Date: 26 August 2022
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): 100 mg

Route(s) of administration: intravenous

Marketing Authorisation Holder: GlaxoSmithKline AG

Marketing Authorisation No.: 67741

Decision and Decision date: temporary authorisation in accordance with Art. 9a TPA approved on 20.06.2022

Note:

Assessment Report as adopted by Swissmedic with all information of a commercially confidential nature deleted.

The SwissPAR is a “final” document, which provides information relating to a submission at a particular point in time and will not be updated after publication.

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1 Terms, Definitions, Abbreviations

ADC	Antibody-drug-conjugate
ADCC	Antibody-dependent cellular cytotoxicity
ADCP	Antibody-dependent cellular phagocytosis
BCMA	B-cell maturation antigen
CGE	Capillary gel electrophoresis
cIEF	Capillary isoelectric focusing
EMA	European Medicines Agency
ERA	Environmental Risk Assessment
FDA	U.S. Food and Drug Administration
GLP	Good Laboratory Practice
HC	Heavy chain
HCT	Haematopoietic cell transplantation
HIC	Hydrophobic interaction chromatography
SE-HPLC	Size exclusion high performance liquid chromatography
ICH	International Council for Harmonisation
Ig	Immunoglobulin
IMiD	Immunomodulatory agent
LC	Light chain
LoQ	List of Questions
mAb	Monoclonal antibody
MAH	Marketing Authorisation Holder
mcMMAF	Maleimidocaproyl monomethyl auristatin F
MM	Multiple myeloma
MRI	Magnetic resonance imaging
ORR	Objective/overall response rate
OS	Overall survival
PI	Proteasome inhibitor
PK	Pharmacokinetics
RMP	Risk Management Plan
SwissPAR	Swiss Public Assessment Report
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)

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2 Background Information on the Procedure

2.1 Applicant's Request(s)

New Active Substance status
The applicant requested the status of a new active entity for the active substance belantamab mafodotin of the medicinal product mentioned above.

Orphan drug status
The applicant requested Orphan Drug Status in accordance with Article 4 a^{decies} no. 2 of the TPA.
The Orphan Status was granted on 22 March 2021.

Temporary authorisation for human medicinal products
The applicant requested a temporary authorisation in accordance with Art. 9a TPA.

2.2 Indication and Dosage

2.2.1 Requested Indication

Belantamab mafodotin is indicated for the treatment of patients with relapsed/refractory multiple myeloma who have received at least four prior therapies including an anti-CD38 antibody, a proteasome inhibitor, and an immunomodulatory agent.

2.2.2 Approved Indication

Blenrep is indicated as monotherapy for the treatment of multiple myeloma in adult patients who have already received at least four prior therapy lines and whose disease is refractory to at least one proteasome inhibitor, one immunomodulatory agent and an anti-CD38 monoclonal antibody, and who demonstrated disease progression during the most recent therapy.
The efficacy and safety of belantamab mafodotin in patients who have previously undergone BCMA-directed CAR-T cell therapy have not been investigated.

2.2.3 Requested Dosage

Summary of the applied standard dosage:
2.5 mg/kg body weight, administered as an intravenous infusion every three weeks

2.2.4 Approved Dosage

(see appendix)

2.3 Regulatory History (Milestones)

Application	8 March 2021
Formal control completed	6 April 2021
List of Questions (LoQ)	3 August 2021
Answers to LoQ	26 October 2021
Predecision	24 January 2022
Answers to Predecision	2 March 2022
Labelling corrections	5 April 2022
Answers to Labelling corrections	2 May 2022
Final Decision	20 June 2022
Decision	approval (temporary authorisation in accordance with Art. 9a TPA)

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3 Medical Context

Multiple myeloma (MM) is characterised by the neoplastic proliferation of plasma cells producing a monoclonal immunoglobulin. The plasma cells proliferate in the bone marrow, which often results in extensive skeletal destruction with osteolytic lesions, osteopenia, and/or pathological fractures. MM is a rare cancer, accounting for approximately 1 to 2 percent of all cancers. Incidence rate of MM in Switzerland is 9.6 per 100,000.
MM treatment is indicated when at least one CRAB-SLiM criteria is fulfilled. These criteria include the following biomarkers or symptoms: SLiM - Sixty percent (60%) or greater of bone marrow plasma cells; light chain ratio of 100 or greater in serum; or MRI with more than 1 focal lesion.
CRAB - Calcium levels increased in blood; renal (kidney) deficiency, anaemia, or bone damage.

MM is a heterogeneous disease, with some patients progressing rapidly despite treatment and others not requiring therapy for a number of years. Survival rates have improved for patients with multiple myeloma, yet relapse remains common, indicating an ongoing need for new therapeutic approaches. Following diagnosis and risk stratification, all patients are assessed to determine eligibility for autologous haematopoietic cell transplantation (HCT).

Treatment options for patients with relapsed or refractory MM include HCT, a re-challenge of the previous chemotherapy regimen, or a trial of a new regimen. Factors used to determine the choice of therapy include a risk stratification of myeloma, prior treatments used, and the duration of response to these treatments.

