 12.6 Immunogenicity

**13 NONCLINICAL TOXICOLOGY**

- 13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

**14 CLINICAL STUDIES**

**15 REFERENCES**

**16 HOW SUPPLIED/STORAGE AND HANDLING**

**17 PATIENT COUNSELING INFORMATION**

\* Sections or subsections omitted from the full prescribing information are not listed.

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## FULL PRESCRIBING INFORMATION

### WARNING: OCULAR TOXICITY

- **BLNREP causes changes in the corneal epithelium resulting in changes in vision, including severe visual impairment, and symptoms such as blurred vision and dry eyes. In the clinical study, corneal ulcers, including cases with infection, also occurred [see Warnings and Precautions (5.1)].**
- **Conduct ophthalmic exams at baseline, before each dose, promptly for new or worsening symptoms, and as clinically indicated. In the clinical study, 83% of patients required a dosage modification due to ocular toxicity. Withhold BLNREP until improvement and resume or permanently discontinue, based on severity [see Dosage and Administration (2.3), Warnings and Precautions (5.1)].**
- **Because of the risk of ocular toxicity, BLNREP is available only through a restricted program called the BLNREP Risk Evaluation and Mitigation Strategy (REMS) [see Warnings and Precautions (5.2)].**

## 1 INDICATIONS AND USAGE

BLNREP is indicated in combination with bortezomib and dexamethasone for the treatment of adult patients with relapsed or refractory multiple myeloma who have received at least two prior lines of therapy, including a proteasome inhibitor and an immunomodulatory agent.

## 2 DOSAGE AND ADMINISTRATION

### 2.1 Important Safety Information

Ophthalmic exams, including slit lamp exam and assessment of best-corrected visual acuity (BCVA), should be conducted by an eye care professional, such as an ophthalmologist or optometrist. Conduct ophthalmic exams at baseline, before each dose of BLNREP, promptly for new or worsening symptoms, and as clinically indicated [see Warnings and Precautions (5.1)].

Counsel patients to promptly inform their healthcare provider of any ocular symptoms. Advise patients to use preservative-free artificial tears at least 4 times a day starting with the first infusion and continuing until end of treatment, and to avoid wearing contact lenses for the duration of therapy. Bandage contact lenses may be used under the direction of an eye care professional [see Warnings and Precautions (5.1)].

### 2.2 Recommended Dosage

The recommended dosage for BLNREP is 2.5 mg/kg of actual body weight once every 3 weeks in combination with bortezomib and dexamethasone (BvD) for the first 8 cycles, followed by BLNREP 2.5 mg/kg of actual body weight once every 3 weeks as

a single agent until disease progression or unacceptable toxicity.

For dosing instructions of agents administered in combination with BLENREP, see *Clinical Studies (14)* and respective Prescribing Information, as appropriate.

BLENREP is administered as an intravenous infusion over approximately 30 minutes.

## 2.3 Dosage Modifications for Adverse Reactions

In the BVd arm of the clinical study, 98% of patients required a dosage modification for any component of treatment for an adverse reaction, including 87% who required a dosage modification of BLENREP [see *Clinical Studies (14)*]. Eighty-three percent of patients required a dosage modification of BLENREP for ocular toxicity based on ophthalmic exam findings or other ocular adverse reactions as defined by the Common Terminology Criteria for Adverse Events (CTCAE) [see *Adverse Reactions (6.1)*]. There were high rates of dosage modifications in early treatment cycles. By Cycle 3, 53% of patients had a dosage interruption or reduction, 7% had discontinued treatment, and only 40% received the planned dose of BLENREP.

The recommended dosage modifications for ocular toxicity based on ophthalmic exam findings are provided in Tables 1 and 2. Ophthalmic exam findings include both corneal exam findings and change in BCVA as assessed by an eye care professional. The overall grade of ophthalmic exam findings is based on the worst finding in the worst affected eye, based on either corneal exam finding or a change in BCVA. Corneal exam findings may or may not be accompanied by changes in BCVA or ocular symptoms.

- Do not re-escalate the dose of BLENREP after a dosage reduction is made for ocular toxicity based on ophthalmic exam findings.
- In the clinical study, 67% of patients required a dosage interruption of BLENREP for ocular toxicity that lasted longer than 3 weeks (time between doses, median: 5.7 weeks [range: 3 to 31 weeks]).

The recommended dosage modifications for other adverse reactions, including dosage modifications for ocular adverse reactions based on the CTCAE, are provided in Table 3.

**Table 1. Recommended Dosage Reductions of BLENREP for Adverse Reactions**

	<b>BLENREP</b>
<b>Reduced Dosage Level 1</b>	1.9 mg/kg every 3 weeks
<b>Reduced Dosage Level 2<sup>a</sup></b>	1.9 mg/kg every 8 weeks

<sup>a</sup> Reduced Dosage Level 2 is specific to dosage reductions due to ocular toxicity based on ophthalmic exam findings.

**Table 2. Recommended Dosage Modifications for Ocular Toxicity Based on Ophthalmic Exam Findings<sup>a</sup>**

<b>Severity</b>	<b>Ophthalmic Exam Findings</b> [see <i>Warnings and Precautions (5.1)</i> ]	<b>Recommended Dosage Modification</b>
<b>Grade 1</b>	<i>Corneal Exam Findings:</i>	Continue treatment at current dosage.

	<p>Mild superficial punctate keratopathy<sup>a</sup></p> <p>and/or</p> <p><i>Change in BCVA:</i></p> <p>Decline from baseline of 1 line on Snellen Equivalent BCVA</p>	
<b>Grade 2</b>	<p><i>Corneal Exam Findings:</i></p> <p>Moderate superficial punctate keratopathy, patchy microcyst-like deposits<sup>b</sup>, peripheral sub-epithelial haze, or a new peripheral stromal opacity</p> <p>and/or</p> <p><i>Change in BCVA:</i></p> <p>Decline from baseline of 2 lines on Snellen Equivalent BCVA and not worse than 20/200</p>	<p>Withhold BLENREP until improvement in both corneal exam findings and change in BCVA to Grade 1 or less. Resume treatment at Reduced Dosage Level 1 as per Table 1. If recurrent Grade 2 or 3 ocular toxicity is experienced, resume treatment at Reduced Dosage Level 2.</p>
<b>Grade 3</b>	<p><i>Corneal Exam Findings:</i></p> <p>Severe superficial punctate keratopathy, diffuse microcyst-like deposits<sup>b</sup> involving the central cornea, central sub-epithelial haze, or a new central stromal opacity</p> <p>and/or</p> <p><i>Change in BCVA:</i></p> <p>Decline from baseline of 3 or more lines on Snellen Equivalent BCVA and not worse than 20/200</p>	
<b>Grade 4</b>	<p><i>Corneal Exam Findings:</i></p> <p>Corneal epithelial defect or corneal ulcer, with or</p>	<p>Consider permanent discontinuation of BLENREP.</p> <p>If continuing treatment, withhold BLENREP until improvement in both</p>

	<p>without infection</p> <p>and/or</p> <p><i>Change in BCVA:</i></p> <p>Decline to Snellen Equivalent BCVA of worse than 20/200</p>	<p>corneal exam findings and change in BCVA to Grade 1 or less. For patients previously on 2.5 mg/kg every 3 weeks, resume treatment at Reduced Dosage Level 1 as per Table 1. For patients previously on 1.9 mg/kg every 3 weeks, resume treatment at Reduced Dosage Level 2.</p> <p>If recurrent Grade 4 ocular toxicity is experienced, permanently discontinue BLENREP.</p>
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BCVA = best-corrected visual acuity.

<sup>a</sup> Mild superficial keratopathy (documented worsening from baseline). Refer to Table 3 for recommended dosage modifications for other ocular adverse reactions.

<sup>b</sup> Microcyst-like deposits are considered at least a Grade 2 finding. Withhold BLENREP if any microcyst-like deposits are observed.

