swissmedic

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Swissmedic, Swiss Agency for Therapeutic Products

Swiss Public Assessment Report

Blenrep

International non-proprietary name:	belantamab mafodotin
Pharmaceutical form:	powder for concentrate for solution for infusion
Dosage strength(s):	70 mg, 100 mg
Route(s) of administration:	intravenous
Marketing authorisation holder:	GlaxoSmithKline AG
Marketing authorisation no.:	69910
Decision and decision date:	approved on 19 June 2025

Note:

This assessment report is as adopted by Swissmedic with all information of a commercially confidential nature deleted.

SwissPARs are final documents that provide information on submissions at a particular point in time. They are not updated after publication.

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1 Terms, Definitions, Abbreviations

ADC	Antibody-drug conjugate
AE	Adverse event
AST	Aspartate aminotransferase
AUC	Area under the plasma concentration-time curve
BCMA	B-cell maturation antigen
BPd	Belantamab mafodotin, pomalidomide, and dexamethasone
CGE	Capillary gel electrophoresis
CI	Confidence interval
cIEF	Capillary isoelectric focussing
CL	Clearance
C_{max}	Maximum observed plasma/serum concentration of drug
DOR	Duration of response
ERA	Environmental risk assessment
GLP	Good Laboratory Practice
HIC	Hydrophobic interaction chromatography
HR	Hazard ratio
ICH	International Council for Harmonisation
Ig	Immunoglobulin
ITT	Intention-to-treat
LoQ	List of Questions
mAB	Monoclonal antibody
MAH	Marketing Authorisation Holder
Max	Maximum
mcMMAF	Maleimidocaproyl monomethyl auristatin F
Min	Minimum
MM	Multiple myeloma
MRD	Minimal residual disease
N/A	Not applicable
NO(A)EL	No observed (adverse) effect level
OS	Overall survival
PFS	Progression-free survival
PK	Pharmacokinetics
PopPK	Population pharmacokinetics
PVd	Pomalidomide, bortezomib and dexamethasone
RMP	Risk management plan
RRMM	Relapsed/refractory multiple myeloma
SAE	Serious adverse event
SE-HPLC	Size exclusion high-performance liquid chromatography
SwissPAR	Swiss Public Assessment Report
TEAE	Treatment-emergent adverse event
TPA	Federal Act of 15 December 2000 on Medicinal Products and Medical Devices (SR 812.21)
TPO	Ordinance of 21 September 2018 on Therapeutic Products (SR 812.212.21)
ULN	Upper limit of normal

2 Background information on the procedure

2.1 Applicant's request(s) and information regarding procedure

New active substance status
The applicant requested new active substance status for belantamab mafodotin in the above-mentioned medicinal product.

Fast-track authorisation procedure
The applicant requested a fast-track authorisation procedure in accordance with Article 7 TPO.

Orphan drug status
The applicant requested orphan drug status in accordance with Article 4 paragraph 1 letter a^{decies} no. 2 TPA.
Orphan drug status was granted on 22 March 2021.

2.2 Indication and dosage

2.2.1 Requested indication

Blenrep is indicated for the treatment of adults with multiple myeloma in combination with pomalidomide and dexamethasone in patients who have received at least one prior therapy including lenalidomide.

2.2.2 Approved indication

Blenrep is indicated for the treatment of relapsed or refractory multiple myeloma in adults in combination with pomalidomide and dexamethasone in patients who have received at least one prior line of therapy, including lenalidomide, and who demonstrated disease progression during the last therapy (see "Clinical efficacy").

2.2.3 Requested dosage

Summary of the requested standard dosage:
Cycles of 4 weeks each.
Cycle 1: 2.5 mg/kg body weight once as i.v. infusion over 30 minutes.
Cycle 2 and onwards: 1.9 mg/kg once every 4 weeks as i.v. infusion over 30 minutes.
Treatment until disease progression.
Other co-medication: 4 times each day apply eye drops with artificial tears to reduce corneal symptoms.

In case of toxicities: reduce frequency of Blenrep administration to 1.9 mg/kg once every 8 weeks.
If further reduction is needed: reduce to 1.4 mg/kg once every 8 weeks.

2.2.4 Approved dosage

(see appendix)

2.3 Regulatory history (milestones)

Application	23 August 2024
Formal control completed	27 August 2024
List of Questions (LoQ)	31 October 2024
Response to LoQ	29 January 2025
Preliminary decision	19 March 2025
Response to preliminary decision	30 April 2025
Labelling corrections and/or other aspects	13 May 2025
Response to labelling corrections and/or other aspects	25 May 2025
2nd round labelling corrections and/or other aspects	28 May 2025
Response to 2nd round labelling corrections and/or other aspects	5 June 2025
Final decision	19 June 2025
Decision	approval

3 Medical context

Multiple myeloma (MM) is a plasma cell neoplasm that accounts for approximately 1 to 2% of all cancers and 10-15% percent of haematological neoplasms. The incidence increases with age, and the median age at onset of MM is approximately 70 years, with approximately two thirds of patients aged older than 65 years.

MM is an incurable disease. Patients will ultimately relapse even if they achieve prolonged and deep initial responses to frontline therapy. Survival rates have improved for patients with MM over the last 5 years based on novel agents such as immunomodulatory drugs, proteasome inhibitors, chemotherapy or novel antibodies, yet relapse remains inevitable, indicating an ongoing need for new therapeutic approaches, particularly in the second-line and third-line settings.

4 Quality aspects

4.1 Drug substance

Belantamab mafodotin drug substance is an antibody-drug conjugate (ADC) composed of an anti-mitotic agent maleimidocaproyl monomethyl auristatin F (mcMMAF) covalently conjugated to a recombinant afucosylated humanised monoclonal $IgG1_K$ antibody specific for B-cell maturation antigen (BCMA). Upon binding, belantamab mafodotin is rapidly internalised and the linker is cleaved, leading to intracellular release of mcMMAF. The mechanisms of action of belantamab mafodotin are designed to enable anti-tumour activity of cells by antibody-dependent cell-mediated cytotoxicity (non-dividing) as well as antibody-drug conjugate activity (dividing cells).
The intermediate drug substance, the antibody belantamab, consists of two identical light chain (LC) polypeptides and two identical heavy chain (HC) polypeptides. The antibody (mAB) is produced from a mammalian cell line (Chinese Hamster Ovary).
The physicochemical and biological properties of the antibody-drug conjugate and its impurities were determined using state-of-the-art methods.
The specifications for release include relevant tests and limits, e.g. for appearance, identity, pH, several purity tests (e.g. SE-HPLC, HIC, cIEF), protein concentration and a potency assay.
Specifications are based on clinical batch experience, batch analysis data (release and stability data) and are in conformance with current compendial and regulatory guidelines.
Batch analysis data for several commercial scale batches from the current manufacturing site are provided. Additional batch data for the drug substance used in clinical trials are presented, and their comparability has been demonstrated. All the analytical methods are described and non- compendial methods have been validated in accordance with ICH guidelines.
The drug substance is stored at appropriate storage conditions. No significant changes have been observed within the proposed shelf life.

4.2 Drug product

The finished product is a sterile lyophilised dosage form of belantamab mafodotin with the strengths of either 70 mg or 100 mg. The finished product is intended for intravenous infusion after reconstitution with sterile water for injection and dilution in 0.9% saline.
All used excipients in the formulated drug product comply with the European Pharmacopoeia.
The finished product manufacturing process has been validated at commercial scale using several validation batches.
The specifications include relevant tests and limits, e.g. for appearance, colour, clarity, identity, cell-based potency assay, pH, moisture content, osmolality, purity and impurity tests (IEF, CGE, HPLC), protein concentration by UV, particles, sterility and bacterial endotoxins. All non-compendial methods have been validated in accordance with ICH guidelines.
Batch analysis data for several batches from the commercial site are provided. The container closure systems in contact with the finished product consist of a glass vial with a bromobutyl rubber stopper and an aluminium/plastic seal/cap. All components coming into contact with the finished product comply with European Pharmacopoeia requirements.
The drug product is stored at 2-8°C. No meaningful changes have been observed within the proposed storage conditions. A shelf life of 48 months has been accepted.

