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 100 mg powder for concentrate for solution for infusion

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

One vial of powder contains 100 mg of belantamab mafodotin.

After reconstitution, the solution contains 50 mg belantamab mafodotin per mL.

Belantamab mafodotin is an antibody-drug conjugate 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).

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 as monotherapy for the treatment of multiple myeloma in adult patients, who have received at least four prior therapies and whose disease is refractory to at least one proteasome inhibitor, one immunomodulatory agent, and an anti-CD38 monoclonal antibody, and who have demonstrated disease progression on the last therapy.

4.2 Posology and method of administration

Treatment with BLENREP should be initiated and supervised 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 at baseline, before the subsequent 3 treatment cycles, and as clinically indicated whilst on treatment (see section 4.4).

Physicians should advise patients to administer preservative-free artificial tears at least 4 times a day beginning on the first day of infusion and continuing until completion of treatment as this may reduce corneal symptoms (see section 4.4).

For patients with dry eye symptoms, additional therapies may be considered as recommended by their eye care professional.

Posology

The recommended dose is 2.5 mg/kg of BLENREP administered as an intravenous infusion once every 3 weeks.

It is recommended that treatment should be continued until disease progression or unacceptable toxicity (see section 4.4).

Dose modifications

Recommended dose modifications for corneal adverse reactions are provided in Table 1. Table 2 provides dose modifications recommended for other adverse reactions.

Management of corneal adverse reactions

Corneal adverse reactions may include findings upon eye examination and/or changes in visual acuity (see sections 4.4 and 4.8). The treating physician should review the patient's ophthalmic examination report before dosing and should determine the dose of BLENREP based on the highest category from the report in the most severely affected eye as both eyes may not be affected to the same degree (Table 1).

During the ophthalmic examination, the eye care professional should assess the following:

- The corneal examination finding(s) and the decline in best corrected visual acuity (BCVA).
- If there is a decline in BCVA, the relationship of corneal examination findings to BLENREP should be determined.
- The highest category grading for these examination findings and BCVA should be reported to the treating physician.

Table 1. Dose modifications for corneal adverse reactions

Category[a]	**Eye examination findings**	**Recommended dose modifications**
Mild	*Corneal examination finding(s)* Mild superficial keratopathy[b] *Change in BCVA*[c] Decline from baseline of 1 line on Snellen Visual Acuity	Continue treatment at current dose.
Moderate	*Corneal examination finding(s)* Moderate superficial keratopathy[c] *Change in BCVA* Decline from baseline of 2 or 3 lines (and Snellen Visual Acuity not worse than 20/200)	Withhold treatment until improvement in examination findings and BCVA to mild severity or better. Consider resuming treatment at a reduced dose of 1.9 mg/kg.
Severe	*Corneal examination finding(s)* Severe superficial keratopathy[d] Corneal epithelial defect[e] *Change in BCVA* Decline from baseline of more than 3 lines	Withhold until improvement in examination findings and BCVA to mild severity or better. For worsening symptoms that are unresponsive to appropriate management, consider discontinuation.

[a] The severity category is defined by the most severely affected eye as both eyes may not be affected to the same degree.
[b] Mild superficial keratopathy (documented worsening from baseline), with or without symptoms.
[c] Moderate superficial keratopathy – with or without patchy microcyst-like deposits, sub-epithelial haze (peripheral), or a new peripheral stromal opacity.
[d] Severe superficial keratopathy with or without diffuse microcyst-like deposits involving the central cornea, sub-epithelial haze (central), or a new central stromal opacity.
[e] A corneal defect may lead to corneal ulcers. These should be managed promptly and as clinically indicated by an eye care professional.

Table 2. Dose modifications for other adverse reactions

Adverse reaction	Severity	Recommended dose modifications
Thrombocytopenia *(see section 4.4)*	Grade 2-3: Platelet count 25,000 to less than 75,000/microlitres	Consider withholding BLENREP and/or reducing the dose of BLENREP to 1.9 mg/kg.
	Grade 4: Platelet count less than 25,000/microlitres	Withhold BLENREP until platelet count improves to Grade 3 or better. Consider resuming at a reduced dose of 1.9 mg/kg.
Infusion-related reactions *(see section 4.4)*	Grade 2 (moderate)	Interrupt infusion and provide supportive treatment. Once symptoms resolve, resume at lower infusion rate by at least 50%.
	Grade 3 or 4 (severe)	Interrupt infusion and provide supportive treatment. Once symptoms resolve, resume at lower infusion rate reduced by at least 50%. If anaphylactic or life-threatening infusion reaction, permanently discontinue the infusion and institute appropriate emergency care.

Adverse reactions were graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE).

Special populations

Elderly
No dose adjustment is required for elderly patients (see section 5.2).

