PART VI: SUMMARY OF THE RISK MANAGEMENT PLAN

Summary of risk management plan for Treprostinil Tillomed 1 mg/ml, 2.5 mg/ml, 5 mg/ml and 10 mg/ml solution for infusion (herein referred as Treprostinil solution for infusion):

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

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

Important new concerns or changes to the current ones will be included in updates of Treprostinil solution for infusion's RMP.

I. The medicine and what it is used for

Treprostinil solution for infusion is indicated in therapy of idiopathic or hereditary Pulmonary Arterial Hypertension (PAH) to improve tolerance and symptoms of the disease in patients classified as New York Heart Association (NYHA) Class III.

Treprostinil solution for infusion contains treprostinil sodium as the active substance and it is given by subcutaneous (under the skin) or intravenous (directly into a vein) route.

II. Risks associated with the medicine and activities to minimise or further characterise the risks

Important risks of Treprostinil solution for infusion, together with measures to minimise such risks and the proposed studies for learning more about Treprostinil solution for infusion'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 PL and SmPC addressed to patients and health care 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 the case of Treprostinil solution for infusion, these measures are supplemented with *additional risk minimisation measures* mentioned under relevant important risks, below.

In addition to these measures, information about adverse reactions is collected continuously and regularly analysed, 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 Treprostinil solution for infusion is not yet available, it is listed under 'missing information' below.

II.A List of important risks and missing information

Important risks of Treprostinil solution for infusion 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 Treprostinil solution for infusion. 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	• Risks attributable to Drug delivery system: CVC-related BSIs and sepsis (IV) • Safety in patients with hepatic dysfunction/insufficiency • Systemic hypotension • Abrupt withdrawal or sudden large dose reduction
Important potential risks	• Bleeding tendencies • Co-administration with CYP2C8 inhibitors/inducers
Missing information	• Safety of use in patients over the age of 65 years • Safety of use in patients less than 18 years of age • Safety of use in patients with renal dysfunction • Effects of treprostinil infusion therapy on pregnancy, pregnancy outcome, labor and delivery, lactation

II.B Summary of important risks

Risks attributable to Drug delivery system: CVC-related BSIs and sepsis (IV)	
Risk minimisation measures	**Routine risk minimisation measures:** • SmPC sections 4.2, 4.4 and 4.8 • PL sections 2, 3 and 4 • SmPC section 4.4 mention that the therapy physician must ensure that the patient is fully instructed in the operation of the selected infusion set • Prescription only medicine **Additional risk minimisation measures:**

	• Educational material in the form of: o Patient brochure o Patient questionnaire o HCP training programme o Events of Special Interest report form for doctors to complete in the event of them becoming aware of a CVC related BSI

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 Treprostinil solution for infusion.

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

There are no studies required for Treprostinil solution for infusion.