After the approval of daratumumab and its wide use in combinations in earlier lines of treatment, a new population of patients has emerged, referred to as triple-class refractory, encompassing those patients with disease refractory to at least one proteasome inhibitor (PI), one immunomodulatory agent (IMiD), and an anti-CD38 monoclonal antibody (mAb). These patients have generally been exposed to all five drugs that have demonstrated single-agent effect (with or without glucocorticoids), including bortezomib, carfilzomib, lenalidomide, pomalidomide, and daratumumab. Most of these patients have already received alkylating agent therapy, other anti-MM drugs, as well as multiple courses of glucocorticoids, they also have numerous comorbidities and receive multiple concomitant medications. There is a clear unmet medical need for new therapies because the treatment options are very limited and their median overall survival is around 5.6-9.2 months.

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4 Quality Aspects

4.1 Drug Substance

Belantamab mafodotin drug substance is an antibody-drug conjugate composed of an antimitotic agent maleimidocaproyl monomethyl auristatin F (mcMMAF) covalently conjugated to a recombinant afucosylated humanised $IgG1_K$ monoclonal antibody (mAb) directed against B-cell maturation antigen. 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. Both HCs contain one oligosaccharide chain in the conserved Fc site (Asn301). The antibody is produced from a mammalian cell line (Chinese Hamster Ovary) using a fed-batch production process in a production bioreactor. The cell culture fluid is harvested and the antibody is purified by several chromatographic and filtration steps, including virus inactivation and virus removal steps. The other drug substance, intermediate mcMMAF, is manufactured by a six-step peptide synthesis process.
The belantamab mafodotin drug substance manufacturing process itself is performed by Sigma-Aldrich Manufacturing LLC, St. Louis, MO, USA, and consists of the reduction of the mAb, followed by the introduction of mcMMAF for conjugation to reduced cysteine residues at the sites of the inter-chain disulfide bonds between LC and HC or between HCs. The target number of drug-linkers conjugated to each antibody molecule (drug-to-antibody ratio = DAR) is four. Impurities are removed by diafiltration and, finally, belantamab mafodotin drug substance is concentrated by ultrafiltration.
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 100 mg belantamab mafodotin intended for intravenous infusion after reconstitution with sterile water for injections and dilution in 0.9% saline. Prior to lyophilisation, the drug product is formulated in an aqueous buffered solution containing sodium citrate/citric acid, trehalose, disodium edetate and polysorbate 80. All excipients comply with the European Pharmacopoeia.
The finished product manufacturing process consists of thawing, pooling and mixing, sterile filtration, filling, lyophilisation/stoppering and inspection steps. Process validation studies were executed 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 fluorinated polymer-coated

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bromobutyl rubber stopper and an aluminium/plastic seal/cap. All components coming into contact with the finished product comply with Ph. Eur. 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 36 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.

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5 Nonclinical Aspects

In line with the indication and the antibody-drug-conjugate (ADC) nature of the drug, the applicant followed the recommendations of the ICH S9, S9 Q&A, S6 and S7A guidelines. Pivotal toxicology studies were performed according to GLP.

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. 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 selected as relevant species.
Belantamab mafodotin also showed affinity to human FcγR I, FcγR IIIa V, FcγR IIIa F, and FcRn, with K_D values of 1.0 µg/mL, 4.3 µg/mL, 35.7 µg/mL, and 7.9 µg/mL at 25°C. These concentrations are within the range of systemic concentrations reached in humans and toxicology species. The applicant did not provide data regarding affinity to Fcγ receptors in the toxicology species.
In vitro studies in different multiple myeloma (MM) cell lines showed that the drug was rapidly internalised upon binding to BCMA. The active cytotoxic part (cys-mcMMAF) was released inside the cell, presumably via endosomal/lysosomal degradation. Minimal active concentrations for binding and internalisation were in the range of 1 µg/mL; *i.e.* lower than C_{trough} (2.43 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, including in primary MM cells with a broad range of BCMA expression. In addition, repetitive exposure increased levels of BCMA expression, potentially increasing the cellular sensitivity. Low bystander cytotoxicity of the drug to cells that express no, or low, levels of BCMA was observed. However, the highest tested concentration was 10 µg/mL, which is lower than exposures reached in patients and toxicology studies. 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. In addition, micropinocytosis enabled unspecific cellular uptake of the drug. These factors support the broad spectrum of findings in toxicity studies. The drug showed *in vitro* activity concerning antibody-dependent cellular cytotoxicity (ADCC) and phagocytosis (ADCP) and enabled 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 dependent on $CD8^+$ T-cells. Furthermore, in cynomolgus monkeys, a single dose of 1 mg/kg belantamab mafodotin resulted in reductions in BCMA-positive plasma cells and IgE levels (50 to 75%), and a modest reduction (<25%) in IgG, IgA, and IgM levels. The delayed increase of pro-inflammatory cytokines observed in some animals in this study suggests some risk of cytokine release.
Safety pharmacology evaluations were incorporated into the repeat-dose toxicity studies in rats and monkeys. The applicant also tested cys-mcMMAF in a hERG assay. Overall, the results of these evaluations did not raise any concerns.

5.2 Pharmacokinetics

Following i.v. administration of belantamab mafodotin, the PK in mice, rats and monkeys was characteristic of that expected for a human monoclonal antibody (mAb), with low clearance and volume of distribution (Vss), and a half-life measured in days. Following single i.v. administration of fluorescently-labelled belantamab mafodotin or belantamab, the fluorescence was associated with connective tissue in the eye and eyelids, muscle in the eyelids, extra-orbital lacrimal and harderian glands, kidneys and liver, but was not observed in the cornea or glands in the eyelids. The signal was higher 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

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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 three days.
The half-life of belantamab mafodotin was longer in rodents (rats ~11 days, mice ~13 days) compared to monkeys (~4 days). The plasma concentrations (ADC and total mAb) were similar within nonclinical species, suggesting stability of the drug conjugate in circulation.