Renal impairment
No dose adjustment is required in patients with mild or moderate renal impairment (eGFR ≥30 mL/min). There are insufficient data in patients with severe renal impairment to support a dose recommendation (see section 5.2).

Hepatic impairment
No dose adjustment is required in patients with mild hepatic impairment (bilirubin greater than ULN to less than or equal to 1.5 × ULN or aspartate transaminase [AST] greater than ULN). There are insufficient data in patients with moderate hepatic impairment and no data in patients with severe hepatic impairment to support a dose recommendation (see section 5.2).

Body weight
BLENREP has not been studied in patients with body weight < 40 kg or > 130 kg (see section 5.2).

Paediatric population
The safety and efficacy of BLENREP in children and adolescents below 18 years of age have not been established. No data are available.

Method of administration

BLENREP is for intravenous use.
BLENREP must be reconstituted and diluted by a healthcare professional prior to administration as an intravenous infusion. BLENREP should be infused over a minimum of 30 minutes (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.

Corneal adverse reactions

Corneal adverse reactions have been reported with the use of BLENREP. The most commonly reported adverse reactions were keratopathy or microcyst-like epithelial changes in corneal epithelium (as seen on eye examination) with or without changes in visual acuity, blurred vision, and dry eye symptoms. Patients with a history of dry eyes were more prone to develop changes in the corneal epithelium. Changes in visual acuity may be associated with difficulty in driving or operating machinery (see section 4.7).

Ophthalmic examinations, including assessment of visual acuity and slit lamp examination, should be performed at baseline, before the subsequent 3 treatment cycles and during treatment as clinically indicated. Patients should be advised to administer preservative-free artificial tears at least 4 times a day during treatment (see section 4.2). Patients should avoid using contact lenses until the end of treatment.

Patients experiencing keratopathy 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 1).

Cases of corneal ulcer (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 1).

Thrombocytopenia

Thrombocytopenic events (thrombocytopenia and platelet count decreased) were frequently reported in study 205678. Thrombocytopenia may lead to serious bleeding events, including gastrointestinal and intracranial bleeding.

Complete blood counts should be obtained at baseline and monitored during treatment, as clinically indicated. Patients experiencing Grade 3 or 4 thrombocytopenia or those on concomitant anticoagulant treatments may require more frequent monitoring and should be managed with a dose delay or dose reduction (see Table 2). Supportive therapy (*e.g.* platelet transfusions) should be provided according to standard medical practice.

Infusion-Related Reactions

Infusion-related reactions (IRR) have been reported with BLENREP. Most IRRs were Grade 1-2 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, administer premedication for subsequent infusions (see Table 2).

Excipients

This medicinal product contains less than 1 mmol sodium (23 mg) per 100 mg dose, that is to say essentially "sodium-free".

4.5 Interaction with other medicinal products and other forms of interaction

No formal drug interaction studies have been performed with belantamab mafodotin.
Based on available *in vitro* and clinical data, there is a low risk of pharmacokinetic or pharmacodynamic drug interactions for belantamab mafodotin (see section 5.2).

4.6 Fertility, pregnancy and lactation

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

Women
The pregnancy status of child-bearing women should be verified prior to initiating therapy with BLENREP.

Women of child-bearing potential should use effective contraception during treatment with BLENREP and for 4 months after the last dose.

Men
Men with female partners of child-bearing potential should use effective contraception during treatment with BLENREP and for 6 months after the last dose.

Pregnancy

There are no data from the use of BLENREP 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 immunoglobulin G (IgG) is known to cross the placenta; therefore, belantamab mafodotin has the potential to be transmitted from the mother to the developing foetus (see section 5.3).

BLENREP should not be used during pregnancy unless the benefit to the mother outweighs the potential risks to the foetus. If a pregnant woman needs to be treated she should be clearly advised on the potential risk to the foetus.

Breast-feeding

It is not known whether belantamab mafodotin is excreted into 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 cause serious adverse reactions in breast-fed children. Women should be advised to discontinue breast-feeding prior to initiating treatment with BLENREP and for 3 months after the last dose.

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, women of childbearing potential who may desire children in the future should be counselled prior to therapy regarding the option of having eggs frozen before treatment. Men being treated with this medicine are advised to have sperm samples frozen and stored before treatment.

4.7 Effects on ability to drive and use machines

BLENREP has a moderate influence on the ability to drive or use machines (see sections 4.4 and 4.8). Patients should be advised to use caution when driving or operating machines as BLENREP may affect their vision.

4.8 Undesirable effects

Summary of the safety profile

Adverse reactions described in this section were reported from 95 patients who received BLENREP 2.5 mg/kg in study 205678. The most frequent adverse reactions (≥30%) were keratopathy (71%) and thrombocytopenia (38%). The most commonly reported serious adverse reactions were pneumonia (7%), pyrexia (7%) and IRRs (3%). Permanent discontinuation due to an adverse reaction occurred in 9% of patients who received BLENREP with 3% related to ocular adverse reactions.