4.3 Quality conclusions

The manufacturing processes (drug substance and drug product) are well described and demonstrate a consistent quality of drug substance and drug product. The shelf-life of the drug substance and drug product is supported by data from recommended storage conditions, as well as accelerated and stress studies. Safety aspects with regard to adventitious agent contaminants were satisfactorily addressed. The risk of adventitious agents is minimised.

5 Nonclinical aspects

In accordance with the drug's indication and its antibody-drug conjugate (ADC) nature, the applicant adhered to the recommendations outlined in the ICH S9, S9 Q&A, S6, and S7A guidelines. Pivotal toxicology studies were conducted in compliance with Good Laboratory Practice (GLP) standards.

5.1 Pharmacology

The affinity (K_D) of belantamab mafodotin to human and cynomolgus monkey B-cell maturation antigen (BCMA) was within a 2-fold range, i.e. 1.3 µg/mL and 0.6 µg/mL at 37°C, showing higher affinity to the monkey BCMA. The applicant stated that the drug did not bind to mouse or rat BCMA and is unlikely to bind to rabbit BCMA. Therefore, the cynomolgus monkey was considered a relevant species.
Belantamab mafodotin also showed affinity to human Fc gamma receptors (FcγR) I, FcγR IIIa V, FcγR IIIa F, and human neonatal Fc receptor (FcRn) with K_D at 25°C of 1.0 µg/mL, 4.3 µg/mL, 35.7 µg/mL, and 7.9 µg/mL. These concentrations are within the range of systemic concentrations reached in humans and toxicology species. The applicant did not provide data regarding affinity to FcγR in the toxicology species.
Upon binding to BCMA, the drug was rapidly internalised, and the cytotoxic part (cys-mcMMAF) was released inside the cell, presumably via endosomal/lysosomal degradation. Minimal active concentrations for binding and internalisation on different multiple myeloma (MM) cell lines were in the range of 1 µg/mL; i.e. lower than C_{trough} (3.6 µg/mL) in humans and therefore in an efficacious range. Upon internalisation, belantamab mafodotin elicited G2/M arrest, apoptosis and immunogenic cell death in a time- and concentration-dependent manner in BCMA expressing cells, including primary MM cells. At 10 µg/mL, low bystander cytotoxicity of the drug to cells that express no, or low, levels of BCMA was observed. However, this concentration is lower than exposures reached in patients and toxicology studies. Furthermore, *in vitro*, macropinocytosis enabled unspecific cellular uptake of the drug. Taken together, this might explain the discrepancy with the *in vivo* toxicity studies, as the spectrum of toxicities was not confined within the BCMA targets of belantamab mafodotin. The delayed increase of pro-inflammatory cytokines occasionally observed in one study suggests some potential risk of cytokine release.
The applicant also demonstrated *in vitro* antibody-dependent cellular cytotoxicity and phagocytosis activity. Overall, the compound demonstrated antitumour activity towards dividing and non-dividing cells.
Belantamab mafodotin induced significant tumour growth regression in xenograft models with different human MM cells. In an immune-competent syngeneic mouse model, results indicated that the regression is $CD8^+$ T-cell dependent. Furthermore, in cynomolgus monkeys, a single dose of 1 mg/kg belantamab mafodotin resulted in reductions in BCMA-positive plasma cells and IgE levels, and a modest reduction of <25% in IgG, IgA, and IgM levels, which reflects target related toxicity.
In combination with lenalidomide, pomalidomide, or bortezomib, belantamab mafodotin improved survival in 2 mouse MM xenograft models. Tumour growth was inhibited after combination with lenalidomide or bortezomib, but not pomalidomide.

Safety pharmacology evaluations were incorporated into the repeat dose toxicology studies in rats and monkeys. The applicant also tested cys-mcMMAF in a hERG assay. Overall, the results of these safety pharmacology evaluations did not raise any concerns.

5.2 Pharmacokinetics

Following intravenous (i.v.) administration of belantamab mafodotin, the PK in mice, rats and monkeys was characteristic of that expected for a human monoclonal antibody, with low clearance (CL) and volume of distribution (Vss) and a half-life measured in days. Following single i.v.

administration of labelled drug, the mAB was associated with connective tissue in the eye and eyelids, extra-orbital lacrimal and Harderian glands and liver, as well as muscle in the eyelids but was not observed in the cornea or glands in the eyelids. Binding was stronger in liver and kidneys than in the eye. Liberated cys-mcMMAF was detected at very low levels in liver, bone marrow, kidney, Harderian gland and extra-orbital lacrimal gland, with no detection in cornea, eyelid or whole eye. *In vitro* (rat, monkey, human) and *in vivo* (rat), the linear isomer of cys-mcMMAF was predominately chemically hydrolysed and dehydrated to the cyclised isomer of cys-mcMMAF, with very low Phase I/II metabolism. Following i.v. dosing of radioactive cys-mcMMAF to rats, the radioactivity was excreted in faeces (83%, mainly cyclised form) and urine (13%, mainly linear form). Belantamab mafodotin was stable in rat, monkey or human plasma, with <3% MMAF being released over 3 days.
The half-life of belantamab mafodotin was longer in rodents (rats ~11 days, mice ~13 days) compared to monkeys (~4 days). Following i.v. administration of the drug, the time to reach C_{max} (T_{max}) was mainly around 0.25 hour. The plasma concentrations (ADC and total monoclonal antibody) were similar within nonclinical species, suggesting stability of the drug conjugate in circulation.
Belantamab mafodotin was cleared slowly in animals. Clearance was much lower than the glomerular filtration rate, indicating little clearance of belantamab mafodotin by the renal routes. The Vss in animals was less than the extracellular fluid volume, suggesting that the compound was mainly confined to the systemic circulation. This is comparable to the human situation.

5.3 Toxicology

Significant nonclinical findings occurred in the repeat-dose toxicity studies. The findings were primarily related to the cytotoxic drug conjugate, cys-mcMMAF, which were in line with the safety profiles reported for other auristatins and microtubule-disrupting agents. The target organs were the kidney, lung, liver, haematopoietic system, male and female reproductive organs and the eye. The spectrum of toxicities is not confined to the BCMA targets of belantamab mafodotin. Overall, the comparison of findings between monkey (pharmacologically relevant species) and rat indicated that, due to the low expression of the target BCMA in healthy monkeys, the adverse effects observed in this species, except for immunosuppression, are also unspecific (i.e. off target). This is possibly due to unspecific processes such as FcR interactions or pinocytosis. The above-mentioned toxic effects are likely to occur in humans as no safety margins exist. However, this is acceptable in view of the indication. The findings are adequately mentioned in the Nonclinical Specifications in the RMP.
The ADC tested positive for genotoxicity in an *in vitro* micronucleus screening assay with human lymphocytes. This is consistent with the pharmacological effect of cys-mcMMAF-mediated disruption of microtubules causing possible aneuploidy, which was substantiated with additional data.
Additionally, the applicant investigated the genotoxic potential of cys-mcMMAF in an Ames test, a mouse lymphoma and an *in vivo* rat bone marrow micronucleus assay. These investigations were all negative.
Following the guidelines, the applicant did not perform carcinogenicity studies.

No dedicated reproductive and developmental toxicity studies were performed. However, as the mechanism of action is to induce cytotoxicity in rapidly dividing cells, the drug is likely to affect a developing embryo. There is also a risk of heritable changes via genotoxicity in female germ cells. Effects on male and female reproductive organs occurred in animals at ~4 times exposure at the maximum recommended human dose. Based on the findings in animals and the mode of action, belantamab mafodotin may impair fertility in females and males of reproductive potential. As human IgG is known to cross the placenta, the drug should not be used during pregnancy unless the clinical condition of the woman requires treatment with belantamab mafodotin. IgG is present in human milk in small amounts. It is not known whether the drug is excreted into human milk. As belantamab mafodotin is a humanised IgG mAB, and based on the cytotoxic mechanism of action, it may cause serious adverse reactions in breast-fed children. Women are advised to discontinue breast-feeding prior to initiating treatment with belantamab mafodotin and for 3 months after the last dose. Women of childbearing potential should use effective contraception during treatment with belantamab mafodotin

and for 4 months after the last dose. Men with female partners of childbearing potential should use effective contraception during treatment with belantamab mafodotin and for 6 months after the last dose.

