Swiss Summary of the Risk Management Plan (RMP)
for
Blenrep

(Belantamab mafodotin)

RMP Summary:	Version 1.0
Based on EU RMP:	Version 1.1.
Marketing Authorisation Holder:	GlaxoSmithKline AG
Date:	03.08.2022

The Risk Management Plan (RMP) is a comprehensive document submitted as part of the application dossier for market approval of a medicine. The RMP summary contains information on the medicine's safety profile and explains the measures that are taken in order to further investigate and follow the risks as well as to prevent or minimise them.

The RMP summary of Blenrep is a concise document and does not claim to be exhaustive.

As the RMP is an international document, the summary might differ from the “Arzneimittelinformation / Information sur le médicament” approved and published in Switzerland, e.g. by mentioning risks occurring in populations or indications not included in the Swiss authorization.

Please note that the reference document which is valid and relevant for the effective and safe use of Blenrep in Switzerland is the “Arzneimittelinformation/ Information sur le médicament” (see www.swissmedic.ch) approved and authorized by Swissmedic.

GlaxoSmithKline AG is fully responsible for the accuracy and correctness of the content of the published summary RMP of Blenrep.

PART VI: SUMMARY OF THE RISK MANAGEMENT PLAN

Summary of risk management plan for BLENREP

This is a summary of the risk management plan (RMP) for belantamab mafodotin. The RMP details important risks of BLENREP, how these risks can be minimised, and how more information will be obtained about BLENREP risks and uncertainties (missing information).

The BLENREP summary of product characteristics (SmPC) and package leaflet give essential information to healthcare professionals and patients on how BLENREP should be used.

This summary of the RMP for BLENREP should be read in the context of all this information including the assessment report of the evaluation and its plain-language summary, all which is part of the European Public Assessment Report (EPAR).

Important new concerns or changes to the current ones will be included in updates to the RMP for BLENREP.

I. The medicine and what it is used for

BLENREP is authorised as monotherapy for the treatment of multiple myeloma in adult patients, who have received at least 4 prior therapies and whose disease is refractory to at least one proteasome inhibitor, one immunomodulatory agent, and an anti-CD38 antibody, and who have demonstrated disease progression on the last therapy. It contains BLENREP as the active substance and it is given intravenously.

Further information about the evaluation of BLENREP's benefits can be found in the BLENREP EPAR, including in its plain-language summary, available on the EMA website, under the medicine's webpage:
https://www.ema.europa.eu/en/medicines/human/EPAR/blenrep

II. Risks associated with the medicine and activities to minimise or further characterise the risks

Important risks of BLENREP, together with measures to minimise such risks and the proposed studies for learning more about BLENREP's risks, are outlined below.

Measures to minimise the risks identified for medicinal products can be:

- Specific information, such as warnings, precautions, and advice on correct use, in the package leaflet and SmPC addressed to patients and healthcare professionals;
- Important advice on the medicine's packaging;
- The authorised pack size — the amount of medicine in a pack is chosen so to ensure that the medicine is used correctly;
- The medicine's legal status — the way a medicine is supplied to the patient (e.g. with or without prescription) can help to minimise its risks.

Together, these measures constitute *routine risk minimisation* measures.

In the case of BLENREP, these measures are supplemented with *additional risk minimization measures* mentioned under relevant important risks, below.

In addition to these measures, information about adverse reactions is collected continuously and regularly analysed so that immediate action can be taken as necessary. These measures constitute *routine pharmacovigilance activities*.

If important information that may affect the safe use of BLENREP is not yet available, it is listed under 'missing information' below.

II.A List of important risks and missing information

Important risks of BLENREP are risks that need special risk management activities to further investigate or minimise the risk, so that the medicinal product can be safely administered. Important risks can be regarded as identified or potential. Identified risks are concerns for which there is sufficient proof of a link with the use of BLENREP. Potential risks are concerns for which an association with the use of this medicine is possible based on available data, but this association has not been established yet and needs further evaluation. Missing information refers to information on the safety of the medicinal product that is currently missing and needs to be collected (e.g. on the long-term use of the medicine);

List of important risks and missing information	
Important identified risks	Keratopathy (or MEC) in the corneal epithelium (as seen on eye examination) with or without changes in visual acuity, blurred vision, or dry eye
Important potential risks	Nephrotoxicity Increased risk of infections due to immunosuppression and/or neutropenia
Missing information	Safety in patients with severe renal impairment Safety in patients with hepatic impairment

II.B Summary of important risks

Important identified risk 1: Keratopathy (or MEC) in the corneal epithelium (as seen on eye examination) with or without changes in visual acuity, blurred vision, or dry eye	
Evidence for linking the risk to the medicine	Corneal events are a class effect reported with other MMAF-containing ADCs and have been reported with BLENREP. 'Keratopathy (or MEC) in the corneal epithelium (as seen on eye examination) with or without changes in visual acuity, blurred vision, or dry eye ' is considered an important identified risk based on the changes in the corneal epithelium on ocular examination that have frequently been observed in the BLENREP clinical trial programme. This finding was most commonly associated with blurred vision, dry eyes, photophobia, and changes in visual acuity.
Risk factors and risk groups	In the DREAMM-2 study, logistic regression analysis showed a statistically significant (p=0.014) association between history of dry eye and the development of a Grade 2 or greater corneal event (DREAMM-2 CSR, Table 3.1280).
Risk minimisation measures	**Routine risk minimisation measures**: SmPC Sections: 4.2, 4.4, 4.8 PL Sections: 2, 4 Recommended treatment modifications are provided in SmPC section 4.2. Instruction regarding symptom evaluation, treatment modifications and interventions are provided in SmPC section 4.4. Prescription only medicine Use restricted to physicians experienced in the use of anticancer medicinal products **Additional risk minimisation measures**: Educational materials for prescribing haematologists/ oncologists, eye care professionals, and patients
Additional pharmacovigilance activities	**Additional pharmacovigilance activities**: 205678 (DREAMM-2): Open-label, randomized study of two doses of BLENREP in participants with relapsed/refractory multiple myeloma who have failed prior treatment with an anti-CD38 antibody 207495 (DREAMM-3): Phase III Study of Single Agent BLENREP versus Pomalidomide plus Low-dose Dexamethasone in Participants with Relapsed/Refractory Multiple Myeloma (RRMM)