5.3 Toxicology

Toxicity following i.v. administration with belantamab mafodotin was evaluated for up to 13 weeks in rats and monkeys. Studies with i.v. administration were performed with belantamab for 4 weeks in monkeys and for 5 days with cys-mcMMAF in rats and monkeys. The cynomolgus monkey was selected as a pharmacologically relevant species for belantamab mafodotin toxicity, as belantamab mafodotin does not bind to rat BCMA.
Significant nonclinical findings occurred in the repeat-dose toxicity studies. The findings were primarily related to the cytotoxic drug conjugate, cys-mcMMAF, and 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 within the BCMA targets of belantamab mafodotin. Overall, comparison of the findings between the monkey (pharmacologically relevant species) and rat (off-target) indicates 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. 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 there were no safety margins. However, this is acceptable in view of the indication. The findings are adequately mentioned in the RMP.
In accordance with ICH S9, the applicant did not conduct definitive genetic toxicology and carcinogenicity studies with belantamab mafodotin. Nonetheless, the drug 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. Additionally, the applicant investigated the genotoxic potential of cys-mcMMAF in an Ames test, a mouse lymphoma assay, and an *in vivo* rat bone marrow micronucleus assay. These investigations were all negative.
No dedicated reproductive or developmental toxicity studies were conducted. Effects on reproductive organs occurred in animals of both sexes at ~4 times exposure at the maximum recommended human dose. Based on these findings, belantamab mafodotin may impair fertility in females and males of reproductive potential. There is also a risk of heritable changes via genotoxicity in germ cells. Further, as the mechanism of action is to induce cytotoxicity in rapidly dividing cells and the toxicity is not confined to BCMA expressing tissues, the drug is likely to affect a developing embryo. As human IgG molecules are known to cross the placenta, the drug should not be used during pregnancy unless the benefit to the mother outweighs the potential risks to the foetus. It is not known whether the drug is excreted into human milk. IgG is present in human milk in small amounts. 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.
Based on the ERA, belantamab mafodotin does not represent a risk for the environment.

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.

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6 Clinical and Clinical Pharmacology Aspects

The evaluation of the clinical and clinical pharmacology data in this application has been carried out in reliance on previous regulatory decisions by the EMA and the FDA. The available assessment report and corresponding product information from EMA and FDA were used as a basis for the clinical and clinical pharmacology evaluation.
For further details concerning clinical pharmacology, dosing recommendations, efficacy and safety, see section 8.1 of this report.

Available efficacy data for belantamab mafodotin in adults with relapsed and refractory multiple myeloma who have received at least four prior therapies including an anti-CD38 monoclonal antibody, a proteasome inhibitor, and an immunomodulatory agent appear to be clinically meaningful. Due to the limited size of the efficacy database, including uncertainties related to the single-arm nature of the submitted pivotal study DREAMM-2 and the missing validation of primary endpoint overall response rate (ORR) as surrogate marker for overall survival (OS), the presently available efficacy data for belantamab mafodotin are not considered sufficient for regular approval. In addition, concerns exist regarding the limited safety data based on single-arm studies only and the potential long-term toxicity of belantamab mafodotin. Therefore, a temporary approval was granted. In order to further confirm the currently available results, the applicant will submit updated efficacy and safety data from study DREAMM-2 and the confirmatory phase 3 study DREAMM-3.

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7 Risk Management Plan Summary

The RMP summaries contain information on the medicinal products' safety profiles and explain the measures that are taken in order 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. Marketing Authorisation Holders are responsible for the accuracy and correctness of the content of the published RMP summaries. 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 occurring in populations or indications not included in the Swiss authorisations.

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8 Appendix

Approved Information for Healthcare Professionals

Please be aware that the following version of the information for healthcare professionals relating to 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 reference document, which is valid and relevant 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. The Authorisation Holder is responsible for the correct translation of the text. Only the information for healthcare professionals approved in one of the official Swiss languages is binding and legally valid.

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▼ 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 is temporarily approved, see “Properties/Effects” section.

BLENREP

Composition

Active substances

Belantamab mafodotin.

Excipients

Sodium citrate dihydrate, citric acid, trehalose dihydrate, disodium edetate (EDTA), polysorbate 80.
Total sodium content: 3.15 mg

Pharmaceutical form and active substance quantity per unit

Powder for a concentrate for the preparation of a solution for infusion.
Each vial contains 100 mg belantamab mafodotin (lyophilised yellow to white powder).
After reconstitution, the solution contains 50 mg belantamab mafodotin per mL.

Indications/Uses

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

“The efficacy and safety of belantamab mafodotin in patients who have previously undergone BCMA-directed CAR-T cell therapy have not been investigated.”

Dosage/Administration

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

Recommended adjuvant treatment

Patients should undergo an ophthalmological examination, including visual acuity test and slit-lamp examination, prior to the initiation of treatment, prior to the three subsequent cycles of treatment and if clinically indicated during the further course of therapy (see “Warnings and precautions”).
Physicians should advise their patients to use preservative-free artificial tears at least four times a day from the first day of infusion until the end of therapy, as this may reduce corneal symptoms (see “Warnings and precautions”).
For patients who show symptoms of eye dryness, additional treatments should be considered according to the recommendations of the ophthalmologist.