This application is only intended for treatment of adults. Furthermore, belantamab mafodotin was granted a full paediatric waiver, on the grounds that multiple myeloma occurs only in adult populations. All relevant nonclinical safety findings are adequately described in the nonclinical part of the safety specification of the RMP. Based on the ERA, a risk for the environment is considered unlikely.

5.4 Nonclinical conclusions

Overall, the submitted nonclinical documentation is considered appropriate to support the approval of belantamab mafodotin in the proposed indication. The pharmaco-toxicological profile has been sufficiently characterised. All nonclinical data that are relevant for safety are adequately mentioned in the Information for healthcare professionals. From the nonclinical standpoint, there is no objection against approval.

6 Clinical aspects

6.1 Clinical pharmacology

Absorption
Maximum concentration for belantamab mafodotin ADC occurred at, or shortly after, the end of infusion, while cys-mcMMAF concentrations peaked roughly 24 hours after infusion.
The following tables describe the pharmacokinetics of belantamab mafodotin for 2.5 mg/kg doses on Day 1 of Cycle 1 at the end of the first three- and four-week intervals.

Belantamab mafodotin pharmacokinetics at the end of the first three-week interval[a]

	AUC[b]	C_{avg21}	C_{max}	C_{tau}
ADC (%)	3950 µg•h/mL (30.6)	7.83 µg/mL (30.6)	43.7 µg/mL (22.1)	2.03 µg/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 the 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.

Belantamab mafodotin pharmacokinetics at the end of the first four-week interval[a]

	AUC[b]	C_{avg28}	C_{max}	C_{tau}
ADC (%)	4504 µg•h/mL (25)	6.70 µg/mL (25)	47.1 µg/mL (18.9)	1.57 µg/mL (53)
cys-mcMMAF (%)	90.5 ng•h/mL (40.9)	0.182 ng/mL (42.7)	0.933 ng/mL (41.7)	–

ADC = antibody drug conjugate; AUC = area under the curve; C_{avg28} = belantamab mafodotin average concentration over 28 days; C_{max} = maximum plasma concentration; C_{tau} = concentration at the end of the dosing interval.

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

[b] AUC for ADC is $AUC_{(0\text{-}28days)}$, and $AUC_{(0\text{-}7days)}$ for cys-mcMMAF.

Accumulation of belantamab mafodotin (ADC) was minimal to moderate as observed in clinical studies with a three-weekly 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%).

Metabolism
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.

Elimination
Based on the population PK analysis, the geometric mean (geometric CV%) belantamab mafodotin (ADC) initial systemic 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 cys-mcMMAF excreted in urine was not substantial (approximately 18% of the dose) after the Cycle 1 dose, with no evidence of other MMAF-related metabolites.

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

Special populations / Intrinsic factors
Age, race, gender and body weight did not have a clinically relevant impact on the PK of belantamab mafodotin or cys-mcMMAF based on the results of the population PK 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 greater than the upper limit of normal (ULN) to ≤1.5 × ULN and any AST or total bilirubin ≤ ULN with AST >ULN) or moderate hepatic impairment (total bilirubin greater than 1.5 x ULN to ≤3 × ULN and any AST).

Renal impairment: The applicant submitted one study in relapsed/refractory multiple myeloma (RRMM) patients with severe renal impairment compared to matched RRMM patients with normal or mildly impaired renal function. Based on the results of this study (belantamab mafodotin C_{max} and AUC were reduced by 23% and 16%, respectively; cys-mcMMAF C_{max} and AUC were reduced by 56% and 44%, respectively) no dose adjustment for belantamab mafodotin is recommended, which is acceptable. In addition, the popPK analysis renal impairment was not identified as a covariate with impact on the PK of belantamab mafodotin or cys-mcMMAF.

Pivotal PopPK analysis
PK data from 977 patients were included in the popPK analysis. The cys-mcMMAF population PK model was linked to the belantamab mafodotin model. The population PK models characterised the PK of belantamab mafodotin and cys-mcMMAF well. The two models characterised the distribution and elimination of the analytes with linear 2-compartment kinetics; the belantamab mafodotin model had time-varying clearance, and the cys-mcMMAF model had a time-varying drug antibody ratio, consistent with belantamab mafodotin models reported previously. The belantamab mafodotin has an initial systemic CL of 0.926 L/day, a V_{ss} of 10.8 L, and an elimination phase half-life of 13.0 days for a typical participant with RRMM in the analysis population. Following monotherapy treatment, CL is reduced by 33.2% to 0.619 L/day over time, resulting in an elimination half-life of 16.8 days. Following combination treatment, CL is reduced by 44.0% to 0.518 L/day, resulting in an elimination half-life of 19.1 days. The time to 50% change in CL was 66.4 days. The time to reach 95% of steady state with respect to CL was approximately 172 days. Over the entire analysis population, the geometric mean (geometric percent CV [CV%]) ADC initial systemic CL was 0.901 L/day (40.0%), V_{ss} was 10.8 L (22.2%), and the elimination half-life was 13.2 days (25.5%). Following treatment, steady-state CL was 0.605 L/day (43.2%) or approximately 32.9% lower than initial systemic CL with an elimination half-life of 17.0 days (31.2%).

Interactions
No formal studies have been carried out on interactions with belantamab mafodotin.
Based on available *in vitro* and clinical data, the risk of pharmacokinetic and pharmacodynamic drug interactions is low for belantamab mafodotin.

The results of in vitro studies showed 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 and bile salt export pump (BSEP) and a possible substrate of P-glycoprotein (P-gp).

Effect of other medicinal products on belantamab mafodotin
A population pharmacokinetic analysis was used to assess the effect of combination therapy on belantamab mafodotin (ADC) and cys-mcMMAF pharmacokinetics (PK). Combination therapies with bortezomib, lenalidomide, pomalidomide and/or dexamethasone did not affect the PK of ADC and cys-mcMMAF.

Effect of belantamab mafodotin on other medicinal products
For combination therapies with lenalidomide, bortezomib and pomalidomide, PK profiles were evaluated in clinical trials and compared with historical data. The observed PK for lenalidomide, bortezomib and pomalidomide suggested a lack of impact of belantamab mafodotin on the PK of the included combination therapies.

Mechanism of action
Belantamab mafodotin is a humanised IgG1 kappa monoclonal antibody conjugated with the 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 (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 cancer 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.

Relationship Between Probabilities of Response and Ocular Safety Endpoints and Cycle 1 ADC C_{avg}
A model-predicted benefit/risk assessment of a 1.9 mg/kg vs. 2.5 mg/kg initial doses of belantamab mafodotin was performed. Decreasing the initial dose of belantamab mafodotin from 2.5 mg/kg to 1.9 mg/kg results in a decreased absolute probability of response for very good partial remission (VGPR+) and complete response (CR+), respectively, while simultaneously resulting in no decreased probability of Grade ≥3 ocular adverse events of special interest, probability of best corrected visual acuity (BCVA) bilateral worsening to 20/50 or worse, or probability of Grade ≥3 corneal events, as exposure-response curves for those ocular safety endpoints are relatively flat.

Thus, the model predictions suggest that a 2.5 mg/kg initial dose of belantamab mafodotin has relatively higher benefit, especially for deeper response (e.g. CR+), with no additional risk compared to an initial dose of 1.9 mg/kg.

6.2 Efficacy

The applicant submitted one pivotal phase 3, randomised (1:1), open label study (DREAMM-8) to support the proposed indication.
DREAMM-8 was a study evaluating the efficacy and safety of the combination of belantamab mafodotin and pomalidomide/dexamethasone (BPd) compared with the combination of pomalidomide and bortezomib/dexamethasone (PVd) in adult patients with a confirmed diagnosis of MM as defined by the International Myeloma Working Group (IMWG) criteria. Patients enrolled were supposed to have received previous treatment with at least 1 prior line of MM therapy including a lenalidomide-containing regimen. For details regarding included patient population, please refer to the attached Information for healthcare professionals.