Tabulated list of adverse reactions

Table 3 summarises adverse drug reactions that occurred in patients receiving the recommended dose of BLENREP 2.5 mg/kg once every 3 weeks.

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) and very rare (< 1/10,000). Within each frequency grouping, where relevant, adverse reactions are presented in order of decreasing seriousness.

Table 3. Adverse reactions reported in multiple myeloma patients treated with BLENREP

System Organ Class	Adverse reactions[a]	Frequency	Incidence (%)	
			Any Grade	Grade 3-4
Infections and infestations	Pneumonia[b]	Very common	11	7
	Upper respiratory tract infection	Common	9	0
Blood and lymphatic system disorders	Thrombocytopenia[c]	Very common	38	22
	Anaemia		27	21
	Lymphopenia[d]		20	17
	Leukopenia[e]		17	6
	Neutropenia[f]		15	11
Eye disorders	Keratopathy[g]	Very common	71	31
	Blurred vision events[h]		25	4
	Dry eye events[i]		15	1
	Photophobia	Common	4	0
	Eye irritation		3	0
	Ulcerative keratitis	Uncommon	1	1
	Infective keratitis		1	1
Gastrointestinal disorders	Nausea	Very common	25	0
	Diarrhoea		13	1

	Vomiting	Common	7	2
General disorders and administration site conditions	Pyrexia	Very common	23	4
	Fatigue		16	2
Investigations	Increased aspartate aminotransferase	Very common	21	2
	Increased gamma glutamyltransferase		11	3
	Increased creatine phosphokinase	Common	5	2
Injury, poisoning and procedural complications	Infusion-related reactions[j]	Very common	21	3

[a] Adverse reactions coded using MedDRA and graded for severity based CTCAE v4.03.
[b] Includes pneumonia and herpes simplex pneumonia
[c] Includes thrombocytopenia and decreased platelet count.
[d] Includes lymphopenia and decreased lymphocyte count.
[e] Includes leukopenia and decreased leukocyte count.
[f] Includes neutropenia and decreased neutrophil count.
[g] Based on eye examination, characterised as corneal epithelium changes with or without symptoms.
[h] Includes diplopia, vision blurred, visual acuity reduced, and visual impairment.
[i] Includes dry eye, ocular discomfort, and eye pruritus.
[j] Includes events determined by investigators to be related to infusion. Infusion reactions may include, but are not limited to, pyrexia, chills, diarrhea, nausea, asthenia, hypertension, lethargy, tachycardia.

Description of selected adverse reactions

Corneal adverse reactions

Corneal adverse reactions were assessed in Study 205678 from the safety population (n = 218) which included patients treated with 2.5 mg/kg (n=95). Eye disorder events occurred in 74% patients and the most common adverse reactions were keratopathy or microcyst-like epithelial changes in corneal epithelium [identified on eye exam, with or without symptoms] (71%), blurred vision (25%), and dry eye symptoms (15%). Decreased vision (Snellen Visual Acuity worse than 20/50) in the better eye was reported in 18% and severe vision loss (20/200 or worse) in the better seeing eye was reported in 1% of patients treated with belantamab mafodotin.
The median time to onset of Grade 2 or above corneal findings (best corrected visual acuity or keratopathy on eye examination) was 36 days (range: 19 to 143 days). The median time to resolution of these corneal findings was 91 days (range: 21 to 201 days).
Corneal findings (keratopathy) led to dose delays in 47% of patients, and dose reductions in 27% of patients. Three percent of patients discontinued treatment due to ocular events.

Infusion-related reactions

In clinical studies, the incidence of infusion-related reactions (IRR) with belantamab mafodotin 2.5 mg/kg was 21%, and most (90%) occurred during the first infusion. Most IRRs were reported as Grade 1 (6%) and Grade 2 (12%) while 3% experienced Grade 3 IRRs. Serious IRRs were reported by 4% of patients and included symptoms of pyrexia and lethargy. Median time to onset and the median duration of the first occurrence of an IRR was 1 day. One patient (1%) discontinued treatment due to IRRs, experiencing Grade 3 IRRs at first and second infusion. No Grade 4 or 5 IRRs were reported.

Thrombocytopenia

Thrombocytopenic events, (thrombocytopenia and platelet count decreased) occurred in 38% of patients treated with belantamab mafodotin 2.5 mg/kg. Grade 2 thrombocytopenic events occurred in 3% of patients, Grade 3 in 9%, and Grade 4 in 13%. Grade 3 bleeding events occurred in 2% of patients and no Grade 4 or 5 events were reported.

