PUBLIC SUMMARY OF THE RISK MANAGEMENT PLAN

HYMPAVZI (Marstacimab)

Marketing Authorization Number 69556

Solution for injection in pre-filled pen; 150 mg/ml

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LIST OF ABBREVIATIONS

EMA	European Medicines Agency
EPAR	European Public Assessment Report
EU	European Union
NO	Nitric Oxide
PL	Package leaflet
PSUR	Periodic Safety Update Report
RMP	Risk Management Plan
SC	Subcutaneous
SmPC	Summary of Product Characteristics (Europe)
SoC	Standard of Care
TFPI	Tissue Factor Pathway Inhibitor

OVERVIEW

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 for Hympavzi 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 marketing authorization.

Please note that the reference document which is valid and relevant for the effective and safe use of Hympavzi in Switzerland is the "Arzneimittelinformation / Information sur le médicament" (see www.swissmedic.ch) approved and authorised by Swissmedic. Pfizer is fully responsible for the accuracy and correctness of the content of the published RMP summary of Hympavzi.

SUMMARY OF RISK MANAGEMENT PLAN FOR HYMPAVZI (MARSTACIMAB)

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

Hympavzi's Summary of Product Characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how Hympavzi should be used.

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

I. The Medicine and What It Is Used For

Hympavzi is authorised for

- Routine prophylaxis of bleeding episodes in patients 12 years of age and older, weighing at least 35 kg, with severe haemophilia A (congenital factor VIII deficiency, FVIII <1%) without FVIII inhibitors, and

- Routine prophylaxis of bleeding episodes in patients 12 years of age and older, weighing at least 35 kg, with severe haemophilia B (congenital factor IX deficiency, FIX <1%) without FIX inhibitors).

It contains marstacimab as the active substance and it is intended for SC administration.

Further information about the evaluation of Hympavzi's benefits can be found in Hympavz's EPAR, including in its plain-language summary, available on the EMA website, under the medicine's webpage link to the EPAR summary landing page.

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

Important risks of Hympavzi, together with measures to minimise such risks and the proposed studies for learning more about Hympavzi'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 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 Hympavzi are risks that need special risk management activities to further investigate or minimise the risk, so that the medicinal product can be safely taken.

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 Hympavzi. 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);

Table 1. List of important risks and missing information

Important identified risks	Thromboembolism*
Important potential risks	Thromboembolism
Missing information	None

* Important identified risk as requested by Swissmedic. Applies to Switzerland only.

II.B. Summary of Important Risks

Table 2. Important Potential Risk: Thromboembolism*

Evidence for linking the risk to the medicine	No cases of thromboembolic events were observed in haemophilia patients receiving marstacimab prophylaxis. The use of other anti-tissue factor pathway inhibitor (anti-TFPI) products has been associated with the development of thromboembolic complications.
Risk factors and risk groups	The incidence of venous thromboembolism and its complications increases with age: 1 case per 1,000,000 children aged<15 years; 72.4 cases per 100,000 adults aged 40 to 54 years; and 280 cases per 100,000 person who are from 85 to 89 years of age. Age-related changes occur in the vascular and haemostatic system, affecting platelet activity, coagulation factors, and coagulation inhibitors, as well as the endothelium. The fibrinolytic system is also impaired by aging, as is shown by increased levels of plasminogen activator inhibitor, which positively correlate with age-related pathological conditions such as diabetes, insulin resistance, and atherosclerosis. Advanced age is also accompanied by vessel stiffness and dilatation due to the degeneration of elastic fibres and increased collagen content and associated with a reduced expression of nitric oxide synthase thus leading to reduced NO production, which may contribute to platelet activation and thrombosis. Hyper-coagulability and vascular wall changes together may increase the incidence of thrombotic events and pulmonary thromboembolism in the elderly patients. Refer to SVII 3.1
Risk minimisation measures	Routine risk minimisation measures:** SmPC section 4.4 PL sections 2 Additional risk minimisation measures: None

Table 2. Important Potential Risk: Thromboembolism*

Additional pharmacovigilance activities	Additional pharmacovigilance activities: Short study name B7841016: A Post-Authorisation Safety Study to Evaluate the Safety of Marstacimab Among Patients with Severe Haemophilia A or B using Real-World Data in European Haemophilia Registers See section II.C of this summary for an overview of the post-authorisation development plan.

* Important identified risk as requested by Swissmedic. Applies to Switzerland only.
** For Switzerland only, the following applies: Presentation of relevant safety information in the local product prescribing information for healthcare professionals and in the local patient information.

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:

There are no studies, which are conditions of the marketing authorisation or specific obligation of marstacimab.

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

Study short name

B7841016: A Post-Authorisation Safety Study to Evaluate the Safety of Marstacimab Among Patients with Severe Haemophilia A or B using Real-World Data in European Haemophilia Registers.

Purpose of the study:

Based on animal studies and clinical trials, thromboembolic events are an important potential risk associated with the use of marstacimab. To assess the potential risk of this primary safety event of interest among patients with severe haemophilia A or B who are treated with marstacimab in the real-world in Europe, an active surveillance study using data from several European haemophilia registers is proposed.

The primary study objective is:

- To evaluate the incidence rate of thromboembolic events among patients with severe haemophilia A or B in the patient cohort treated with marstacimab during routine clinical care.

The secondary study objective is:

- To evaluate the incidence rate of thromboembolic events among patients with severe haemophilia A or B in the patient cohort unexposed to marstacimab and receiving standard-of-care (SoC) treatment (e.g., prophylaxis factor replacement).

- To describe clinical characteristics of patients (exposed to marstacimab and unexposed to marstacimab and receiving standard-of-care treatment [e.g., prophylaxis factor replacement]) who experience a thromboembolic event.

The safety event of interest, noted above, is based on current understanding of identified and potential risks with marstacimab. However, other safety events may be added/updated as understanding of the safety profile of marstacimab evolves and feasibility of their assessment permits.