Patients in the BPd arm received belantamab mafodotin 2.5 mg/kg at the initial dose in Cycle 1 followed by 1.9 mg/kg in Cycle 2 and beyond every 4 weeks. Dose selection of belantamab in combination with pomalidomide/dexamethasone (BPd) was based on data from the Phase 1/2 ALGONQUIN study [1] and can be accepted even though the data provided do not allow any conclusion regarding an optimal dose. The choice of the combination partners (pomalidomide and dexamethasone) in the BPd arm is also acceptable. For details regarding dosing, please refer to the attached Information for healthcare professionals.

The primary endpoint of the study was progression-free survival (PFS), and the key secondary efficacy endpoints were overall survival (OS), duration of response (DOR), and minimal residual disease (MRD) negativity rate. Endpoints were tested within a hierarchical testing procedure with fixed sequence for PFS, OS and MRD negativity rate.

Overall, 302 patients were enrolled in the study,155 patients were randomised in the BPd arm and 147 patients were randomised in the PVd arm. Baseline characteristics were overall balanced. The median age was 67 years, 64% of patients were male, and 86% were White. In total, 53% of patients had one prior line of therapy and 47% of patients two or more prior lines of therapy. Please refer to the attached Information for healthcare professionals for details regarding demographics and baseline characteristics.

The results of the second interim analysis were presented as per a data cut-off date of 19 February 2024.
A total of 142 events of progression or death were reported, 60 events (40%) in the BPd group and 80 events (54%) in the PVd group. The treatment with BPd resulted in a statistically significant improvement in PFS assessed by independent review committee with a hazard ratio (HR) of 0.52 (95% CI: 0.37, 0.73; p-value <0.001).

OS was not mature at the second interim analysis, with a total of 105 death events in the intent-to-treat (ITT) population (49 events [32%] in the BPd arm and 56 events [38%] in the PVd arm). OS analysis was not statistically significant; median OS was not reached in any of the treatment groups and HR was 0.77 (95% CI:0.53, 1.14). The OS p-value (0.095) did not cross the pre-defined OS boundary adjusting for the observed number of events at the time of analysis. The follow-up for OS is ongoing and will continue until the next planned interim analysis of OS.
Considering that OS was not statistically significant, MRD negativity was not formally tested.

6.3 Safety

The pooled safety analysis included data from 516 patients treated with a triplet combination including belantamab mafodotin, pomalidomide, bortezomib, and dexamethasone.

Treatment-emergent adverse events (TEAEs) occurred in 99% of patients. The most common TEAEs (>20%) were decreased visual acuity, corneal examination findings, thrombocytopenia, blurred vision, neutropenia, dry eyes, foreign body sensation in the eyes, eye irritation, photosensitivity, eye pain, diarrhoea, fatigue, upper respiratory tract infection, pneumonia, and anaemia.

Grade 3 and 4 TEAEs were observed in 93% of patients. Serious adverse events (SAEs) were observed in 53% of patients. The most common SAEs reported in more than 2% of patients were pneumonia, neutropenia, fever, febrile neutropenia, thrombocytopenia, and anaemia.

[1] Trudel S, McCurdy A, Louzada ML, Parkin S, White D, Chu MP, Kotb R, Mian H, Othman I, Su J, Khan A, Gul E, Reece D. Belantamab mafodotin, pomalidomide and dexamethasone in refractory multiple myeloma: a phase 1/2 trial. Nat Med. 2024 Feb;30(2):543-551. doi: 10.1038/s41591-023-02703-y

TEAEs leading to study drug interruption or delay was reported in 93% of patients, and TEAEs leading to drug discontinuation were reported in 23% of patients.

In total, grade 5 TEAEs were reported in 8% of the patients. The most frequent events leading to death were pneumonia (10 patients), and COVID-19 pneumonia (7 patients).

Ocular adverse events are identified as adverse events of special interest for the drug. In the pooled safety analysis set, ocular adverse events were observed in 83% of patients. The most common ocular adverse reactions were decreased visual acuity (90%; 59% Grades 3 and 4) and corneal examination findings (89%; 71% Grades 3 and 4) based on ophthalmological examination results, blurred vision (62%; 17% Grades 3 and 4), dry eyes (44%; 6% Grades 3 and 4), foreign body sensation (40%; 3% Grades 3 and 4), photosensitivity (37%; 2% Grades 3 and 4), eye irritation (35%; 4% Grades 3 and 4), and eye pain (27%; <1% Grades 3 and 4). The median time to onset of the first event was 30 days (range:1-666 days). Grade 3 and 4 events occurred in 42% (217/516) of patients, with blurred vision being the most common (17%). Ocular adverse events resulted in dose delay in 79% of patients. Considering the importance of this event, including grade 3-4 adverse events, a boxed warning was added to the Information for healthcare professionals. An ophthalmological examination must be carried out before each cycle (for details please refer to the attached Information for healthcare professionals).

6.4 Final clinical benefit risk assessment

Multiple myeloma is an incurable disease with a high unmet medical need for second-line treatment in multiple myeloma patients, especially for those who are pre-treated with lenalidomide and anti-CD38 antibody.

This study met its predefined primary endpoint and showed a statistically significant improvement in terms of PFS. Overall survival data are still immature; however, early separation of the OS Kaplan-Meier curves in favour of BPd treatment has been observed, with no early detriment. Follow-up for OS data is ongoing and expected to be available by July 2025.

The toxicity of the triplet combinations is manageable, and relevant risks are described in the Information for healthcare professionals, including monitoring and dose modifications. Of concern was the high rate of ocular toxicity occurring in patients treated with the experimental drug. Considering the importance of this toxicity, a boxed warning has been implemented (see attached Information for healthcare professionals).

In summary, in the light of the high unmet medical need, the overall benefit risk is positive. Updated OS analyses were requested as a condition.

7 Risk management plan summary

The RMP summaries contain information on the medicinal products′ safety profiles and explain the measures that are taken to further investigate and monitor the risks, as well as to prevent or minimise them.
The RMP summaries are published separately on the Swissmedic website. It is the responsibility of the marketing authorisation holder to ensure that the content of the published RMP summaries is accurate and correct. As the RMPs are international documents, their summaries might differ from the content in the Information for healthcare professionals / product information approved and published in Switzerland, e.g. by mentioning risks that occur in populations or indications not included in the Swiss authorisations.

8 Appendix

Approved Information for healthcare professionals

Please be aware that the following version of the Information for healthcare professionals for Blenrep was approved with the submission described in the SwissPAR. This Information for healthcare professionals may have been updated since the SwissPAR was published.

Please note that the valid and relevant reference document for the effective and safe use of medicinal products in Switzerland is the Information for healthcare professionals currently authorised by Swissmedic (see www.swissmedicinfo.ch).

Note:
The following Information for healthcare professionals has been translated by the MAH. It is the responsibility of the authorisation holder to ensure the translation is correct. The only binding and legally valid text is the Information for healthcare professionals approved in one of the official Swiss languages.

▼ 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 new or serious adverse reactions. See the "Undesirable effects" section for advice on the reporting of adverse reactions.

BLENREP

IMPORTANT WARNING: OCULAR UNDESIRABLE EFFECTS

Most patients experienced corneal changes while taking Blenrep, some with serious consequences, such as significantly reduced vision or corneal ulcers, and symptoms such as blurred vision or dry eyes (see “Warnings and precautions”, “Effects on ability to drive and use machines” and “Undesirable effects”).

An ophthalmological examination must be carried out before each cycle.

Depending on the severity of the findings, a dose adjustment (delay and/or reduction) or discontinuation of treatment is necessary (see “Dosage/Administration”).

Additional educational materials for prescribers, ophthalmologists and patients regarding the risk of ocular undesirable effects are available for Blenrep.

Composition

Active substances

Belantamab mafodotin (genetically engineered using CHO [Chinese Hamster Ovary] cells).

