ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See section 4.8 for how to report adverse reactions.

1. NAME OF THE MEDICINAL PRODUCT

Blenrep 70 mg powder for concentrate for solution for infusion
Blenrep 100 mg powder for concentrate for solution for infusion

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Belantamab mafodotin is an antibody-drug conjugate (ADC) that contains belantamab, an afucosylated humanised monoclonal IgG1k antibody specific for B cell maturation antigen (BCMA), produced using recombinant DNA technology in a mammalian cell line (Chinese hamster ovary) that is conjugated with maleimidocaproyl monomethyl auristatin F (mcMMAF).

Blenrep 70 mg powder for concentrate for solution for infusion

One vial of powder contains 70 mg of belantamab mafodotin.

After reconstitution with 1.4 mL of water for injections, each mL of solution contains 50 mg belantamab mafodotin.

Excipient with known effect

Each vial of reconstituted solution contains 0.28 mg polysorbate 80 per 1.4 mL of withdrawable solution.

Blenrep 100 mg powder for concentrate for solution for infusion

One vial of powder contains 100 mg of belantamab mafodotin.

After reconstitution with 2 mL of water for injections, each mL of solution contains 50 mg belantamab mafodotin.

Excipient with known effect

Each vial of reconstituted solution contains 0.4 mg polysorbate 80 per 2 mL of withdrawable solution.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Powder for concentrate for solution for infusion (powder for concentrate).

Lyophilised white to yellow powder.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Blenrep is indicated in adults for the treatment of relapsed or refractory multiple myeloma:

- in combination with bortezomib and dexamethasone in patients who have received at least one prior therapy; and
- in combination with pomalidomide and dexamethasone in patients who have received at least one prior therapy including lenalidomide.

4.2 Posology and method of administration

Treatment with Blenrep is initiated and monitored by physicians experienced in the treatment of multiple myeloma.

Recommended supportive care

Patients should have an ophthalmic examination (including visual acuity and slit lamp examination) performed by an eye care professional before each of the first 4 doses of Blenrep treatment, and as clinically indicated thereafter (see section 4.4).

Posology

Administration of Blenrep is to be continued according to the recommended schedule until disease progression or unacceptable toxicity. Blenrep is administered in combination with other treatments (see Table 1). For other medicinal products that are administered with Blenrep, see section 5.1 and the respective current Summary of Product Characteristics.

Table 1: Recommended starting dose schedule for Blenrep in combination with other therapies

Combination regimen	Recommended starting dose schedule
With bortezomib and dexamethasone (BVd)[a] (Cycle length = 3 weeks)	2.5 mg/kg administered once every 3 weeks
With pomalidomide and dexamethasone (BPd) (Cycle length = 4 weeks)	Cycle 1: 2.5 mg/kg administered once Cycle 2 onwards: 1.9 mg/kg administered once every 4 weeks

[a] Bortezomib and dexamethasone are administered for the first 8 cycles.

If a planned dose of Blenrep is missed due to reasons other than adverse reactions, it is recommended that Blenrep be resumed with the start of the next planned treatment cycle.

If a planned dose of Blenrep is missed due to adverse reactions, it is recommended that Blenrep be resumed with the start of the next planned treatment cycle after recovery of adverse reactions (see Table 3).

Dose modifications

Dose modifications are required for nearly all patients to manage safety and tolerability. Dose reduction levels for Blenrep are provided in Table 2. Recommended modifications to manage adverse reactions are provided in Table 3.

Table 2: Dose reduction schedule for Blenrep

	Combination with bortezomib and dexamethasone	**Combination with pomalidomide and dexamethasone**
Recommended starting dose schedule	2.5 mg/kg every 3 weeks	2.5 mg/kg once on cycle 1 then 1.9 mg/kg every 4 weeks starting on cycle 2
Reduced dose level 1	1.9 mg/kg every 3 weeks	1.9 mg/kg every 8 weeks
Reduced dose level 2	NA[a]	1.4 mg/kg every 8 weeks

NA = Not applicable.

[a] There is no reduced dose level 2.

Ocular adverse reactions

Ocular events were graded based on ophthalmic examination findings that include the combination of corneal examination findings and best corrected visual acuity (BCVA). The patient's ophthalmic examination findings should be reviewed by the treating physician before determining the dose of Blenrep.

The corneal examination findings may or may not be accompanied by changes in BCVA. Ocular adverse reaction severity is defined by the most severely affected eye as both eyes may not be affected to the same degree. It is important for physicians to consider not only corneal examination findings but also visual acuity changes and reported symptoms as they evaluate dose delays and reductions.

Do not re-escalate dose after a dose reduction is made for ocular adverse reactions. Re-escalation of dose for non-ocular adverse reactions is to be based on clinical judgement, if applicable.

Table 3: Recommended dose modifications for adverse reactions

Adverse reaction	**Severity[a]**	**Recommended dose modifications**
Ocular adverse reactions[b] (see section 4.4)	Mild (Grade 1) *Corneal examination finding(s)* Mild superficial punctate keratopathy with worsening from baseline, with or without symptoms. *Change in BCVA* Decline from baseline of 1 line on snellen equivalent visual acuity.	Treatment should be continued at the current dose.

Adverse reaction	Severity[a]	Recommended dose modifications
	Moderate (Grade 2) *Corneal examination finding(s)* Moderate superficial punctate keratopathy, patchy microcyst-like deposits, peripheral sub-epithelial haze, or a new peripheral stromal opacity. *Change in BCVA* Decline from baseline of 2 lines (and snellen equivalent visual acuity not worse than 20/200). Or Severe (Grade 3) *Corneal examination finding(s)* Severe superficial punctate keratopathy, diffuse microcyst-like deposits involving the central cornea, central sub-epithelial haze, or a new central stromal opacity. *Change in BCVA* Decline from baseline of 3 or more lines (and snellen equivalent visual acuity not worse than 20/200).	Withhold treatment until improvement in both corneal examination findings and BCVA to mild severity or better. Resume treatment at reduced dose level 1 as per Table 2. If toxicity is identified prior to dosing cycle 2 for BPd, reduce Blenrep dose at 1.9 mg/kg every 4 weeks for cycle 2 and all subsequent cycles.
	Corneal Epithelial Defect such as Corneal Ulcers or Change of BCVA worse than 20/200 (Grade 4) *Corneal examination finding(s)* Corneal epithelial defect such as corneal ulcers.[b] *Change in BCVA* Decline to snellen equivalent visual acuity of worse than 20/200.	Withhold until improvement in both corneal examination findings and BCVA to mild severity or better. Resume treatment at reduced dose level 1 for BVd and reduced dose level 2 for BPd as per Table 2, if applicable. For worsening symptoms that are unresponsive to appropriate management, consider permanent discontinuation.

Adverse reaction	Severity[a]	Recommended dose modifications
Thrombocytopenia[c] (see section 4.4)	Grade 3	Without bleeding: • For patients on 2.5 mg/kg, reduce Blenrep to 1.9 mg/kg. For BVd, may consider reverting to previous dose, if appropriate once thrombocytopenia recovers to Grade 2 or better. • For patients on 1.9 mg/kg or lower, continue at same dose. With bleeding: • Withhold Blenrep until improvement to Grade 2 or better. For patients previously on 2.5 mg/kg, resume Blenrep at 1.9 mg/kg. For patients on 1.9 mg/kg or lower, resume at same dose. Consider additional supportive treatment (e.g., transfusion), as clinically indicated and per local practice.
	Grade 4	Withhold the dose. Consider restarting if recovered to Grade 3 or better, and only if there is no active bleeding at time of treatment restart. For patients previously on 2.5 mg/kg, resume Blenrep at 1.9 mg/kg. For patients on 1.9 mg/kg or lower, resume at same dose.
Infusion-related reactions (see section 4.4)	Grade 2	Interrupt infusion and provide supportive treatment. Once symptoms resolve to Grade 1 or better, resume at a decreased infusion rate by at least 50% and may consider premedication.
	Grade 3	Interrupt infusion and provide supportive treatment. Once resolved, resume dosing with a slower infusion rate. For future infusion, consider premedication.
	Grade 4	Permanently discontinue Blenrep. • If anaphylactic or life-threatening infusion reaction, permanently discontinue the infusion and institute appropriate emergency care.
Pneumonitis (see section 4.8)	Grade ≥3	Permanently discontinue Blenrep.
Other adverse reactions (see section 4.8)	Grade 3	Withhold Blenrep until improvement to Grade 1 or better. For patients previously on 2.5 mg/kg, resume Blenrep at 1.9 mg/kg. For patients on 1.9 mg/kg or lower, resume at same dose.
	Grade 4	Consider permanent discontinuation of Blenrep. If continuing treatment, withhold Blenrep until improvement to Grade 1 or better. For patients previously on 2.5 mg/kg, resume Blenrep at 1.9 mg/kg. For patients on 1.9 mg/kg or lower, resume at same dose.

BCVA = best corrected visual acuity; BPd = Blenrep with pomalidomide and dexamethasone;
BVd = Blenrep with bortezomib and dexamethasone.

[a] Non-ocular adverse reactions were graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE).
[b] A corneal defect may lead to corneal ulcers. These should be managed promptly and as clinically indicated by an eye care professional. Corneal ulcer, by definition, means an epithelial defect with underlying stromal infiltration.
[c] If thrombocytopenia is considered disease-related, is not accompanied by bleeding, and recovers with transfusion to >25 x10^9/L platelets, continuing treatment at the current dose may be considered.

Special populations

Elderly
No dose adjustment is recommended for patients who are aged 65 years or over (see sections 4.8 and 5.2).

Renal impairment
No dose adjustment is recommended in patients with mild (eGFR 60-89 mL/min), moderate (eGFR 30-59 mL/min), severe renal impairment (eGFR < 30 mL/min not requiring dialysis), or end-stage renal disease (eGFR < 15 mL/min requiring dialysis) (see section 5.2).

Hepatic impairment
No dose adjustment is recommended in patients with mild hepatic impairment (total bilirubin greater than upper limit of normal [ULN] to ≤ 1.5 × ULN and any aspartate transaminase [AST] or total bilirubin ≤ ULN with AST > ULN). There are limited data in patients with moderate hepatic impairment (total bilirubin greater than 1.5 × ULN to ≤ 3.0 × ULN and any AST level), or in patients with severe hepatic impairment (total bilirubin greater than > 3.0 × ULN and any AST level) to support a dose recommendation; Blenrep should only be used in these patients if the potential benefits outweigh any potential risks (see section 5.2).

Body weight
Blenrep is dosed based on baseline actual body weight and has been studied in patients with body weight 37 to 170 kg (see section 5.2). For changes of body weight >10% during treatment, re-calculate dose based on the actual body weight at the time of dosing.

Paediatric population
There is no relevant use of Blenrep in the paediatric population for the treatment of relapsed or refractory multiple myeloma.

Method of administration

Blenrep is for intravenous infusion only and is administered by an intravenous infusion pump using an infusion set made of polyvinyl chloride or polyolefin over approximately 30 minutes. In the event of an infusion-related reaction (IRR), the administration time may be extended beyond 30 minutes, provided that the total in-use time, including both preparation and administration of the dose, does not exceed the allowable 6-hour duration.

Blenrep must not be administered as an intravenous push or bolus injection.

Blenrep must be diluted before administration.