Infections

Upper respiratory tract infections were commonly reported across the belantamab mafodotin clinical programme and were mostly mild to moderate (Grade 1 to 3), occurring in 9% of patients treated with belantamab mafodotin 2.5 mg/kg. There were no SAEs of upper respiratory tract infections reported. Pneumonia was the most frequent infection reported in 11% of patients treated with belantamab mafodotin 2.5 mg/kg. Pneumonia was also the most frequent SAE, reported in 7% of patients. Infections with a fatal outcome were primarily due to pneumonia (1%).

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 has been no experience of overdosage in clinical studies.

There is no known specific antidote for belantamab mafodotin overdose. In the event of an overdose, the patient should be monitored for any signs or symptoms of adverse effects and appropriate supportive treatment should be instituted immediately.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: antineoplastic agents, monoclonal antibodies, ATC code: L01XC39

Mechanism of action

Belantamab mafodotin is a humanised IgG1κ monoclonal antibody conjugated with a cytotoxic agent, maleimidocaproyl monomethyl auristatin F (mcMMAF). Belantamab mafodotin binds to cell surface BCMA and is rapidly internalised. Once inside the tumour cell, the cytotoxic agent is released disrupting the microtubule network, leading to cell cycle arrest and apoptosis. The antibody 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
Based on exposure-QT_c analysis, belantamab mafodotin had no meaningful QTc prolongation (>10 ms) at the recommended dose of 2.5 mg/kg once every 3 weeks.

Immunogenicity

In clinical studies in patients with multiple myeloma, <1% of patients (2/274) tested positive for anti-belantamab mafodotin antibodies after receiving belantamab mafodotin. One of the two patients tested positive for neutralising anti-belantamab mafodotin antibodies.

Clinical efficacy

Study 205678 was an open-label, two arm, Phase II, multicentre study which evaluated belantamab mafodotin as monotherapy in patients with multiple myeloma who had relapsed following treatment with at least 3 prior therapies, and who were refractory to an immunomodulatory agent, a proteasome inhibitor and an anti-CD38 antibody alone or in combination. Patients were included if they had undergone autologous stem cell transplant or were considered transplant ineligible and had measurable disease by International Myeloma Working Group (IMWG) criteria.

Patients were randomised to receive 2.5 mg/kg (N=97) or 3.4 mg/kg (N=99) belantamab mafodotin by intravenous infusion every 3 weeks until disease progression or unacceptable toxicity (see Table 4). The data presented below is from the 2.5 mg/kg cohort who received the recommended therapeutic dose based on overall benefit risk assessment (see section 4. 2).

Table 4: Baseline demographics and disease characteristics

Baseline Characteristics		**2.5 mg/kg (N=97)**
Age	Median (range) Interquartile range	65.0 (39-85) 60-70
Gender	Male Female	51 (53%) 46 (47%)
ECOG at baseline	0/1 2	33%, 50%, 17%
ISS stage at screening	II III	33 (34%) 42 (43%)
Cytogenetics risk	High risk*	26 (27%)
Number of prior lines	Median Range	7 (3-21)
Duration of exposure	Median Range	9 weeks (2-75)
Treatment cycles	Median Range	3 (1-17)

*High risk cytogenetic factors [positive for t (4;14), t (14;16), and 117p13del]

The primary endpoint was overall response rate as evaluated by an Independent Review Committee (IRC) based on the IMWG Uniform Response Criteria for Multiple Myeloma. Table 5 provides the results of study 205678.

Table 5. Efficacy of BLENREP in patients with multiple myeloma in study 205678

Clinical response	**2.5 mg/kg (N = 97)**
Overall response rate (ORR), % (97.5% CI)	32% (22, 44)
Stringent complete response (sCR), n (%)	2 (2%)
Complete response (CR), n (%)	5 (5%)
Very good partial response (VGPR), n (%)	11 (11%)
Partial response (PR), n (%)	13 (13%)
Clinical benefit rate*, n (%) (95% CI)	36 (26.6, 46.5)
Median duration of response in months (95% CI)	11 (4.2 to Not reached)
Probability of Maintaining Response at 12 Months (95% CI)	0.50 (0.29, 0.68)
Median time to response in months (95% CI)	1.5 (1.0, 2.1)
Median time to best response in months (95% CI)	2.2 (1.5, 3.6)
Median overall survival (OS) in months (95% CI)	13.7 (9.9 to Not reached)
Survival probability at 12 Months (95% CI)	0.57 (0.46, 0.66)

*CBR: sCR+CR+VGPR+PR+Minimal response

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).

This medicinal product has been authorised under a so-called 'conditional approval' scheme. This means that further evidence on this medicinal product is awaited.

The European Medicines Agency will review new information on this medicinal product at least every year and this SmPC will be updated as necessary.