Excipients

Sodium citrate dihydrate, citric acid, trehalose dihydrate, edetate disodium (EDTA), polysorbate 80 (0.2 mg/mL reconstituted solution).

70 mg: total sodium content: 2.2 mg per vial.

100 mg: total sodium content: 3.15 mg per vial.

Pharmaceutical form and active substance quantity per unit

Powder for a concentrate for making a solution for infusion.

Each vial contains 70 mg or 100 mg belantamab mafodotin (lyophilised white to yellow powder).

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

Indications/Uses

Blenrep is indicated for the treatment of relapsed or refractory multiple myeloma in adults in combination with pomalidomide and dexamethasone in patients who have received at least one prior line of therapy, including lenalidomide, and who demonstrated disease progression during the last therapy (see “Clinical efficacy”).

Dosage/Administration

Treatment with Blenrep should be initiated and supervised by physicians experienced in the treatment of multiple myeloma.

Mode of administration

Blenrep is a cytotoxic anticancer medicinal product. Proper handling procedures should be followed. Instructions on reconstitution and further dilution are provided in the “*Dosage/Administration*” and “*Instructions for handling*” sections.

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

To ensure the traceability of biotechnologically produced medicinal products, it is recommended that the trade name and batch number be documented for each treatment.

Recommended supportive care

An ophthalmological examination must be carried out before each cycle (see "Warnings and precautions" and "Boxed warning").

Physicians should encourage patients to inform them of any ocular symptoms. Additionally, they should advise patients to administer preservative-free artificial tears at least four times a day, beginning on the first day of infusion and continuing until completion of treatment, as this may reduce ocular symptoms (see “Warnings and precautions”).

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

Usual dosage

The recommended starting dosage of Blenrep in combination with other therapies is presented in Table 1.

Table 1. Recommended starting dosage in combination with other therapies

Combination regimen	Recommended starting dosage[a]
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] For dosage instructions of medicinal products administered together with Blenrep, see "Clinical efficacy" and their respective prescribing information.

Treatment with Blenrep should be continued until disease progression or unacceptable toxicity.

Dose adjustment following undesirable effects

The dosage of Blenrep should be adjusted for each patient.
Recommended dose adjustments are provided in Tables 2 and 3 (dose adjustment following undesirable effects).
Ocular events were graded based on ophthalmic examination findings that include the combination of corneal examination findings and best corrected visual acuity (BCVA).
The treating physician should review the patient's ophthalmic examination findings before administration and determine the dose of Blenrep based on the highest degree of severity of findings for the more severely affected eye, as both eyes may not be affected to the same degree (Table 3).
During the ophthalmic examination, the ophthalmologist should assess the following:

- The corneal examination finding(s) and the decline in BCVA.
- If there is a decline in BCVA, the relationship with Blenrep should be determined.
- The category grading for these examination findings and BCVA should be communicated to the treating physician.

The corneal examination findings may or may not be accompanied by changes in BCVA. Note: one eye may be more severely affected than the other. 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.
The Blenrep dose must not be re-escalated after a dose reduction is made following ocular undesirable effects.

Table 2. Dose reduction schedule for Blenrep

	Combination with pomalidomide and dexamethasone[a] (cycle length = 4 weeks)
Recommended starting dose	Cycle 1: 2.5 mg/kg administered once. Cycle 2 onwards: 1.9 mg/kg administered every 4 weeks
Reduced dose level 1	1.9 mg/kg every 8 weeks

Reduced dose level 2	1.4 mg/kg every 8 weeks

[a] Extended dosing intervals were observed during the clinical studies (see “Undesirable effects”).

Table 3. Dose adjustments following undesirable effects

Undesirable effect	Severity[a]	Recommended dose adjustments
Ocular undesirable effects (see “Warnings and precautions”)[b]	***Mild (Grade 1)*** *Corneal examination finding(s)* Mild superficial punctate keratopathy with worsening from baseline, without or without symptoms. *Change in BCVA* Decline from baseline of 1 line on Snellen-equivalent visual acuity.	Continue treatment at current dose.
	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).	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.[c]
	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*	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.[c]

Undesirable effect	Severity[a]	Recommended dose adjustments
	Decline from baseline of 3 or more lines (and Snellen-equivalent visual acuity not worse than 20/200).	
	Corneal epithelial defect or change in BCVA of 20/200 or worse (Grade 4) *Corneal examination finding(s)* Corneal epithelial defect[d] *Change in BCVA* Decline to Snellen-equivalent visual acuity of worse than 20/200.	Withhold treatment until improvement in both corneal examination findings and BCVA to mild severity (Grade 1) or better. Resume treatment at reduced dose level 2 as per Table 2, if applicable. For worsening symptoms that are unresponsive to appropriate management, permanent discontinuation should be considered.
Thrombocytopenia (see "Warnings and precautions")	***Grade 3***	No bleeding: For patients on 2.5 mg/kg, reduce Blenrep dose to 1.9 mg/kg. For patients on 1.9 mg/kg or lower, continue treatment at same dose.[e] With bleeding: Withhold Blenrep until improvement to Grade 2 or better. For patients previously on 2.5 mg/kg, resume treatment with Blenrep at 1.9 mg/kg. For patients on 1.9 mg/kg or lower, resume treatment at same dose. Consider additional supportive treatment (e.g., transfusion) as clinically indicated and per local practice.
	Grade 4	Discontinue treatment and consider restarting if recovered to

Undesirable effect	Severity[a]	Recommended dose adjustments
		Grade 3 or better, and only if there is no active bleeding at time of restarting treatment. For patients previously on 2.5 mg/kg, resume treatment with Blenrep at 1.9 mg/kg. For patients on 1.9 mg/kg or lower, resume treatment at same dose. If thrombocytopenia is considered disease-related, is not accompanied by bleeding and recovers with transfusion to >25 $x10^9$/L, continuation of treatment at the current dose may be considered.
Infusion-related reactions (see "Warnings and precautions")	***Grade 2***	Interrupt infusion and initiate supportive treatment. Once symptoms resolve to Grade 1 or better, resume infusion at an infusion rate that is decreased by at least 50%.
	Grade 3	Interrupt infusion and initiate supportive treatment. Once symptoms resolve to Grade 1 or better, resume infusion with premedication and at a lower infusion rate extended to 2 to 4 hours. Any future infusion requires premedication.
	Grade 4	Permanently discontinue Blenrep. • In the event of an anaphylactic or life-threatening infusion reaction, permanently discontinue the infusion

Undesirable effect	Severity[a]	Recommended dose adjustments
		and institute appropriate emergency care.
Other undesirable effects (see "Undesirable effects")	***Grade 3***	Discontinue treatment with Blenrep until improvement to Grade 1 or better. For patients previously on 2.5 mg/kg, resume treatment with Blenrep at 1.9 mg/kg. For patients on 1.9 mg/kg or lower, resume treatment 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 treatment with Blenrep at 1.9 mg/kg. For patients on 1.9 mg/kg or lower, resume treatment at same dose.

BCVA = best corrected visual acuity.

[a] Non-ocular undesirable effects were graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE).

[b] Ocular undesirable effect severity is defined by the most severely affected eye, as both eyes may not be affected to the same degree.

[c] If toxicity is identified prior to administration of belantamab mafodotin with pomalidomide and dexamethasone in Cycle 2, treatment with 1.9 mg/kg should be given every 4 weeks.

[d] A corneal defect may lead to corneal ulcers. These should be managed promptly and as clinically indicated by an ophthalmologist.

[e] For belantamab mafodotin with bortezomib and dexamethasone, consideration can be given to reverting to the previous dose, if appropriate, once thrombocytopenia recovers to Grade 2 or better.

Special dosage instructions

Patients with hepatic disorders

No dose adjustment is required in patients with mild hepatic impairment (total bilirubin greater than ULN to ≤1.5 × ULN and any aspartate transaminase [AST] or total bilirubin ≤ULN with AST >ULN). There are limited data on patients with moderate hepatic impairment, and therefore, dosing of belantamab mafodotin in these patients should be carefully considered (see “Pharmacokinetics” – Kinetics in specific patient groups). There are no data in patients with severe hepatic impairment to support a dose recommendation.