Filtration of the diluted solution is not required. However, if the diluted solution is filtered, 0.2 µm or 0.22 µm polyethersulfone (PES) based filter is recommended.

For instructions on dilution, precaution before manipulating or administering the medicinal product, handling, and disposal of the vials, see section 6.6.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Traceability

In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.

Ocular adverse reactions

Ocular adverse reactions (e.g., blurred vision, dry eye, eye irritation, and photophobia) have been reported with the use of Blenrep. The most commonly reported corneal examination findings include superficial punctuate keratopathy, microcyst-like epithelial changes, and haze, with or without changes in visual acuity or symptoms. Clinically relevant changes in visual acuity may be associated with temporary difficulty in driving or operating machinery (see sections 4.7 and 4.8). Patients should be advised to temporarily avoid activities such as driving or operating machinery if visual symptoms occur (see section 4.7) and to report any changes in vision promptly. Regular ophthalmologic monitoring is recommended.

Physicians should also encourage patients to inform them of any ocular symptoms. Ophthalmic examinations, including assessment of visual acuity and slit lamp examination, should be performed before each of the first 4 doses of Blenrep and during treatment as clinically indicated.

Patients should be advised to administer preservative-free artificial tears at least 4 times a day during treatment. Patients should avoid using contact lenses until the end of treatment. Bandage contact lenses may be used under the direction of an ophthalmologist.

Patients experiencing corneal examination findings (keratopathies such as superficial punctate keratopathy or microcyst-like deposits) with or without changes in visual acuity may require a dose modification (delay and/or reduction) or treatment discontinuation based on severity of findings (see Table 3).

Cases with changes in the subbasal nerve plexus of the cornea (e.g., nerve fibre fragmentation and loss of nerve fibres) resulting in hypoesthesia of the cornea and cases of corneal ulcers (ulcerative and infective keratitis) have been reported (see section 4.8). These should be managed promptly and as clinically indicated by an eye care professional. Treatment with Blenrep should be interrupted until the corneal ulcer has healed (see Table 3).

Thrombocytopenia

Thrombocytopenic events (thrombocytopenia and platelet count decreased) have been reported with the use of Blenrep. Thrombocytopenia may lead to serious bleeding events, including gastrointestinal and intracranial bleeding (see section 4.8).

Complete blood counts (CBC) with differential and including platelet counts should be frequently monitored throughout treatment. Patients experiencing Grade 3 or 4 thrombocytopenia or those on concomitant anticoagulant treatments may require more frequent monitoring and may be managed with a dose delay or dose reduction (see Table 3). Supportive therapy (e.g., platelet transfusions) may be provided according to standard medical practice.

Infusion-related reactions

Infusion-related reactions (IRRs) have been reported with the use of Blenrep. Most IRRs were Grade 1 or 2 and resolved within the same day (see section 4.8). If a Grade 2 or higher infusion-related reaction occurs during administration, reduce the infusion rate, or stop the infusion depending on the severity of the symptoms. Institute appropriate medical treatment and restart infusion at a slower rate if the patient's condition is stable. If Grade 2 or higher IRR occurs, consider premedication for subsequent infusions (see Table 3).

Pneumonitis

Cases of pneumonitis, including fatal events, have been observed with Blenrep. Evaluation of patients with new or worsening unexplained pulmonary symptoms (e.g., cough, dyspnoea) must be performed to exclude possible pneumonitis. In case of suspected or confirmed Grade 3 or higher pneumonitis, it is recommended that Blenrep is discontinued and appropriate treatment initiated.

Hepatitis B virus reactivation

Hepatitis B virus (HBV) reactivation can occur in patients treated with medicinal products directed against B cells, including Blenrep, and in some cases, may result in fulminant hepatitis, hepatic failure, and death. Patients with evidence of positive HBV serology must be monitored for clinical and laboratory signs of HBV reactivation as per clinical guidelines. In patients who develop reactivation of HBV while on Blenrep, treatment with Blenrep must be withheld and patients must be treated according to clinical guidelines.

Excipients with known effect

Polysorbate 80
This medicinal product contains polysorbate 80 (E433), which may cause allergic reactions. Each 70 mg vial contains 0.28 mg of polysorbate 80 (E433) in 1.4 mL of withdrawable reconstituted solution, and each 100 mg vial contains 0.4 mg of polysorbate 80 (E433) in 2 mL of withdrawable reconstituted solution.

Sodium
This medicinal product contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially "sodium-free".

4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies have been performed. Based on available *in vitro* and clinical data, there is a low risk of pharmacokinetic or pharmacodynamic drug interactions for belantamab mafodotin. Clinical pharmacokinetic assessments of belantamab mafodotin in combination with bortezomib, lenalidomide, pomalidomide, and/or dexamethasone indicated no clinically relevant drug-drug interaction between belantamab mafodotin and these small molecule medicinal products.

4.6 Fertility, pregnancy, and lactation

Women of child-bearing potential/Contraception in females and males

Women
The pregnancy status of women of child-bearing potential must be verified prior to initiating therapy with Blenrep. Women of child-bearing potential have to use effective contraception during treatment with Blenrep and for at least 4 months after the last dose.

Men
Men with female partners of child-bearing potential have to use effective contraception during treatment with Blenrep and for at least 6 months after the last dose.

Pregnancy

There are no data from the use of belantamab mafodotin in pregnant women. Based on the mechanism of action of the cytotoxic component monomethyl auristatin F (MMAF), belantamab mafodotin can cause embryo-foetal harm when administered to a pregnant woman (see section 5.3). Human immunoglobulins (IgG) are known to cross the placental barrier, and therefore, being an IgG, belantamab mafodotin has the potential to be transmitted from the mother to the developing foetus.

Blenrep is not recommended during pregnancy unless the benefit to the mother outweighs the potential risks to the foetus. If a pregnant woman needs to be treated she must be clearly advised on the potential risk to the foetus.

Breast-feeding

It is unknown whether belantamab mafodotin is excreted in human milk. Immunoglobulin G (IgG) is present in human milk in small amounts. Since belantamab mafodotin is a humanised IgG monoclonal antibody, and based on the mechanism of action, it may potentially cause serious adverse reactions in breastfed newborns or infants of treated mothers.

Blenrep is not to be used during breast-feeding and breast-feeding is to be avoided for at least 3 months after the last dose of Blenrep.

Fertility

Based on findings in animals and the mechanism of action, belantamab mafodotin may impair fertility in females and males of reproductive potential (see section 5.3).

Therefore, physicians may counsel women of childbearing potential and men being treated with Blenrep who desire children in the future regarding fertility preservation.

4.7 Effects on ability to drive and use machines

Blenrep has a moderate influence on the ability to drive and use machines.

Patients must be advised to use caution when driving or operating machines while on Blenrep as it may affect patients' vision and influence their ability to drive or use machines due to impact on visual acuity and other ocular adverse reactions (see sections 4.4 and 4.8).

4.8 Undesirable effects

Summary of the safety profile

The most common adverse reactions (any grade) were corneal examination findings (including keratopathy) (84%), visual acuity reduced (81%), thrombocytopenia (62%), vision blurred (52%), dry eye (36%), foreign body sensation in eyes (32%), photophobia (30%), eye irritation (28%), neutropenia (27%), anaemia (23%), diarrhoea (23%), neuropathies (23%), and eye pain (21%).

The most common serious adverse reactions (any grade) were pneumonia (9%), pyrexia (4%), COVID-19 (3%), COVID-19 pneumonia (3%), and thrombocytopenia (2%).

The proportion of subjects with treatment discontinuation due to adverse reactions was 24%. The most common adverse reaction leading to treatment discontinuation was ocular events (7%).

The frequency of dose reduction due to adverse reactions was 63%. The most common adverse reactions leading to dose reduction were ocular events (39%), thrombocytopenia (12%), platelet count

decreased (6%), insomnia (5%), peripheral sensory neuropathy (5%), neuropathy peripheral (5%), neutropenia (4%), fatigue (3%), and neutrophil count decreased (2%).

The frequency of dose delay due to adverse reactions was 83%. The most common adverse reactions leading to dose delay were ocular events (67%), thrombocytopenia (16%), COVID-19 (11%), platelet count decreased (8%), neutropenia (8%), upper respiratory tract infection (7%), pneumonia (7%), diarrhoea (4%), pyrexia (4%), neutrophil count decreased (4%), peripheral sensory neuropathy (4%), bronchitis (3%), COVID-19 pneumonia (3%), cataract (3%), neuropathy peripheral (3%), and alanine aminotransferase increased (3%).

Tabulated list of adverse reactions

The adverse reaction frequencies are based on all-cause adverse event frequencies, from patients with multiple myeloma exposed to belantamab mafodotin, for which, after thorough assessment, a causal relationship between the medicinal product and the adverse event is at least a reasonable possibility.

The safety of belantamab mafodotin has been evaluated in more than 7500 patients with multiple myeloma, including 516 patients who received belantamab mafodotin in triplet combinations as part of the DREAMM-6 (a Phase 1/2, open-label dose exploration study), DREAMM-7, and DREAMM-8 studies, 312 patients who received belantamab mafodotin as monotherapy in the DREAMM-2 and DREAMM-3 studies, and including patients from the post-marketing setting.

Adverse reactions are listed in Table 4 by system organ class and by frequency.

Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness. Frequencies are defined as:
Very common: ≥1/10
Common: ≥1/100 to <1/10
Uncommon: ≥1/1 000 to <1/100
Rare: ≥1/10 000 to <1/1 000
Very rare: <1/10 000
Not known: frequency cannot be estimated from the available data

Table 4: Adverse reactions in multiple myeloma patients treated with belantamab mafodotin in clinical trials and post-marketing

System organ class (SOC)	Adverse reaction	Frequency	Incidence (%)	
			Any grade	Grade 3-4
Infections and infestations	COVID-19	Very common	18	3
	Upper respiratory tract infection	Very common	15	<1
	Pneumonia	Very common	13	7
	Urinary tract infection	Common	9	2
	Bronchitis	Common	5	<1
	COVID-19 pneumonia	Common	3	2
	Hepatitis B reactivation	Uncommon	<1	<1
Blood and lymphatic system disorders	Thrombocytopenia[a]	Very common	62	47
	Neutropenia[b]	Very common	27	22
	Anaemia	Very common	23	12
	Lymphopenia[c]	Very common	10	7
	Leukopenia[d]	Common	9	4
	Febrile neutropenia	Common	1	1