Usual dosage

The recommended dose for Blenrep is 2.5 mg/kg body weight, administered as an intravenous infusion every three weeks.
It is recommended that treatment should be continued until disease progression or unacceptable toxicity.
To ensure the traceability of biotechnologically produced medicinal products, it is recommended to document the trade name and batch number for each treatment.

Dose adjustment following undesirable effects

The recommended dose adjustments for corneal adverse reactions are listed in Table 1 and those for other undesirable effects in Table 2.
Undesirable corneal effects may include abnormalities on eye examination and/or changes in visual acuity (see “Warnings and precautions”). The treating physician should consider the patient's ophthalmic examination report prior to dose administration and determine the dose of Blenrep based on the highest degree of severity of findings for the most severely affected eye, as both eyes may not be affected to the same degree (Table 1).
During the ophthalmological examination, the ophthalmologist should assess the following:

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

Table 1: Dose adjustments for undesirable corneal effects

Degree of severity[a]	**Findings of the ophthalmological examination**	**Recommended dose adjustments**

Mild	*Corneal examination finding(s)* Mild superficial keratopathy[b] *Change in BCVA* Decrease in Snellen visual acuity by one line compared to baseline	Continuation of treatment with current dose.
Moderate	*Corneal examination finding(s)* Moderate superficial keratopathy[c] *Change in BCVA* Decrease by two or three lines compared to baseline (and Snellen visual acuity not worse than 20/200)	Discontinue treatment until the findings and best-corrected visual acuity have reached a degree of severity of mild or lower. Consider resuming treatment at a reduced dose of 1.9 mg/kg body weight.
Severe	*Corneal examination finding(s)* Severe superficial keratopathy[d] Epithelial defect of the cornea[e] *Change in BCVA* Decrease in visual acuity according to Snellen by more than three lines compared to baseline	Discontinue treatment until the findings and best-corrected visual acuity have reached a degree of severity of mild or lower. If symptoms worsen and there is no response to appropriate treatment, discontinuation should be considered.

[a] The degree of 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 deterioration from baseline) with or without symptoms.

[c] Moderate superficial keratopathy - with or without patchy microcyst-like deposits, subepithelial opacity (peripheral) or a new peripheral stromal opacity.

[d] Severe superficial keratopathy with or without diffuse microcyst-like deposits on the cornea, subepithelial opacity (central) or a new opacity of the central stroma.

[e] A corneal defect can lead to corneal ulcers. These should be treated promptly by an ophthalmologist as clinically indicated.

Table 2: Dose adjustments due to other undesirable effects

Undesirable effect	Degree of severity	Recommended dose adjustments

Thrombocytopenia (see “Warnings and precautions”)	Grade 2-3: thrombocyte count 25,000 to < 75,000/microlitre	Possibly discontinue treatment with Blenrep and/or reduce the dose of Blenrep to 1.9 mg/kg body weight.
	Grade 4: thrombocyte count < 25,000/microlitre	Discontinue treatment with Blenrep until thrombocyte count improves to Grade 3 or lower. Consider resuming therapy at a reduced dose of 1.9 mg/kg body weight.
Infusion-related reactions (see “Warnings and precautions”)	Grade 2 (moderate)	Discontinue infusion and initiate adjuvant treatment. As soon as the symptoms subside, continue the infusion at an infusion rate that is at least 50% lower.
	Grade 3 or 4 (heavy)	Discontinue infusion and initiate adjuvant treatment. As soon as symptoms subside, continue infusion at an infusion rate that is at least 50% lower. In the event of an anaphylactic or life-threatening infusion reaction, permanently stop infusion and initiate appropriate emergency care.
Other undesirable effects (see “Undesirable effects”)	Grade 3	Discontinue treatment with Blenrep until improvement to Grade 1 or lower. Consider resuming therapy at a reduced dose.
	Grade 4	Consider permanent discontinuation of Blenrep. If treatment is continued, discontinue until improvement to Grade 1 or lower and resume at a reduced dose.

The degree of severity of undesirable effects was graded based on the National Cancer Institute's Common Terminology Criteria for Adverse Events (CTCAE).

Special dosage instructions

Patients with impaired hepatic function

No dose adjustment is required in patients with mildly impaired hepatic function (bilirubin greater than ULN to less than or equal to 1.5 × ULN or aspartate transaminase [AST] greater than ULN). There are insufficient data on patients with moderately impaired hepatic function and no data at all on patients with severe hepatic impairment on which to base a dose recommendation (see “Pharmacokinetics - Special patient populations”).

Patients with impaired renal function

No dose adjustment is required in patients with mild to moderately impaired renal function (eGFR ≥ 30 mL/min/1.73m^2). There are insufficient data on which to base a dose recommendation in patients with severe renal impairment (see “Pharmacokinetics - Special patient populations”).

Elderly patients

No dose adjustment is required in patients over 65 years of age (see “Pharmacokinetics - Special patient groups”).

Children and adolescents

The safety and efficacy of Blenrep in children and adolescents under 18 years of age has not been established.

Mode of administration

Blenrep is a cytotoxic anti-cancer medicinal product. The appropriate handling procedures must be followed. For instructions on reconstitution and further dilution, see *Handling instructions*.
Blenrep is administered as an intravenous infusion over approximately 30 minutes.

Contraindications

Hypersensitivity to the active substance or one of the excipients.