Patients with renal disorders

No dose adjustment is required in patients with mild, moderate or severe renal impairment or kidney failure (eGFR <30 mL/min) (see “Pharmacokinetics” – Kinetics in specific patient groups).

Elderly patients
No dose adjustment is required in patients over 65 years of age (see “Pharmacokinetics” – Kinetics in specific patient groups).

Children and adolescents
Belantamab mafodotin is not approved for use in the paediatric population.

Contraindications

Hypersensitivity to the active substance or one of the excipients.

Warnings and precautions

Ocular undesirable effects
Ocular undesirable effects (e.g., blurred vision, dry eye, eye irritation and photophobia) have been reported in association with treatment with Blenrep.
The most commonly reported corneal examination findings included superficial punctate keratopathy, microcyst-like epithelial changes and haze, with or without changes in visual acuity. Clinically relevant changes in visual acuity may be associated with difficulty in driving or using machines.
An ophthalmological examination must be carried out before each cycle.
Patients should be advised to administer preservative-free artificial tears at least four times a day during treatment (see “Dosage/Administration”). Patients should avoid using contact lenses until the end of treatment.
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

adjustment (delay and/or reduction) or treatment discontinuation based on severity of findings (see “Dosage/Administration”).
Cases of corneal ulcer (ulcerative and infectious keratitis) have been reported (see “Undesirable effects”). These should be managed promptly and as clinically indicated by an ophthalmologist. Treatment with Blenrep should be interrupted until the corneal ulcer has healed (see “Dosage/Administration”).

Thrombocytopenia
Thrombocytopenic events (thrombocytopenia and reduced platelet count) have been reported with Blenrep. Thrombocytopenia may lead to serious bleeding, 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 closer monitoring and, under certain circumstances, longer dosing intervals or smaller doses (see “Dosage/Administration”). Supportive therapy (e.g., platelet transfusions) should be provided according to standard medical practice.

Infusion reactions
Infusion-related reactions (IRR) have been reported with Blenrep. Most IRRs were Grade 1 or 2 and resolved within the same day (see “Undesirable effects”). If a Grade 2 or higher IRR occurs during administration, the infusion rate should be reduced or the infusion terminated depending on the severity of the symptoms. Appropriate medical treatment should be initiated and the infusion restarted at a slower rate if the patient’s condition is stable. If a Grade 2 or Grade 3 IRR occurs, premedication should be administered for all subsequent infusions (see “Dosage/Administration”). For Grade 4 IRRs, Blenrep should be permanently discontinued.

Pneumonitis
Cases of pneumonitis, including fatal events, have been observed in association with the use of Blenrep. Patients with new or worsening unexplained pulmonary symptoms (e.g., cough, dyspnoea) should be evaluated for pneumonitis. In the case of suspected Grade 2 or higher pneumonitis, Blenrep should not be used. If Grade 2 or higher pneumonitis is confirmed, systemic corticosteroid treatment should be started immediately (e.g., ≥1 mg/kg/day prednisolone or equivalent treatment) and continued for at least 14 days, followed by gradual tapering over at least four weeks. Treatment with Blenrep should only be resumed after an evaluation of the benefit and risk. For Grade 3 or 4 pneumonitis, Blenrep should be permanently discontinued.

Excipients
This medicinal product contains less than 1 mmol sodium (23 mg) per vial, i.e., it is virtually sodium-free.

Interactions

No formal studies have been carried out on interactions with belantamab mafodotin.
Based on available in vitro and clinical data, the risk of pharmacokinetic and pharmacodynamic drug interactions is low for belantamab mafodotin.
The results of in vitro studies showed 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 and bile salt export pump (BSEP) and a possible substrate of P-glycoprotein (P-gp).
Effect of other medicinal products on belantamab mafodotin
A population pharmacokinetic analysis was used to assess the effect of combination therapy on belantamab mafodotin ADC and cys-mcMMAF pharmacokinetics (PK). Combination therapies with bortezomib, lenalidomide, pomalidomide and/or dexamethasone did not affect the PK of ADC and cys-mcMMAF.
Effect of belantamab mafodotin on other medicinal products
For combination therapies with lenalidomide, bortezomib and pomalidomide, PK profiles were evaluated in clinical trials and compared with historical data. The observed PK for lenalidomide, bortezomib and pomalidomide suggested lack of impact of belantamab mafodotin on the PK of the included combination therapies.

Pregnancy, lactation

Women of child-bearing age/contraception in men and women
The pregnancy status of women of child-bearing age should be verified prior to initiating treatment with Blenrep. Women of child-bearing age should use an effective contraceptive method during treatment with Blenrep and for four months after the last dose.
Men with female partners of child-bearing age should use an effective contraceptive method during treatment with Blenrep and for six 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), Blenrep can cause embryo-foetal harm when administered to a pregnant woman (see “Preclinical data”). Human immunoglobulin G (IgG) is known to cross the placenta; therefore, Blenrep has the potential to be transmitted from the mother to the developing foetus.
Blenrep should not be used during pregnancy unless treatment with Blenrep is necessary due to the clinical condition of the woman.
If a pregnant woman needs to be treated, she must be clearly advised on the potential risk to the foetus.

Lactation

It is not known whether Blenrep is excreted into human milk. Immunoglobulin G (IgG) is present in human milk in small amounts. Since Blenrep is a humanised IgG monoclonal antibody, and based on its mechanism of action, it may cause serious undesirable effects in breastfed children. Women should be advised to discontinue breastfeeding prior to initiating treatment with Blenrep and for three months after the last dose.

Fertility

Based on findings in animals and the mechanism of action, Blenrep may impair fertility in females and males of reproductive potential (see “Preclinical data”).

Effects on ability to drive and use machines

When taking Blenrep, most patients experienced corneal changes, sometimes with serious consequences, such as significantly reduced vision or corneal ulcers and symptoms such as blurred vision and dry eyes (see “Warnings and precautions”, “Undesirable effects” and “Boxed Warning”). Blenrep has a major influence on the ability to drive or use machines.

Undesirable effects

Clinical trial data

The safety of belantamab mafodotin was evaluated in 516 patients with multiple myeloma who received belantamab mafodotin in combination therapies (DREAMM-6, DREAMM-7, DREAMM-8 studies).

The frequencies were calculated from the pooled results of these clinical trials. Where the frequency varied between studies, the highest frequency category was reported in this section. The listed frequencies of undesirable effects may not be exclusively attributable to the medicinal product but may also be influenced by the underlying disease or other medicinal products used in combination with Blenrep.

The most common adverse reactions were reduced visual acuity (91%), corneal examination findings (89%), thrombocytopenia (87%), blurred vision (79%), neutropenia (63%), dry eyes (61%), foreign body sensation in eyes (61%), eye irritation (50%), photophobia (47%), eye pain (33%), diarrhoea (32%), fatigue (27%), upper respiratory tract infection (27%), pneumonia (24%), anaemia (23%), increased alanine aminotransferase (19%), pyrexia (19%), nausea (17%), increased aspartate aminotransferase (15%), increased gamma glutamyl transferase (15%), deterioration of vision (15%), lymphopenia (12%) and leukopenia (10%).

The most common serious adverse reactions in ≥2% of patients were pneumonia (18%), neutropenia (6%), pyrexia (5%), febrile neutropenia (3%), thrombocytopenia (3%) and anaemia (2%).

Undesirable effects leading to permanent discontinuation of any component of therapy occurred in 31% of patients, of which 9% were due to ocular events, including ocular undesirable effects, changes in visual acuity or corneal examination findings.
Undesirable effects leading to dose delay of any component of therapy occurred in 91% of patients and in 83% of patients with ocular events.
Undesirable effects leading to dose reduction of any component of therapy occurred in 69% of patients and in 59% of patients with ocular events.
Table 4 summarises adverse drug reactions that occurred in patients receiving the recommended dose of belantamab mafodotin for all indications, during clinical trials in patients receiving combination therapy or during post-marketing experience associated with belantamab mafodotin monotherapy. Frequencies are defined as follows: 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) and not known (cannot be estimated from the available data). Within each frequency category, undesirable effects are presented in order of decreasing severity.

