GlaxoSmithKline AG

Swiss Summary of the Risk Management Plan (RMP) for

Jemperli

(Dostarlimab)

RMP Summary: Version 1, 12 April 2022
EU RMP: Version 1.1, 12 April 2021

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 minimize them.

The RMP summary of Jemperli 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 Jemperli 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 Jemperli

PART VI: SUMMARY OF THE RISK MANAGEMENT PLAN

Summary of risk management plan for JEMPERLI (dostarlimab)

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

JEMPERLI's summary of product characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how JEMPERLI should be used.

This summary of the RMP for JEMPERLI 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 of JEMPERLI's RMP.

I. The medicine and what it is used for

JEMPERLI is indicated as monotherapy for the treatment of patients with mismatch repair deficient/microsatellite instability-high (dMMR/MSI-H) recurrent or advanced endometrial cancer (EC) who have progressed on or after treatment with a platinum-containing regimen (see SmPC for the full indication). It contains dostarlimab as the active substance and it is given by infusion.

Further information about the evaluation of JEMPERLI's benefits can be found in JEMPERLI's 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/jemperli

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

Important risks of JEMPERLI, together with measures to minimise such risks and the proposed studies for learning more about dostarlimab'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 addition to these measures, information about adverse reactions is collected continuously and regularly analysed, including periodic safety update report (PSUR) assessmentso that immediate action can be taken as necessary. These measures constitute *routine pharmacovigilance activities*.

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

II.A List of important risks and missing information

Important risks of JEMPERLI 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 JEMPERLI. 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	▪ IrARs (such as immune-related pneumonitis, colitis, endocrinopathies, immune-related skin adverse reactions, nephritis, systemic inflammatory response syndrome, myositis and other irARs) ▪ Infusion-related reactions
Important potential risks	None
Missing information	▪ Long-term safety

II.B Summary of important risks

Important identified risk: IrARs (such as immune-related pneumonitis, colitis, endocrinopathies, immune-related skin adverse reactions, nephritis, systemic inflammatory response syndrome, myositis and other irARs)	
Evidence for linking the risk to the medicine	**Non-clinical**: Non-clinical observations in cynomolgus monkeys included increased incidence of liquid faeces, dermatitis, mild mixed cell inflammation in the liver, mild to moderate mononuclear infiltrates with or without minimal degeneration in the kidney and heart.

	Clinical: In subjects with dMMR/MSI-H EC, 47 (36.4%) subjects experienced potential irARs and 29 (22.5%) subjects reported treatment-related irARs. Grade ≥3 irARs were reported in 17 (13.2%) subjects, SAEs were reported in 10 (7.8%) subjects, and irARs leading to permanent treatment discontinuation were reported in 6 (4.7%) subjects. **Class effect**: 'IrARs' is a risk for all drugs in the class: Keytruda (pembrolizumab), Opdivo (Nivolumab), Tecentriq (Atezolizumab), Bavencio (Avelumab), Imfinzi (Durvalumab), and Libtayo (cemiplimab).
Risk factors and risk groups	A retrospective medical record review showed that a higher BMI and multiple cycles of pembrolizumab were associated with higher risk of irARs. A derived neutrophil-lymphocyte ratio greater than 3 at baseline was correlated with low risk of irARs. Patients with pre-existing autoimmune disease may be at increased risk of exacerbation of their autoimmune condition and for *de novo* irARs, however, use in this population is not predicted to be associated with unexpected risks or risks of clinical significance that would not be manageable with appropriate intervention.
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**: Patient Card

Important identified risk: Infusion-related reactions	
Evidence for linking the risk to the medicine	**Clinical**: Infusion-related reactions were not experienced by any of the patients in GARNET Cohort A1 (N=129), although 1.4% of the patients in the overall clinical programme treated with dostarlimab monotherapy (N=515) experienced infusion-related reactions. These infusion-related reactions were reported as infusion-related reaction (1.2%) and hypersensitivity (0.2%), occurring within 1 day of infusion. None of the cases was serious. One subject experienced a Grade ≥3 infusion-related reaction and 2 subjects experienced infusion-related reactions/hypersensitivity that resulted in treatment discontinuation.

	Class effect: 'Infusion-related reactions' is a risk for all drugs in the PD-1/PD-L1 inhibitor class: Keytruda (pembrolizumab), Opdivo (Nivolumab), Tecentriq (Atezolizumab), Bavencio (Avelumab), Imfinzi (Durvalumab), and Libtayo (cemiplimab).
Risk factors and risk groups	No specific risk factors or risk groups are known, all patients are at risk.
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 and 4.4. Prescription only medicine Use restricted to physicians experienced in the use of anticancer medicinal products **Additional risk minimisation measures**: No risk minimisation measures

Missing information: Long-term safety	
Risk minimisation measures	**Routine risk minimisation measures**: None **Additional risk minimisation measures**: No risk minimisation measures

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:

GARNET, a Phase I dose escalation and cohort expansion study of dostarlimab in subjects with advanced solid tumors – cohort A1.

Purpose of the study: The primary objective is to confirm the clinical benefit of dostarlimab for patients with recurrent or advanced endometrial cancer.

RUBY, a randomized, double-blind Phase III multicenter study of dostarlimab in combination with chemotherapy versus chemotherapy alone in subjects with recurrent or primary advanced endometrial cancer.

Purpose of the study: The primary objective is to confirm the clinical benefit of dostarlimab with chemotherapy for patients with recurrent or primary advanced endometrial cancer.

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

There are no studies required for JEMPERLI.