System organ class (SOC)	Adverse reaction	Frequency	Incidence (%)	
			Any grade	Grade 3-4
Immune system disorders	Hypogammaglobulinemia	Common	2	<1
Metabolism and nutrition disorders	Decreased appetite	Common	8	<1
Psychiatric disorders	Insomnia	Very Common	13	1
Nervous system disorders	Neuropathies[e]	Very common	23	2
Eye disorders	Corneal examination findings (including keratopathy)[f,g]	Very common	84	62
	Visual acuity reduced[f]	Very common	81	50
	Vision blurred	Very common	52	13
	Dry eye	Very common	36	5
	Foreign body sensation in eyes	Very common	32	2
	Photophobia	Very common	30	1
	Eye irritation	Very common	28	3
	Eye pain	Very common	21	<1
	Cataract	Very common	13	4
	Visual impairment	Common	8	5
	Lacrimation increased	Common	5	<1
	Diplopia	Common	3	<1
	Eye pruritus	Common	2	<1
	Ocular discomfort	Common	1	<1
	Corneal ulcer[h]	Common	1	<1
	Corneal hypoesthesia	Not known	-	-
Respiratory, thoracic and mediastinal disorders	Cough	Very common	11	<1
	Dyspnoea	Common	9	1
	Pneumonitis	Uncommon	<1	<1
Gastrointestinal disorders	Diarrhoea	Very common	23	2
	Nausea	Very common	17	<1
	Constipation	Very common	15	<1
	Vomiting	Common	7	<1
Hepatobiliary Disorders	Increased aspartate aminotransferase	Very common	15	2
	Increased alanine aminotransferase	Very common	13	3
	Increased gamma glutamyltransferase	Very common	11	5
	Porto-sinusoidal vascular disorder[i]	Uncommon	<1	<1
Skin and subcutaneous tissue disorders	Rash	Common	4	<1
Musculoskeletal	Arthralgia	Very common	11	<1

System organ class (SOC)	Adverse reaction	Frequency	Incidence (%)	
			Any grade	Grade 3-4
and connective tissue disorders	Back pain	Very common	11	1
	Increased creatine phosphokinase	Common	3	1
Renal and urinary disorders	Albuminuria[j]	Common	3	<1
General disorders and administration site conditions	Fatigue	Very common	19	3
	Pyrexia	Very common	18	<1
	Asthenia	Common	6	1
Injury, poisoning and procedural complications	Infusion-related reactions[k]	Very Common	11	<1

[a] Includes thrombocytopenia and platelet count decreased.
[b] Includes neutropenia and neutrophil count decreased.
[c] Includes lymphopenia and lymphocyte count decreased.
[d] Includes leukopenia and white blood cell count decreased.
[e] Includes peripheral sensory neuropathy, neuropathy peripheral, neuralgia, polyneuropathy, peripheral motor neuropathy, sensory loss, peripheral sensorimotor neuropathy.
[f] Based on ophthalmic examination findings.
[g] Includes superficial punctate keratopathy, microcyst-like epithelial changes, stippled vortex staining pattern, sub-epithelial haze, corneal epithelial defects, and stromal opacity with or without changes in visual acuity.
[h] Includes infective keratitis and ulcerative keratitis.
[i] Signs or symptoms may include abnormal liver function tests, portal hypertension, varices, and ascites.
[j] Includes albuminuria, albumin urine present, urine albumin/creatinine ratio increased, and microalbuminuria.
[k] Includes adverse reactions determined to be related to infusion. Infusion reactions may include, but are not limited to, pyrexia, chills, diarrhoea, nausea, asthenia, hypertension, lethargy, and tachycardia.

Description of selected adverse reactions

Ocular adverse reactions

Across pooled datasets from 3 trials of belantamab mafodotin in combination with other therapies (n = 516), DREAMM-6 (a Phase 1/2, open-label dose exploration study), DREAMM-7 and DREAMM-8, ocular events were reported and included ophthalmic examination findings and ocular adverse reactions. The most common (> 25%) were reduced visual acuity (90%), corneal examination findings based on the ophthalmic examination findings (89%), blurred vision (62%), dry eye (44%), foreign body sensation in eyes (40%), photophobia (37%), eye irritation (35%), and eye pain (27%).

Corneal examination findings (keratopathies such as superficial punctate keratopathy and microcyst-like deposits) were reported based on the ophthalmic examination findings as Grade 1 in 5% of patients, Grade 2 in 14%, Grade 3 in 59% and Grade 4 in 12%. Cases of corneal ulcer (ulcerative and infective keratitis) were reported in < 1% of patients (n = 5). At least 1 corneal examination finding or BCVA-related event (Grade ≥ 2) was reported by 86% of patients.

Table 5 includes a summary of decreased vision in patients with normal baseline (snellen equivalent visual acuity 20/25 or better in at least one eye) and corneal examination findings from pooled data of belantamab mafodotin in combination with other therapies.

Table 5: Median duration and resolution of the first ocular events in clinical trials (DREAMM-6, DREAMM-7, DREAMM-8; n = 516)

	Bilateral reduction in BCVA		Corneal examination findings (Grade 2+ events)
	20/50 or worse	20/200 or worse	
Patients with event, n (%)	161 (31)	8 (2)	423 (82)
Median time to first onset (days)	85	99	43
Improvement of first event[a], n (%)	155 (96)	8 (100)	NA
Resolution of first event[b], n (%)	145 (90)[c]	6 (75)[c]	355 (84)[d]
Median time to resolution of first event, days (range)	57 (8, 908)	86.5 (22, 194)	106 (8, 802)
Ongoing first event[b], n (%)	16 (10)	2 (25)	68 (16)
On treatment and follow-up ongoing, n (%)	3 (2)	-	4 (< 1)
Discontinued treatment and follow-up ongoing, n (%)	2 (1)	-	8 (2)
Discontinued treatment and follow-up ended, n (%)	11 (7)	2 (25)	56 (13)

NA = Not applicable.

[a] Improvement was defined as no longer 20/50, or 20/200, or worse in at least one eye.

[b] At time of data cut-off (DREAMM-6: 28 FEB 2023; DREAMM-7: 02 OCT 2023; DREAMM-8: 29 JAN 2024).

[c] Resolution of BCVA was defined as 20/25 or better in at least one eye.

[d] Resolution of corneal examination findings was defined as Grade 1 or better based on the ophthalmic examination findings.

Infusion-related reactions

Across DREAMM-6, DREAMM-7, and DREAMM-8 (n = 516), the incidence of IRRs was 6%. Nearly all IRRs were reported as Grade 1 (2%) and Grade 2 (4%), while < 1% experienced Grade 3 IRRs. One patient discontinued treatment due to IRRs. The incidence of IRRs was 4% during the first infusion, < 1% during the second infusion, and 2% during the subsequent infusions. IRRs were managed in 3% of patients with an event by dose reductions and 41% by dose delays, while 50% required additional premedication.

Thrombocytopenia

Across DREAMM-6, DREAMM-7, and DREAMM-8 (n = 516), thrombocytopenic events (thrombocytopenia and platelet count decreased) occurred in 74% of patients. Grade 2 thrombocytopenic events occurred in 10% of patients, Grade 3 in 26%, and Grade 4 in 33%. Clinically significant bleeding (≥ Grade 2) occurred in 5% of patients with concomitant low platelet levels (Grades 3 to 4). These clinically significant bleeding events included: thrombocytopenia, platelet count decreased, epistaxis, urinary tract haemorrhage, haemorrhoidal haemorrhage, gastrointestinal haemorrhage, mouth haemorrhage, cerebral haemorrhage, and haematuria, and were Grade 2 in < 1%, Grade 3 in 2%, Grade 4 in 3%, and Grade 5 in < 1% of patients. The median time to onset for the first occurrence of thrombocytopenia was 8 days (range: 1, 659). The median duration of the first occurrence of thrombocytopenia was 15 days (range: 1, 361). Thrombocytopenia was managed in 35% of patients with an event by dose reduction and 44% by dose delay, while 2% required permanent discontinuation.

Infections

Across DREAMM-6, DREAMM-7, and DREAMM-8 (n = 516), COVID-19 was reported in 23% of patients with 4% in Grade 3 and < 1% in Grade 4. A fatal outcome occurred in < 1% of patients, 16% had an event that led to dose delay, while < 1% required permanent discontinuation.

Across DREAMM-6, DREAMM-7, and DREAMM-8 (n = 516), pneumonia was reported in 18% of patients with 9% in Grade 3 and < 1% in Grade 4. Of pneumonia events occurring, 2% had a fatal outcome, < 1% led to dose reduction, 11% led to dose delay, while 2% required permanent discontinuation.

Across DREAMM-6, DREAMM-7, and DREAMM-8 (n = 516), COVID-19 pneumonia was reported in 5% of patients with 3% in Grade 3 and < 1% in Grade 4. A fatal outcome occurred in 1% of patients, 4% had an event that led to dose delay, while < 1% required permanent discontinuation.

Elderly

Across DREAMM-6, DREAMM-7, and DREAMM-8 (n = 516), 226 patients were less than 65 years of age, 211 patients were 65 to less than 75 years of age, and 79 patients were 75 years of age or older. Serious adverse events occurred in 45% of patients less than 65 years of age, compared with 60% in those aged 65 to less than 75 years of age and 56% in those 75 years of age or older. The most common serious adverse reaction was pneumonia in 9% of patients less than 65 years of age, 17% in the 65 to less than 75 years of age group, and 9% in the 75 years of age or older group.

Ocular events (Grade 3 or 4) occurred in 76% of patients under 65 years of age, compared with 79% in those aged 65 to less than 75 years of age, and 71% in those 75 years of age or older.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V.

4.9 Overdose

There is no known specific antidote for belantamab mafodotin overdose. If overdose is suspected, patients must be monitored for any signs or symptoms of adverse reactions and appropriate supportive treatment instituted.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: antineoplastic agents, monoclonal antibodies, and antibody drug conjugates, ATC code: L01FX15.

Mechanism of action

Belantamab mafodotin is a humanised IgG1 kappa monoclonal antibody conjugated with a cytotoxic agent, mcMMAF. Belantamab mafodotin binds to cell surface BCMA and is rapidly internalised. Once inside the tumour cell, the cytotoxic agent (cys-mcMMAF) is released disrupting the microtubule network, leading to cell cycle arrest and apoptosis. The antibody also enhances recruitment and activation of immune effector cells, killing tumour cells by antibody-dependent cellular cytotoxicity and phagocytosis. Apoptosis induced by belantamab mafodotin is accompanied

by markers of immunogenic cell death, which may contribute to an adaptive immune response to tumour cells.

Pharmacodynamic effects

Cardiac electrophysiology
Belantamab mafodotin or cys-mcMMAF had no meaningful QTc prolongation (> 10 ms) at doses of up to 3.4 mg/kg once every 3 weeks.

Immunogenicity
Anti-drug antibodies (ADA) were rarely detected. No evidence of ADA impact on pharmacokinetics, efficacy or safety was observed.

Clinical efficacy and safety

DREAMM-7: belantamab mafodotin in combination with bortezomib and dexamethasone
The efficacy and safety of belantamab mafodotin in combination with bortezomib and dexamethasone (BVd) were investigated in a multicentre, randomised (1:1), open-label, Phase 3 study conducted in patients with multiple myeloma (MM) who had relapsed following treatment with at least one prior line of therapy.

In the BVd arm (N = 243), patients received belantamab mafodotin 2.5 mg/kg by intravenous infusion every 3 weeks on day 1 of each cycle; bortezomib 1.3 mg/m^2 (subcutaneously) on days 1, 4, 8, and 11 of cycles 1 to 8 (21-day cycles); and dexamethasone 20 mg (intravenous infusion or orally) on the day of and the day after bortezomib treatment. In the daratumumab, bortezomib, and dexamethasone (DVd) arm (N = 251), patients received daratumumab 16 mg/kg (IV) in 21-day cycles: every week for cycles 1 to 3 and every 3 weeks for cycles 4 to 8. Dexamethasone and bortezomib schedules were the same in both arms. Treatment continued in both arms until disease progression, death, unacceptable toxicity, withdrawal of consent, or study end. Patients were stratified by the Revised International Staging System (R-ISS), prior exposure to bortezomib, and the number of prior lines of therapy.