Table 4. Undesirable effects reported in multiple myeloma patients treated with belantamab mafodotin

System organ class	Undesirable effects
Infections and infestations	**Very common** Upper respiratory tract infection 27%, pneumonia 24%
Blood and lymphatic system disorders	**Very common** Thrombocytopenia 87%, neutropenia 63%, anaemia 23%, lymphopenia 12%, leukopenia 10%
Eye disorders	**Very common** Visual acuity reduced[a] 91%, corneal examination findings 89% (including keratopathy)[a], blurred vision 79%, dry eyes 61%, foreign body sensation in eyes 61%, photophobia 47%, eye irritation 50%, eye pain 33%, deterioration of vision 15% **Common** Lacrimation increased, diplopia, eye pruritus, ocular discomfort, corneal ulcer[b]
Respiratory, thoracic and mediastinal disorders	**Uncommon** Pneumonitis[c]

System organ class	Undesirable effects
Gastrointestinal disorders	**Very common** Diarrhoea 32%, nausea 17% **Common** Vomiting
Renal and urinary disorders	**Common** Albuminuria[d]
General disorders and administration site conditions	**Very common** Fatigue 27%, pyrexia 19%
Hepatobiliary disorders	**Very common** Increased alanine aminotransferase 19%, increased aspartate aminotransferase 15%, increased gamma glutamyl transferase 15%
Musculoskeletal and connective tissue disorders	**Common** Increased creatine phosphokinase
Injury, poisoning and procedural complications	**Common** Infusion-related reactions[e]

[a] Based on ophthalmic examination findings.

[b] Includes infectious keratitis and ulcerative keratitis.

[c] Including fatal cases.

[d] Includes albuminuria, albumin present in urine, albumin/creatinine ratio in urine increased and microalbuminuria.

[e] Includes events determined to be related to infusion. Infusion reactions may include pyrexia, chills, diarrhoea, nausea, asthenia, hypertension, lethargy and tachycardia.

Throughout the study, the recommended dose adjustments, which included dose delays and reductions, managed undesirable effects and enabled patients to continue treatment. The mean dose per patient was 2 mg/kg (median 2 mg/kg). Dose delays of Blenrep occurred in 93% of patients. Of those patients, 66% experienced ≥3 dose delays with a median duration of delay of 7.6 weeks (IQR 3.6, 11.7). Time between doses per patient increased within each time interval with a mean of 5.3 weeks (median 4.1 weeks; IQR 4, 5) in the first 6 months, 11.9 weeks (median 11.8 weeks; IQR 5, 16) in the 6 to 12-month period, and 14.2 weeks (median 14.1 weeks; IQR 10, 18) in the greater than 12 month period.

Description of selected undesirable effects

Ocular undesirable effects

Across pooled datasets for belantamab mafodotin in combination therapies (n = 516), ocular adverse events occurred in 83% of patients (n = 430/516). The most common ocular adverse reactions were reduced visual acuity (90%; 59% Grades 3 and 4) and corneal examination findings (89%; 71% Grades 3 and 4) based on the ophthalmic examination results; blurred vision (62%; 17% Grades 3 and 4); dry eyes (44%; 6% Grades 3 and 4); foreign body sensation in eyes (40%; 3% Grades 3 and 4); photophobia (37%; 2% Grades 3 and 4); eye irritation (35%; 4% Grades 3 and 4); and eye pain (27%; <1% Grades 3 and 4). The median time to onset of the first event was 30 days. Grade 3 and 4 events occurred in 42% (217/516) of patients, of which the most common was blurred vision (17%). Ocular adverse events led to dose delay in 79% of patients. One serious ocular adverse event was reported.

Ophthalmic examination findings (corneal examination findings or BCVA changes) occurred in 91% (472/516) of patients. The median time to onset of the first event (Grade 2 or worse) was 43 days. Grade 3 and 4 events occurred in 394 patients. Ophthalmic examination findings (corneal examination findings or BCVA changes) led to dose delay in 383 patients (74%).

Decreased bilateral visual acuity to 20/50 or worse (Snellen) at the same visit occurred in 161 patients who had a baseline of 20/25 or better in at least one eye. The median time to onset of the first event was 85 days.

Infusion-related reactions

In the pooled results of clinical trials involving combination therapies, the incidence of infusion-related reactions (IRR) was 6% (n = 32/516). The majority of IRRs were reported as Grade 1 (2%) and Grade 2 (4%), while Grade 3 IRRs were observed in <1%. One patient discontinued treatment due to IRR.

Thrombocytopenia

In the pooled results of clinical trials involving combination therapies, thrombocytopenic events (thrombocytopenia and reduced platelet count) occurred in 74% of patients (n = 382/516), with 59% reported as Grade 3 or 4. Clinically significant bleeding (Grade 2) occurred in 5% of patients with concomitant low platelet levels (Grades 3 to 4).

Infections

In the pooled results of clinical trials involving combination therapies, pneumonia was reported in 18% (n = 93/516) of patients, with 12% reported as Grade ≥3. Ten patients had a pneumonia event with a fatal outcome.

Reporting suspected adverse reactions after authorisation of the medicinal product is very important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any new or serious suspected adverse reactions online via the ElViS portal (Electronic Vigilance System). You can obtain information about this at www.swissmedic.ch.

Overdose

Signs and symptoms

There has been no experience of overdose of belantamab mafodotin in clinical studies.

Treatment

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

Further management should be as clinically indicated.

Properties/Effects

ATC code

L01FX15

Mechanism of action

Belantamab mafodotin is a humanised IgG1 kappa monoclonal antibody conjugated with the 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 (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 cancer 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.

Pharmacodynamics

Dose-response relationship

For BVd and BPd combination therapies, higher belantamab mafodotin Cycle 1 exposure was associated with higher probability of response (e.g., very good partial response [VGPR+]) and higher incidence of some safety-related undesirable effects (e.g., Grade ≥2 corneal examination findings). For most of the range of belantamab mafodotin Cycle 1 exposure, the probability of VGPR or better was higher than the probability of ocular undesirable effects and BCVA-related endpoints.

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 three weeks.

Immunogenicity

The incidence of anti-belantamab mafodotin antibodies (ADAs) was consistently low in patients treated with belantamab mafodotin in combination therapies, with no observed clinical impact on pharmacokinetics, safety and efficacy.

In the pivotal combination therapy studies (DREAMM-7 and DREAMM-8) and the combination therapy supportive study (DREAMM-6), 3% of patients (15/515) tested positive for treatment-emergent ADAs. Two patients tested positive for neutralising anti-belantamab mafodotin antibodies (NAb).

Clinical efficacy

DREAMM-8: Combination with pomalidomide and dexamethasone

DREAMM-8 was an open-label, Phase III, multicentre study which evaluated belantamab mafodotin in combination with pomalidomide and dexamethasone (BPd) compared with pomalidomide, bortezomib and dexamethasone (PVd) in patients with relapsed or refractory multiple myeloma.

Eligible patients had a confirmed diagnosis of multiple myeloma (MM) as defined by IMWG criteria, had previously been treated with at least 1 prior line of MM therapy, including lenalidomide, and must have had documented disease progression during or after their most recent therapy.

According to the protocol, no more than 50% of the included patients were allowed to have ≥2 prior lines of therapy. Included patients must have been deemed ineligible for prior ASCT, or ASCT had to be carried out more than 100 days prior to the first dose of Blenrep, to be considered eligible. Patients previously treated with or who had intolerance to pomalidomide were excluded. Furthermore, patients who were intolerant to or refractory to bortezomib, as well as patients with prior treatment with BCMA-targeted therapy, were excluded.

Patients were randomised in a 1:1 ratio to receive either BPd or PVd, stratified by the number of prior lines of treatment, prior exposure to bortezomib, prior anti-CD38 treatment and International Staging

System (ISS) status. In the BPd arm (n = 155), patients received belantamab mafodotin 2.5 mg/kg (IV) once on Day 1 in Cycle 1 (28-day cycle) followed by belantamab mafodotin 1.9 mg/kg (IV) every four weeks on Day 1 in 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 PVd arm (n = 147), patients received pomalidomide 4 mg (PO) every three 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 administration of bortezomib. The dose 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, end of study or death.