**Table 3. Recommended Dosage Modifications for Other Adverse Reactions<sup>a</sup>**

<b>Adverse Reaction</b>	<b>Severity</b>	<b>Recommended Dosage Modification</b>
Thrombocytopenia [see Warnings and Precautions (5.3)]	<b>Platelet count between 25,000/mcL and 50,000/mcL without bleeding</b>	For patients on 2.5 mg/kg, reduce to Reduced Dosage Level 1 as per Table 1. <sup>b</sup> For patients on 1.9 mg/kg, continue at same dosage.
	<b>Platelet count between 25,000/mcL and 50,000/mcL with bleeding</b>	Withhold BLENREP until bleeding resolves. For patients previously on 2.5 mg/kg, resume at Reduced Dosage Level 1 as per Table 1. For patients on 1.9 mg/kg, resume at same dosage.
	<b>Platelet count less than 25,000/mcL</b>	Withhold BLENREP until platelet count recovers to 25,000/mcL or higher. For patients previously on 2.5 mg/kg, resume at Reduced Dosage Level 1 as per Table 1. For patients on 1.9 mg/kg, resume at same dosage.
Infusion-related Reactions	<b>Grade 2</b>	Interrupt infusion and provide supportive care. Once symptoms resolve to Grade 1 or less, resume infusion at 50% of the initial rate prior to the event. Consider premedication for subsequent infusions.

	<b>Grade 3</b>	Interrupt infusion and provide supportive care. Once symptoms resolve to Grade 1 or less, resume at 50% of the initial rate prior to the event. Administer premedication for subsequent infusions.
	<b>Grade 4</b>	Permanently discontinue BLENREP. If anaphylactic or life-threatening infusion reaction, permanently discontinue the infusion and institute appropriate emergency care.
Other Adverse Reactions <i>[see Adverse Reactions (6.1)]</i>	<b>Grade 3</b>	Withhold BLENREP until adverse reaction improves to Grade 1 or less. For patients previously on 2.5 mg/kg, resume at Reduced Dosage Level 1 as per Table 1. For patients on 1.9 mg/kg, resume at same dosage.
	<b>Grade 4</b>	Consider permanent discontinuation of BLENREP. If continuing treatment, withhold BLENREP until adverse reaction improves to Grade 1 or less. For patients previously on 2.5 mg/kg, resume at Reduced Dosage Level 1 as per Table 1. For patients on 1.9 mg/kg, resume at same dosage.

<sup>a</sup> Adverse reactions were graded according to the Common Terminology Criteria for Adverse Events v5.0.

<sup>b</sup> Consider reverting to previous dose, if appropriate once platelet count recovers to 50,000/mcL or higher.

## 2.4 Preparation and Administration

BLENREP is a hazardous drug. Follow applicable special handling and disposal procedures.<sup>1</sup>

Calculate the dose (mg), total volume (mL) of solution required, and the number of vials of BLENREP needed based on the patient's actual body weight. More than one vial may be needed for a full dose.

### Reconstitution

- Remove the vial(s) of BLENREP from the refrigerator and allow to stand for approximately 10 minutes to reach room temperature (68°F to 77°F [20°C to 25°C]).

- Reconstitute each 70 mg vial of BLENREP with 1.4 mL of Sterile Water for Injection, USP, to obtain a final concentration of 50 mg/mL. Gently swirl the vial to aid dissolution. **Do not shake.**
- If the reconstituted solution is not used immediately, store in the original container refrigerated at 36°F to 46°F (2°C to 8°C) or at room temperature (68°F to 77°F [20°C to 25°C]) for up to 4 hours. Discard if not diluted within 4 hours. **Do not freeze.**
- Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. The reconstituted solution should be a clear to opalescent, colorless to yellow to brown liquid. Discard if extraneous particulate matter is observed.

### Dilution

- Withdraw the calculated volume of BLENREP from the appropriate number of vials and dilute in a 250 mL infusion bag of 0.9% Sodium Chloride Injection, USP, to a final concentration of 0.2 mg/mL to 2 mg/mL. The infusion bag must be made of polyvinylchloride (PVC) or polyolefin (PO).
- Mix the diluted solution by gentle inversion. **Do not shake.**
- Discard any unused reconstituted solution of BLENREP left in the vial(s).
- If the diluted infusion solution is not used immediately, store refrigerated at 36°F to 46°F (2°C to 8°C) for up to 24 hours. **Do not freeze.** Once removed from refrigeration, administer the diluted infusion solution of BLENREP within 6 hours (including infusion time).
- Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. The diluted infusion solution should be clear and colorless. Discard if particulate matter is observed.

### Administration

- If refrigerated, allow the diluted infusion solution to equilibrate to room temperature (68°F to 77°F [20°C to 25°C]) prior to administration. Diluted infusion solution may be kept at room temperature for no more than 6 hours (including infusion time).
- Administer by intravenous infusion over approximately 30 minutes using an infusion set made of PVC or PO.
- Filtration of the diluted solution is not required; however, if the diluted solution is filtered, use a polyethersulfone (PES)-based filter (0.2 micron).

Do not mix or administer BLENREP with other products. The product does not contain a preservative.

## **3 DOSAGE FORMS AND STRENGTHS**

For injection: 70 mg of belantamab mafodotin-blmf as a white to yellow lyophilized powder in a single-dose vial for reconstitution and further dilution.

## **4 CONTRAINDICATIONS**

None.



## 5 WARNINGS AND PRECAUTIONS

### 5.1 Ocular Toxicity

BLNREP causes ocular toxicity, defined as changes in the corneal epithelium and changes in BCVA based on ophthalmic exam (including slit lamp exam), or other ocular adverse reactions as defined by the CTCAE [see *Adverse Reactions (6.1)*].

In DREAMM-7, ocular toxicity occurred in 92% of patients, including Grade 3 or 4 in 77% of patients. The most common ocular toxicities (>25%) were reduction in BCVA (89%) and corneal exam findings (86%) based on ophthalmic exam findings, blurred vision (66%), dry eye (51%), photophobia (47%), foreign body sensation in eyes (44%), eye irritation (43%), and eye pain (33%) [see *Adverse Reactions (6.1)*].

Ocular toxicity based on ophthalmic exam findings was reported as Grade 2 in 9% of patients, Grade 3 in 56% of patients, and Grade 4 in 21% of patients. The median time to onset of the first Grade 2 to 4 ophthalmic exam findings was 43 days (range: 15 to 611 days). The median duration of all Grade 2 to 4 ophthalmic exam findings was 85 days (range: 5 to 813 days). Patients experienced a median of 3 episodes (range: 1 to 11 episodes) of ocular toxicity based on ophthalmic exam findings. Of the patients with Grade 2 to 4 ophthalmic exam findings, 42% had improvement of the last event to Grade 1 or better; 22% had resolution of the last event based on return to baseline or normal ophthalmic exam findings.

The most commonly reported corneal exam findings included superficial punctate keratopathy, microcyst-like deposits, epithelial changes, and haze. Cases of corneal ulcer, including cases with infection, have been reported and should be managed promptly by an eye care professional [see *Adverse Reactions (6.1)*].

A reduction in BCVA to 20/50 or worse in at least one eye occurred in 69% of patients, including 29% who experienced a change in BCVA to 20/100 or worse, and 12% who experienced a change in BCVA to 20/200 or worse. Of the patients with reduced BCVA to 20/50 or worse in at least one eye, 61% had resolution of the last event to baseline or better. Of the patients with reduced BCVA to 20/100 or worse, 57% had resolution of the last event. Of the patients with reduced BCVA to 20/200 or worse, 48% had resolution of the last event.

Ophthalmic exams (including slit lamp exam and BCVA assessment) should be conducted by an eye care professional, such as an ophthalmologist or optometrist, at baseline, before each dose of BLNREP, promptly for new or worsening symptoms, and as clinically indicated. Perform baseline exam within 4 weeks prior to the first dose. Perform each follow-up exam within 10 days prior to the next planned dose. All effort should be made to schedule the exam as close to BLNREP dosing as possible. Withhold BLNREP until improvement in both corneal exam findings and change in BCVA to Grade 1 or less and resume at same or reduced dose or permanently discontinue based on severity [see *Dosage and Administration (2.1, 2.3)*].

Counsel patients to promptly inform their healthcare provider of any ocular symptoms. Counsel patients to use preservative-free artificial tears at least 4 times a day starting with the first infusion and continuing until the end of treatment, and to avoid wearing contact lenses for the duration of therapy. Bandage contact lenses may be used under the direction of an eye care professional [see *Dosage and Administration (2.1)*].

Changes in visual acuity may be associated with difficulty for driving and reading. Counsel patients to use caution when driving or operating machinery.

BLNREP is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) [see *Warnings and Precautions* (5.2)].

## **5.2 BLNREP Risk Evaluation and Mitigation Strategy (REMS)**

BLNREP is available only through a restricted program called the BLNREP REMS because of the risk of ocular toxicity [see *Warnings and Precautions* (5.1)].