5.2 Pharmacokinetic properties

Absorption

Maximum concentration for belantamab mafodotin occurred at or shortly after the end of infusion while cys-mcMMAF concentrations peaked ~24 hours after dosing. Geometric mean belantamab mafodotin C_{max} and $AUC_{(0\text{-}tau)}$ concentrations were 43 mcg/mL and 4,666 mcg.h/mL, respectively. Geometric mean cys-mcMMAF C_{max} and $AUC_{(0\text{-}168h)}$ concentrations were 0.90 ng/mL and 84 ng.h/mL, respectively.

Distribution

The mean steady-state volume of distribution of belantamab mafodotin was 10.8 L.

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 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).

Elimination

Belantamab mafodotin was cleared slowly with total plasma clearance of 0.92 L/day and a terminal phase half-life of 12 days. Over time, clearance was reduced to 0.72 L/day with an elimination half-life of 14 days. Predose cys-mcMMAF concentrations at each dose were typically below the limit of quantification (0.05 ng/mL).

In an animal study, approximately 83% of the radioactive dose was excreted in the faeces; urinary excretion (approximately 13%) was a minor route; intact cys-mcMMAF was detected in human urine, 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 patients (≥65 years old)

No formal studies have been conducted in elderly patients. Age was not a significant covariate in population pharmacokinetic analyses.

Renal impairment
No formal studies have been conducted in patients with renal impairment. Renal function was not a significant covariate in population pharmacokinetic analyses that included patients with normal renal function and mild or moderate renal impairment.

Hepatic impairment
No formal studies have been conducted in patients with hepatic impairment. Hepatic function was not a significant covariate in population pharmacokinetic analyses that included patients with normal hepatic function or mild hepatic impairment.

Body weight
Body weight was a significant covariate in population pharmacokinetic analyses. Belantamab mafodotin C_{tau} was predicted to be +10% at a body weight of 100 kg (+20% for 130 kg) and -10% at a body weight of 55 kg (-20% for 40 kg) compared to the typical patient (75 kg).

5.3 Preclinical safety data

Animal toxicology and/or pharmacology

In non-clinical studies, the principal adverse findings (directly related to belantamab mafodotin) in the rat and monkey, at exposures ≥1.2 times of 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. 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* 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. Luteinized 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
Citric acid
Trehalose dihydrate
Disodium edetate
Polysorbate 80

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

18 months.

Reconstituted solution

The reconstituted solution can be stored for up to 4 hours at room temperature (20ºC to 25ºC) or stored in a refrigerator (2°C to 8°C) 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 (2ºC to 8ºC) 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 (20ºC to 25ºC) for a maximum of 6 hours (including infusion time).

6.4 Special precautions for storage

Store in a refrigerator (2ºC to 8ºC).

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

6.5 Nature and contents of container

Type 1 glass vial sealed with bromobutyl rubber stopper and aluminium overseal with a plastic removable cap containing 100 mg powder.

Pack size: 1 vial

6.6 Special precautions for disposal and other handling

Preparation of solution for infusion

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

The recommended dose of BLENREP is 2.5 mg/kg administered as an intravenous infusion once every 3 weeks.

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 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 vial 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 (2ºC to 8ºC) 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 (20ºC to 25ºC) for a maximum of 6 hours (including infusion time).

Administration Instructions

1. Administer the diluted solution by intravenous infusion over a minimum of 30 minutes using an infusion set made of polyvinyl chloride or polyolefin.
2. Filtration of the diluted solution is not required. However, if the diluted solution is filtered, 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 (Ireland) Limited
12 Riverwalk, Citywest Business Campus
Dublin 24
Ireland

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/20/1474/001

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

10. DATE OF REVISION OF THE TEXT

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

ANNEX II

A. MANUFACTURER OF THE BIOLOGICAL ACTIVE SUBSTANCE AND 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

E. SPECIFIC OBLIGATION TO COMPLETE POST-AUTHORISATION MEASURES FOR THE CONDITIONAL MARKETING AUTHORISATION

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

Name and address of the manufacturer of the biological active substance

Sigma-Aldrich Manufacturing LLC
3300 South Second Street,
St. Louis, MO 63118
USA

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 periodic safety update report 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**

The educational programme is aimed at helping haematologists/oncologists, eye care professionals and patients understand the corneal risks associated with belantamab mafodotin, so that corneal examination findings, and/or visual changes can be promptly identified and managed according to the product labelling.

Prior to the launch of BLENREP (belantamab mafodotin) in each Member State the MAH must agree about 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 (belantamab mafodotin) is marketed, all healthcare professionals and patients/carers who are expected to prescribe, dispense and receive BLENREP (belantamab mafodotin) have access to/are provided with the following educational materials to be disseminated through professional bodies consisting of the following:

- Educational materials for Healthcare professionals (HCPs) (includes haematologists/oncologists/eye care professionals):
    - Corneal adverse reaction guides
    - Eye care screening sheet

- Educational materials for the patient
    - Corneal adverse reaction guides
    - Patient and pharmacy eye drop wallet cards.