A total of 302 patients with MM were evaluated for efficacy in the DREAMM-8 study. Baseline demographics and characteristics were similar across both arms. Baseline characteristics for the BPd arm (n = 155) were: median age: 67 years (46% aged 65 to 74 years and 12% aged 75 years or older); 64% male, 36% female; 86% white, 13% Asian, <1% Native Hawaiian or other Pacific Islander, <1% mixed race; ISS stage at screening: I (60%), II (25%), III (14%); 34% high cytogenetic risk; 53% of patients received one prior line of therapy and 47% of patients received two or more lines of prior treatment (median number of 1 prior line of therapy); 86% of patients relapsed more than 12 months after initiation of first-line treatment; 13% with EMD present; and of those who received treatment (n = 150), ECOG PS 0 (53%), 1 (45%) 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 had previously received ASCT. 82% of patients were refractory to immunomodulator therapy, 26% to proteasome inhibitor therapy and 23% to anti-CD38 therapy.

The primary endpoint was progression-free survival (PFS), as evaluated by a blinded independent review committee (IRC) based on the International Myeloma Working Group (IMWG) criteria for multiple myeloma.

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 5.

Table 5. Efficacy results of belantamab mafodotin in DREAMM-8

	Belantamab mafodotin plus pomalidomide and dexamethasone (BPd)[a] N = 155	**Pomalidomide plus bortezomib and dexamethasone (PVd)[a] N = 147**
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	
Probability of PFS at 12 months (95% CI)[h]	71% (63; 78)	51% (42; 60)
Overall survival (OS)		
Median in months (95% CI)[c]	NR (33, NR)	NR (25.2, NR)
Hazard ratio (95% CI)[f]	0.77 (0.53; 1.14)	

CI = confidence interval; NR = not reached.

[a] Efficacy data are based on the intent-to-treat (ITT) population, except DOR, which is based on responders only.

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

[c] According to the Brookmeyer-Crowley method.

[d] Median follow-up of 21.8 months.

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

[f] Based on stratified Cox regression model.

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

[h] According to the Kaplan-Meier method.

Pharmacokinetics

Absorption

Maximum concentration for belantamab mafodotin ADC occurred at or shortly after the end of infusion, while cys-mcMMAF concentrations peaked roughly 24 hours after infusion.
Tables 6 and 7 describe the pharmacokinetics of belantamab mafodotin for 2.5 mg/kg doses on Day 1 of Cycle 1 at the end of the first three- and four-week intervals.

Table 6. Belantamab mafodotin pharmacokinetics at the end of the first three-week interval[a]

	AUC[b]	C_{avg21}	C_{max}	C_{tau}
ADC (%)	3950 µg•h/mL (30.6)	7.83 µg/mL (30.6)	43.7 µg/mL (22.1)	2.03 µg/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 the 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.

Table 7. Belantamab mafodotin pharmacokinetics at the end of the first four-week interval[a]

	AUC[b]	C_{avg28}	C_{max}	C_{tau}
ADC (%)	4504 µg•h/mL (25)	6.70 µg/mL (25)	47.1 µg/mL (18.9)	1.57 µg/mL (53)
cys-mcMMAF (%)	90.5 ng•h/mL (40.9)	0.182 ng/mL (42.7)	0.933 ng/mL (41.7)	–

ADC = antibody drug conjugate; AUC = area under the curve; C_{avg28} = belantamab mafodotin average concentration over 28 days; C_{max} = maximum plasma concentration; C_{tau} = concentration at the end of the dosing interval.

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

[b] AUC for ADC is $AUC_{(0\text{-}28days)}$, and $AUC_{(0\text{-}7days)}$ for cys-mcMMAF.

Accumulation of belantamab mafodotin (ADC) was minimal to moderate as observed in clinical studies with a three-weekly 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%).

Metabolism

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.

Elimination

Based on the population PK analysis, the geometric mean (geometric CV%) belantamab mafodotin (ADC) initial systemic 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 cys-mcMMAF excreted in urine was not substantial (approximately 18% of the dose) after the 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.

Kinetics in specific patient groups

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 greater than ULN to ≤1.5 × ULN and any AST or total bilirubin ≤ ULN with AST >ULN) or moderate hepatic impairment (total bilirubin greater than 1.5 x ULN to ≤3 × ULN and any AST).

Renal impairment
In patients with severe renal impairment (eGFR: 15 to 29 mL/min), belantamab mafodotin C_{max} decreased by 23% and $AUC_{(0\text{-}tau)}$ decreased by 16% compared with patients with normal or mild renal impairment (eGFR ≥60 mL/min). For cys-mcMMAF, C_{max} and $AUC_{(0\text{-}168h)}$ decreased by 56% and 44% respectively compared to patients with normal or mild renal impairment. Renal function (eGFR: 12 to 150 mL/min) was not a significant covariate in population pharmacokinetic analyses that included patients with normal or mild, moderate, or severe renal impairment or kidney failure.
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 endpoints based on a dose-response analysis.

Elderly patients

Age was not a significant covariate in population pharmacokinetic analyses that included patients aged 32 to 89 years.

Children and adolescents

No pharmacokinetic data are available on children and adolescents.

Body weight

Body weight (37 to 170 kg) was a significant covariate in population pharmacokinetic analyses, but this effect was not clinically relevant with the weight-proportional dosing regimen.

Preclinical data

Repeated dose toxicity

In animal studies on rats and monkeys, the key undesirable effects (directly related to belantamab mafodotin) at exposures of ≥1.1 times the clinical dose of 2.5 mg/kg were the following: elevated liver enzymes, sometimes associated with hepatocellular necrosis (at ≥10 mg/kg in rats and ≥3 mg/kg in monkeys), and increases in alveolar macrophages associated with eosinophilic deposits in the lungs at ≥3 mg/kg (rats 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 rats and rabbits. 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.

Carcinogenicity/mutagenicity

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 toxicity

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 also has rapidly dividing cells. There is also a potential risk of hereditary 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 four times the exposure of the clinical dose. Luteinised anovulatory follicles were seen in the ovaries of rats after three weekly doses. Findings in male reproductive organs of rats that were adverse and progressed following repeated dosing included marked

degeneration/atrophy of seminiferous tubules that generally did not reverse following dosing cessation.

Other information

Incompatibilities
In the absence of compatibility studies, the reconstituted concentrate and diluted solution for infusion must not be mixed with other medicinal products.

Shelf life

The medicinal product must not be used after the date marked "EXP" on the packaging.

Shelf life after opening

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

Diluted solution
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 six hours (including infusion time).

Special precautions for storage instructions

Store in a refrigerator (2-8°C). Do not freeze.
Store in the original packaging.
Keep out of the reach of children.

Instructions for handling

Blenrep is a cytotoxic anticancer medicinal product. Proper handling procedures should be followed.
Use aseptic technique for the reconstitution and dilution of the reconstituted solution.
Calculate the necessary 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 injection to obtain a solution with a concentration of 50 mg/mL.

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

3. Visually inspect the reconstituted solution for particulate matter and discolouration. The reconstituted solution should be a clear to opalescent and colourless to yellow to brown liquid. Discard the vial containing 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 0.9% (9 mg/mL) sodium chloride solution for injection. Mix the diluted solution by gentle inversion. The final concentration of the diluted solution should be between 0.2 mg/mL and 2 mg/mL. DO NOT SHAKE.
3. Discard any unused reconstituted solution of Blenrep left in the vial.

Instructions for use

1. Administer the diluted solution by intravenous infusion over approximately 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, a polyethersulfone (PES)-based filter is recommended.

Disposal

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

Authorisation number

69910

Packs

Blenrep vials 70 mg: 1 [A]
Blenrep vials 100 mg: 1 [A]

Marketing authorisation holder

GlaxoSmithKline AG, 6340 Baar

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March 2025