Warnings and precautions

Ophthalmological toxicity
Undesirable effects on the cornea have been reported in association with the use of Blenrep. The most commonly reported adverse reactions were keratopathy, including microcyst-like epithelial changes of the corneal epithelium (detected during ophthalmological examinations) with or without changes in visual acuity, blurred vision and symptoms of dry eyes. Patients with a history of dry eyes were more prone to corneal epithelial changes. Changes in visual acuity may be associated with difficulty driving or operating machinery.

Ophthalmological examinations, including assessment of visual acuity and slit-lamp examination, should be performed prior to the initiation of treatment, prior to the three subsequent cycles of treatment and during the further course of treatment if clinically indicated. Patients are advised to use preservative-free artificial tears at least four times daily during treatment (see “Dosage/Administration”).
Patients should avoid wearing contact lenses until the end of treatment unless prescribed otherwise by an ophthalmologist.

In patients who experience keratopathy with or without changes in visual acuity, a dose adjustment (delay and/or reduction) or discontinuation of treatment may be required depending on the degree of severity of the findings (see “Dosage/Administration - Table 1”).

Cases of corneal ulceration (ulcerative and infectious keratitis) have been reported (see “Undesirable effects”). These should be treated promptly by an ophthalmologist as clinically indicated. Treatment with Blenrep should be discontinued until the corneal ulcer has healed (see "Dosage/Administration - Table 1”).

Thrombocytopenia

Thrombocytopenia events (thrombocytopenia and decreased thrombocyte count) were frequently reported in study 205678. Thrombocytopenia can lead to severe bleeding, including gastrointestinal and intracranial bleeding.

A complete blood count should be requested prior to the initiation of treatment and during treatment if clinically indicated. Patients with Grade 3 or 4 thrombocytopenia and patients receiving concomitant anticoagulant therapy may require closer monitoring and may require longer dosing intervals or lower doses (see “Dosage/Administration - Table 2”). Adjuvant therapies (e.g. platelet transfusion) should be used in accordance with standard medical practice.

Infusion reactions

Infusion-related reactions (IRR) have been reported in association with Blenrep. In most cases, these were Grade 1 or 2 and resolved the same day (see “Undesirable effects”). If a Grade 2 or higher IRR occurs during administration, the infusion rate is reduced or the infusion is stopped, depending on the degree of severity of the symptoms. Appropriate medical treatment should be initiated and the infusion restarted at a lower rate if the patient's condition is stable. If a Grade 2 or higher IRR occurs, premedication should be given for all subsequent infusions (see “Dosage/Administration - Table 2”).

Pneumonitis

Cases of pneumonitis from spontaneous reports and named patient programs, including fatal events, have been observed with Blenrep. Patients with new or worsening unexplained pulmonary symptoms (e.g. cough, dyspnoea) should be evaluated for pneumonitis. In case of suspected Grade 2 or higher pneumonitis, Blenrep should be withheld. If Grade 2 or higher pneumonitis is confirmed, a systemic corticosteroid treatment should be started immediately (e.g., ≥1 mg/kg/day prednisolone or an equivalent treatment) and continued for at least 14 days, followed by gradual tapering over at least four weeks. Blenrep should only be resumed after an evaluation of the benefits and risks.

Excipients

This medicinal product contains less than 1 mmol sodium (23 mg) per 100 mg vial, i.e. it is almost sodium-free.

Interactions

No formal studies have been conducted to detect interactions with belantamab mafodotin.

According to the results from *in vitro studies,* cys-mcMMAF is a substrate for the organic anion-transporting polypeptides OATP1B1 and OATP1B3, the multidrug resistance-associated protein MRP1, MRP2, MRP3 as well as the bile salt export pump (BSEP) and a potential substrate for P-glycoprotein (P-gp).

Pregnancy, lactation

Women of childbearing age/contraception in men and women
Before starting treatment with Blenrep, the pregnancy status of women of childbearing age should be reviewed. Women of childbearing potential should use an effective method of contraception during treatment with Blenrep and for a period of four months after the last dose.
Men with partners of childbearing age should use an effective method of contraception during treatment with Blenrep and for a period of six months after the last dose.

Pregnancy

No data are available on the use of Blenrep in pregnant women. Due to the mechanism of action of the cytotoxic component monomethyl auristatin F (MMAF), belantamab mafodotin may cause damage to the embryo or foetus when administered to pregnant women (see “Preclinical data”). Human immunoglobulin G (IgG) is known to cross the placenta; therefore, belantamab mafodotin can potentially be transferred from the mother to the developing foetus.
Blenrep must not be used during pregnancy, unless treatment with Blenrep is required because of the woman's clinical condition. Pregnant women for whom treatment is necessary must be clearly informed of the potential risks to the foetus.

Lactation

It is not known whether belantamab mafodotin is excreted in breast milk. Immunoglobulin G (IgG) is present in small amounts in breast milk. Due to the mechanism of action of belantamab mafodotin and the fact that it is a humanised monoclonal IgG antibody, the preparation may cause serious undesirable effects in breastfed infants. Women should be advised to stop breastfeeding before starting therapy with Blenrep and not to breastfeed until three months after the last dose.

Fertility

Based on results in animals and the mechanism of action, belantamab mafodotin may impair fertility in women and men of reproductive potential (see “Preclinical data”).

Effects on ability to drive and use machines

Visual deterioration has been reported in some patients treated with belantamab mafodotin in clinical trials (see “Warnings and precautions”, “Undesirable effects”). Patients should be advised to exercise caution when driving or using machines as Blenrep may impair vision.

