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.

JEMPERLI is indicated in combination with carboplatin and paclitaxel for the treatment of adult patients with mismatch repair deficient (dMMR)/microsatellite instability-high (MSI-H) primary advanced or recurrent endometrial cancer (EC) and who are candidates for systemic therapy.

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 JEMPERLI'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) assessment 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 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	▪ Immune-related adverse reactions (including pneumonitis, colitis, hepatitis, endocrinopathies, immune-related skin adverse reactions, nephritis and other irARs)
Important potential risks	None
Missing information	▪ Long-term safety

II.B Summary of important risks

Important identified risk: Immune-related adverse reactions (including pneumonitis, colitis, hepatitis, endocrinopathies, immune-related skin adverse reactions, nephritis 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**: **GARNET: Dostarlimab monotherapy study for 2L EC (dMMR/MSI-H EC patients N=153)** In subjects with dMMR/MSI-H EC, 59 (38.6%) subjects experienced potential irARs and 42 (27.5%) subjects reported treatment-related irARs. Grade ≥3 irARs were reported in 20 (13.1%) subjects, SAEs were reported in 16 (10.5%) subjects, and irARs leading to permanent treatment discontinuation were reported in 14 (9.2%) subjects. **RUBY: Dostarlimab combination therapy for 1L EC (Part 1; All EC patients N= 241 and dMMR/MSI-H EC patients N= 52)** In all EC patients receiving dostarlimab plus carboplatin and paclitaxel, 137 (56.8%) experienced irARs and 92 (38.2%) reported treatment-related irARs. Grade ≥3 irARs were reported in 40 (16.6%) patients, SAEs were reported in 14 (5.8%) patients, and irARs leading to permanent treatment discontinuation were reported in 19 (7.9%) subjects. In dMMR/MSI-H EC patients receiving dostarlimab plus carboplatin and paclitaxel, 38 (73.1%) experienced potential irARs and 25 (48.1%) reported treatment-related irARs. Grade ≥3 irARs were reported in 10 (19.2%) patients, SAEs were reported in 2 (3.8%) patients, and irARs leading to permanent treatment discontinuation were reported in 2 (3.8%) 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

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 study is a condition of the marketing authorisation:

RUBY, a randomized, double blind Phase III multicenter study of dostarlimab in combination with carboplatin and paclitaxel versus carboplatin and paclitaxel 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 carboplatin and paclitaxel 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.