Notable requirements of the BLNREP REMS include the following:

- Prescribers must be certified in the BLNREP REMS by enrolling and completing training.
- Prescribers must counsel patients receiving BLNREP on the risk of ocular toxicity, the need for monitoring via ophthalmic exams before each dose, and provide patients with the BLNREP REMS Patient Guide.
- Patients must be enrolled in the BLNREP REMS and adhere to monitoring.
- Healthcare settings that dispense BLNREP must be certified in the BLNREP REMS by enrolling and must obtain authorization prior to dispensing.
- Wholesalers and distributors must distribute BLNREP only to certified healthcare settings.

Further information is available at [www.BLNREPREMS.com](http://www.BLNREPREMS.com) and 1-855-690-9572.

## **5.3 Thrombocytopenia**

Thrombocytopenia of any grade occurred in 100% of patients in DREAMM-7 [see *Adverse Reactions* (6.1)].

Grade 2 thrombocytopenia occurred in 10% of patients, Grade 3 in 29% of patients, and Grade 4 in 45% of patients. Clinically significant bleeding (Grade  $\geq 2$ ) occurred in 7% of patients with concomitant low platelet levels (Grade 3 or 4).

Monitor complete blood cell counts at baseline and periodically during treatment as clinically indicated. Withhold or reduce the dose of BLNREP based on severity [see *Dosage and Administration* (2.3)].

## **5.4 Embryo-fetal Toxicity**

Based on its mechanism of action, BLNREP 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 BLNREP and for 4 months after the last dose. Advise males with female partners of reproductive potential to use effective contraception during treatment with BLNREP and for 6 months after the last dose [see *Use in Specific Populations* (8.1, 8.3)].

## **6 ADVERSE REACTIONS**

The following clinically significant adverse reactions are described elsewhere in the

labeling:

- Ocular Toxicity [see *Warnings and Precautions (5.1)*]
- Thrombocytopenia [see *Warnings and Precautions (5.3)*]

## 6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared with rates in the clinical trials of another drug and may not reflect the rates observed in practice.

### Relapsed or Refractory Multiple Myeloma in Combination with Bortezomib and Dexamethasone

The safety of BLENREP with bortezomib and dexamethasone (n = 242) compared with daratumumab with bortezomib and dexamethasone (n = 246) was evaluated in DREAMM-7 in patients with relapsed or refractory multiple myeloma who received at least one prior line of therapy [see *Clinical Studies (14)*]. Patients received BLENREP 2.5 mg/kg of actual body weight once every 3 weeks in combination with bortezomib and dexamethasone (BVd) for the first 8 cycles, followed by BLENREP as a single agent or daratumumab in combination with bortezomib and dexamethasone (DVd) for the first 8 cycles, followed by daratumumab as a single agent. Among patients who received BLENREP, 69% were exposed for 6 months or longer and 55% were exposed for greater than one year. The safety of BLENREP in combination with bortezomib and dexamethasone in patients who received only one prior line of therapy (n = 125) has not been established.

Serious adverse reactions occurred in 50% of patients who received BVd. Serious adverse reactions in  $\geq 2\%$  of patients included pneumonia (18%), pyrexia (5%), thrombocytopenia (5%), COVID-19 (5%), upper respiratory tract infection (4%), sepsis (4%), second primary malignancy (3%), and anemia (2%). Fatal adverse reactions occurred in 10% of patients who received BVd. Fatal adverse reactions which occurred in  $>1$  patient included pneumonia (4%), sepsis (2%), COVID-19 (1%), respiratory failure ( $<1\%$ ), and intracranial hemorrhage ( $<1\%$ ).

Permanent discontinuation of BLENREP due to an adverse reaction occurred in 17% of patients. Adverse reactions which resulted in permanent discontinuation of BLENREP in  $\geq 3\%$  of patients included ocular toxicity (9%) and pneumonia (4%).

Dosage interruptions of BLENREP due to an adverse reaction occurred in 78% of patients. Adverse reactions which required dosage interruption of BLENREP in  $\geq 3\%$  of patients included ocular toxicity based on ophthalmic exam findings (74%), blurred vision (32%), upper respiratory tract infection (20%), dry eye (14%), photophobia (14%), pneumonia (14%), eye irritation (13%), COVID-19 (12%), foreign body sensation in eyes (12%), eye pain (10%), thrombocytopenia (9%), visual impairment (7%), cataract (5%), diarrhea (4%), and neutropenia (4%).

Dosage reductions of BLENREP due to an adverse reaction occurred in 36% of patients. Adverse reactions which required dosage reductions for BLENREP in  $\geq 3\%$  of patients included ocular toxicity based on ophthalmic exam findings (30%), thrombocytopenia (14%), and blurred vision (10%).

The most common adverse reactions ( $\geq 20\%$ ) were reduction in BCVA, corneal exam findings, blurred vision, dry eye, photophobia, foreign body sensation in eyes, eye

irritation, upper respiratory tract infection, hepatotoxicity, eye pain, diarrhea, fatigue, pneumonia, cataract, and COVID-19. The most common Grade 3 or 4 laboratory abnormalities ( $\geq 10\%$ ) were decreased platelets, decreased lymphocytes, decreased neutrophils, increased gamma glutamyltransferase, decreased white blood cells, and decreased hemoglobin.

Table 4 summarizes the adverse reactions in DREAMM-7.

**Table 4. Adverse Reactions ( $\geq 10\%$ ) in Patients with Relapsed or Refractory Multiple Myeloma Who Received BLENREP in DREAMM-7**

Adverse Reaction <sup>a</sup>	BLENREP + Bortezomib and Dexamethasone N = 242		Daratumumab + Bortezomib and Dexamethasone N = 246	
	All Grades (%)	Grades 3-4 (%)	All Grades (%)	Grades 3-4 (%)
<b>Eye disorders</b>				
Reduction in BCVA <sup>b</sup>	89	57	44	9
Corneal exam findings <sup>b</sup>	86	72	19	3
Blurred vision	66	22	11	0.8
Dry eye <sup>c</sup>	51	7	7	0
Photophobia	47	2	2	0
Foreign body sensation in eyes <sup>c</sup>	44	3	4	0
Eye irritation	43	5	5	0
Eye pain <sup>c</sup>	33	0.8	4	0.4
Cataract <sup>c</sup>	24	8	14	3
Visual impairment	11	5	2	0.4
<b>Gastrointestinal disorders</b>				
Diarrhea	32	4	31	4
Nausea	16	0.8	12	0
<b>Infections</b>				
Upper respiratory tract infection <sup>c,d</sup>	38	2	36	2
Pneumonia <sup>c,d</sup>	26	16	17	5
COVID-19 <sup>d</sup>	24	5	20	2
<b>Hepatobiliary disorders</b>				

Hepatotoxicity <sup>c</sup>	33	14	16	2
<b>General disorders and administration site conditions</b>				
Fatigue <sup>c</sup>	26	6	27	4
Pyrexia <sup>c,d</sup>	19	0.4	11	2

BCVA = best-corrected visual acuity; BVd = BLENREP + bortezomib and dexamethasone; DVd = daratumumab + bortezomib and dexamethasone.

<sup>a</sup> Adverse reactions, except ophthalmic exam findings, were graded according to Common Terminology Criteria for Adverse Events v5.0.

<sup>b</sup> Based on ophthalmic exam findings.

<sup>c</sup> Grouped term includes other related terms.

<sup>d</sup> Includes the following fatal adverse reactions: BVd: pneumonia (n = 10), COVID-19 (n = 3), upper respiratory tract infection (n = 1); DVd: pneumonia (n = 7), COVID-19 (n = 5), pyrexia (n = 1).

Clinically relevant adverse reactions in <10% of patients who received BVd included: increased lacrimation, vomiting, diplopia, albuminuria, sepsis, eye pruritus, infusion-related reactions, corneal ulcer (including cases with infection), and pneumonitis.

Table 5 summarizes the laboratory abnormalities in DREAMM-7.

