Understanding Blenrep
(belantamab mafodotin-blmf)
for injection
Founded in 1990, the International Myeloma Foundation (IMF) is the first and largest organization focusing specifically on multiple myeloma. The IMF’s reach extends to more than 525,000 members in 140 countries worldwide. The IMF is dedicated to improving the quality of life of myeloma patients while working toward prevention and a cure through our four founding principles: Research, Education, Support, and Advocacy.

**RESEARCH** The signature project of the IMF’s Research division is the Black Swan Research Initiative®, a groundbreaking and collaborative effort to develop the first definitive cure for myeloma. Each year, the IMF also awards Brian D. Novis Grants, which promote research for better myeloma treatments, management, and practices in the field. In addition, more than 200 leading myeloma researchers comprise the IMF’s International Myeloma Working Group (IMWG), a research body that has developed myeloma guidelines that are followed around the world. Finally, the IMF’s Nurse Leadership Board (NLB), comprised of nurses from leading myeloma treatment centers, develops recommendations for the nursing care of myeloma patients.

**EDUCATION** The IMF Patient & Family Seminars and Regional Community Workshops are held around the world to provide up-to-date information presented by leading myeloma specialists and researchers directly to patients and their families. The IMF’s library of more than 100 publications, for patients and caregivers as well as for healthcare professionals, is updated annually and available free of charge. Publications are available in more than 20 languages.

**SUPPORT** The IMF’s InfoLine is staffed by information specialists who answer myeloma-related questions and provide support via phone and email to thousands of families each year. In addition, the IMF sustains a network of more than 150 myeloma support groups and offers training for the hundreds of dedicated patients, caregivers, and nurses who volunteer to lead these groups in their communities.

**ADVOCACY** The IMF’s Advocacy team has educated and empowered thousands of individuals who make a positive impact each year on issues critical to the myeloma community. Working in the US at both federal and state levels, we lead coalitions to advocate for parity in insurance coverage. We also represent the myeloma community’s interests before the US Congress and agencies such as the National Institutes of Health, the Food and Drug Administration, the Centers for Medicare and Medicaid Services, and the Veterans Administration. Outside the US, the IMF’s Global Myeloma Action Network (GMAN) works to help patients gain access to treatment.

Learn more about the ways the IMF is helping to improve the quality of life of myeloma patients while working toward prevention and a cure. Contact us at 818.487.7455 or 800.452.CURE, or visit myeloma.org.

Improving Lives Finding the Cure®
# Table of contents

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>What you will learn from this booklet</td>
<td>4</td>
</tr>
<tr>
<td>What is Blenrep and how does it work?</td>
<td>4</td>
</tr>
<tr>
<td>Who is a candidate for Blenrep?</td>
<td>5</td>
</tr>
<tr>
<td>How is Blenrep given?</td>
<td>5</td>
</tr>
<tr>
<td>What are the dose and schedule of Blenrep?</td>
<td>5</td>
</tr>
<tr>
<td>What are the possible side effects of Blenrep, and how are they managed?</td>
<td>5</td>
</tr>
<tr>
<td>Pregnancy, lactation, and reproductive potential</td>
<td>8</td>
</tr>
<tr>
<td>Access to Blenrep</td>
<td>9</td>
</tr>
<tr>
<td>Terms and definitions</td>
<td>9</td>
</tr>
</tbody>
</table>
What you will learn from this booklet

The IMF’s Understanding series of booklets is designed to inform you about treatments and supportive care measures for multiple myeloma (which we refer to simply as “myeloma”). Words in bold+blue type are explained in the “Terms and definitions” section at the end of this booklet, as well as in a more complete compendium of myeloma-related vocabulary, the IMF’s Glossary of Myeloma Terms and Definitions, located at glossary.myeloma.org.

It is important and helpful for you to learn as much as possible about myeloma and its treatment options in order to be empowered to play an active role in your own medical care and to make good decisions about your care with your doctor. The information in this booklet will help you in discussions with your healthcare team.

What is Blenrep and how does it work?

Blenrep (belantamab mafodotin-blmf) is an antibody-drug conjugate (ADC), the first in a new class of treatments for myeloma. Blenrep is the combination of a monoclonal antibody (mAb) that binds to a specific receptor on the surface of myeloma cells called B-cell maturation antigen (BCMA), coupled with monomethyl auristatin F (MMAF), a drug that can kill myeloma cells.

BCMA is involved in myeloma cell growth and survival, and is found on the surface of cells in all patients with myeloma. When the monoclonal antibody portion of Blenrep attaches to BCMA, Blenrep enters the cell and releases MMAF, which leads to cell death. The antibody part of the ADC attracts your body’s own immune system to recognize the cancerous myeloma cells and attack them.

What is the clinical trial experience with Blenrep?