Undesirable effects

Summary of the safety profile

The following section summarises the adverse reactions that occurred in patients (N=264) receiving belantamab mafodotin as monotherapy in pooled clinical trials. The most frequent undesirable effects (≥30%) were keratopathy (64%), thrombocytopenia (34%), anaemia (32%) and blurred vision (31%). The most commonly reported serious adverse reactions were pneumonia (10%), pyrexia (5%) and IRRs (3%).
Permanent discontinuation due to an undesirable effect occurred in 12% of patients receiving belantamab mafodotin, 3% of which were related to undesirable ocular effects.

List of undesirable effects

Table 3 summarises the adverse drug reactions in patients receiving belantamab mafodotin as monotherapy.
The frequencies are defined as follows: very common (≥ 1/10), common (≥ 1/100, < 1/10), uncommon (≥ 1/1,000, < 1/100), rare (≥ 1/10,000, < 1/1,000), very rare (< 1/10,000) and not known (frequency cannot be assessed on the basis of the available data). Within each frequency category, the undesirable effects that occurred are listed in descending degree of severity.

Table 3: Reported adverse reactions in patients treated with belantamab mafodotin.

System organ class	Undesirable effects[a]	Frequency	Incidence (%)	
			All degrees	Grade 3-4
Infections and parasitic diseases	Pneumonia[b]	Very common	14	9
	Upper respiratory tract infections	Very common	17	<1
Blood and lymphatic system disorders	Thrombocytopenia[c]	Very common	34	23
	Anaemia		32	22
	Lymphopenia[d]	Common	5	3
	Leukopenia[e]		6	2
	Neutropenia[f]	Very common	11	7
Eye disorders	Keratopathy[g]	Very common	64	20
	Events of blurred vision[h]		31	3

	Dry eye events[i]		20	1
	Photophobia		11	0
	Eye irritation	Common	3	0
	Ulcerative keratitis	Uncommon	<1	<1
	Infectious keratitis		<1	<1
Respiratory, thoracic and mediastinal disorders	Pneumonitis[K]	Not known		
Diseases of the gastrointestinal tract	Nausea	Very common	28	<1
	Diarrhoea		16	2
	Vomiting		13	<1
Renal and urinary disorders	Albuminuria	Uncommon	<1	0
General diseases and administration site conditions	Fever	Very common	23	3
	Exhaustion		25	3
Examinations	Increased aspartate aminotransferase	Very common	25	5
	Increased gamma-glutamyltransferase		13	5
	Increased creatine phosphokinase	Common	5	2
Injury, poisoning and complications due to surgery	Infusion-related reactions[j]	Very common	13	2

[a] Adverse events coded according to MedDRA and classified by degree of severity based on CTCAE v4.03.
[b] Including pneumonia and herpes simplex pneumonia.
[c] Including thrombocytopenia and reduced thrombocyte count.
[d] Including lymphopenia and reduced lymphocyte count.
[e] Including leukopenia and reduced leucocyte count.
[f] Including neutropenia and decreased neutrophil count.
[g] Characterised as changes in the corneal epithelium with or without symptoms according to opthalmological examination.
[h] Including double vision, blurred vision, reduced visual acuity and visual deterioration.
[i] Including dry eye, eye disorders and eye itching.

[j] Including events that the investigators judged to be due to the infusion. Infusion reactions include but are not limited to pyrexia, chills, diarrhoea, nausea, asthenia, hypertension, lethargy, tachycardia.
[K] Including fatal cases.
NA = not applicable

Description of specific undesirable events and additional information

Corneal undesirable events

In study 205678 (n=95), ocular events occurred in 74% of patients; the most common adverse events were keratopathy or microcystic epithelial changes of the corneal epithelium (71%, noted during ophthalmological examinations, with or without symptoms), blurred vision (25%) and dry eye symptoms (15%). Decreased visual acuity (Snellen visual acuity worse than 20/50) in the better eye was reported in 18% and severe loss of vision (20/200 or worse) in the better eye in 1% of patients treated with belantamab mafodotin.

The median time to the occurrence of corneal findings of Grade 2 or above (best-corrected visual acuity or keratopathy at ophthalmological examination) was 36 days (range: 19 to 143 days). The median time to regression of these corneal findings (first appearance) was 91 days (range: 21 to 201 days).

Corneal findings (keratopathy) led to dose deferral in 47% of patients and dose reductions in 27% of patients. 3% of patients discontinued treatment due to ocular events.

Infusion-related reactions

In clinical trials, the incidence of infusion-related reactions (IRRs) with belantamab mafodotin 2.5 mg/kg was 21%; of these, most (90%) occurred during the first infusion. Most IRRs were reported as Grade 1 (6%) and Grade 2 (12%), while Grade 3 IRRs were present in 3%. Severe IRRs were reported in 4% of patients and included symptoms of pyrexia and lethargy. The median time to onset and median duration of the first onset of an IRR was one day. One patient (1%) discontinued treatment after Grade 3 IRRs occurred during the first and second infusions. Grade 4 or 5 IRRs were not reported.

Thrombocytopenia

Thrombocytopenic events (thrombocytopenia and decreased thrombocyte count) occurred in 38% of patients treated with 2.5 mg/kg belantamab mafodotin. Grade 2 thrombocytopenic events occurred in 3%, Grade 3 in 9% and Grade 4 in 13% of patients. Grade 3 bleeding events occurred in 2% of patients; Grade 4 or 5 events were not reported.