- Summary of the Product Characteristics (SmPC) and Package Leaflet (PL)

Key elements to be included

The healthcare professional's corneal adverse reaction guides

The HCPs corneal adverse reaction guides will contain the following key information:

Relevant information of the safety concern keratopathy or microcyst-like epithelial changes in the corneal epithelium:

- Advise patients that corneal adverse reactions may occur during treatment.
- Patients with a history of dry eyes are more prone to develop changes in the corneal epithelium.

Details on how to minimise the safety concern addressed by the additional risk minimisation measures through appropriate monitoring:

- Ophthalmic examinations, including assessment of visual acuity and slit lamp examination, should be performed at baseline, before the subsequent 3 treatment cycles, and as clinically indicated whilst on treatment.
- Patients experiencing keratopathy with or without changes in visual acuity may require a dose modification (delay and/or reduction) or treatment discontinuation based on severity of findings.
- Emphasise the need to consult the SmPC.

<u>Key messages to convey during patient counselling</u>:

- 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 corneal adverse reactions occur.
- Patients who report corneal symptoms should be referred to an eye care professional.
- Patients should be advised to use caution when driving or operating machinery.

<u>Healthcare professionals' training material</u>

Anatomy and physiology of the eye:

- Images of the eye are provided and reviewed.
- Keratopathy is characterised based on exam findings and patient reported outcomes.

Description of eye exams:

- Use of slit lamp exams provide detailed information on the anatomical structures in the eye. They can help detect a range of conditions, including keratopathy or microcyst-like epithelial changes in the corneal epithelium (as seen on eye examination).
- Description of visual acuity provides a measure of the visual system's ability to discern fine distinctions in the visual environment.
- Best corrected visual acuity (BCVA) refers to the visual acuity achieved with correction (such as glasses), as measured on the standard Snellen Visual Acuity Chart, monocularly and binocularly.
- Summary of visual acuity scores (20/20 vs <20/20) and how a score less than 20/20 can be corrected and managed by the patients.

Eye care screening sheet:

- Includes important information related to corneal adverse reactions associated with belantamab mafodotin, adverse event management, and instructions to facilitate communication between prescribers and eye care professionals for patients.

Patient corneal adverse reaction guides

The patient corneal adverse reaction guides will contain the following key information:

- Corneal adverse reactions may occur during treatment. Patients with a history of dry eyes are more prone to develop changes in the corneal epithelium.
- Ophthalmic examinations, including assessment of visual acuity and slit lamp examination, should be performed at baseline, before the subsequent 3 treatment cycles, and as clinically indicated whilst on treatment.
- Patients experiencing keratopathy with or without changes in visual acuity may require a dose modification (delay and/or reduction) or treatment discontinuation based on severity of findings.
- Tell your haematologist/oncologist about any history of vision or eye problems.
- Consult the PL.

A description of the sign and symptoms of the risk of keratopathy:

- If you experience changes with your vision whilst on belantamab mafodotin, contact your haematologist/oncologist. Symptoms include the following:
    - redness, dryness, itching, burning sensation, or sandy or gritty sensation in their eyes;
    - sensitivity to light;
    - blurred vision;
    - pain in their eyes;
    - excessive watering of their eyes.

- If you experience changes in your vision or eyes after initiating treatment (changes have improved, persisted, or worsened since your last appointment), contact your haematologist/oncologist.

- Your HCP will ask you to use eye drops called preservative-free artificial tears during treatment. Administer them as instructed.

Patient eye drop wallet card:

- Patient wallet card indicates the patient is on treatment with belantamab mafodotin and contains contact information for the haematologist/oncologist and the eye care professional.
- Present to HCPs during follow up visits.

Pharmacy eye drop wallet card:

- Patients to present the pharmacy wallet card to the pharmacist to find eye drops called preservative-free artificial tears for use, as directed.

E. SPECIFIC OBLIGATION TO COMPLETE POST-AUTHORISATION MEASURES FOR THE CONDITIONAL MARKETING AUTHORISATION

This being a conditional marketing authorisation and pursuant to Article 14-a(4) of Regulation (EC) No 726/2004, the MAH shall complete, within the stated timeframe, the following measures:

Description	**Due date**
In order to confirm the efficacy and safety of BLENREP in relapsed/refractory multiple myeloma adult patients, who have received at least four prior therapies and whose disease is refractory to at least one proteasome inhibitor, one immunomodulatory agent, and an anti-CD38 monoclonal antibody, and who have demonstrated disease progression on the last therapy, the MAH should submit the results of the DREAMM-2 (205678) study investigating the efficacy of belantamab mafodotin in patients with multiple myeloma who had 3 or more prior lines of treatment, are refractory to a proteasome inhibitor and an immunomodulatory agent and have failed an anti-CD38 antibody.	April 2021
In order to confirm the efficacy and safety of BLENREP in multiple myeloma adult patients, who have received at least four prior therapies and whose disease is refractory to at least one proteasome inhibitor, one immunomodulatory agent, and an anti-CD38 monoclonal antibody, and who have demonstrated disease progression on the last therapy, the MAH should submit the results of the DREAMM-3 (207495) study comparing the efficacy of belantamab mafodotin vs. pomalidomide plus low dose dexamethasone (pom/dex) in patients with relapsed/refractory multiple myeloma.	July 2024

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

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, citric acid, trehalose dihydrate, disodium edetate, polysorbate 80.