Important potential risk 1: Nephrotoxicity	
Evidence for linking the risk to the medicine	Non-clinical safety studies have demonstrated dose dependent and reversible primary glomerular injury and tubular degeneration (in rat and monkey) directly related to BLENREP, accompanied by large molecular proteinuria (albuminuria) and enzymuria. Single cell necrosis of the kidney and bladder urothelium was also noted in the 13-week monkey study. Severe tubular degeneration/regeneration and marked glomerulonephritis exacerbated by immune complex disease, likely associated with ADA, following 5 weekly doses of 10 mg/kg, led to the early euthanasia of one monkey. Glomerulonephritis associated with immune complex formation is not expected to be reversible.
Risk factors and risk groups	Patients with multiple myeloma have an increased risk of renal impairment.
Risk minimisation measures	**Routine risk minimisation measures**: Prescription only medicine Use restricted to physicians experienced in the use of anticancer medicinal products **Additional risk minimisation measures**: None
Additional pharmacovigilance activities	**Additional pharmacovigilance activities**: 205678 (DREAMM-2): Open-label, randomized study of two doses of BLENREP in participants with relapsed/refractory multiple myeloma who have failed prior treatment with an anti-CD38 antibody 207495 (DREAMM-3): Phase III Study of Single Agent BLENREP versus Pomalidomide plus Low-dose Dexamethasone in Participants with Relapsed/Refractory Multiple Myeloma (RRMM)

Important potential risk 2: Increased risk of infections due to immunosuppression and/or neutropenia	
Evidence for linking the risk to the medicine	Decreases in immunoglobulins were seen in monkeys at all doses. Decreases in lymphoid cellularity/necrosis (dose-responsive in severity) was noted in the spleen and/or lymph nodes at ≥3 mg/kg/week, which was associated with decreases in thymic cellularity in rats.
Risk factors and risk groups	MM subjects frequently are immunodeficient due to the underlying condition, and concomitant hypogammaglobulinemia. Patients with underlying immunosuppression may be at risk for infection. Assessment of changes in immunoglobulin levels is challenging in patients with MM.
Risk minimisation measures	**Routine risk minimisation measures**: Prescription only medicine Use restricted to physicians experienced in the use of anticancer medicinal products **Additional risk minimisation measures**: None
Additional pharmacovigilance activities	**Additional pharmacovigilance activities:** **205678 (DREAMM-2):** Open-label, randomized study of two doses of BLENREP in participants with relapsed/refractory multiple myeloma who have failed prior treatment with an anti-CD38 antibody **207495 (DREAMM-3):** Phase III Study of Single Agent BLENREP versus Pomalidomide plus Low-dose Dexamethasone in Participants with Relapsed/Refractory Multiple Myeloma (RRMM)

Missing information 1: Safety in patients with severe renal impairment	
Risk minimisation measures	**Routine risk minimisation measures**: Prescription only medicine Use restricted to physicians experienced in the use of anticancer medicinal products **Additional risk minimisation measures**: None
Additional pharmacovigilance activities	**Additional pharmacovigilance activities:** **209626 (DREAMM-12)**: A Phase 1 open label study of GSK2857916 in relapsed/refractory multiple myeloma patients with renal impairment

Missing information 2: Safety in patients with hepatic impairment	
Risk minimisation measures	**Routine risk minimisation measures**: Prescription only medicine Use restricted to physicians experienced in the use of anticancer medicinal products **Additional risk minimisation measures**: None
Additional pharmacovigilance activities	**Additional pharmacovigilance activities:** **209627 (DREAMM-13)**: A Phase 1 open label study of GSK2857916 in patients with relapsed/refractory multiple myeloma and hepatic impairment

II.C Post-authorisation development plan

II.C.1 Studies which are conditions of the marketing authorisation

The following studies are conditions of the marketing authorisation:

DREAMM-2

Study short name and title:

Open-label, randomized study of two doses of BLENREP in participants with relapsed/refractory multiple myeloma who have failed prior treatment with an anti-CD38 antibody (DREAMM-2)

Purpose of the Study:

To evaluate the clinical efficacy of 2 doses of BLENREP in participants with relapsed/refractory multiple myeloma

DREAMM-3

Study short name and title:

Phase III Study of Single Agent BLENREP versus Pomalidomide plus Low-dose Dexamethasone in Participants with Relapsed/Refractory Multiple Myeloma (RRMM) (DREAMM-3)

Purpose of the Study:

To compare the efficacy with BLENREP vs pomalidomide plus low dose dexamethasone (pom/dex) in participants with relapsed/refractory multiple myeloma (RRMM)

II.C.2 Other studies in post-authorisation development plan

There are no studies required for BLENREP.