Infections

Upper respiratory tract infections were frequently reported throughout the entire belantamab mafodotin clinical programme. They were mostly mild to moderate (Grade 1 to 3) and occurred in 9%

of patients treated with 2.5 mg/kg belantamab mafodotin. No serious adverse events concerning upper respiratory tract infections were reported.
Pneumonia was the most common infection and was reported in 11% of patients treated with 2.5 mg/kg belantamab mafodotin. Pneumonia was also the most common serious adverse event and was reported as such in 7% of patients. Infections with a fatal outcome were primarily due to pneumonia (1%).

Undesirable effects after market launch
Pneumonitis
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 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 are no experiences of overdoses of belantamab mafodotin in clinical trials.

Treatment

There is no known specific antidote in the event of an overdose of belantamab mafodotin. In case of overdose, the patient should be monitored for signs or symptoms of undesirable effects and initiate appropriate adjuvant treatment immediately.
The further procedure depends on the clinical requirements.

Properties/Effects

ATC code

L01XC39

Mechanism of action

Belantamab mafodotin is a humanised monoclonal IgG1-kappa antibody conjugated to the cytotoxic agent maleimidocaproyl monomethylauristatin F (mcMMAF). Belantamab mafodotin binds to the BCMA on the cell surface and is rapidly internalised. In the tumour cell, the cytotoxic agent is released and destroys the microtubule network. This leads to cell cycle arrest and apoptosis. The antibody enhances the recruitment and activation of immune effector cells, which kill cancer cells via antibody-dependent cellular cytotoxicity and phagocytosis. Apoptosis induced by belantamab mafodotin is accompanied by markers of immunogenic cell death, which could contribute to an adaptive immune response to tumour cells.

Pharmacodynamics

Cardiac electrophysiology

Belantamab mafodotin at the recommended dose of 2.5 mg/kg once every three weeks did not cause significant QTc prolongation (> 10 ms).

Immunogenicity

In clinical trials in patients with multiple myeloma, < 1% of patients (2/274) tested positive for antibodies to belantamab mafodotin after receiving belantamab mafodotin. In one of the two cases, patients tested positive for neutralising antibodies to belantamab mafodotin.

Clinical efficacy

In the open-label, two-arm phase II multicentre study 205678, belantamab mafodotin was studied as monotherapy in patients with multiple myeloma that had relapsed after at least three prior courses of therapy and who were refractory to either monotherapy or combination therapy with an immunomodulatory agent, a proteasome inhibitor and an anti-CD38 antibody. Patients were included if they had undergone autologous stem cell transplant or were considered transplant ineligible and had measurable disease in accordance with International Myeloma Working Group (IMWG) criteria. Patients were randomised to receive either 2.5 mg/kg (N = 97) or 3.4 mg/kg (N = 99) of belantamab mafodotin as an intravenous infusion every three weeks until disease progression or unacceptable toxicity. The data below are from the 2.5 mg/kg cohort, which is the recommended therapeutic dose. Baseline demographic data and disease characteristics for the group of patients treated with belantamab mafodotin 2.5mg/kg (N=97) were as follows:
The median value (range) for age was 65 (39 to 85) years. 53% percent of patients were male and 47% of patients were female. 33% of patients had an ECOG score of 0 at baseline, 50% of patients had a score of 1 and 17% of patients had a score of 2. 34% of patients had a ISS stage II and 43% of patients had a ISS stage III at screening. 27% of patients had cytogenetic high-risk factors (positive for t [4;14], t [14;16] and 17p13del). The median value (range) for number of previous courses of therapy was 7 (3 to 21). The median value (range) for duration of exposure was 9 (2 to 75) weeks. The median value (range) for treatment cycles was 3 (1 to 17).

The primary endpoint was overall response rate, which was assessed by an independent review committee (IRC) using the IMWG Uniform Response Criteria for Multiple Myeloma. Table 5 shows 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), (%)	2 %
Complete Response (CR), (%)	5 %
Very Good Partial Response (VGPR), (%)	11 %
Partial Response (PR), (%)	13 %
Median duration of response in months (95% CI)	11 (4.2 to not reached)

Temporary authorisation

Due to incomplete clinical data at the time of the review of the marketing authorisation application, the medicinal product Blenrep is granted temporary authorisation (Art. 9a Therapeutic Products Act). The temporary authorisation is subject to the timely fulfillment of conditions. Once these conditions have been fulfilled, the temporary authorisation can be converted into a regular authorisation.

Pharmacokinetics

Absorption

The highest concentration of belantamab mafodotin was measured at the end of infusion or shortly thereafter, while the concentration of cys-mcMMAF peaked approximately 24 hours after infusion. The geometric mean C_{max}- and $AUC_{(0\text{-}tau)}$ concentrations of belantamab mafodotin were 43 µg/mL and 4666 µg·h/mL, respectively, for Cycle 1 at the 2.5 mg/kg dose level.
The time to reach steady state was ~70 days; accumulation of belantamab mafodotin was ~70% from Cycle 1 to Cycle 3 with a dosing interval of every three weeks.

Distribution

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

Metabolism

The monoclonal antibody portion of belantamab mafodotin is expected to be broken down by ubiquitous proteolytic enzymes into small peptides and individual amino acids. Cys-mcMMAF showed limited metabolic clearance in incubation studies with the human hepatic S9 fraction.