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

GlaxoSmithKline (Ireland) Limited, 12 Riverwalk, Citywest Business Campus, Dublin 24, Ireland.

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/20/1474/001

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 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 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,** a *monoclonal antibody* connected to an anticancer substance that can kill multiple myeloma cells. 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 anticancer substance is released and kills the cancer cells.

BLENREP is used to treat adults who have cancer of the bone marrow called multiple myeloma.

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

Do not receive 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

Eye problems

BLENREP can cause dry eyes, blurred vision or other eye problems.
You should have an eye examination by an eye specialist before starting treatment and for the next three doses of BLENREP. Your doctor may request further eye tests whilst on treatment with BLENREP. Even if your vision seems fine, it is important that you get your eyes checked during treatment with BLENREP because some changes can happen without symptoms and may only be seen on an eye examination.

➔ **Do not use contact lenses** while you are receiving treatment.

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.

If you notice changes with your vision, your doctor may hold treatment with BLENREP or adjust the dose or ask you to see an eye specialist. Your doctor may decide to stop treatment with BLENREP.

➔ **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 counts (*thrombocytopenia*) include:

- abnormal bruising under the skin,
- bleeding longer than usual after a test,
- 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*.

➔ See 'Infusion-related reactions' in Section 4.

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

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

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 and fertility

If you are pregnant or breast-feeding, 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 **contraception** during treatment and for 4 months after your last dose of BLENREP.

Women being treated with this medicine who wish to have children are advised to seek fertility counselling and consider options to freeze eggs/embryos before treatment.

If you are a man who could father a child:

- You must use effective **contraception** during treatment and for 6 months after your last dose of BLENREP.

Men being treated with this medicine are advised to have sperm samples frozen and stored before treatment.

Breast-feeding

You must not breast-feed during treatment and for 3 months after your last dose of BLENREP.

It is not known if the medicine passes into breast milk. Talk to your doctor about this.

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 sodium
This medicine contains less than 1 mmol sodium (23 mg) per 100 mg 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.

The recommended dose is 2.5 mg of BLENREP per kilogram of your body weight. It is given by your doctor or nurse as a drip into a vein *(intravenous infusion)* every three weeks.

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

If you given more BLENREP than you should

This medicine will be given by your doctor or nurse. In the unlikely event that you are given too much (an overdose) your doctor will check you for side effects.

If a dose of BLENREP is missed

It is very important to go to all your appointments, to make sure your treatment works. 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.

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 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.

Other side effects

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 disorder of the cornea of the eye (*keratopathy*), blurred vision, and dry eyes.

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

- low number of a type of blood cell called platelets which help to clot blood (*thrombocytopenia*), causing abnormal bruising and bleeding

➔ **Read the information** under 'Abnormal bruising and bleeding' in Section 2 of this leaflet.

- infection of the lungs (*pneumonia*)
- fever
- 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 (*lymphopenia, leukopenia, neutropenia*).
- abnormal blood levels of enzymes indicating liver problems (*aspartate aminotransferase, gamma glutamyltransferase*).
- nausea
- feeling tired (*fatigue*)
- diarrhoea

Common: may affect up to 1 in 10 people

- cold or cold-like symptoms such as cough, runny nose or sore throat.
- vomiting
- abnormal levels of creatinine phosphokinase
- sensitivity to light (photophobia)
- eye irritation

Uncommon: may affect up to 1 in 100 people

- eye sores, possibly with infection (*ulcerative and infective keratitis*)

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

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 (2ºC–8ºC).

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. 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 100 mg of belantamab mafodotin. After reconstitution the solution contains 50 mg belantamab mafodotin per mL.

The other ingredients are sodium citrate, citric acid, trehalose dihydrate, disodium edetate and polysorbate 80 (see section 2 “BLENREP contains sodium”).

What BLENREP looks like and contents of the pack

BLENREP is 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.