The key eligibility criteria for the study were having a confirmed diagnosis of MM as defined by International Myeloma Working Group (IMWG) criteria, having previously been treated with at least 1 prior line of MM therapy, and having had documented disease progression during or after their most recent therapy. Patients were excluded if they were intolerant to bortezomib, refractory to twice weekly bortezomib, previously treated with BCMA-targeted therapy, had ongoing ≥ Grade 2 peripheral neuropathy or neuropathic pain, or had current corneal epithelial disease except for mild punctate keratopathy.

The primary efficacy outcome measure was progression-free survival (PFS) as evaluated by a blinded Independent Review Committee (IRC) based on the IMWG criteria for MM.

A total of 494 patients were evaluated for efficacy in DREAMM-7. Baseline demographics and characteristics were similar across both arms including: median age: 65 years (36% aged 65-74 years and 14% aged 75 years or older); 55% male, 45% female; 83% White, 12% Asian, 4% Black, < 1% mixed race; R-ISS stage at screening I (41%), II (53%), III (5%); 28% high cytogenetics risk, median number of 1 prior line of therapy; 8% with extramedullary disease (EMD) present; and of those who received treatment (N = 488), Eastern Cooperative Oncology Group Performance Status (ECOG PS) 0 (48%), 1 (48%), or 2 (4%). In the BVd arm, 90% of patients received prior proteasome inhibitor therapy (bortezomib, carfilzomib, ixazomib), 81% of patients received prior immunomodulator therapy (lenalidomide, thalidomide, pomalidomide), and 67% of patients previously received autologous stem cell transplantation (ASCT). There were 9% of patients refractory to proteasome inhibitor therapy and 39% of patients refractory to immunomodulator therapy. In the DVd arm, 86% of patients received prior proteasome inhibitor therapy (bortezomib, carfilzomib, ixazomib), 86% of patients received prior immunomodulator therapy (lenalidomide, thalidomide, pomalidomide), and 69% of patients previously received autologous stem cell transplantation (ASCT). Ten percent of

patients refractory to proteasome inhibitor therapy and 41% of patients refractory to immunomodulator therapy.

Patients treated with belantamab mafodotin in combination with bortezomib and dexamethasone had a statistically significant improvement in PFS, overall survival (OS), and minimal residual disease (MRD) negativity rate compared with daratumumab, bortezomib, and dexamethasone. Efficacy results at the time of the first interim analysis (data cut-off 2 October 2023), except OS where data is presented from the second interim analysis data cut-off (7 October 2024) are presented in Table 6 and Figures 1 and 2.

Table 6: Efficacy results in DREAMM-7

	Belantamab mafodotin plus bortezomib and dexamethasone (BVd)[a] N = 243	**Daratumumab plus bortezomib and dexamethasone (DVd)[a] N = 251**
Primary endpoint		
Progression-free survival (PFS)[b]		
Number (%) of patients with event	91 (37)	158 (63)
Median in months (95% CI)[c]	36.6 (28.4, NR)	13.4 (11.1, 17.5)
Hazard ratio (95% CI)[d]	0.41 (0.31, 0.53)	
p-value[e]	<0.00001	
Secondary endpoints		
Overall survival (OS)		
Number (%) of patients with event	68 (28)	103 (41)
Median in months (95% CI)[c]	NR (NR, NR)	NR (41, NR)
Hazard ratio (95% CI)[d]	0.58 (0.43, 0.79)	
p-value	0.00023	
Minimal residual disease (MRD) negativity rate[b,f,g]		
Percent of patients, (95% CI)	24.7 (19.4, 30.6)	9.6 (6.2, 13.9)
p-value[h]	<0.00001	

CI = Confidence interval; NR = Not reached.

[a] Efficacy data is based on the intent-to-treat (ITT) population.

[b] Response was based on IRC per IMWG criteria.

[c] By Brookmeyer and Crowley method.

[d] Based on stratified Cox regression model.

[e] One-sided p-value based on stratified log-rank test.

[f] For patients with a complete response or better.

[g] Assessed by Next Generation Sequencing (NGS) at 10^{-5} threshold.

[h] Two-sided p-value based on stratified Cochran-Mantel-Haenszel test.

Figure 1: Kaplan-Meier curve of progression-free survival per IRC in DREAMM-7

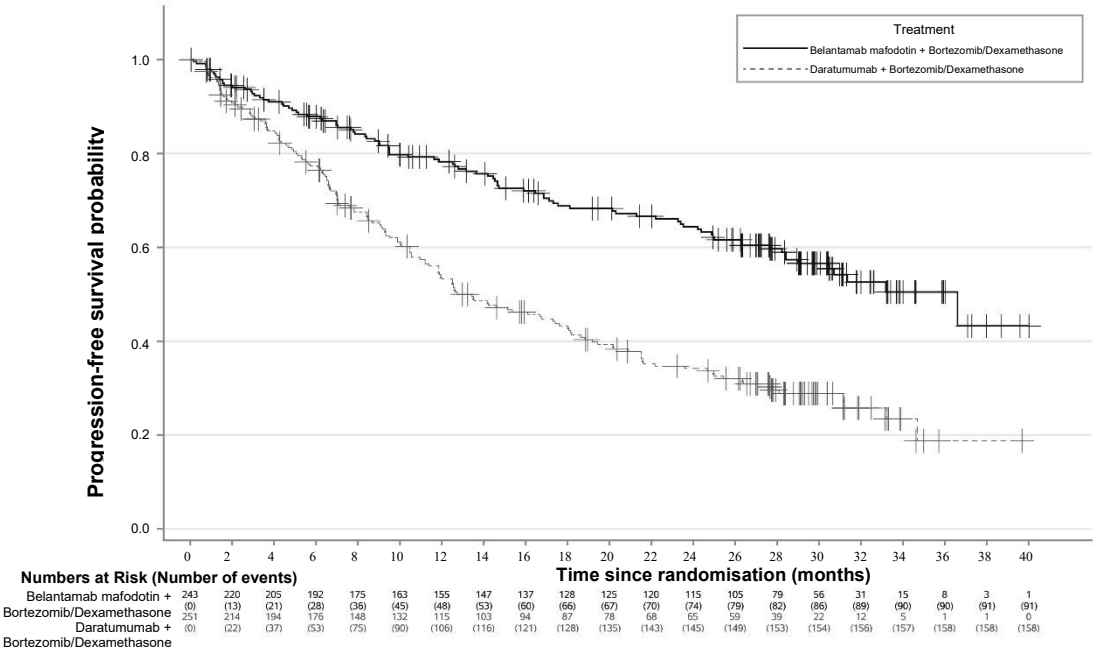
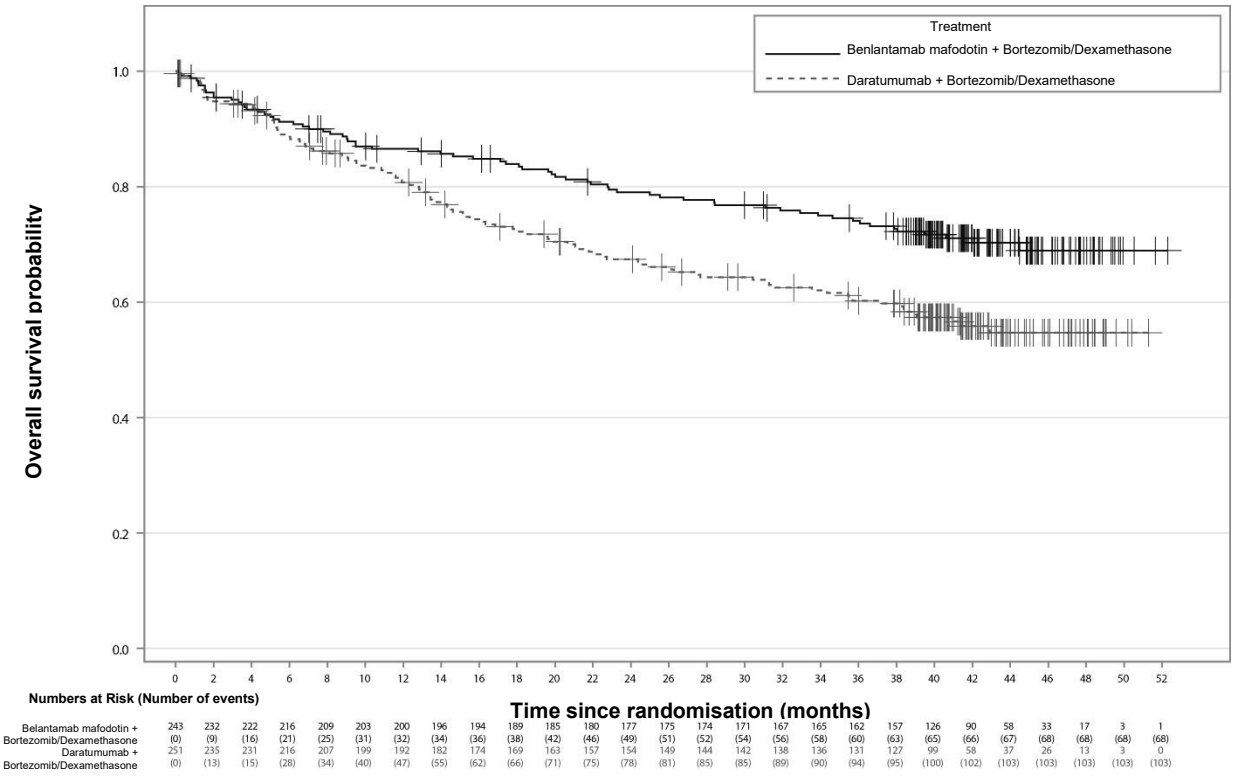


Figure 2: Kaplan-Meier curve of overall survival in DREAMM-7



DREAMM-8: belantamab mafodotin in combination with pomalidomide and dexamethasone
The efficacy and safety of belantamab mafodotin in combination with pomalidomide and dexamethasone (BPd) were investigated in a multicentre, randomised (1:1), open-label, Phase 3 study conducted in patients with multiple myeloma (MM) who had relapsed following treatment with at least one prior line of therapy, including lenalidomide.

In the BPd arm (N = 155), patients received belantamab mafodotin 2.5 mg/kg by intravenous infusion once on day 1 in cycle 1 (28-day cycle) followed by belantamab mafodotin 1.9 mg/kg by intravenous infusion every 4 weeks on day 1 of cycle 2 onwards (28-day cycles); pomalidomide 4 mg (orally [PO]) administered on days 1 to 21; and dexamethasone 40 mg PO on days 1, 8, 15, and 22 in all cycles (28-day cycles). In the pomalidomide, bortezomib, and dexamethasone (PVd) arm (N = 147), pomalidomide 4 mg PO was administered every 3 weeks on days 1 to 14 in all cycles (21-day cycles); bortezomib 1.3 mg/m^2 was administered subcutaneously on days 1, 4, 8, and 11 in cycles 1 to 8, and on days 1 and 8 in cycle ≥ 9 (21-day cycles). Dexamethasone 20 mg PO was administered on the day of and the day after bortezomib. The dose level of dexamethasone in each arm was reduced by half in patients aged 75 years and older. Treatment in both arms continued until disease progression, unacceptable toxicity, withdrawal of consent, initiation of another anticancer therapy, or end of study/death. Patients were stratified by the number of prior lines of treatment, prior exposure to bortezomib, prior anti-CD38 treatment, and International Staging System (ISS) status.