**Table 5. Select Laboratory Abnormalities (>10%) That Worsened from Baseline in Patients with Relapsed or Refractory Multiple Myeloma Who Received BLENREP in DREAMM-7**

<b>Laboratory Abnormality</b>	<b>BLENREP + Bortezomib and Dexamethasone<sup>a</sup></b>		<b>Daratumumab + Bortezomib and Dexamethasone<sup>a</sup></b>	
	<b>All Grades (%)</b>	<b>Grades 3-4 (%)</b>	<b>All Grades (%)</b>	<b>Grades 3-4 (%)</b>
<b>Hematology</b>				
Platelets decreased	100	74	88	48
Lymphocytes decreased	90	53	92	56
Leukocytes decreased	59	11	67	17
Neutrophils decreased	52	17	53	13
Hemoglobin decreased	51	10	60	12
<b>Chemistry</b>				
Aspartate aminotransferase increased	88	5	40	0
Gamma glutamyltransferase increased	73	15	44	3

Alanine aminotransferase increased	71	5	54	1
Creatinine increased	51	2	53	<1
Creatine phosphokinase increased	48	3	31	3

BVd = BLENREP + bortezomib and dexamethasone; DVd = daratumumab + bortezomib and dexamethasone.

<sup>a</sup> The denominator used to calculate the rate varied from 238 to 241 (BVd) and 243 to 246 (DVd) based on the number of patients with a baseline value and at least one post-treatment value.

Patient-reported ocular symptoms were assessed using the Patient-Reported Outcomes Common Terminology Criteria for Adverse Events (PRO-CTCAE) and Ocular Surface Disease Index (OSDI).

PRO-CTCAE assessments were collected at baseline and then every 3 weeks until treatment discontinuation. Completion rates in both arms were  $\geq 90\%$  at baseline and  $\geq 81\%$  at subsequent timepoints where  $>50\%$  of patients remained on treatment. OSDI assessments were collected every 3 weeks until the 6<sup>th</sup> dose and then every 6 weeks thereafter until treatment discontinuation for BVd and every 3 weeks until Cycle 6 and then every 12 weeks thereafter until treatment discontinuation for DVd. Completion rates in both arms were  $\geq 90\%$  at baseline and  $\geq 52\%$  at subsequent timepoints where  $>50\%$  of patients remained on treatment.

Table 6 summarizes the patient-reported symptom of blurred vision as assessed by PRO-CTCAE.

**Table 6. Patient-Reported Symptom of Blurred Vision Assessed by PRO-CTCAE in Patients with Relapsed or Refractory Multiple Myeloma in DREAMM-7**

Symptom (Attribute) <sup>a</sup>	Any Symptom Before Treatment <sup>b</sup>		Score 3 or 4 Before Treatment <sup>c</sup>		Any Symptom on Treatment <sup>d,e</sup>		Score 3 or 4 on Treatment <sup>d,f</sup>	
	BVd (%) n = 232	DVd (%) n = 227	BVd (%) n = 232	DVd (%) n = 227	BVd (%) n = 238	DVd (%) n = 239	BVd (%) n = 238	DVd (%) n = 239
Blurred vision (severity)	28	24	<1	2	93	74	55	15

BVd = BLENREP + bortezomib and dexamethasone; DVd = daratumumab + bortezomib and dexamethasone; PRO-CTCAE = patient-reported outcomes common terminology criteria for adverse events.

<sup>a</sup> Symptom attribute scoring defined as severity with a score of 0 = 'none'; 1 = 'mild'; 2 = 'moderate'; 3 = 'severe'; 4 = 'very severe'.

<sup>b</sup> Percentage of patients whose symptom score before treatment was 1 to 4.

- <sup>c</sup> Percentage of patients whose symptom score before treatment was 3 or 4.  
<sup>d</sup> Number of patients who provided at least one on-treatment score.  
<sup>e</sup> Percentage of patients whose maximum post-baseline score was 1 to 4 on treatment.  
<sup>f</sup> Percentage of patients whose maximum post-baseline score was 3 or 4 on treatment.

Driving at night was assessed using the OSDI. At baseline, the proportion of patients who reported limitations with driving at night “all of the time” or “most of the time” during the last week was 9% in the BVd arm and 4% in the DVd arm. The proportion of patients who reported limitations with driving at night “all of the time” or “most of the time” during the last week was highest in the BVd arm at 47% at Week 13 and in the DVd arm at 12% at Week 76.

## **8 USE IN SPECIFIC POPULATIONS**

### **8.1 Pregnancy**

#### Risk Summary

Based on its mechanism of action, BLENREP can cause fetal harm when administered to a pregnant woman, because it contains a genotoxic compound (the microtubule inhibitor, MMAF) and it targets actively dividing cells [see *Clinical Pharmacology (12.1)*, *Nonclinical Toxicology (13.1)*]. Human immunoglobulin G (IgG) is known to cross the placenta; therefore, belantamab mafodotin-blmf has the potential to be transmitted from the mother to the developing fetus. There are no available data on the use of BLENREP in pregnant women to evaluate for drug-associated risk. No animal reproduction studies were conducted with BLENREP. Advise pregnant women of the potential risk to a fetus.

In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

#### Data

*Animal Data:* Animal reproductive or developmental toxicity studies were not conducted with belantamab mafodotin-blmf. The cytotoxic component of BLENREP, mcMMAF, disrupts microtubule function, is genotoxic, and can be toxic to rapidly dividing cells, suggesting it has the potential to cause embryo-fetal toxicity.

### **8.2 Lactation**

#### Risk Summary

There are no data on the presence of belantamab mafodotin-blmf in human milk or the effects on the breastfed child or milk production. Because of the potential for serious adverse reactions in the breastfed child, advise women not to breastfeed during treatment with BLENREP and for 3 months after the last dose.

### **8.3 Females and Males of Reproductive Potential**

BLENREP can cause fetal harm when administered to pregnant women [see *Use in Specific Populations (8.1)*].

#### Pregnancy Testing

Verify the pregnancy status of females of reproductive potential prior to initiating BLENREP.

### Contraception

*Females:* Advise females of reproductive potential to use effective contraception during BLENREP treatment and for 4 months after the last dose.

*Males:* Because of the potential for genotoxicity, advise males with female partners of reproductive potential to use effective contraception during treatment with BLENREP and for 6 months after the last dose [see *Nonclinical Toxicology (13.1)*].

### Infertility

Based on findings in animal studies, BLENREP may impair fertility in females and males. The effects were not reversible in male rats but were reversible in female rats [see *Nonclinical Toxicology (13.1)*].

## **8.4 Pediatric Use**

The safety and effectiveness of BLENREP in pediatric patients have not been established.

## **8.5 Geriatric Use**

Of 242 patients who received BLENREP in DREAMM-7, 121 patients (50%) were aged 65 years or older and 37 patients (15%) were 75 years or older. No overall differences in the safety of BLENREP were observed between patients 65 years of age and older and younger adult patients.

Of the 108 patients who received BLENREP and were evaluated for efficacy in the DREAMM-7 study, there was an insufficient number of older adult patients to determine if the effectiveness in patients 65 years of age and older is different than in younger adult patients.

## **8.6 Hepatic Impairment**

No dose adjustment is recommended for patients with mild hepatic impairment (total bilirubin > upper limit of normal [ULN] to  $\leq 1.5 \times \text{ULN}$  and any aspartate aminotransferase [AST] or total bilirubin  $\leq \text{ULN}$  with AST >ULN).

The recommended dose of BLENREP has not been established in patients with moderate or severe hepatic impairment [see *Clinical Pharmacology (12.3)*].

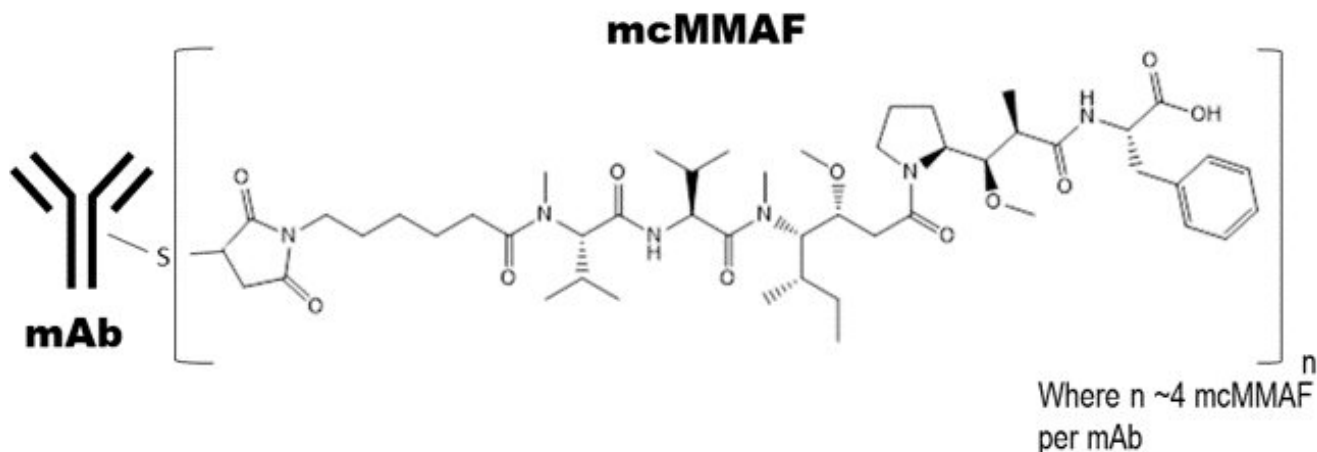
## **11 DESCRIPTION**

Belantamab mafodotin-blmf is a B-cell maturation antigen (BCMA)-directed antibody and microtubule inhibitor conjugate. Belantamab mafodotin-blmf is an antibody conjugate composed of 3 components: 1) afucosylated, humanized immunoglobulin G1 monoclonal antibody covalently linked to 2) the microtubule inhibitor mcMMAF via 3) a protease-resistant maleimidocaproyl linker.