The first study with Blenrep in human beings, the DREAMM-1 clinical trial, showed that Blenrep was safe and well tolerated. Sixty percent of the heavily pretreated patients in the DREAMM-1 clinical trial responded to Blenrep, including 15% with complete response (CR). The median time until there were signs that the myeloma had progressed was 12 months.

When a new drug is approved by the US Food and Drug Administration (FDA), the results of an important clinical trial, called a registration trial, are the basis for the request for drug approval. The FDA approval of Blenrep was based on the results of the DREAMM-2 clinical trial, which evaluated the safety and efficacy of two doses – 2.5 mg/kg (milligrams per kilogram of body weight) and 3.4 mg/kg – of Blenrep in patients who
had received at least 3 prior lines of therapy that included a proteasome inhibitor (Velcade® [bortezomib], Ninlaro® [ixazomib], or Kyprolis® [carfilzomib]) and an immunomodulatory drug (Revlimid® [lenalidomide] or Pomalyst® [pomalidomide]), and were relapsed and/or refractory to treatment with an anti-CD38 monoclonal antibody (Darzalex® [daratumumab]). The patients in the DREAMM-2 clinical trial had more advanced myeloma, poorer prognosis, and a greater number of prior lines of therapy than the patients in the DREAMM-1 clinical trial. In DREAMM-2, patients needed to be refractory or intolerant to an anti-CD38, and had to be refractory to an immunomodulatory drug and a proteasome inhibitor.

Results of the DREAMM-2 clinical trial were published in The Lancet Oncology in December 2019. Of the 97 patients in the of 2.5 mg/kg arm of the study, 31% had a partial response (PR) or better to treatment with Blenrep, 18% had a very good partial response (VGPR) or better, including 2 patients with a complete response (CR) and 1 patient with a stringent complete response (sCR). Patients in the study had received a median of seven prior lines of treatment. The median duration of response had not been reached at six months of follow-up.

To further explore the use of Blenrep in combination therapies, several DREAMM clinical trials are either already recruiting patients or are planned to open in the future. As of this writing, clinicaltrials.gov has information about the following studies: DREAMM-2 through DREAMM-9, DREAMM-12, and DREAMM-13.

**Who is a candidate for Blenrep?**

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

**How is Blenrep given?**

Blenrep is given as an intravenous (IV) infusion over approximately 30 minutes.

**What are the dose and schedule of Blenrep?**

Blenrep is given once every 3 weeks, at a dose of 2.5 mg/kg, until disease progression or unacceptable toxicity.

**What are the possible side effects of Blenrep, and how are they managed?**

Your doctor can anticipate these problems before they occur, and manage these possible side effects.
Ocular toxicity (connected with the eyes or vision)

In the 2.5 mg/kg arm of the DREAMM-2 clinical trial, 71% of patients experienced keratopathy (with or without symptoms), 25% had blurred vision, 15% had dry eye, and some patients experienced photophobia (extreme sensitivity to light). MMAF is known to cause corneal changes, the transparent front part of the eye that covers the iris, pupil, and anterior chamber. Corneal problems leading to discontinuation of Blenrep occurred in 1% of the patients in the 2.5 mg/kg arm of the DREAMM-2. You must report to your doctor any changes in your vision and/or any unusual bruising or bleeding.

Ocular toxicity occurred in 77% of the 218 patients in the pooled safety population. The pooled safety population includes patients who received Blenrep at a dose of 2.5 mg/kg or at the higher dose of 3.4 mg/kg (1.4 times the recommended dose). Adverse events included keratopathy (76%), changes in visual acuity (55%), blurred vision (27%), and dry eye (19%). Among patients with keratopathy, 49% had 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.

Keratopathy was reported as Grade 1 in 7% of patients, Grade 2 in 22%, Grade 3 in 45%, and Grade 4 in 0.5% per the keratopathy visual acuity (KVA) scale. Cases of corneal ulcer (ulcerative and infective keratitis) have been reported. Most keratopathy events developed within the first two treatment cycles (cumulative incidence of 65% by Cycle 2). Of the patients with Grade 2 to Grade 4 keratopathy, 39% recovered to Grade 1 or lower after median follow-up of 6.2 months. Of the 61% who had ongoing keratopathy, 28% were still on treatment, 9% were in follow-up, and in 24% the follow-up ended due to ongoing corneal issues. For patients in whom events resolved, the median time to resolution was 2 months (range: 11 days to 8.3 months).

A clinically significant decrease in visual acuity of worse than 20/40 in the better-seeing eye was observed in 19% of the 218 patients and of 20/200 or worse in the better-seeing eye in 1.4%. Of the patients with decreased visual acuity of worse than 20/40, 88% resolved and the median time to resolution was 22 days (range: 7 days to 4.2 months). Of the patients with decreased visual acuity of 20/200 or worse, all resolved and the median duration was 22 days (range: 15 to 22 days).

