Swiss Summary of the Risk Management Plan (RMP)

Winrevair®

(Sotatercept for Subcutaneous Injection)

Active substance(s): Sotatercept

Product(s) concerned: WINREVAIR®

Based on EU-RMP V1.0

Version 1.0 (October 2024)

Marketing Authorisation Holder: MSD Merck Sharp & Dohme AG, Lucerne

Disclaimer:

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 Winrevair® 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 Winrevair® in Switzerland is the «Arzneimittelinformation/ Information sur le médicament» (see www.swissmedic.ch) approved and authorized by Swissmedic. MSD Merck Sharp and Dohme AG is fully responsible for the accuracy and correctness of the content of the published summary RMP of Winrevair®.

Summary of risk management plan for Winrevair (sotatercept)

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

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

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

I. The Medicine and What it is Used for

Winrevair is authorised for the treatment of pulmonary arterial hypertension (PAH) in adults. PAH is a type of high blood pressure in the arteries of your lungs (see SmPC for the full indication). It contains sotatercept as the active substance, and it is given subcutaneously (as an injection just under the skin).

Further information about the evaluation of Winrevair's benefits can be found in Winrevair's EPAR, including in its plain-language summary, available on the European Medicines Agency (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 Characterize the Risks

Important risks of Winrevair, together with measures to minimise such risks and the proposed studies for learning more about risks of Winrevair, 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 (eg, 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 analyzed 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 Winrevair is not yet available, it is listed under 'missing information' below.

II.A List of Important Risks and Missing Information

Important risks of Winrevair 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 Winrevair. 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 II.A.1: List of Important Risks and Missing Information

List of Important Risks and Missing Information	
Important identified risks	Erythrocytosis
Important potential risks	Severe thrombocytopenia
	Embryo-foetal toxicity
Missing information	Long-term safety

II.B Summary of Important Risks

The safety information in the product labeling is aligned to the reference medicinal product.

Table II.B.1: Important Identified Risk: Erythrocytosis

Evidence for linking the risk to the medicine	Mechanism of action: strong evidence Animal studies: moderate evidence Clinical studies: strong evidence
Risk factors and risk groups	Increased hemoglobin (a molecule in the blood that carries oxygen) can cause the blood to become thicker than usual, which could lead to blood clotting in the blood vessels. Therefore, patients with increased hemoglobin and a history of blood clots may be at increased risk for developing blood clots that could break off and block another blood vessel.
Risk minimisation measures	**Routine risk minimisation measures:** SmPC Sections 4.2 Posology and method of administration, 4.4 Special warnings and precautions for use, and 4.8 Undesirable effects. Package leaflet Section 2 What you need to know before you use Winrevair and Section 4 Possible side effects. **Additional risk minimisation measures:** None.

Table II.B.2: Important Potential Risk: Severe Thrombocytopenia

Evidence for linking the risk to the medicine	Animal studies: weak evidence Clinical studies: moderate evidence
Risk factors and risk groups	From published research, men with idiopathic PAH (PAH of unknown cause) are more likely than women to have thrombocytopenia (a decrease in platelet count [cells involved in forming blood clots]). Thrombocytopenia is associated with the use of prostacyclin analogues, medications used to treat PAH.
Risk minimisation measures	**Routine risk minimisation measures:** SmPC Sections 4.2 Posology and method of administration, 4.3 Contraindications, 4.4 Special warnings and precautions for use, and 4.8 Undesirable effects. Package leaflet Section 2 What you need to know before you use Winrevair and Section 4 Possible side effects. **Additional risk minimisation measures:** None.

Table II.B.3: Important Potential Risk: Embryo-foetal Toxicity

Evidence for linking the risk to the medicine	Animal studies: strong evidence
Risk factors and risk groups	Women of child-bearing potential who do not adhere to using effective contraception.
Risk minimisation measures	**Routine risk minimisation measures:** SmPC Section 4.6 Fertility, pregnancy and lactation. Package leaflet Section 2 What you need to know before you use Winrevair. **Additional risk minimisation measures:** None.

Table II.B.4: Missing Information: Long-term Safety

Risk minimisation measures	**Routine risk minimisation measures:** SmPC Section 4.8 Undesirable effects. **Additional risk minimisation measures:** None.
Additional pharmacovigilance activities	**Additional pharmacovigilance activities:** SOTERIA.

II.C Post-Authorisation Development Plan

II.C.1 Studies Which are Conditions of the Marketing Authorisation

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

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

One clinical trial is being conducted to address missing information.

1) SOTERIA

Purpose of the study:

SOTERIA is being conducted to assess the long-term safety, tolerability, and efficacy of sotatercept in PAH.

The primary objective of this long-term follow-up study is to evaluate the long-term safety and tolerability of sotatercept when added to background PAH therapy in adult participants with PAH. The secondary objective is to follow participants from parent sotatercept studies that were treated with sotatercept or placebo and assess continued efficacy.