HERCEPTIN®

Pulver für ein Konzentrat zur Herstellung einer Infusionslösung, Zul.-Nr. 55’065

HERCEPTIN®subkutan

Lösung zur subkutanen Injektion, Zul.-Nr. 65’964

Public Risk Management Plan (RMP) Summary

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The Risk Management Plan (RMP) is a comprehensive document submitted as part of the application dossier for market approval of a medicinal products. 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 “Herceptin” 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 “Herceptin” in Switzerland is the “Arzneimittelinformation / Information sur le médicament” (see www.swissmedic.ch) approved and authorized by Swissmedic. “Roche Pharma (Schweiz) AG” is fully responsible for the accuracy and correctness of the content of the published summary RMP of Herceptin.

PART VI: SUMMARY OF THE RISK MANAGEMENT PLAN

SUMMARY OF RISK MANAGEMENT PLAN FOR HERCEPTIN

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

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

This summary of the RMP for Herceptin® 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 Herceptin® RMP.

I. THE MEDICINE AND WHAT IT IS USED FOR

Herceptin® 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 and subcutaneous.

Further information about the evaluation of Herceptin® benefits can be found in Herceptin® EPAR, including in its plain-language summary, available on the European Medicines Agency (EMA) website, under the medicine's webpage

http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/human/medicines/000278/human_med_000818.jsp&mid=WC0b01ac058001d124

II. RISKS ASSOCIATED WITH THE MEDICINE AND ACTIVITIES TO MINIMIZE OR FURTHER CHARACTERIZE THE RISKS

Important risks of Herceptin®, together with measures to minimize such risks and the proposed studies for learning more about Herceptin® 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 the case of Herceptin®, these measures are supplemented with *additional risk minimization* measures mentioned under relevant risks, below.

In addition to these measures, information about adverse events is collected continuously and regularly analyzed: 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 Herceptin® 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 Herceptin®. 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	Cardiac dysfunction Administration-Related Reactions (ARRs) Oligohydramnios
Important potential risks	None
Missing information	None

II.B Summary of Important Risks

Important Identified Risk	
Cardiac dysfunction	
Evidence for linking the risk to the medicine	MBC: M77001 and BO16216. EBC: Joint Analysis (NSABP B-31 and NCCTG N9831), BCIRG 006 (H2296s)/GO00773, BO16348, MO16432, BO22227, MO22982, MO28048 GC: BO18255. QTc-study H4613g (HerQLes). Global Safety Database
Risk factors and risk groups	Patient with Early Breast Cancer (EBC)
Risk minimization measures	**Routine risk communication:** SmPC Section 4.4 Warnings and Precautions for Use SmPC Section 4.8 Undesirable effects **Routine risk minimization activities recommending specific clinical measures to address the risk:** Monitoring to identify patients who develop cardiac dysfunction and clinical recommendation algorithm to deal with LVEF decreases that are associated with the cardiac dysfunction has been adequately covered in Section 4.4 of SmPC **Other risk minimization measures beyond the Product Information:** Pack size: Each carton contains one vial Legal Status: Herceptin is a prescription only medicine **Additional risk minimization measures:** None
Additional pharmacovigilance activities	Additional pharmacovigilance activities: None

Important Identified Risk	
Administration-Related Reactions (ARRs)	
Evidence for linking the risk to the medicine	EBC: Studies BO16348, BO22227, MO22982, and MO28048. Global Safety Database. Drug Safety Reports, DSR 1036301 dated 12 December 2009, DSR 1056779 dated 27 June 2013 and DSR 1060413 dated 15 May 2014
Risk factors and risk groups	There are currently no reliable predictors of patients who may or may not be susceptible to administration related reactions to Herceptin. However, the SPC indicates that patients, who are experiencing dyspnea at rest due to complications of advanced malignancy or co-morbidities, may be at greater risk of severe reactions including fatal outcomes.
Risk minimization measures	**Routine risk communication:** SmPC Section 4.2 Posology and Method of Administration SmPC Section 4.4 Warnings and Precautions for Use SmPC Section 4.8 Undesirable effects **Routine risk minimization activities recommending specific clinical measures to address the risk**: Guidance on observation period after administration has been adequately captured in Section 4.2 of E.U. SmPC. **Other risk minimization measures beyond the Product Information**: Pack Size: Each carton contains one vial Legal Status: Herceptin is a prescription only medicine. *Additional risk minimization measures:* No risk minimization measures
Additional pharmacovigilance activities	There are no additional pharmacovigilance activities

Important Identified Risk	
Oligohydramnios	
Evidence for linking the risk to the medicine	Global Safety Database, Drug safety reports #1030381, 1040470 and 10156279. Pregnancy registry MotHER [H4621g/GE28099 is closed].
Risk factors and risk groups	There are no reliable indicators of patients who may or may not be at risk
Risk minimization measures	**Routine risk communication:** SmPC Section 4.6 Fertility, pregnancy and lactation **Routine risk minimization activities recommending specific clinical measures to address the risk:** If a pregnant woman is treated with Herceptin or if a patient becomes pregnant while receiving Herceptin or within 7 months following last dose of Herceptin, close monitoring by a multidisciplinary team is desirable. This has been captured in Section 4.6 of E.U. SmPC. **Other risk minimization measures beyond the Product Information:** Pack size: Each carton contains one vial Legal Status: Herceptin is a prescription only medicine *Additional risk minimization measures:* No risk minimization measures
Additional pharmacovigilance activities	Additional pharmacovigilance activities: None

II.C Post-Authorization Development Plan

II.C.1 Studies That Are Conditions of the Marketing Authorization

Not applicable.

II.C.2 Other Studies in Post-Authorization Development Plan

Not Applicable