The key eligibility criteria included having confirmed diagnosis of MM as defined by IMWG criteria, having previously been treated with at least 1 prior line of MM therapy, including lenalidomide, and having had documented disease progression during or after their most recent therapy. Patients were excluded if they received prior treatment with or intolerant to pomalidomide, were previously treated with BCMA-targeted therapy, or had current corneal disease except for mild punctate keratopathy.

The primary efficacy outcome measure was PFS as evaluated by a blinded IRC based on the IMWG criteria for MM.

A total of 302 patients were evaluated for efficacy in DREAMM-8. Baseline demographics and characteristics were similar across both arms including: median age: 67 years (43% aged 65-74 years and 18% aged 75 years or older); 60% male, 40% female; 86% White, 12% Asian, < 1% Native Hawaiian or other Pacific Islander, < 1% mixed race; ISS stage at screening I (59%), II (26%), III (15%); 33% high cytogenetic risk, median number of 1 prior line of therapy; 10% with EMD present; and of those who received treatment (N = 295), ECOG PS 0 (55%), 1 (42%), or 2 (3%). In the BPd arm, 100% of patients received prior immunomodulator therapy (lenalidomide, thalidomide), 90% of patients received prior proteasome inhibitor therapy (bortezomib, carfilzomib, ixazomib), 25% of patients received prior anti-CD38 therapy (daratumumab, isatuximab), and 64% of patients previously received ASCT. There were 82% of patients refractory to immunomodulator therapy, 26% of patients refractory to proteasome inhibitor therapy, and 23% of patients refractory to anti-CD38 therapy. In the PVd arm, 100% of patients received prior immunomodulator therapy (lenalidomide, thalidomide), 93% of patients received prior proteasome inhibitor therapy (bortezomib, carfilzomib, ixazomib), 29% of patients received prior anti-CD38 therapy (daratumumab, isatuximab, anti-CD38), and 56% of patients previously received ASCT. There were 76% of patients refractory to immunomodulator therapy, 24% of patients refractory to proteasome inhibitor therapy, and 24% of patients refractory to anti-CD38 therapy.

Patients treated with belantamab mafodotin in combination with pomalidomide and dexamethasone had a statistically significant improvement in PFS in the overall population compared with pomalidomide, bortezomib and dexamethasone. Efficacy results at the time of the first interim analysis (data cut-off 29 January 2024) are presented in Table 7 and Figures 3 and 4.

Table 7: Efficacy results in DREAMM-8

	Belantamab mafodotin plus pomalidomide and dexamethasone (BPd)[a] N = 155	**Pomalidomide plus bortezomib and dexamethasone (PVd)[a] N = 147**
Primary endpoint		
Progression-free survival (PFS)[b]		
Number (%) of patients with event	62 (40)	80 (54)
Median in months (95% CI)[c,d,e]	NR (20.6, NR)	12.7 (9.1, 18.5)
Hazard ratio (95% CI)[f]	0.52 (0.37, 0.73)	
p-value[g]	<0.001	
Secondary endpoints[h]		
Overall survival (OS)		
Number (%) of patients with event	49 (32)	56 (38)
Median in months (95% CI)[c]	NR (33, NR)	NR (25.2, NR)
Hazard ratio (95% CI)[f]	0.77 (0.53, 1.14)	
Minimal residual disease (MRD) negativity rate[b,i,j]		
Percent of patients (95% CI)	23.9 (17.4, 31.4)	4.8 (1.9, 9.6)

CI = Confidence interval; NR = Not reached.

[a] Efficacy data is based on the intent-to-treat (ITT) population.

[b] Response was based on IRC per IMWG criteria.

[c] By Brookmeyer and Crowley method.

[d] Median follow-up of 21.8 months.

[e] At the time of the data cut-off (29 JAN 2024).

[f] Based on stratified Cox regression model.

[g] One-sided p-value based on stratified log-rank test.

[h] Results have not reached statistical significance.

[i] For patients with a complete response or better.

[j] Assessed by NGS at 10^{-5} threshold.

Figure 3: Kaplan-Meier curve of progression-free survival per IRC in DREAMM-8

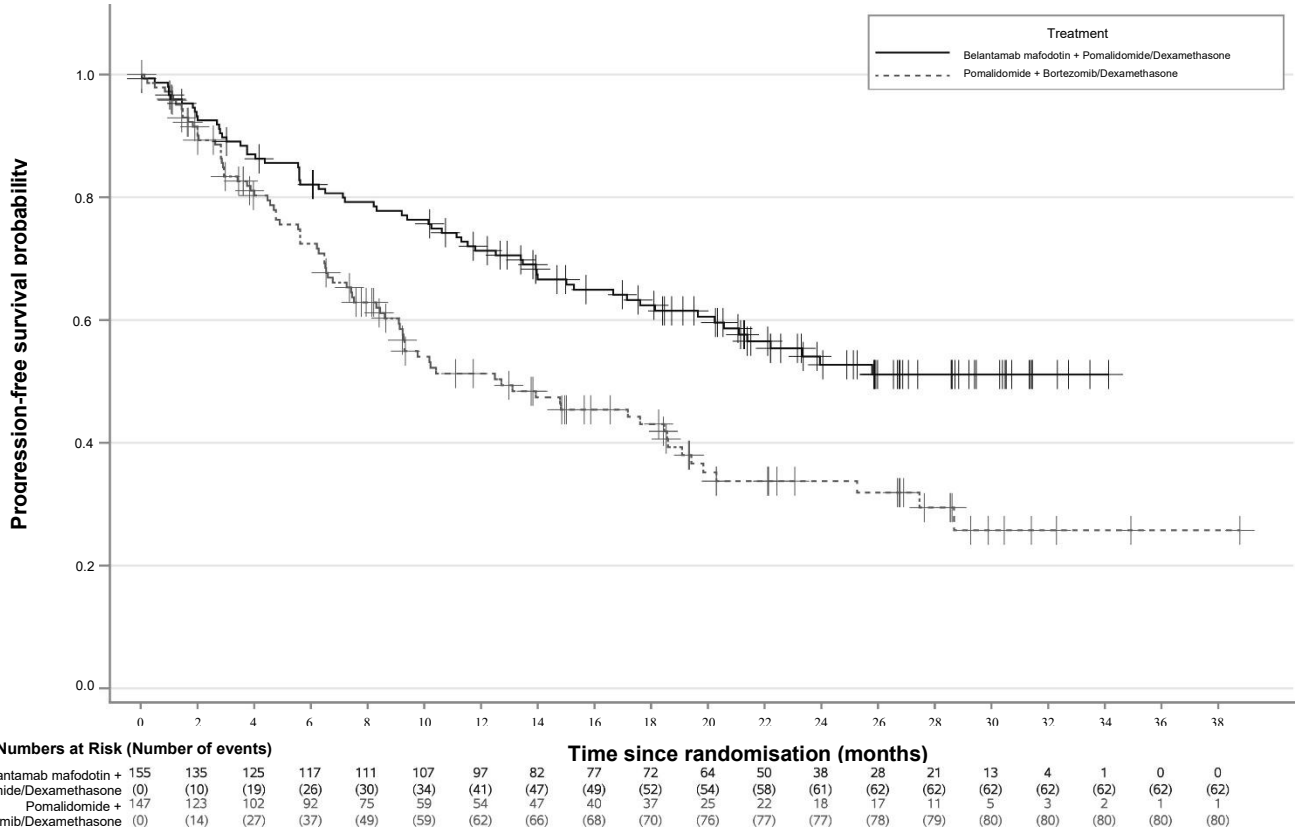
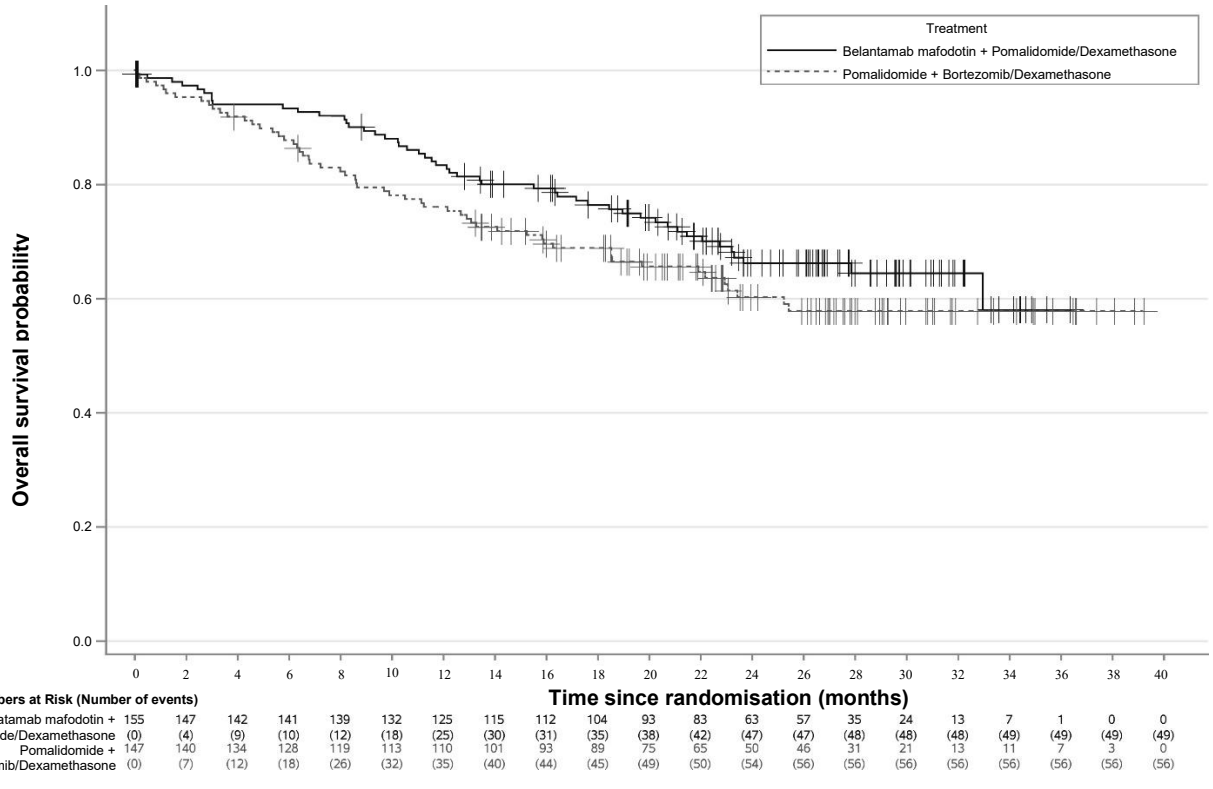


Figure 4: Kaplan-Meier curve of overall survival in DREAMM-8



Paediatric population

The European Medicines Agency has waived the obligation to submit the results of studies with Blenrep in all subsets of the paediatric population in multiple myeloma (see section 4.2 for information on paediatric use).

5.2 Pharmacokinetic properties

Absorption

Maximum concentration for belantamab mafodotin ADC occurred at or shortly after the end of infusion while cys-mcMMAF concentrations peaked ~24 hours after dosing.

