Remodulin®

Infusionslösung

Active substance: Treprostinil

Summary of the Risk Management Plan (RMP)

Based on EU-RMP V7.0
Version 2.0 (October 2023)
Marketing Authorisation Holder: Gebro Pharma AG, Liestal

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 "Remodulin" 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 "Remodulin" in Switzerland is the "Arzneimittelinformation/ Information sur le médicament" (see www.swissmedic.ch) approved and authorized by Swissmedic. "Name of the marketing authorisation holder" is fully responsible for the accuracy and correctness of the content of the published summary RMP of "Remodulin".

Part VI: Summary of the Risk Management Plan

Summary of risk management plan for REMODULIN (Treprostinil)

This is a summary of the RMP for Remodulin (treprostinil). The RMP details important risks of Remodulin, how these risks can be minimized, and how more information will be obtained about Remodulin's risks and uncertainties (missing information).

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

I. The medicine and what it is used for

Remodulin is authorized for treatment of idiopathic or heritable PAH to improve exercise tolerance and symptoms of the disease in patients classified as NYHA FC class III (see SmPC for the full indication). It contains treprostinil as the active substance and it is given by solution for infusion in 1 mg/mL, 2.5 mg/mL, 5 mg/mL, and 10 mg/mL via SC or IV routes.

II. Risks associated with the medicine and activities to minimize or further characterize the risks

Important risks of Remodulin, together with measures to minimize such risks and the proposed studies for learning more about Remodulin'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 the case of Remodulin, 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, including PSUR assessment 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 Remodulin is not yet available, it is listed under ‘missing information’ below.

II.A List of important risks and missing information

Important risks of Remodulin 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 Remodulin. 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: central venous catheter (CVC)-related bloodstream infections (BSIs) and sepsis (IV)
Important potential risks	None.
Missing information	None.

II.B Summary of important risks

Important identified risk: Risks attributable to Drug Delivery System: Central venous catheter (CVC) related bloodstream infections (BSIs) and sepsis (IV)	
Evidence for linking the risk to the medicine	A CDC retrospective survey of seven centers in the United States that used IV Remodulin for the treatment of PAH found an incidence rate for catheter-related BSIs of 1.1 events per 1000 catheter days. Since utilizing the classification "Bloodstream infection – ESI" in 2017, a total of 233 case reports (1 from clinical studies, 232 from the post-marketing setting) describing 402 events pertaining to BSIs and sepsis with IV treprostinil have been identified. Section 3 of the RSI for SC/IV treprostinil states that "Chronic IV infusions of treprostinil delivered using an external infusion pump with an indwelling CVC are associated with risk of BSIs and sepsis, which may be fatal". CVC related BSIs are therefore considered an important identified risk for IV treprostinil.
Risk factors and risk groups	All patients with an indwelling CVC used for chronic, continuous administration of IV medication are at risk of developing catheter-related BSI. The level of risk varies between patients and is dependent on a number of factors, particularly the attention paid to scrupulous infection control procedures during manipulation of the medication reservoir and infusion delivery system.
Risk minimization measures	Routine risk minimization measures: *SmPC Section 4.2 provides advice on minimizing the risk of CVC-BSIs* *SmPC Section 4.4 indicates that the preferred method of drug delivery is via SC infusion based on the CVC-BSI risk.* Additional risk minimization measures:

	General catheter care based on international catheter care guidelines for Remodulin and Flolan provided by the US Pulmonary Hypertension Association *Recommendations include:* - *To protect the catheter and connecting device with an impermeable cover during a shower.* - *hand hygiene.* - *catheter hub instructions, including use of a closed-hub system and prostanoid reconstitution and administration guidelines* *Materials used to convey these recommendations include:* - *Slide lecture kit for doctors and nurses that presents CVC-related BSI risk minimization techniques and best practice recommendations* - *Patient brochure for patients started on IV administration* - *Dear Doctor Letter to be sent to all potential prescribers informing them of the risks* - *Patient Questionnaire on practicalities of CVC-related BSI prevention techniques* - *Events of Special Interest report form for doctors to complete in the event of them becoming aware of a CVC-related BSI.*
Additional pharmacovigilance activities	None.

II.C Post-authorization development plan

II.C.1 Studies which are conditions of the marketing authorization

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

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

None.