The antibody is produced in a mammalian cell line (Chinese Hamster Ovary) using recombinant DNA technology and the microtubule inhibitor and linker are produced by chemical synthesis. Approximately 4 molecules of mafodotin are attached to each antibody molecule. The molecular weight of belantamab mafodotin-blmf is approximately



152 kDa. Belantamab mafodotin-blmf has the following structure:



BLNREP (belantamab mafodotin-blmf) for injection is a sterile, preservative-free, white to yellow, lyophilized powder in a single-dose vial for reconstitution and further dilution prior to intravenous use. BLNREP is supplied as 70 mg per vial and requires reconstitution with 1.4 mL of Sterile Water for Injection, USP, to obtain a concentration of 50 mg/mL. Each mL of reconstituted solution contains belantamab mafodotin-blmf (50 mg) and the inactive ingredients, citric acid monohydrate (0.46 mg), edetate disodium (0.017 mg), polysorbate 80 (0.2 mg), sodium citrate (5.88 mg), and trehalose (68.4 mg). The pH of the reconstituted solution is 6.2.

## 12 CLINICAL PHARMACOLOGY

### 12.1 Mechanism of Action

Belantamab mafodotin-blmf is an antibody-drug conjugate (ADC). The antibody component is an afucosylated IgG1 directed against BCMA, a protein expressed on normal B lymphocytes and multiple myeloma cells. The small molecule component is mcMMAF, a microtubule inhibitor. Upon binding to BCMA, belantamab mafodotin-blmf is internalized followed by release of the cytotoxic agent (cys-mcMMAF) via proteolytic cleavage. The released cys-mcMMAF intracellularly disrupts the microtubule network, leading to cell cycle arrest and apoptosis.

Belantamab mafodotin-blmf had antitumor activity in multiple myeloma cells and mediated killing of tumor cells through cys-mcMMAF-induced apoptosis, as well as by tumor cell lysis through antibody-dependent cellular cytotoxicity and antibody-dependent cellular phagocytosis.

### 12.2 Pharmacodynamics

#### Exposure-Response Relationships

When BLNREP was used in combination with Vd, higher belantamab mafodotin-blmf Cycle 1 exposure was associated with a higher incidence of some safety adverse reactions (e.g., Grade  $\geq 2$  corneal exam findings).

#### Cardiac Electrophysiology

Belantamab mafodotin-blmf had no meaningful QT<sub>c</sub> prolongation (>10 ms) at the recommended dosage.

### 12.3 Pharmacokinetics

Belantamab mafodotin-blmf exhibited dose-proportional pharmacokinetics, with a gradual decrease in clearance over time. After a planned infusion duration of 30 minutes, maximum belantamab mafodotin-blmf plasma concentrations occurred at or shortly after the end of the infusion. Accumulation of belantamab mafodotin-blmf was minimal to moderate for the ADC (Cycle 3 to Cycle 1 ratio was 1.13 for C<sub>max</sub> and 1.58 for AUC) as observed with a dosing regimen of every 3 weeks.

Table 7 describes the pharmacokinetics of belantamab mafodotin-blmf for the 2.5 mg/kg dose on Cycle 1 at the end of the first 3-week intervals.

**Table 7. Summary of Pharmacokinetic Parameters<sup>a</sup>**

	<b>AUC<sup>b</sup></b>	<b>C<sub>max</sub></b>	<b>C<sub>tau</sub></b>
ADC (%)	3,950 mcg•h/mL (30.6)	43.7 mcg/mL (22.1)	2.03 mcg/mL (62.5)
cys-mcMMAF (%)	94.2 ng•h/mL (42.3)	0.976 ng/mL (45.3)	–

ADC = antibody drug conjugate; AUC = area under the curve; C<sub>max</sub> = maximum plasma concentration; C<sub>tau</sub> = concentration at the end of a dosing interval.

<sup>a</sup> Data presented as geometric mean (CV%).

<sup>b</sup> AUC for ADC is AUC<sub>(0-21days)</sub> and for cys-mcMMAF is AUC<sub>(0-7days)</sub>.

#### Distribution

In vitro, cys-mcMMAF exhibited low protein binding (70% unbound at a concentration of 5 ng/mL) in human plasma.

The geometric mean (CV%) steady-state volume of distribution of belantamab mafodotin-blmf was 10.8 L (22.2%).

#### Elimination

The geometric mean (CV%) belantamab mafodotin-blmf (ADC) initial systemic clearance (CL) was 0.901 L/day (40%), and the elimination half-life was 13 days (26%). Following treatment, steady-state CL was 0.605 L/day (43%) or approximately 33% lower than initial systemic CL with an elimination half-life of 17 days (31%).

The fraction of intact cys-mcMMAF excreted in urine was approximately 18% of the dose in Cycle 1, with no evidence of other mcMMAF-related metabolites.

*Metabolism:* The monoclonal antibody portion of belantamab mafodotin-blmf is expected to undergo proteolysis to small peptides and individual amino acids by ubiquitous proteolytic enzymes. Cys-mcMMAF had limited metabolic clearance in human hepatic S9 fraction incubation studies.

#### Specific Populations

No clinically significant differences in the pharmacokinetics of belantamab

mafodotin-blmf were observed based on age (32 to 89 years), sex, race (White vs. Black vs. Asian), body weight (37 to 170 kg), mild to severe renal impairment and kidney failure (eGFR <30 mL/min), or mild hepatic impairment (total bilirubin >ULN to  $\leq 1.5 \times \text{ULN}$  and any AST or total bilirubin  $\leq \text{ULN}$  with AST >ULN).

The effects of moderate (total bilirubin  $>1.5 \times \text{ULN}$  to  $\leq 3 \times \text{ULN}$  and any AST) or severe hepatic impairment (total bilirubin  $>3 \times \text{ULN}$  and any AST) on the pharmacokinetics of belantamab mafodotin-blmf are unknown.

#### *In Vitro Studies:*

**Cytochrome P450 (CYP) Enzymes:** Cys-mcMMAF is not an inhibitor, an inducer, or a sensitive substrate of cytochrome P450 enzymes.

**Transporter Systems:** Cys-mcMMAF is a substrate of organic anion transporting polypeptide (OATP)1B1 and OATP1B3, multidrug resistance-associated protein (MRP)1, MRP2, and MRP3, bile salt export pump (BSEP), and a possible substrate of P-glycoprotein (P-gp).

## **12.6 Immunogenicity**

The observed incidence of anti-drug antibodies is highly dependent on the sensitivity and specificity of the assay. Differences in assay methods preclude meaningful comparisons of the incidence of anti-drug antibodies in the studies described below with the incidence of anti-drug antibodies (ADAs) in other studies, including those of BLENREP or of other belantamab mafodotin-blmf products.

In the combination therapy studies, 3% of patients (15/515) tested positive for treatment-emergent belantamab mafodotin-blmf ADAs. Among the 15 patients who tested positive for ADAs, 2 patients tested positive for neutralizing anti-belantamab mafodotin-blmf antibodies.

## **13 NONCLINICAL TOXICOLOGY**

### **13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility**

Carcinogenicity studies have not been conducted with belantamab mafodotin-blmf.

Belantamab mafodotin-blmf was genotoxic in an in vitro micronucleus assay in human lymphocytes through an aneugenic mechanism. These results are consistent with the pharmacological effect of MMAF binding to tubulin causing microtubule depolymerization resulting in spindle disorganization during cell division. Cys-mcMMAF was not mutagenic in the bacterial reverse mutation assay (Ames test), the L5178Y mouse lymphoma forward mutation assay, or the in vivo rat bone marrow micronucleus assay.