Table 8 describes the pharmacokinetics of belantamab mafodotin for 2.5 mg/kg doses on cycle 1 Day 1 at the end of the first 3-week interval.

Table 8: Belantamab mafodotin pharmacokinetics at the end of the first 3-week interval[a]

	AUC[b]	**C_{avg21}**	**C_{max}**	**C_{tau}**
ADC (%)	3 950 mcg•h/mL (30.6)	7.83 mcg/mL (30.6)	43.7 mcg/mL (22.1)	2.03 mcg/mL (62.5)
cys-mcMMAF (%)	94.2 ng•h/mL (42.3)	0.243 ng/mL (42.4)	0.976 ng/mL (45.3)	–

ADC = antibody drug conjugate; AUC = Area under the curve; C_{avg21} = belantamab mafodotin average concentration over 21 days; C_{max} = maximum plasma concentration; C_{tau} = concentration at the end of a dosing interval.

[a] Data presented as geometric mean (%CV), based on population PK models.

[b] AUC for ADC is $AUC_{(0\text{-}21days)}$ and $AUC_{(0\text{-}7days)}$ for cys-mcMMAF.

Accumulation of belantamab mafodotin (ADC) was minimal to moderate (the ratio from cycle 3 to cycle 1 was 1.13 for C_{max} and 1.58 for AUC) and accumulation of cys-mcMMAF was negligible as observed in clinical trials with a every 3 weeks dosing regimen.

Distribution

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

Based on the population PK analysis, the geometric mean (geometric CV%) for steady-state volume of distribution of belantamab mafodotin was 10.8 L (22%).

Biotransformation

The monoclonal antibody portion of belantamab mafodotin 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.

Drug interactions

In vitro studies demonstrated that cys-mcMMAF is not an inhibitor, an inducer, or a sensitive substrate of cytochrome P450 enzymes, but is a substrate of organic anion transporting polypeptide (OATP)1B1 and OATP1B3, multidrug resistance-associated protein (MRP)1, MRP2, MRP3, bile salt export pump (BSEP), and a possible substrate of P-glycoprotein (P-gp). Clinically relevant drug-drug interactions with inhibitors or inducers of these enzymes and transporters are not expected.

Elimination

Based on the population PK analysis from patients treated with belantamab mafodotin monotherapy or in combination with other medicinal products, the geometric mean (geometric CV%) belantamab mafodotin (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 not substantial (approximately 18% of the dose) after cycle 1 dose, with no evidence of other MMAF-related metabolites.

Linearity/non-linearity

Belantamab mafodotin exhibits dose-proportional pharmacokinetics over the recommended dose range with a reduction in clearance over time.

Special populations

Elderly
Based on a population of patients aged 32 to 89 years, age was not a significant covariate in population pharmacokinetics analyses.

Renal impairment
In patients with severe renal impairment (eGFR 15-29 mL/min, n = 8), belantamab mafodotin C_{max} decreased by 23% and $AUC_{(0\text{-}tau)}$ decreased by 16% compared with patients with normal renal function or mild renal impairment (eGFR ≥ 60 mL/min, n = 8). For cys-mcMMAF, C_{max} and $AUC_{(0\text{-}168h)}$ decreased by 56% and 44%, respectively compared to patients with normal renal function or mild renal impairment. Renal function (eGFR 12-150 mL/min) was not a significant covariate in population pharmacokinetic analyses that included patients with normal renal function, mild (eGFR 60-89 mL/min), moderate (eGFR 30-59 mL/min), or severe renal impairment (eGFR < 30 mL/min not requiring dialysis). No impact on belantamab mafodotin PK was observed for patients with end stage renal disease (eGFR < 15 mL/min requiring dialysis, n = 5).

Belantamab mafodotin is not expected to be removed via dialysis due to its molecular size. While free cys-mcMMAF may be removed via dialysis, cys-mcMMAF systemic exposure is very low and has not been shown to be associated with efficacy or safety based on exposure-response analysis.

Hepatic impairment
No formal studies have been conducted in patients with hepatic impairment. Hepatic function as per the National Cancer Institute Organ Dysfunction Working Group classification, was not a significant covariate in population pharmacokinetic analyses that included patients with normal hepatic function, mild (total bilirubin > ULN to ≤ 1.5 × ULN and any AST or total bilirubin ≤ ULN with AST > ULN) or moderate hepatic impairment (total bilirubin > 1.5 x ULN to ≤ 3 × ULN and any AST). Limited data are available for patients with moderate (n = 5) or severe hepatic impairment (n = 1, total bilirubin > 3 × ULN and any AST) in the population pharmacokinetic analyses.

Body weight
Body weight (37 to 170 kg) was a significant covariate in population pharmacokinetic analyses, but this effect will be adjusted by the weight-proportional dosing regimen (see section 4.2).

5.3 Preclinical safety data

Animal toxicology and/or pharmacology

In non-clinical trials, the principal adverse findings (directly related to belantamab mafodotin) in the rat and monkey, at similar exposures to the recommended clinical dose of 2.5 mg/kg, were elevated

liver enzymes sometimes associated with hepatocellular necrosis at ≥ 10 and ≥ 3 mg/kg, respectively, and increases in alveolar macrophages associated with eosinophilic material in the lungs at ≥ 3 mg/kg (rat only). Most findings in animals were related to the cytotoxic drug conjugate, the histopathological changes observed in the testes and lungs, were not reversible in rats.

Single cell necrosis in the corneal epithelium and/or increased mitoses of corneal epithelial cells was observed in rat and rabbit. Inflammation of the corneal stroma correlating with superficial haze and vascularisation was observed in rabbits. Belantamab mafodotin was taken up into cells throughout the body by a mechanism unrelated to BCMA receptor expression on the cell membrane.

Carcinogenesis/mutagenesis

Belantamab mafodotin was genotoxic in an *in vitro* micronucleus screening assay in human lymphocytes, consistent with the pharmacological effect of cys-mcMMAF-mediated disruption of microtubules causing aneuploidy.

No carcinogenicity or definitive genotoxicity studies have been conducted with belantamab mafodotin.

Reproductive toxicology

No animal studies have been performed to evaluate the potential effects of belantamab mafodotin on reproduction or development. The mechanism of action is to kill rapidly dividing cells which would affect a developing embryo which has rapidly dividing cells. There is also a potential risk of heritable changes via aneuploidy in female germ cells.

Effects on male and female reproductive organs have been observed in animals at doses of ≥ 10 mg/kg, which is approximately 4 times the exposure of the clinical dose. Luteinised nonovulatory follicles were seen in the ovaries of rats after 3 weekly doses. Findings in male reproductive organs that were adverse and progressed following repeat dosing in rat, included marked degeneration/atrophy of seminiferous tubules that generally did not reverse following dosing cessation.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium citrate dihydrate
Citric acid monohydrate (E330)
Trehalose dihydrate
Disodium edetate
Polysorbate 80 (E433)

6.2 Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3 Shelf life

Unopened vial

4 years.

Reconstituted solution

The reconstituted solution can be stored for up to 4 hours at room temperature (20 ºC – 25 ºC) or stored in a refrigerator (2 ºC – 8 ºC) for up to 4 hours. Do not freeze.

Diluted solution

From a microbiological point of view, the product should be used immediately.

If not used immediately, the diluted solution can be stored in a refrigerator (2 ºC – 8 ºC) prior to administration for up to 24 hours. Do not freeze. If refrigerated, allow the diluted solution to equilibrate to room temperature prior to administration.

The diluted infusion solution may be kept at room temperature (20 ºC – 25 ºC) for a maximum of 6 hours (including infusion time).

6.4 Special precautions for storage

Store in a refrigerator (2 ºC – 8 ºC).

For storage conditions after reconstitution of the medicinal product, see section 6.3.

6.5 Nature and contents of container

Blenrep 70 mg powder for concentrate for solution for infusion
Type 1 glass vial of 6 mL containing 70 mg powder sealed with bromobutyl rubber stopper and aluminium overseal with a plastic removable cap.

Pack size: 1 vial

Blenrep 100 mg powder for concentrate for solution for infusion
Type 1 glass vial of 6 mL containing 100 mg powder sealed with bromobutyl rubber stopper and aluminium overseal with a plastic removable cap.

Pack size: 1 vial

6.6 Special precautions for disposal and other handling

Caution should be used during handling and preparation of Blenrep. Follow procedures for proper handling and disposal of anticancer medicinal products.

Preparation of solution for infusion

Blenrep is a cytotoxic anticancer medicinal product. Proper handling procedures must be followed. Use aseptic technique for the reconstitution and dilution of the dosing solution.

Calculate the dose (mg), total volume (mL) of solution required and the number of vials needed based on the patient's actual body weight (kg).

Reconstitution

1. Remove the vial(s) of Blenrep from the refrigerator and allow to stand for approximately 10 minutes to reach room temperature.
2. Reconstitute each 70 mg vial with 1.4 mL of water for injections to obtain a concentration of 50 mg/mL. Gently swirl the vial to aid dissolution. Do not shake.

Reconstitute each 100 mg vial with 2 mL of water for injections to obtain a concentration of 50 mg/mL. Gently swirl the vial to aid dissolution. Do not shake.

3. Visually inspect the reconstituted solution for particulate matter and discoloration. The reconstituted solution should be a clear to opalescent, colourless to yellow to brown liquid. Discard the reconstituted solution if extraneous particulate matter other than translucent to white proteinaceous particles is observed.

Dilution

1. Withdraw the necessary volume for the calculated dose from each vial.
2. Add the necessary amount of Blenrep to the infusion bag containing 250 mL of sodium chloride 9 mg/mL (0.9%) solution for injection. Mix the diluted solution by gentle inversion. The final concentration of the diluted solution should be between 0.2 mg/mL to 2 mg/mL. Do not shake.
3. Discard any unused reconstituted solution of Blenrep left in the vial.

If the diluted solution is not used immediately, it may be stored in a refrigerator (2 ºC – 8 ºC) for up to 24 hours prior to administration. If refrigerated, allow the diluted solution to equilibrate to room temperature prior to administration. The diluted solution may be kept at room temperature (20 ºC – 25 ºC) for a maximum of 6 hours (including infusion time).

Administration

1. Administer the diluted solution by intravenous infusion only and approximately over 30 minutes using an infusion set made of polyvinyl chloride or polyolefin. In the event where the administration time may be extended beyond 30 minutes, do not exceed the allowable 6-hour duration in-use time, including both preparation and administration of the dose.
2. Filtration of the diluted solution is not required. However, if the diluted solution is filtered, 0.2 µm or 0.22 µm polyethersulfone (PES) based filter is recommended.

Disposal

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

GlaxoSmithKline Trading Services Limited
12 Riverwalk
Citywest Business Campus
Dublin 24
Ireland
D24 YK11

8. MARKETING AUTHORISATION NUMBER(S)

Blenrep 70 mg powder for concentrate for solution for infusion
EU/1/25/1948/001

Blenrep 100 mg powder for concentrate for solution for infusion
EU/1/25/1948/002

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation:

10. DATE OF REVISION OF THE TEXT

Detailed information on this medicinal product is available on the website of the European Medicines Agency https://www.ema.europa.eu.

