Summary of the risk management plan for Herwenda

This is a summary of the RMP for Herwenda, a biosimilar to Herceptin. The RMP details important risks of Herwenda, how these risks can be minimized, and how more information will be obtained about Herwenda's risks and uncertainties (missing information).

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

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

I. The medicine and what it is used for

Herwenda was developed as a biosimilar to the reference product Herceptin, and the proposed indications, dosage, and route of administration for Herwenda are identical to those for Herceptin. Comparable efficacy, safety, PK, PD and immunogenicity of Herwenda with Herceptin had been demonstrated during the development program including data derived from analytical, animal, and clinical studies. Therefore, the benefit and risks of Herwenda are comparable to those of Herceptin.

Herwenda is authorized for metastatic breast cancer (MBC), early breast cancer (EBC) and metastatic gastric cancer (MGC) (see SmPC for the full indication). It contains trastuzumab as the active substance and it is given by intravenous infusion.

Further information about the evaluation of Hervenda's benefits can be found in Herwenda'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/herwenda

II. Risks associated with the medicine and activities to minimize or further characterize the risks

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

Measures to minimize 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 authorized 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 minimize its risks.

Together, these measures constitute routine risk minimization measures.

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

II.A. List of important risks and missing information

Important risks of Herwenda are risks that need special risk management activities to further investigate or minimize 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 Herwenda. 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).

There is currently no missing information for trastuzumab.

List of important risks and missing information

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Important identified risks	Cardiac dysfunction Administration-related reactions Oligohydramnios
Important potential risks	Medication error (subcutaneous administration)
Missing information	None

II.B. Summary of important risks

The safety information in the proposed SmPC is aligned to the reference product Herceptin.

Important identified risk: Cardiac dysfunction

Evidence for linking the risk to the medicine	EG12014 and Herceptin clinical trial data, Herceptin RMP and Herceptin product labels.
Risk factors and risk groups	Patient with Early Breast Cancer (EBC) and Metastatic Breast Cancer (MBC). The risk factors described for the development of trastuzumab-induced cardiotoxicity include age >50 years, borderline LVEF before trastuzumab treatment, history of cardiovascular disease, cardiovascular risk factors such as diabetes, dyslipidaemia or elevated body mass index (>30), sequence in which chemotherapy is administered and prior treatment with anthracyclines (cumulative doses >300 mg/m^2).
Risk minimisation measures	Routine risk minimization measures: SmPC section 4.2, 4.4 and 4.8 Additional risk minimization measures: None

Important identified risk: Administration-related reactions

Evidence for linking the risk to the medicine	EG12014 and Herceptin clinical trial data, Herceptin RMP and Herceptin product labels.
Risk factors and risk groups	No risk groups or risk factors are known. However, patients with dyspnoea at rest due to complications of advanced

	malignancy and comorbidities may be at increased risk of severe reactions including fatal outcomes.
Risk minimisation measures	Routine risk minimization measures: SmPC section 4.2, 4.4 and 4.8 Additional risk minimization measures: none

Important identified risk: Oligohydramnios

Evidence for linking the risk to the medicine	EG12014 and Herceptin clinical trial data, Herceptin RMP and Herceptin product labels.
Risk factors and risk groups	There are no reliable indicators of patients who may or may not be at risk.
Risk minimisation measures	Routine risk minimization measures: SmPC section 4.6 and 4.8 Targeted questionnaire for follow-up of any reports of pregnancy to further characterize the risk and analyse any adverse event of foetal harm for causal factors. Additional risk minimization measures: none

Important potential risk: Medication error (subcutaneous administration)

Evidence for linking the risk to the medicine	Herwenda is only available as a formulation for IV administration. while the reference medicinal product, Herceptin is available both as formulation for IV and for SC administration. Herceptin RMP and Herceptin product labels
Risk factors and risk groups	There are no reliable indicators of patients who may or may not be at risk.
Risk minimisation measures	Routine risk minimization measures: SmPC section 4.2 Targeted questionnaire for follow-up of any reports of medication errors to further characterize the risk. Additional risk minimization measures: none

II.C. Post-authorization development plan

Not applicable.

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

There are no studies which are conditions of the marketing authorization or specific obligation of Herwenda.

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

There are no studies required for Herwenda.