Prevention and treatment of ocular toxicity

Your doctor will conduct eye examinations as follows:

- At baseline (within 3 weeks prior to your first dose of Blenrep),
Prior to each dose (at least 1 week after the previous dose and within 2 weeks prior to the next dose), and

Promptly for worsening symptoms (report any eye side effects to your doctor promptly, and your dose of Blenrep will be withheld until improvement of the side effects, then resumed at same or reduced dose, or permanently discontinued).

You must use preservative-free lubricant eye drops at least 4 times a day, starting with the first infusion of Blenrep and continuing until end of treatment. Avoid use of contact lenses unless directed by an ophthalmologist.

NOTE: Changes in visual acuity may be associated with difficulty for driving and reading. Use caution when driving or operating machinery.

**Thrombocytopenia (low levels of platelets)**

Platelets (thrombocytes) help blood to clot, which means low levels of platelets can lead to bleeding. In the Blenrep 2.5 mg/kg arm in the DREAMM-2 clinical trial, 21% of the patients had low platelet levels that were considered serious (Grade 3 or 4). 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 one patient. Fatal adverse reactions included cerebral hemorrhage in two patients.

**Prevention and treatment of thrombocytopenia**

Your doctor will monitor your platelet counts before you begin treatment with Blenrep and over the course of your treatment. If your platelets are too low, your doctor may interrupt, delay, or discontinue your dose of Blenrep. Thrombocytopenia may be treated either with medication or with platelet infusion.

**Infusion-related reactions**

Infusion-related reactions are common with Blenrep, and can be serious. Infusion-related reactions occurred in 18% of 218 patients in the pooled safety population. Tell your doctor right away if you get any of the following signs or symptoms while receiving Blenrep:

- Chills or shaking
- Redness of your face (flushing)
- Itching or rash
Shortness of breath, cough, or wheezing
Swelling of your lips, tongue, throat, or face
Dizziness
Feel like passing out
Tiredness
Fever
Feel like your heart is racing (palpitations)

**Prevention and treatment of infusion-related reactions**
Immediately report any signs and symptoms of infusion-related reactions to your doctor.

Your doctor will monitor you for infusion-related reactions and may slow down or stop your infusion. Depending on the severity of the infusion-related reaction, your doctor may give you medication prior to your future infusions or may need to stop treatment.

**Other common side effects of Blenrep**
Other common adverse events with Blenrep were nausea, low blood cell counts, fever, tiredness, and changes in kidney and liver function tests.

Red blood cells contain **hemoglobin**, a protein that contains iron and transports oxygen from the lungs to the body’s organs and tissues. A low level of hemoglobin (**anemia**) results in low levels of oxygen in the body, which may cause shortness of breath and feelings of exhaustion. In the DREAMM-2 clinical trial, 20% of the patients had Grade 3 or 4 anemia. If you develop anemia, your doctor will determine which treatment regimen for anemia is best and safest for you.

**Pregnancy, lactation, and reproductive potential**
Blenrep may impair fertility in females and males. Blenrep can cause fetal harm when administered to pregnant women. Pregnancy testing is recommended for females of reproductive potential prior to initiating treatment with Blenrep. Due to the potential for serious adverse reactions in the breastfed child, women are advised not to breastfeed during treatment with Blenrep and for 3 months after the last dose. Females of reproductive potential must use effective contraception during treatment with Blenrep and for 4 months after the last dose. Males with female partners of reproductive potential must use effective contraception during treatment with Blenrep and for 6 months after the last dose.
Access to Blenrep

Blenrep can be prescribed in a normal fashion by the treating doctor. However, due to the potential for eye toxicities the doctor, patient, and the clinic or healthcare facility must all enroll and complete training in the “Blenrep REMS” (Risk Evaluation and Mitigation Strategy) program. This ensures that eye examinations occur before each dose of Blenrep with dose and/or schedule adjustments as necessary. Blenrep REMS requirements include the following:

- Prescribers must counsel patients receiving Blenrep about the risk of ocular toxicity and the need for ophthalmic examinations.
- Patients must be enrolled in the Blenrep REMS program and must comply with monitoring.
- Healthcare facilities must be certified with the program and verify that patients are authorized to receive Blenrep.

For more information about the REMS program, visit blenrepREMS.com or call 1-855-209-9188.

In addition, GSK Oncology provides Blenrep access and reimbursement services to help patients with their Blenrep treatment journey. Please visit bit.ly/blenrep or call 1-844-447-5662.

Terms and definitions

**Anemia**: A decrease in hemoglobin, a protein which is contained in red blood cells and carries oxygen to the body’s tissues and organs. Anemia is usually defined as hemoglobin below 10 g/dL, and/or as a decrease of ≥ 2 g/dL from the normal level for an individual. Over 13–14 g/dL is considered normal.