ANNEX II

A. MANUFACTURER OF THE BIOLOGICAL ACTIVE SUBSTANCEAND MANUFACTURER RESPONSIBLE FOR BATCH RELEASE

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

A. MANUFACTURER OF THE BIOLOGICAL ACTIVE SUBSTANCE AND MANUFACTURER RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer of the biological active substance

GlaxoSmithKline Manufacturing SpA
Strada Provinciale Asolana, 90,
San Polo di Torrile, Parma 43056,
Italy

Name and address of the manufacturer responsible for batch release

GlaxoSmithKline Manufacturing SpA
Strada Provinciale Asolana, 90,
San Polo di Torrile, Parma 43056,
Italy

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Medicinal product subject to restricted medical prescription (see Annex I: Summary of Product Characteristics, section 4.2).

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

- **Periodic safety update reports (PSURs)**

The requirements for submission of PSURs for this medicinal product are set out in the list of Union reference dates (EURD list) provided for under Article 107c (7) of Directive 2001/83/EC and any subsequent updates published on the European medicines web-portal.

The marketing authorisation holder (MAH) shall submit the first PSUR for this product within 6 months following authorisation.

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

- **Risk management plan (RMP)**

The marketing authorisation holder (MAH) shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the marketing authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:

- At the request of the European Medicines Agency;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

- **Additional risk minimisation measures**

Prior to the launch of Blenrep in each Member State, the Marketing Authorisation Holder (MAH) must agree the content and format of the educational materials, including communication media,

distribution modalities, and any other aspects of the programme with the National Competent Authority.

The MAH shall ensure that in each Member State where Blenrep is marketed, all healthcare professionals who are expected to prescribe, or dispense Blenrep, and patients who receive Blenrep have access to/are provided with the following educational materials to be disseminated in line with NCA agreed implementation pathways:

- Educational materials for healthcare professionals
- Patient education materials
- Patient Card

The educational materials for healthcare professionals contains the following key messages:

- Detailed information on the ocular effects of belantamab mafodotin, including proper grading
- Description of required ocular exams for patients receiving belantamab mafodotin before each of the first 4 doses of belantamab mafodotin, and as clinically indicated thereafter:
    - Slit lamp examination to provide detailed information on the impact of belantamab mafodotin on the eye, including corneal examination, findings such as superficial punctate keratopathy, microcyst-like epithelial changes and haze, with or without changes in visual acuity.
    - Measurement of best corrected visual acuity to provides a measure of the impact of any corneal exam findings on the visual acuity.
- Key messages to convey during patient counselling:
    - Advise to patients that ocular adverse reactions may occur during treatment.
    - Patients should be advised to administer preservative-free artificial tears at least 4 times a day during treatment.
    - Patients should avoid using contact lenses until the end of treatment.
    - Patients should consult their haematologist/oncologist if ocular adverse reactions occur.

The patient educational materials contains the following key messages:

- Description of eye problems reported with belantamab mafodotin which may occur during treatment.
- Eye exams should be performed before each of the first 4 doses of belantamab mafodotin, and as clinically indicated thereafter.
- Basic details on the anatomy and physiology of the eye and a description of eye exams.
- Patients experiencing eye-related problems may require a dose adjustment to their treatment with belantamab mafodotin, which means either reducing the dose or changing the time between the doses. Your doctor might also ask you to see an eye care professional.
- Tell your haematologist/oncologist about any history of vision or eye problems.
- If you experience changes with your vision whilst on belantamab mafodotin, contact your haematologist/oncologist.
- Your doctor will ask you to use eye drops called preservative-free artificial tears during treatment. Administer them as instructed.
- Trackers for eye drops and appointments.

The Patient Card contains the following key messages:

- Indicates the patient is on treatment with belantamab mafodotin, known to cause serious ocular effects (including keratopathy), and contains contact information for the prescribing haematologist/oncologist and the ECP.
- Present to doctor during regular follow up visits.
- Patients to present the Patient Card to the pharmacist to find preservative-free artificial tears for use, as directed.

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON

1. NAME OF THE MEDICINAL PRODUCT

BLENREP 70 mg powder for concentrate for solution for infusion
belantamab mafodotin

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each vial contains 70 mg of belantamab mafodotin (50 mg/mL after reconstitution).

3. LIST OF EXCIPIENTS

Also contains: sodium citrate dihydrate, citric acid monohydrate, trehalose dihydrate, disodium edetate, polysorbate 80. See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Powder for concentrate for solution for infusion
1 vial.

5. METHOD AND ROUTE OF ADMINISTRATION

For intravenous infusion after reconstitution and dilution.
Read the package leaflet before use.
For single use only.

Press here to open

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

Cytotoxic: handle with caution.

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

GlaxoSmithKline Trading Services Limited, 12 Riverwalk, Citywest Business Campus, Dublin 24, Ireland, D24 YK11

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/25/1948/001

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Justification for not including Braille accepted.

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

VIAL LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

BLENREP 70 mg powder for concentrate
belantamab mafodotin
IV
cytotoxic

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

70 mg

6. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON

1. NAME OF THE MEDICINAL PRODUCT

BLENREP 100 mg powder for concentrate for solution for infusion
belantamab mafodotin

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each vial contains 100 mg of belantamab mafodotin (50 mg/mL after reconstitution).

3. LIST OF EXCIPIENTS

Also contains: sodium citrate dihydrate, citric acid monohydrate, trehalose dihydrate, disodium edetate, polysorbate 80. See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Powder for concentrate for solution for infusion
1 vial.

5. METHOD AND ROUTEOF ADMINISTRATION

For intravenous infusion after reconstitution and dilution.
Read the package leaflet before use.
For single use only.

Press here to open

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

Cytotoxic: handle with caution.

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

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12. MARKETING AUTHORISATION NUMBER(S)

EU/1/25/1948/002

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Justification for not including Braille accepted.

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

VIAL LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

BLENREP 100 mg powder for concentrate
belantamab mafodotin
IV
cytotoxic

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

100 mg

6. OTHER

B. PACKAGE LEAFLET

Package leaflet: Information for the patient

Blenrep 70 mg powder for concentrate for solution for infusion
Blenrep 100 mg powder for concentrate for solution for infusion
belantamab mafodotin

▼This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

Read all of this leaflet carefully before you are given this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or nurse.
- If you get any side effects, talk to your doctor or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Blenrep is and what it is used for

Blenrep contains the active substance belantamab mafodotin. It is used in combination with other cancer medicines to treat adults who have a cancer of the bone marrow called multiple myeloma.

Belantamab mafodotin consists of a *monoclonal antibody* connected to a cytotoxic agent (a type of cancer medicine). The monoclonal antibody is a protein designed to find the multiple myeloma cancer cells in your body and bind to them. Once attached to the cancer cells, the cytotoxic agent is released inside the cells and kills them.

Blenrep will be given to you together with other cancer medicines used to treat multiple myeloma:
- bortezomib and dexamethasone, or
- pomalidomide and dexamethasone.

It is important you read the patient leaflets for these other medicines. If you have any questions about these medicines, ask your doctor.

2. What you need to know before you are given Blenrep

You should not be given Blenrep:
- if you are allergic to belantamab mafodotin or any of the other ingredients of this medicine (listed in section 6).

  ➔ **Check with your doctor** if you think this applies to you.

Warnings and precautions
Talk to your doctor or nurse before you are given Blenrep if you have:

Eye problems

This medicine can cause changes to the surface of your eye which can result in changes in vision, blurred vision, and dry eyes.

You should have an eye examination by an eye care professional before each of the first 4 doses of this medicine. Your doctor may order further eye tests for you while you are on treatment with Blenrep. Even if your vision seems fine, it is important that you get your eyes checked during treatment with this medicine because some changes can happen without symptoms and may only be seen during an eye examination.

➔ **Do not use contact lenses** while you are receiving treatment unless instructed to do so by your eye care professional.

Your doctor will ask you to use eye drops called preservative-free artificial tears at least 4 times a day during treatment to moisten and lubricate your eyes. You should apply them as instructed.

Tell your doctor if you notice changes with your vision. Your doctor may reduce the dose or change the time between doses. Your doctor might also ask you to see an eye care professional.

➔ **Contact your doctor** if you have blurred vision or other eye problems.

Abnormal bruising and bleeding

Blenrep can decrease the number of blood cells called platelets which help to clot your blood. Symptoms of low platelets levels (*thrombocytopenia*) include:

- abnormal bruising under the skin,
- bleeding longer than usual after a blood test or cut to the skin,
- bleeding from your nose or your gums, or more serious bleeding.

Your doctor will ask you to have a blood test before you start treatment, and regularly during treatment with Blenrep, to check that your platelet levels are normal.

➔ **Tell your doctor** if you develop abnormal bleeding or bruising, or any symptoms that worry you.

Infusion-related reactions

Blenrep is given by a drip (*infusion*) into a vein. Some people who receive infusions develop *infusion-related reactions*. These reactions can happen during the infusion or within 24 hours after the infusion. In rare cases, you may have a severe allergic reaction which may include a swollen face, lips, mouth, tongue or throat, difficulty swallowing or breathing or any itchy rash (*hives*).

➔ For more signs of an infusion-related reaction, see section 4.

➔ **Get medical help immediately** if you think you may be having an allergic reaction.

If you have previously had a reaction to an infusion of this medicine, or any other medicine:

➔ **Tell your doctor or nurse** before you receive another infusion.

Lung inflammation

Severe and life-threatening inflammation of the lungs *(pneumonitis)* has occurred in some people who received Blenrep.

Possible symptoms of lung inflammation include:

- shortness of breath,
- chest pain,
- new onset or worsening cough.

If you have symptoms of pneumonitis, your doctor may decide to delay or stop treatment with Blenrep.

➔ **Tell your doctor** if you develop any lung problems or breathing-related symptoms that worry you.

If you have or have previously had a hepatitis B-infection

Talk to your doctor if you might have or have previously had a hepatitis B infection. This medicine may cause a reactivation of the infection. Your doctor may check you for signs of infection before and during treatment.

➔ **Tell your doctor** if you notice any of the following signs or symptoms: worsening tiredness, yellowing of the skin or white part of the eyes, and dark urine. If you have symptoms of hepatitis B infection, your doctor may decide to delay or stop treatment with Blenrep.

Children and adolescents

This medicine is not intended for use in children or adolescents below 18 years of age.

Other medicines and Blenrep

➔ **Tell your doctor** if you are taking, have recently taken or might take any other medicines.

Pregnancy, breast-feeding and fertility

Pregnancy

It is not known if Blenrep affects an unborn baby. Use of this medicine during pregnancy is not recommended.

If you are pregnant, think you may be pregnant or are planning to have a baby:

➔ **Tell your doctor** before you are given this medicine.

If you are a woman who could become pregnant:

- Your doctor will ask you to take a pregnancy test before you start treatment with Blenrep.
- You must use effective **birth control** (*contraception)* during treatment and for 4 months after your last dose of Blenrep.

If you are a man who could father a child:

- You must use effective **birth control** (*contraception*) during treatment and for 6 months after your last dose of Blenrep.

Breast-feeding

It is not known if Blenrep passes into breast milk. You must not breast-feed during treatment and for 3 months after your last dose of this medicine.

Talk to your doctor if you are breast-feeding or planning to breast-feed.

Fertility

Fertility counselling is recommended for men and women who are going to be treated with this medicine and wish to have children.