Elimination

Elimination of belantamab mafodotin was slow, with a total plasma clearance of 0.92 L/day and a terminal half-life of 12 days. Over time, clearance decreased by 28%, which led to an elimination half-life of 14 days. In an animal study, about 83% of the radioactive dose of cys-mcMMAF was excreted

in the faeces; urinary excretion (about 13%) played a minor role. 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 decreasing clearance over time.

Kinetics in specific patient groups

Hepatic impairment

No formal studies have been conducted in patients with impaired liver function. In population pharmacokinetic analyses, which included patients with healthy livers as well as patients with mild hepatic impairment, liver function was not found to be a relevant covariate.

Renal impairment

No formal studies have been conducted in patients with impaired renal function. In population pharmacokinetic analyses that included patients with healthy kidneys as well as patients with mild to moderate renal impairment, renal function was not found to be a significant covariate.

Elderly patients

No formal studies have been conducted in elderly patients. In population pharmacokinetic analyses, performed in patients aged 34 to 89 years, age was not found to be a significant covariate.

Children and adolescents

No pharmacokinetic data are available on children and adolescents.

Body weight

In population pharmacokinetic analyses, body weight proved to be a relevant covariate. The C_{tau} of belantamab mafodotin was predicted to be +10% at a body weight of 100 kg (+20% at 130 kg) and -10% at a body weight of 55 kg (-20% at 40 kg) compared to the typical patient (75 kg).

Preclinical data

Repeat dose toxicity

In animal experimental studies on rats and monkeys, the most significant undesirable effects (directly related to belantamab mafodotin) at exposures ≥1.2 times the recommended 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 at ≥3 mg/kg in monkeys) and increases in alveolar macrophages associated with eosinophilic deposits in the lung 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 lung were not reversible in rats.
Single cell necrosis of corneal epithelium and/or increased mitotic rates of corneal epithelial cells were observed in rats and rabbits. Belantamab mafodotin entered cells throughout the body by a mechanism unrelated to cell membrane BCMA receptor expression.

Carcinogenicity / mutagenicity

In an *in vitro* screening test with human lymphocytes, belantamab mafodotin was found to be genotoxic. This is consistent with the pharmacological effect of cysmcMMAF-mediated inhibition of microtubules causing aneuploidy.
No studies on the complete clarification of genotoxicity or carcinogenicity of belantamab mafodotin have been conducted.

Reproductive toxicity

No animal studies have been performed to evaluate the potential effects of belantamab mafodotin on reproduction or development. The mechanism of action results in the destruction of rapidly dividing cells and is therefore likely to have an effect on the development of the embryo, whose cells also divide rapidly. There is also a potential risk of heritable changes due to 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 following a clinical dose. Luteinised nonovulatory follicles were seen in the ovaries of rats after three doses one week apart. Undesirable findings in the male reproductive organs of rats that progressed following repeat dosing included marked degeneration/atrophy of seminiferous tubules that generally did not reverse following dosing cessation.

Other information

Incompatibilities

As no compatibility studies have been carried out, the reconstituted concentrate and the diluted infusion solution must not be mixed with other medicinal products.

Shelf life

The medicinal product may only be used until the date marked "EXP" on the pack.

Shelf life after opening

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

Diluted solution

If the diluted solution is not used immediately, it can be stored in the refrigerator (2 °C to 8 °C) for up to 24 hours before use. Do not freeze. Allow refrigerated diluted solution to reach room temperature before administration.
The diluted infusion solution can be stored at room temperature (20 °C to 25 °C) for up to six hours (including infusion time).

Special precautions for storage

Store in the 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 anti-cancer medicinal product. The appropriate procedures must be followed during handling. Reconstitution and dilution of the ready-to-use solution must be carried out under aseptic conditions.
The required dose (mg), the required total volume of solution (mL) and the required number of vials should be calculated based on the patient's current body weight (kg).

Reconstitution

1. Remove the Blenrep vial(s) from the refrigerator and wait about ten minutes until it/they has/have reached room temperature.
2. Reconstitute the content of each vial with 2 mL of water for injection purposes to make a solution with a concentration of 50 mg/mL. Gently swirl the vial to help the product dissolve. Do not shake.
3. Inspect the reconstituted solution for visible suspended particles and discolouration. The reconstituted solution should be a clear to opalescent and colourless or yellow-to-brown-coloured liquid. Discard the vial of reconstituted solution if foreign particles other than transparent to white proteinaceous particles are visible.

Dilution instructions for intravenous use

1. Take the volume needed for the calculated dose from each vial.
2. Add the required amount of Blenrep to an infusion bag containing 250 mL of 0.9% (9 mg/mL) sodium chloride solution for injection purposes. Mix the diluted solution by gently inverting the bag. The final concentration of the diluted solution should be between 0.2 mg/mL and 2 mg/mL. DO NOT SHAKE.
3. Any unused residues of the reconstituted solution of Blenrep in the vial should be discarded.

Administration instructions

1. The diluted solution is administered as an intravenous infusion over approximately 30 minutes using a polyvinyl chloride or polyolefin infusion set.

2. Filtration of the diluted solution is not required. If the solution is nevertheless filtered, it is recommended to use a polyethersulfone (PES) based filter.

Disposal

Unused medicinal product or waste material shall be disposed of in accordance with national requirements.

Authorisation number

67741

Packs

Blenrep, 100 mg vials: 1 [A]

Marketing authorisation holder

GlaxoSmithKline AG, 3053 Münchenbuchsee

Date of revision of the text

June 2022