Fertility studies have not been conducted with belantamab mafodotin-blmf. Results of repeat-dose toxicity studies with intravenous administration of belantamab mafodotin-blmf in rats indicate the potential for impaired male and female reproductive function and fertility. In rats, weekly dosing for 3 weeks at doses  $\geq 10 \text{ mg/kg}$  (approximately 5 times the exposure at the maximum recommended human dose [MRHD] of  $2.5 \text{ mg/kg}$  based on AUC) resulted in degeneration and atrophy of seminiferous tubules in the testes and luteinized nonovulatory follicles in the ovaries. Findings in females were reversible; findings in the testes were not reversible at the end of the 12-week recovery period with weekly dosing or when given every 3 weeks for

13 weeks at doses  $\geq 10$  mg/kg. In male monkeys, the highest dose tested of 10 mg/kg (approximately 5 times the exposure at the MRHD based on AUC) given weekly for 13 weeks resulted in seminiferous tubules degeneration in the testes that was fully reversed following the 12-week recovery period.

## 14 CLINICAL STUDIES

### Relapsed or Refractory Multiple Myeloma in Combination with Bortezomib and Dexamethasone

The efficacy of BLENREP in combination with bortezomib and dexamethasone (BVd) compared with daratumumab, bortezomib, and dexamethasone (DVd) was evaluated in DREAMM-7 (NCT04246047), an open-label, randomized, multicenter study in adult patients with relapsed or refractory multiple myeloma. Patients received at least one prior line of therapy and had documented disease progression during or after their most recent line of treatment. Patients who were refractory or intolerant to daratumumab or bortezomib, or with prior exposure to anti-BCMA therapy were excluded. Patients with existing corneal disease, except for mild punctate keratopathy, were excluded.

Patients were randomized 1:1 to the following treatment arms:

- BLENREP 2.5 mg/kg (IV) every 3 weeks on Day 1 of each 21-day cycle. Bortezomib 1.3 mg/m<sup>2</sup> (subcutaneously) on Days 1, 4, 8, and 11 and dexamethasone 20 mg (IV or orally) on the day of, and the day after, bortezomib treatment of Cycles 1–8 (21-day cycles). From Cycle 9 onward, treatment with BLENREP was continued as a single agent.
- Daratumumab 16 mg/kg (IV) every week for Cycles 1–3 and every 3 weeks for Cycles 4–8. Bortezomib 1.3 mg/m<sup>2</sup> (subcutaneously) on Days 1, 4, 8, and 11 and dexamethasone 20 mg (IV or orally) on the day of, and the day after, bortezomib treatment of Cycles 1–8 (21-day cycles). From Cycle 9 onward, treatment with daratumumab was continued as a single agent.

The dose level of dexamethasone in each arm was reduced by half in patients aged 75 years or older. Treatment with BLENREP or daratumumab was continued until disease progression or unacceptable toxicity.

Efficacy was established based on progression-free survival (PFS) and overall survival (OS).

A total of 217 patients who received at least two prior lines of therapy, including a proteasome inhibitor and immunomodulatory agent, were evaluated for efficacy: 108 in the BVd arm and 109 in the DVd arm. Baseline demographics and characteristics were similar across arms. The median age was 65 years (range: 39 to 86); 43% were age 65 to 74 years, 11% age 75 years or older; 53% were male; 86% were White, 11% Asian, 2% Black; R-ISS stage at screening was stage I in 37%, stage II in 56%, stage III in 6%; high-risk cytogenetics (presence of t (11;14), t (14;16) or 17p13del) were present in 29%; extramedullary disease was present in 11%. The median number of prior lines of therapy was 3 (range: 2 to 7); 2% received a prior anti-CD38 monoclonal antibody, and 71% previously received autologous stem cell transplantation. Overall, 19% of patients were refractory to proteasome inhibitors and 59% were refractory to immunomodulatory agents.

Efficacy results are summarized in Table 8 and Figures 1 and 2.

**Table 8. Efficacy Results from DREAMM-7**

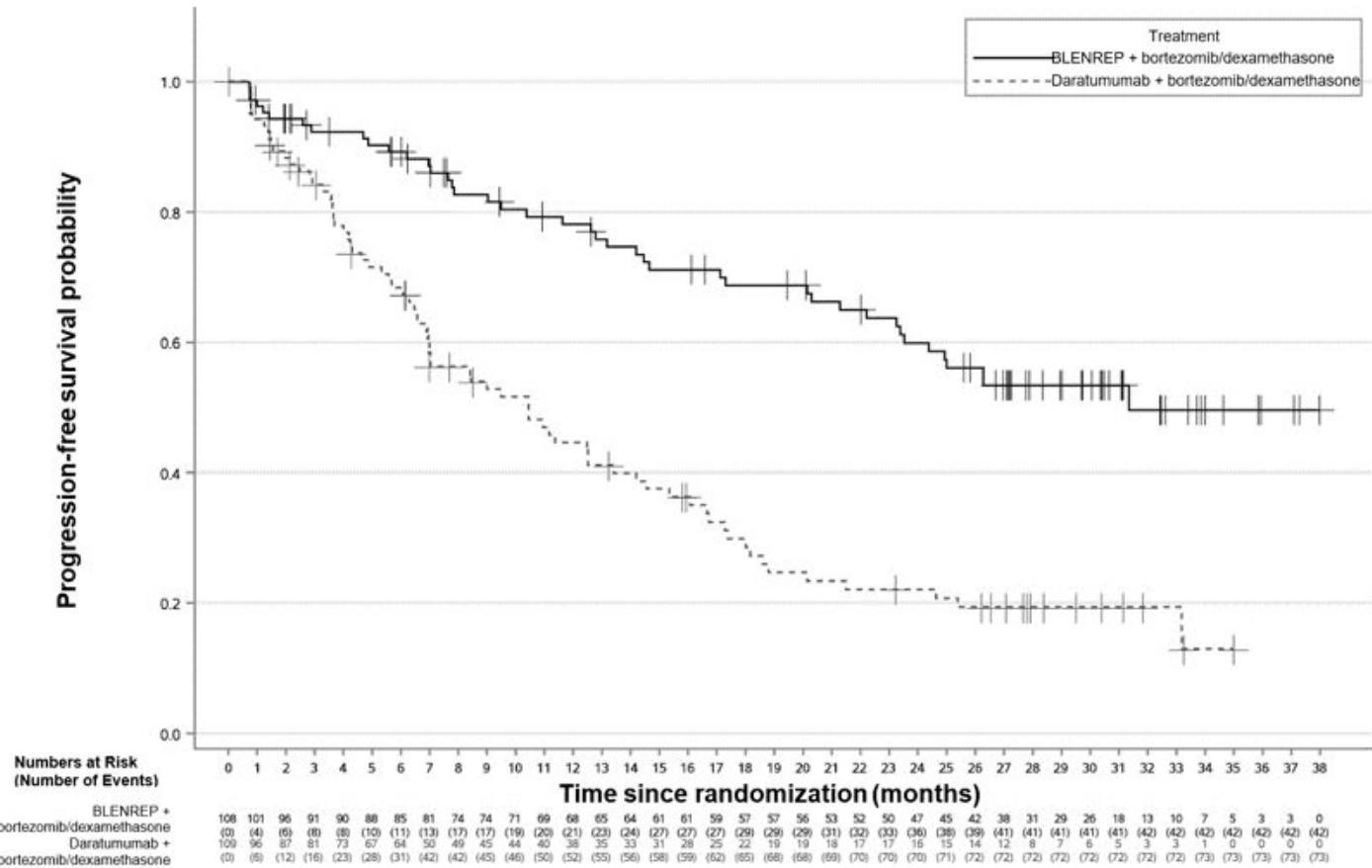
	<b>BLNREP + Bortezomib and Dexamethasone N = 108</b>	<b>Daratumumab + Bortezomib and Dexamethasone N = 109</b>
<b>Progression-Free Survival (PFS)<sup>a,b,c</sup></b>		
Number (%) of patients with event	42 (39)	73 (67)
Median in months (95% CI) <sup>d</sup>	31.3 (23.5, NR)	10.4 (7, 13.4)
Hazard ratio (95% CI) <sup>e</sup>	0.31 (0.21, 0.47)	
<b>Overall Survival (OS)<sup>a,f</sup></b>		
Number (%) of patients with event	33 (31)	57 (52)
Median in months (95% CI) <sup>d</sup>	NR (NR, NR)	35.7 (21.1, NR)
Hazard ratio (95% CI) <sup>e</sup>	0.49 (0.32, 0.76)	
<b>Overall Response Rate (ORR)<sup>a,b,c,g</sup>, % (95% CI)</b>	81.5 (72.9, 88.3)	56.9 (47, 66.3)
Stringent complete response (sCR), n (%)	15 (13.9)	4 (3.7)
Complete response (CR), n (%)	19 (17.6)	5 (4.6)
Very good partial response (VGPR), n (%)	34 (31.5)	23 (21.1)
Partial response (PR), n (%)	20 (18.5)	30 (27.5)
<b>Minimal Residual Disease (MRD) Negativity Rate<sup>a,b,h</sup>, n (%)</b>	25 (23.1)	3 (2.8)
95% CI	(15.6, 32.2)	(0.6, 7.8)
<b>MRD Negativity Rate in Patients with CR or Better<sup>b,h</sup></b>		
Number of patients with CR or better	34	9
MRD negativity rate, n (%)	25 (73.5)	3 (33.3)
(95% CI)	(55.6, 87.1)	(7.5, 70.1)

NR = not reached.