Driving and using machines

Blenrep can cause problems with vision that can affect your ability to drive or use machines.

➔ **Do not drive or use machines** unless you are sure your vision is not affected. Talk to your doctor if you are not sure.

Blenrep contains polysorbate and sodium
This medicine contains 0.28 mg of polysorbate 80 (E433) in each 70 mg vial and 0.4 mg of polysorbate 80 (E433) in each 100 mg vial, which is equivalent to 0.2 mg/mL in each vial. Polysorbates may cause allergic reactions. Tell your doctor if you have any known allergies.

This medicine contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially "sodium-free".

3. How Blenrep is given

Your doctor will decide on the correct dose of Blenrep. The dose is calculated based on your body weight.

Blenrep is given together with other medicines used to treat multiple myeloma.

- When given with bortezomib and dexamethasone, the recommended starting dose of Blenrep is 2.5 mg per kilogram of your body weight, every 3 weeks.
- When given with pomalidomide and dexamethasone, the recommended starting dose of Blenrep is 2.5 mg per kilogram of your body weight for the first dose, then 1.9 mg per kilogram of your body weight, every 4 weeks.

Your doctor or nurse will give you this medicine as a drip (*infusion*) into a vein over 30 minutes.

Your doctor will agree with you how many treatments are needed. The treatment will continue until your disease gets worse or you develop unacceptable side effects. Your doctor will discuss the duration of treatment with you.

Before your infusion, you must apply lubricating and moistening eye drops (*preservative-free artificial tears*). You must continue to use the eye drops at least 4 times a day whilst you are receiving treatment with Blenrep.

➔ **Read the information** under 'Eye problems' in section 2 of this leaflet.

If you are given more Blenrep than you should

Your doctor or nurse will give you this medicine. In the unlikely event that you are given too much (an overdose), your doctor will monitor you for side effects.

If a dose of Blenrep is missed

To make sure your treatment works, it is very important to go to all your appointments. If you miss an appointment, make another one as soon as possible.

➔ Contact your doctor or hospital as soon as possible to re-schedule your appointment.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Serious side effects

Some side effects could be serious. Seek medical help immediately if you experience the following serious side effects:

Very common: may affect more than 1 in 10 people

- COVID-19. Symptoms may include:

- fever
- chills
- cough
- sore throat
- congestion or runny nose
- new loss of taste or smell.

- infection of the lungs (*pneumonia*). Symptoms may include:
  - shortness of breath
  - chest pain
  - new onset or worsening cough.
- abnormal bruising and bleeding, due to low number of a type of blood cell called platelets, which help to clot blood (*thrombocytopenia*)

  ➔ **Read the information** under 'Abnormal bruising and bleeding' in section 2 of this leaflet.
- low number of white blood cells (*neutropenia*), which may increase risk of infections. Symptoms may include:
  - fever
  - chills
  - feeling tired.
- fever (*pyrexia*). Symptoms may include:
  - chills
  - flushing.

Common: may affect up to 1 in 10 people

- COVID-19 lung infection (*pneumonia*). Symptoms may include:
  - shortness of breath or trouble breathing
  - cough
  - chest pain
  - fever
  - extreme tiredness (*fatigue*)
  - confusion.

- Infusion-related reactions
  Some people may have allergic-like reactions when they receive an infusion. These usually develop within minutes or hours but may develop up to 24 hours after treatment. Symptoms may include:
  - flushing
  - chills
  - fever
  - difficulty breathing
  - rapid heartbeat
  - drop in blood pressure.

  ➔ **Get medical help immediately** if you think you may be having a reaction.

Uncommon: may affect up to 1 in 100 people

- disorder of the blood vessels in the liver (*porto-sinusoidal vascular disorder*). This can lead to:
  - abnormal liver blood tests and long-term problems such as increased pressure of the blood vessels in the abdomen (*portal hypertension*)
  - swelling of blood vessels (*varices*) of the tube that leads from the mouth to the stomach (*oesophagus*)

- or a build-up of fluid in the abdomen which can cause abdominal pain, weight gain or swelling of the abdomen (*ascites*).

Other side effects

The following side effects have been reported with Blenrep when given with bortezomib and dexamethasone and Blenrep when given with pomalidomide and dexamethasone. Tell your doctor or nurse if you notice any of the following side effects:

Very common: may affect more than 1 in 10 people

- eye problems, including:
  - blurred vision
  - changes to the surface of your eye
  - dry eyes
  - sensitivity to light (*photophobia*)
  - feeling of something in your eye (foreign body sensation in eyes)
  - eye irritation
  - eye pain
  - decreased vision
  - clouding of the lens (*cataract*).

➔ **Read the information** under 'Eye problems' in section 2 of this leaflet.

- cold or cold-like symptoms such as cough, runny nose or sore throat (*upper respiratory tract infection*)
- low number of red blood cells which carry oxygen in the blood (*anaemia*), causing weakness and fatigue
- low number of white blood cells in the blood which help to fight infections (*lymphopenia*)
- difficulty falling and staying asleep, and poor quality of sleep (*insomnia*)
- nerve damage (*neuropathies*)
- cough
- diarrhoea
- nausea
- constipation
- abnormal blood tests indicating liver problems (*alanine aminotransferase, aspartate aminotransferase, and gamma glutamyltransferase*)
- joint pain
- back pain
- feeling tired (*fatigue*).

Common: may affect up to 1 in 10 people

- other eye problems, including:
  - increased tear production (*lacrimation*)
  - double vision (*diplopia*)
  - itchy eyes (*eye pruritus*)
  - discomfort in eye
  - eye sores, possibly with infection (*corneal ulcer*)
  - problems with vision.
- infection of the parts of the body that collect and pass out urine (*urinary tract infection*)

- inflammation of the airways in the lungs (*bronchitis*)
- low levels of white blood cells which help to fight infection (*leukopenia*)
- low levels of white blood cells with fever (*febrile neutropenia*)
- low levels of antibodies called 'immunoglobulins' in the blood which help to fight infection (*hypogammaglobulinemia*)
- decreased appetite
- difficulty breathing (*dyspnoea*)
- vomiting
- rash
- abnormal blood levels of creatine phosphokinase
- foamy, frothy, or bubbly urine indicating a high level of protein in your urine (*albuminuria*)
- weakness (*asthenia*).

Uncommon: may affect up to 1 in 100 people

- recurrence of hepatitis B infection when you have had hepatitis B in the past

➔ **Read the information** under 'If you have or have previously had hepatitis B infection' in section 2 of this leaflet.

- shortness of breath, chest pains and cough, due to inflammation of the lungs (*pneumonitis*)

➔ **Read the information** under 'Lung inflammation' in section 2 of this leaflet.

Other side effects that have been reported (frequency not known):

- decreased sensitivity (*hypoesthesia)* of the cornea (the transparent layer in front of the eye that covers the pupil and iris).

Reporting of side effects
If you get any side effects, talk to your doctor or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Blenrep

Your doctor, pharmacist or nurse is responsible for storing this medicine and disposing of any unused product correctly. The following information is intended for healthcare professionals.

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the label and carton after EXP. The expiry date refers to the last day of that month.

Store in a refrigerator (2 ºC – 8 ºC).

The reconstituted solution can be stored for up to 4 hours at room temperature (20 ºC – 25 ºC) or stored in a refrigerator (2 ºC – 8 ºC) for up to 4 hours. Do not freeze.

The diluted solution can be stored in a refrigerator (2 ºC – 8 ºC) prior to administration for up to 24 hours. Do not freeze. If refrigerated, allow the diluted solution to equilibrate to room temperature prior to administration. The diluted solution for infusion may be kept at room temperature (20 ºC – 25 ºC) for a maximum of 6 hours.

Do not throw away any medicines via wastewater or household waste. Your healthcare professional will throw away medicines that are no longer used. These measures will help protect the environment.

6. Contents of the pack and other information

What Blenrep contains

The active substance is belantamab mafodotin. One vial of powder contains either 70 mg or 100 mg of belantamab mafodotin, respectively. After reconstitution the solution contains belantamab mafodotin 50 mg per mL.

The other ingredients are sodium citrate dihydrate, citric acid monohydrate (E330), trehalose dihydrate, disodium edetate and polysorbate 80 (E433) (see section 2 ‘Blenrep contains polysorbate and sodium’).

What Blenrep looks like and contents of the pack

Blenrep 70 mg powder for concentrate for solution for infusion (powder for concentrate) and Blenrep 100 mg powder for concentrate for solution for infusion (powder for concentrate) are presented as a white to yellow powder in a glass vial with a rubber stopper and a plastic removable cap. Each carton contains one vial.

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This leaflet was last revised in

Other sources of information

Detailed information on this medicine is available on the European Medicines Agency web site: https://www.ema.europa.eu

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The following information is intended for healthcare professionals only:

Step-by-step instructions for use and handling, reconstitution, and administration

The trade name and batch number of the administered product should be clearly recorded in the patient file.

Caution should be used during handling and preparation of Blenrep. Follow procedures for proper handling and disposal of anticancer medicinal products.

Preparation of solution for infusion

Blenrep is a cytotoxic anticancer medicinal product. Proper handling procedures must be followed. Use aseptic technique for the reconstitution and dilution of the dosing solution.

Calculate the dose (mg), total volume (mL) of solution required and the number of vials needed based on the patient's actual body weight (kg).

Reconstitution

1. Remove the vial(s) of Blenrep from the refrigerator and allow to stand for approximately 10 minutes to reach room temperature.
2. Reconstitute each **70 mg** vial with **1.4 mL** of sterile water for injections to obtain a concentration of 50 mg/mL. Gently swirl the vial to aid dissolution. Do not shake.

   Reconstitute each **100 mg** vial with **2 mL** of sterile water for injections to obtain a concentration of 50 mg/mL. Gently swirl the vial to aid dissolution. Do not shake.
3. Visually inspect the reconstituted solution for particulate matter and discoloration. The reconstituted solution should be a clear to opalescent, colourless to yellow to brown liquid. Discard the reconstituted solution if extraneous particulate matter other than translucent to white proteinaceous particles is observed.

Dilution instructions for intravenous use

1. Withdraw the necessary volume for the calculated dose from each vial.
2. Add the necessary amount of Blenrep to the infusion bag containing 250 mL of sodium chloride 9 mg/mL (0.9%) solution for injection. Mix the diluted solution by gentle inversion. The final concentration of the diluted solution should be between 0.2 mg/mL to 2 mg/mL. Do not shake.
3. Discard any unused reconstituted solution of Blenrep left in the vial.

If the diluted solution is not used immediately, it may be stored in a refrigerator (2 ºC – 8 ºC) for up to 24 hours prior to administration. If refrigerated, allow the diluted solution to equilibrate to room temperature prior to administration. The diluted solution may be kept at room temperature (20 ºC – 25 ºC) for a maximum of 6 hours (including infusion time).

Administration instructions

1. Administer the diluted solution by intravenous infusion only over approximately 30 minutes using an infusion set made of polyvinyl chloride or polyolefin. In the event where the administration time may be extended beyond 30 minutes, do not exceed the allowable 6-hour duration in-use time, including both preparation and administration of the dose.
2. Filtration of the diluted solution is not required. However, if the diluted solution is filtered, 0.2 μm or 0.22 μm polyethersulfone (PES) based filter is recommended.

Disposal

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.