

SUMMARY OF THE RISK MANAGEMENT PLAN

FOR

TRAZIMERA[®] 21mg/mL (TRASTUZUMAB)

Powder for concentrate for solution for infusion

This RMP Summary is based on Part VI of the EU RMP for Trazimera (Trastuzumab) version 1.2, dated 19-April-2018

SUMMARY OF THE RISK MANAGEMENT PLAN

Summary of risk management plan for Trazimera (Trastuzumab)

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 Trazimera 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 Trazimera in Switzerland is the “Arzneimittelinformation / Information sur le médicament” (see www.swissmedic.ch) approved and authorized by Swissmedic.

Pfizer PFE Switzerland GmbH is fully responsible for the accuracy and correctness of the content of the published summary RMP of Trazimera.

I. The Medicine and What It Is Used For

Trazimera has been developed as a biosimilar to Herceptin (trastuzumab). The comparable efficacy, safety, PK, pharmacodynamics, and immunogenicity of Trazimera with Herceptin had been demonstrated during the development programme. Therefore, the treatment benefits of Trazimera are comparable to those of Herceptin. It is intended for the treatment of Metastatic Breast cancer (MBC), Early Breast cancer (EBC) and Metastatic Gastric Cancer (MGC) (see the Information for Professionals for the full indication). It contains trastuzumab as the active substance and it is given by intravenous (IV) infusion.

II. Risks Associated With the Medicine and Activities to Minimise or Further Characterise the Risks

Important risks of Trazimera, together with measures to minimise such 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 Information for Professionals 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 public (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 events is collected continuously and regularly analysed 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 Trazimera 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 Trazimera. 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.

Currently, there are no important potential risks for trastuzumab. Missing information refers to information on the safety of the medicinal product that is currently missing and needs to be collected (eg, on the long-term use of the medicine). There is currently no missing information for trastuzumab.

Table 1. List of Important Risks and Missing Information

Important identified risks	Cardiac dysfunction Administration-related reactions Oligohydramnios
Important potential risks	None
Missing information	None

II.B. SUMMARY OF IMPORTANT RISKS

Summary of Important Risks or Missing Information

All medicines have a product information ("Arzneimittelinformation / Information sur le médicament") which provides physicians, pharmacists and other health care professionals with details on how to use the medicine, the risks and recommendations for minimising them. The measures in these documents are known as routine risk minimisation measures.

The product information for Trazimera can be found on www.swissmedicinfo.ch.

This medicine has no additional risk minimisation measures.

Table 2. Important Identified Risks

Cardiac Dysfunction	
Evidence for linking the risk to the medicine	Trastuzumab and Herceptin clinical trial data, Herceptin RMP and Herceptin product labels.
Risk factors and risk groups	<p>General considerations Patients treated with trastuzumab are at increased risk for developing congestive heart failure (CHF) (New York Heart Association [NYHA] class II-IV) or asymptomatic cardiac dysfunction. These events have been observed in patients receiving trastuzumab therapy alone or in combination with Paclitaxel or Docetaxel, particularly following anthracycline (doxorubicin or epirubicin) containing chemotherapy. These may be moderate to severe and have been associated with death. In addition, caution should be exercised in treating patients with increased cardiac risk, eg hypertension, documented coronary artery disease, CHF, Left Ventricular Ejection Fraction (LVEF) of <55%, older age.</p> <p>Metastatic Breast Cancer (MBC) Patients with MBC who have previously received anthracyclines are at increased risk of cardiac dysfunction with trastuzumab treatment.</p> <p>Early Breast Cancer (EBC) In adjuvant and neoadjuvant EBC setting, the patients with history of myocardial infarction (MI), angina pectoris requiring medical treatment, history of or existing CHF (NYHA II–IV), LVEF of < 55%, other cardiomyopathy, cardiac arrhythmia requiring medical treatment, clinically significant cardiac valvular disease, poorly controlled hypertension (hypertension controlled by standard medical treatment eligible), and haemodynamic effective pericardial effusion are at are increased risk of cardiac dysfunction, therefore treatment cannot be recommended in such patients.</p> <p>In patients with EBC an increase in the incidence of symptomatic and asymptomatic cardiac events was observed when trastuzumab was administered after anthracycline-containing chemotherapy compared to administration with a non-anthracycline regimen of Docetaxel and Carboplatin and was more marked when trastuzumab was administered concurrently with taxanes than when administered sequentially to taxanes. Regardless of the regimen used, most symptomatic cardiac events occurred within the first 18 months.</p> <p>Risk factors for a cardiac event identified in 4 large adjuvant studies included advanced age (> 50 years), low LVEF (<55%) at baseline, prior to or following the initiation of Paclitaxel treatment, decline in LVEF by 10-15 points, and prior or concurrent use of anti-hypertensive medicinal products. In patients receiving trastuzumab after completion of adjuvant chemotherapy the risk of cardiac dysfunction was associated with a higher cumulative dose of anthracycline given prior to initiation of trastuzumab and a Body Mass Index (BMI) >25 kg/m².</p>

Table 2. Important Identified Risks

Cardiac Dysfunction	
Administration-Related Reactions	
Evidence for linking the risk to the medicine	Trazimera and Herceptin clinical trial data, Herceptin RMP and Herceptin product labels.
Risk factors and risk groups	There are currently no reliable predictors of patients who may or may not be susceptible to Administration-Related Reactions (ARRs) to trastuzumab. However, patients, who are experiencing dyspnoea at rest due to complications of advanced malignancy or co-morbidities, may be at greater risk of severe reactions including fatal outcomes.
Oligohydramnios	
Evidence for linking the risk to the medicine	Trazimera 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.

II.C. POST-AUTHORISATION DEVELOPMENT PLAN

Not applicable.