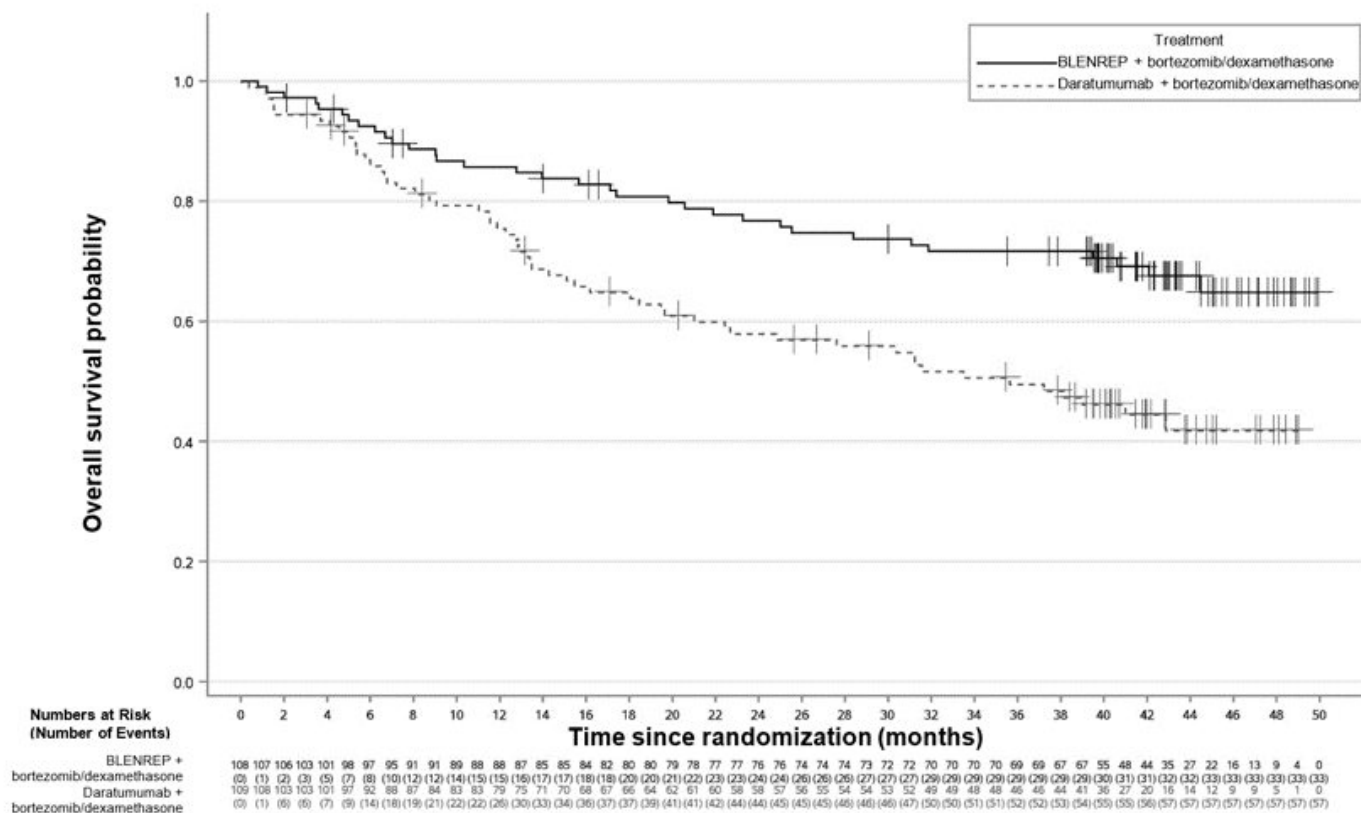
<sup>a</sup> Based on all randomized patients who received at least two prior lines of therapy, including a proteasome inhibitor and immunomodulatory agent.

- <sup>b</sup> Median follow-up of 27.9 months.
- <sup>c</sup> Response was based on Independent Review Committee per International Myeloma Working Group criteria.
- <sup>d</sup> By Brookmeyer and Crowley method.
- <sup>e</sup> Based on stratified Cox regression model.
- <sup>f</sup> Median follow-up of 38.7 months.
- <sup>g</sup> ORR: sCR+CR+VGPR+PR.
- <sup>h</sup> Assessed by next generation sequencing assay (clonoSEQ) at 10<sup>-5</sup> threshold.

**Figure 1: Kaplan-Meier Curve for Progression-Free Survival in DREAMM-7**



**Figure 2: Kaplan-Meier Curve for Overall Survival in DREAMM-7**



In patients who achieved response, the median time to response was 1.43 months (range: 0.7 to 8.4 months) in the BVd arm and 1.03 months (range: 0.7 to 11.1 months) in the DVd arm.

## 15 REFERENCES

1. "OSHA Hazardous Drugs." *OSHA*.  
<http://www.osha.gov/SLTC/hazardousdrugs/index.html>.

## 16 HOW SUPPLIED/STORAGE AND HANDLING

BLNREP (belantamab mafodotin-blmf) for injection is a sterile, preservative-free, white to yellow lyophilized powder for reconstitution and further dilution prior to intravenous use.

BLNREP is supplied in a carton containing one 70 mg single-dose vial with a rubber stopper (not made with natural rubber latex) and aluminum overseal with removable cap (NDC 0173-0913-01).

Store vials refrigerated at 36°F to 46°F (2°C to 8°C).

BLNREP is a hazardous drug. Follow applicable special handling and disposal procedures.<sup>1</sup>

## 17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Medication Guide).

### Ocular Toxicity

- Advise patients that ocular toxicity may occur during treatment with BLENREP [see *Warnings and Precautions (5.1)*].
- Advise patients to promptly tell their healthcare provider if they notice any new or worsening eye symptoms [see *Dosage and Administration (2.1)*, *Warnings and Precautions (5.1)*].
- Advise patients that they will be sent to an eye care professional to obtain ophthalmic exams before starting BLENREP, before each dose, promptly for any new or worsening eye symptoms, and as clinically indicated [see *Dosage and Administration (2.1)*, *Warnings and Precautions (5.1)*].
- Advise patients to administer preservative-free artificial tears at least 4 times per day starting with the first infusion and continuing until the end of treatment and to avoid wearing contact lenses for the duration of therapy. Bandage contact lenses may be used under the direction of an eye care professional [see *Dosage and Administration (2.1, 2.3)*, *Warnings and Precautions (5.1)*].
- Advise patients to use caution when driving or operating machinery as BLENREP may adversely affect their vision [see *Warnings and Precautions (5.1)*].

### BLENREP REMS

- Advise patients that because of the risk of ocular toxicity, BLENREP is available only through a restricted program called the BLENREP REMS [see *Warnings and Precautions (5.2)*].
- Patients must receive counseling about the risk of ocular toxicity, enroll in the REMS, and adhere to ongoing monitoring via ophthalmic exams. Patients will be given the BLENREP REMS Patient Guide. This guide describes the risk of ocular toxicity with BLENREP [see *Warnings and Precautions (5.2)*].

### Thrombocytopenia

- Advise patients to inform their healthcare provider if they develop signs or symptoms of bleeding [see *Warnings and Precautions (5.3)*].