**Antibody-drug conjugate (ADC)**: An anti cancer therapy that links a monoclonal antibody directed at myeloma cells with a drug (cytotoxic agent) that is toxic to cancer cells. The ADC binds to specific receptors on the surface of the cancer cells, then the linked drug enters the cancer cells and kills them.

**B-cell maturation antigen (BCMA)**: Also known as tumor necrosis factor receptor superfamily member 17 (TNFRSF17), it is a protein involved in myeloma cell growth and survival. BCMA is found on the surface of cells in all patients with myeloma.

**Hemoglobin**: A protein in red blood cells that carries oxygen.

**Immunomodulatory drug**: An agent that affects, enhances, or suppresses the immune system. Sometimes called an IMiD® compound.

**Intravenous (IV)**: Administered into a vein.

**Keratopathy**: Any noninflammatory disease of the cornea, the eye’s protective outer layer.

**Median**: The middle number or the mean of the two central numbers in a series of numbers. For example, “median progression-free survival (PFS)” means that half the patients had remissions that were shorter than the median PFS, and half the patients had remissions that were longer than the median PFS.
**Monoclonal antibody (mAb):** An antibody manufactured in a lab rather than produced in the human body. Monoclonal antibodies are specifically designed to find and bind to cancer cells and/or immune system cells for diagnostic or treatment purposes. Monoclonal antibodies can be used alone, or they can be used to deliver drugs, toxins, or radioactive material directly to tumor cells.

**Multiple myeloma:** A cancer of the bone marrow plasma cells, white blood cells that make antibodies. The cancerous plasma cells are called myeloma cells.

**Photophobia:** Extreme sensitivity to light. Photophobia isn’t a condition, but rather is a symptom of another problem.

**Proteasome inhibitor:** Any drug that interferes with the normal function of the proteasome, an enzyme complex responsible for breaking down and recycling unwanted proteins in both normal cells and cancer cells.

**Refractory:** Disease that is no longer responsive to standard treatments. Patients with refractory myeloma have had progressive disease either during treatment or within 60 days following treatment. Most clinical trials for advanced disease are for patients with relapsed and/or refractory myeloma.

**Registration trial:** A well-controlled clinical trial intended to provide the substantial evidence of safety and efficacy required by a governmental regulatory agency to be completed as a prerequisite to approval and sale of a product. For drugs sold in the United States, the regulatory agency is the US Food and Drug Administration (FDA). For drugs sold in the European Union, it is the European Medicines Agency (EMA).

**Relapse:** The reappearance of signs and symptoms of a disease after a period of improvement. Patients with relapsed disease have been treated, then developed signs and symptoms of myeloma at least 60 days after treatment ended. Most clinical trials for advanced disease are for patients with relapsed and/or refractory myeloma.

**Response or remission:** Complete or partial disappearance of the signs and symptoms of cancer. Remission and response are interchangeable terms.

- **Stringent complete response (sCR)** – sCR is CR (as defined below) plus normal FLC ratio and absence of clonal cells in bone marrow by immunohistochemistry or immunofluorescence.

- **Complete response (CR)** – For myeloma, CR is negative immunofixation on serum (blood) and urine, and disappearance of any soft tissue plasmacytomas, and ≤ 5% plasma cells in bone marrow. CR is not the same as a cure.

- **Very good partial response (VGPR)** – VGPR is less than CR. VGPR is serum M-protein and urine M-protein detectable by immunofixation but not on electrophoresis, or 90% or greater reduction in serum M-protein, plus urine M-protein less than 100 mg per 24 hours.

- **Partial response (PR)** – PR is a level of response in which there is at least a 50% reduction in M-protein, and reduction in 24-hour urinary M-protein by at least 90% (or to less than 200 mg per 24 hours).
You are not alone.
The IMF is here to help.

Myeloma is a cancer that is not known to most patients and caregivers at the time of diagnosis. To be empowered to play an active role in your own medical care and to make good decisions about your care with your doctor, it is important and helpful to learn as much as possible about myeloma and its treatment options.

The IMF produces an extensive library of publications and periodicals to help arm you with an important weapon in the fight against myeloma: INFORMATION.

All IMF educational materials are always free of charge. Publications are available in English, and selected titles are also available in other languages.

Visit publications.myeloma.org to read, download, or order printed copies of IMF materials. And visit subscribe.myeloma.org to subscribe to IMF print and electronic communications.

As always, the IMF urges you to discuss all medical issues with your doctor, and to contact the IMF’s InfoLine with your myeloma questions and concerns.

818.487.7455          800.452.CURE
TheIMF@myeloma.org
myeloma.org