RXADVANCE
2 Park Central Drive
Southborough, MA 01772

NEW DRUG APPROVAL

Brand Name	BLENREP
Generic Name	belantamab mafodotin-blmf
Drug Manufacturer	GlaxoSmithKline

New Drug Approval

FDA Approval Date: August 5, 2020
Review Designation: Orphan
Type of Review: Biologics License Application 761158

Place in Therapy

DISEASE DESCRIPTION & EPIDEMIOLOGY

Multiple myeloma is a type of blood cancer that affects plasma cells. In multiple myeloma, malignant plasma cells accumulate in bone marrow - the soft, spongy tissue at the center of your bones - crowding out the normal plasma cells that help fight infection. These malignant plasma cells then produce an abnormal antibody called M protein, which offers no benefit to the body and may cause tumors, kidney damage, bone destruction and impaired immune function. The hallmark characteristic of multiple myeloma is a high level of M protein in the blood. It is the second most common hematologic malignancy in the US, with over 30,000 new cases diagnosed annually, and is becoming increasingly more common. Novel therapies have improved the estimated life expectancy of MM patients from a 5-year relative survival rate of 35% in 2000 to over 50% today. Nevertheless, MM remains incurable and fatal, with most patients dying of the disease.

MM is always preceded by monoclonal gammopathy of undetermined significance (MGUS) and smoldering multiple myeloma (SMM). Those clinically detectable but asymptomatic premalignant conditions progress to malignant MM in a subset of patients for reasons that are poorly understood. Our limited understanding of disease progression is due, in part, to the limited study populations on which estimates of prevalence and progression risk are based. MGUS is present in roughly 3% of the general population aged 50 years or older and progresses to overt MM at a rate of about 1% per year. However, in some patients, the risk of progression is reported to be as high as 58% in 20 years. SMM has an annual risk of progression of 10% in the first 5 years, but in some patients, the risk is as high as 70% in 5 years.

Efficacy

The efficacy of BLENREP was evaluated in DREAMM-2, an open-label, multicenter study (NCT 03525678). Eligible patients had relapsed or refractory multiple myeloma, had previously received 3 or more prior therapies, including an anti-CD38 monoclonal antibody, and were refractory to an immunomodulatory agent and a proteasome inhibitor.

Patients received either BLENREP 2.5 mg/kg or 3.4 mg/kg intravenously once every 3 weeks until disease progression or unacceptable toxicity.The major efficacy outcome measure was overall response rate as evaluated by an Independent Review Committee (IRC) based on the IMWG Uniform Response Criteria for Multiple Myeloma.

A total of 97 patients received BLENREP at a dose of 2.5 mg/kg administered intravenously once every 3 weeks. The median age was 65 years (range: 39 to 85 years), 53% were male, 74% were White, and 16% were Black.

Efficacy results are summarized in below table.

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	BLENREP N = 97
Overall response rate (ORR), n (%) (97.5% CI)	30 (31%) (21%, 43%)
Stringent complete response (sCR), n (%)	2 (2%)
Complete response (CR), n (%)	1 (1%)
Very good partial response (VGPR), n (%)	15 (15%)
Partial response (PR), n (%)	12 (12%)
Median duration of response in monthsa (range)	Not reached (NR) [NR to NR]

Safety

ADVERSE EVENTS

- The most common adverse reactions (≥20%) are keratopathy (corneal epithelium change on eye exam), decreased visual acuity, nausea, blurred vision, pyrexia, infusion-related reactions, and fatigue.
- The most common grade 3 or 4 laboratory abnormalities (≥5%) are platelets decreased, lymphocytes decreased, hemoglobin decreased, neutrophils decreased, creatinine increased, and gamma-glutamyl transferase increased.

WARNINGS & PRECAUTIONS

- **Thrombocytopenia**: Perform complete blood counts at baseline and during treatment as clinically indicated. Consider withholding and/or reducing the dose based on severity.
- **Infusion-Related Reactions**: Monitor patients for infusion-related reactions. Interrupt and then reduce the rate or permanently discontinue based on the severity.
- **Embryo-Fetal Toxicity**: Can cause fetal harm. Advise females of reproductive potential of the potential risk to a fetus and to use effective contraception.

CONTRAINDICATIONS

None.

Clinical Pharmacology

MECHANISMS 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 MMAF, a microtubule inhibitor. Upon binding to BCMA, belantamab mafodotin-blmf is internalized followed by release of MMAF via proteolytic cleavage. The released MMAF 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 MMAF-induced apoptosis, as well as by tumor cell lysis through antibody-dependent cellular cytotoxicity (ADCC) and antibody-dependent cellular phagocytosis (ADCP).

Dose & Administration

ADULTS

The recommended dosage is 2.5 mg/kg as an intravenous infusion over approximately 30 minutes once every 3 weeks.

PEDIATRICS

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

GERIATRICS

Refer to adult dosing

RENAL IMPAIRMENT

No dose adjustment is recommended for patients with mild or moderate renal impairment. The recommended dosage has not been established in patients with severe renal impairment or end-stage renal disease (ESRD).

HEPATIC IMPAIRMENT

No dose adjustment is recommended for patients with mild hepatic impairment. The recommended dosage of BLENREP has not been established in patients with moderate or severe hepatic impairment.

Product Availability

DOSAGE FORM(S) & STRENGTH(S)

For injection: 100 mg as a lyophilized powder in a single-dose vial for reconstitution and further dilution.