### Embryo-fetal Toxicity

- Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to inform their healthcare provider of a known or suspected pregnancy [see *Warnings and Precautions (5.4)*, *Use in Specific Populations (8.1, 8.3)*].
- Advise females of reproductive potential to use effective contraception during treatment with BLENREP and for 4 months after the last dose [see *Warnings and Precautions (5.4)*, *Use in Specific Populations (8.3)*].
- Advise males with female partners of reproductive potential to use effective contraception during treatment with BLENREP and for 6 months after the last dose [see *Use in Specific Populations (8.3)*, *Nonclinical Toxicology (13.1)*].

### Lactation

- Advise women not to breastfeed during treatment with BLENREP and for 3 months



after the last dose [see *Use in Specific Populations (8.2)*].

### Infertility

- Advise males and females of reproductive potential that BLENREP may impair fertility [see *Use in Specific Populations (8.3)*].

### Pneumonitis

- Advise patients to immediately report any new or worsening respiratory symptoms to their healthcare provider [see *Adverse Reactions (6.1)*].

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BLP:1PI

## **MEDICATION GUIDE BLENREP (BLEN-REP) (belantamab mafodotin-blmf) for injection, for intravenous use**

**What is the most important information I should know about BLENREP?**  
**BLENREP can cause serious side effects, including:**

- **Eye problems.** Eye problems are common with BLENREP and can also be severe. BLENREP can cause changes to the surface of your eye, which can lead to symptoms of eye problems, including:
  - o decreased vision
  - o blurred vision
  - o dry eyes
  - o sensitivity to light
  - o feeling like something is in your eyes
  - o eye irritation
  - o eye pain

Ulcers on the surface of the eye (corneal ulcers), including with infection, may also happen during treatment with BLENREP.

**Tell your healthcare provider right away** if you notice any new or worsening eye symptoms or vision changes during treatment with BLENREP.

Your healthcare provider will refer you to an eye care specialist (such as an ophthalmologist or optometrist) to check your eyes before you start treatment, before you receive each dose of BLENREP, and as needed for any new or worsening eye problems. **It is important that you:**

- o Keep all of your eye care appointments because some changes can happen without symptoms and may only be seen on an eye exam.
- o Use preservative-free artificial tears at least 4 times per day starting with your first infusion and continuing until the end of treatment with BLENREP.
- o Avoid wearing contact lenses during treatment with BLENREP unless directed by your eye care specialist.
- o Use caution when driving or operating machinery because BLENREP may cause changes to your vision.

**Because of the risk of eye problems, BLENREP is available only through a restricted program called the BLENREP Risk Evaluation and Mitigation Strategy (REMS).** Your healthcare provider will give you the BLENREP REMS Patient Guide, which describes the risk of eye problems, and will explain the REMS program to you. To receive BLENREP, you must enroll in the REMS program and receive eye exams during treatment. See **“What are the possible side effects of BLENREP?”** for more information about side effects.

### **What is BLENREP?**

BLENREP is a prescription medicine used in combination with the medicines bortezomib and dexamethasone to treat adults with multiple myeloma who:

- have received at least 2 prior treatments, including a proteasome inhibitor and an immunomodulatory agent, and
- their cancer has come back or did not respond to prior treatment.

It is not known if BLENREP is safe and effective in children.

**Before receiving BLENREP, tell your healthcare provider about all of your medical conditions, including if you:**

- have or had vision or eye problems.
- have or had bleeding problems.
- are pregnant or plan to become pregnant. BLENREP can harm your unborn baby.

### **Females who are able to become pregnant:**

- o Your healthcare provider will do a pregnancy test before you start treatment with BLENREP.
- o Use effective birth control during treatment with BLENREP and for 4 months after the last dose. Talk to your healthcare provider about birth control methods you can use during this time.
- o Tell your healthcare provider if you become pregnant or think you may be pregnant during treatment with BLENREP.

### **Males with female partners who are able to become pregnant:**

- o Use effective birth control during treatment with BLENREP and for 6 months after the last dose.
- are breastfeeding or plan to breastfeed. It is not known if BLENREP passes into your breast milk. Do not breastfeed during treatment with BLENREP and for 3 months after the last dose.

**Tell your healthcare provider about all the medicines you take,** including

prescription and over-the-counter medicines, vitamins, and herbal supplements.

### **How will I receive BLENREP?**

- Your healthcare provider will give you BLENREP as an infusion into your vein over about 30 minutes.
- BLENREP is usually given every 3 weeks.
- Your healthcare provider will decide how many treatments you will need.
- If you miss any appointments, call your healthcare provider as soon as possible to reschedule your appointment.

### **What are the possible side effects of BLENREP?**

#### **BLENREP can cause serious side effects, including:**

- **See “Eye Problems” in “What is the most important information I should know about BLENREP?”**
- **Decrease in platelets (thrombocytopenia)** is common with BLENREP and can also be severe. Platelets are a type of blood cell that help your blood to clot. Your healthcare provider will check your blood cell counts before you start treatment with BLENREP and during treatment as needed. Tell your healthcare provider if you get any bleeding or bruising during treatment with BLENREP.

#### **The most common side effects of BLENREP when given with bortezomib and dexamethasone include:**

- See **“Eye problems” in “What is the most important information I should know about BLENREP?”**
- upper respiratory tract infection
- liver problems
- diarrhea
- tiredness
- pneumonia
- cataract
- COVID-19

**The most common severe abnormal blood test results during treatment with BLENREP include** decreases in platelets, white blood cells, and hemoglobin, and increases in certain liver enzymes.

Tell your healthcare provider right away if you get new or worsening unexplained signs or symptoms of lung problems, including shortness of breath, chest pain, or cough.

Your healthcare provider may decrease your dose, temporarily stop, or completely stop treatment with BLENREP if you get serious side effects.

BLENREP may affect fertility in males and females, which may affect your ability to have children. Talk to your healthcare provider if this is a concern for you.

These are not all of the possible side effects of BLENREP.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

### **General information about the safe and effective use of BLENREP.**

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. You can ask your pharmacist or healthcare provider for information about BLENREP that is written for health professionals.

### **What are the ingredients in BLENREP?**

**Active Ingredient:** belantamab mafodotin-blmf

**Inactive Ingredients:** citric acid monohydrate, edetate disodium, polysorbate 80, sodium citrate, and trehalose.

Manufactured by:  
GlaxoSmithKline LLC  
Philadelphia PA, 19104  
U.S. License No. 1727

For:  
GlaxoSmithKline, Durham, NC 27701  
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licensor.  
BLP:1MG

For more information, call GlaxoSmithKline (GSK) at 1-888-825-5249.  
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This Medication Guide has been approved by the U.S. Food and Drug  
Administration. Revised: 10/2025

**NDC 0173-0913-01**

**BLNREP**

**(belantamab mafodotin-blmf)**

**for injection**

**70 mg/vial**

**Rx Only**

For intravenous infusion after reconstitution and dilution.

**CAUTION: Hazardous Drug.**

No preservative.

**Dispense the enclosed Medication Guide to each patient.**

**Contains one Single-Dose vial.**

**Discard Unused Portion.**

**2025 GSK group of companies or its licensor.**

**Product Italy**

Rev. 04/25

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NDC 0173-0913-01  
Rx Only



# BLENREP

(belantamab mafodotin-blmf)  
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## BLENREP

belantamab mafodotin injection, powder, for solution

### Product Information

Product Type	HUMAN PRESCRIPTION DRUG	Item Code (Source)	NDC:0173-0913
Route of Administration	INTRAVENOUS		

### Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
BELANTAMAB MAFODOTIN (UNII: DB1041CXDG) (BELANTAMAB MAFODOTIN - UNII:DB1041CXDG)	BELANTAMAB MAFODOTIN	50 mg in 1 mL

## Inactive Ingredients

Ingredient Name	Strength
<b>CITRIC ACID MONOHYDRATE</b> (UNII: 2968PHW8QP)	
<b>EDETATE DISODIUM</b> (UNII: 7FLD91C86K)	
<b>POLYSORBATE 80</b> (UNII: 6OZP39ZG8H)	
<b>SODIUM CITRATE, UNSPECIFIED FORM</b> (UNII: 1Q73Q2JULR)	
<b>TREHALOSE</b> (UNII: B8WCK70T7I)	

## Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:0173-0913-01	1 in 1 CARTON	10/23/2025	
1		1.4 mL in 1 VIAL; Type 0: Not a Combination Product		

## Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
BLA	BLA761440	10/23/2025	

**Labeler** - GlaxoSmithKline LLC (167380711)

Revised: 10/2025

GlaxoSmithKline LLC