Marketing Authorisation Holder
GlaxoSmithKline (Ireland) Limited
12 Riverwalk
Citywest Business Campus
Dublin 24
Ireland

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

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

België/Belgique/Belgien
GlaxoSmithKline Pharmaceuticals s.a./n.v.
Tél/Tel: + 32 (0) 10 85 52 00

България
ГлаксоСмитКлайн ЕООД
Тел.: + 359 2 953 10 34

Česká republika
GlaxoSmithKline, s.r.o.
Tel: + 420 222 001 111
cz.info@gsk.com

Danmark
GlaxoSmithKline Pharma A/S
Tlf: + 45 36 35 91 00
dk-info@gsk.com

Deutschland
GlaxoSmithKline GmbH & Co. KG
Tel.: + 49 (0)89 36044 8701
produkt.info@gsk.com

Eesti

Lietuva
GlaxoSmithKline Lietuva UAB
Tel: + 370 5 264 90 00
info.lt@gsk.com

Luxembourg/Luxemburg
GlaxoSmithKline Pharmaceuticals s.a./n.v.
Belgique/Belgien
Tél/Tel: + 32 (0) 10 85 52 00

Magyarország
GlaxoSmithKline Kft.
Tel.: + 36 1 225 5300

Malta
GlaxoSmithKline (Malta) Limited
Tel: + 356 21 238131

Nederland
GlaxoSmithKline BV
Tel: + 31 (0) 33 2081100

Norge

GlaxoSmithKline Eesti OÜ
Tel: + 372 6676 900
estonia@gsk.com

Ελλάδα
GlaxoSmithKline Μονοπρόσωπη A.E.B.E.
Τηλ: + 30 210 68 82 100

España
GlaxoSmithKline, S.A.
Tel: + 34 900 202 700
es-ci@gsk.com

France
Laboratoire GlaxoSmithKline
Tél: + 33 (0)1 39 17 84 44
diam@gsk.com

Hrvatska
GlaxoSmithKline d.o.o.
Tel: +385 1 6051999

Ireland
GlaxoSmithKline (Ireland) Limited
Tel: + 353 (0)1 4955000

Ísland
Vistor hf.
Sími: + 354 535 7000

Italia
GlaxoSmithKline S.p.A.
Tel: + 39 (0)45 9218 111

Κύπρος
GlaxoSmithKline (Cyprus) Ltd
Τηλ: + 357 22 39 70 00
gskcyprus@gsk.com

Latvija
GlaxoSmithKline Latvia SIA
Tel: + 371 67312687
lv-epasts@gsk.com

GlaxoSmithKline AS
Tlf: + 47 22 70 20 00

Österreich
GlaxoSmithKline Pharma GmbH
Tel: + 43 (0)1 97075 0
at.info@gsk.com

Polska
GSK Services Sp. z o.o.
Tel.: + 48 (0)22 576 9000

Portugal
GlaxoSmithKline – Produtos Farmacêuticos, Lda.
Tel: + 351 21 412 95 00
FI.PT@gsk.com

România
GlaxoSmithKline (GSK) S.R.L.
Tel: + 4021 3028 208

Slovenija
GlaxoSmithKline d.o.o.
Tel: + 386 (0)1 280 25 00
medical.x.si@gsk.com

Slovenská republika
GlaxoSmithKline Slovakia s. r. o.
Tel: + 421 (0)2 48 26 11 11
recepcia.sk@gsk.com

Suomi/Finland
GlaxoSmithKline Oy
Puh/Tel: + 358 (0)10 30 30 30
Finland.tuoteinfo@gsk.com

Sverige
GlaxoSmithKline AB
Tel: + 46 (0)8 638 93 00
info.produkt@gsk.com

United Kingdom
GlaxoSmithKline UK Ltd
Tel: + 44 (0)800 221441
customercontactuk@gsk.com

This leaflet was last revised in <{MM/YYYY}><{month YYYY}>.

This medicine has been given ‘conditional approval’. This means that there is more evidence to come about this medicine.
The European Medicines Agency will review new information on this medicine at least every year and this leaflet will be updated as necessary.

Other sources of information

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

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.

Preparation of solution for infusion

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

The recommended dose of BLENREP is 2.5 mg/kg administered as an intravenous infusion once every 3 weeks.

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 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 vial 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 (2ºC to 8ºC) 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 (20ºC to 25ºC) for a maximum of 6 hours (including infusion time).

Administration Instructions

1. Administer the diluted solution by intravenous infusion over a minimum of 30 minutes using an infusion set made of polyvinyl chloride or polyolefin.
2. Filtration of the diluted solution is not required. However, if the diluted solution is filtered, polyethersulfone (PES) based filter is recommended.

Disposal

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

Annex IV

Conclusions on the granting of the conditional marketing authorisation and similarity presented by the European Medicines Agency

Conclusions presented by the European Medicines Agency on:

- **Conditional marketing authorisation**

The CHMP having considered the application is of the opinion that the risk-benefit balance is favourable to recommend the granting of the conditional marketing authorisation as further explained in the European Public Assessment Report.

- **Similarity**

The CHMP is of the opinion that Blenrep is not similar to authorised orphan medicinal products within the meaning of Article 3 of Commission Regulation (EC) No. 847/2000 as further explained in the European Public Assessment Report.