OrPha Swiss

Summary of the Risk Management Plan (RMP)

for

RAPIBLOC (landiolol hydrochloride)

Injektionslösung im Fertigpen

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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 "Bezeichnung des Arzneimittels" 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 Rapibloc in Switzerland is the "Arzneimittelinformation/ Information sur le médicament" (see www.swissmedic.ch) approved and authorized by Swissmedic. OrPha Swiss GmbH is fully responsible for the accuracy and correctness of the content of the published summary RMP of Rapibloc.

Part VI: Summary of the risk management plan

Summary of risk management plan for Rapibloc 300 mg powder for solution for infusion

This is a summary of the risk management plan (RMP) for Rapibloc 300 mg powder for solution for infusion.

The RMP details important risks of Rapibloc 300 mg powder for solution for infusion and how more information will be obtained about Rapibloc 300 mg powder for solution for infusion, risks and uncertainties (missing information).

Rapibloc 300 mg powder for solution for infusion summary of product characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how Rapibloc 300 mg powder for solution for infusion should be used.

Important new concerns or changes to the current ones will be included in updates of Rapibloc 300 mg powder for solution for infusion RMP.

I. The medicine and what it is used for

Rapibloc 300 mg powder for solution for infusion are indicated for:

- Supraventricular tachycardia and for the rapid control of ventricular rate in patients with atrial fibrillation or atrial flutter in perioperative, postoperative, or other circumstances where short-term control of the ventricular rate with a short acting agent is desirable.
- Non-compensatory sinus tachycardia where, in the physician's judgment the rapid heart rate requires specific intervention.

Landiolol HCl is not intended for use in chronic settings.

It contains the active substance landiolol hydrochloride and is intended for i.v. use in a monitored setting.

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

Important risks of Rapibloc 300 mg powder for solution for infusion, , 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 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.

If important information that may affect the safe use of Rapibloc 300 mg powder for 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 Rapibloc 300 mg powder for 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 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 Rapibloc 300 mg powder for 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).

Summary of safety concerns	
Important identified risks	• Severe hypotension • Severe bradycardia • Cardiac arrest
Important potential risks	• None
Missing information	• Use in paediatric population (<18 years old) • Use in pregnancy and breastfeeding

II.B Summary of important risks

Important identified risk 1: Severe hypotension	
Evidence for linking the risk to the medicine	Hypotension has been frequently reported with landiolol in published clinical trials, post-marketing experience, including published results of the post-marketing survey. The effect is rapidly reversible with dosage reduction or discontinuation. Close monitoring of the heart rate, ECG and blood pressure and dosage adjustment or discontinuation, if required, is recommended.
Risk factors and risk groups	Patients with hypotension or with small circulating blood volume, e.g. due to heavy bleeding during surgery.
Risk minimisation measures	<u>Routine risk minimisation measures:</u> • SmPC sections “Posology and method of administration”, “Contraindications”, “Warnings and precautions, “Interactions”, “Undesirable effects”, “Overdose” • PL sections “Warnings and precautions, “How the product is given”, “Side effects” • Legal status: Prescription only medicine (POM) • Used only by well-qualified health care professional in a monitored setting <u>Additional risk minimisation measures:</u> • No risk minimisation measures.

Important identified risk 2: Severe bradycardia	
Evidence for linking the risk to the medicine	Bradycardia has been frequently reported with landiolol in published clinical trials, post-marketing experience, including published results of the post-marketing survey. The effect is rapidly reversible with dosage reduction or discontinuation. Close monitoring of the heart rate, ECG and blood pressure and dosage adjustment or discontinuation, if required, is recommended.
Risk factors and risk groups	Patients with a history of cardiac diseases

Important identified risk 2: Severe bradycardia	
Risk minimisation measures	Routine risk minimisation measures: • SmPC sections "Posology and method of administration", "Contraindications", "Warnings and precautions, "Interactions", "Undesirable effects", "Overdose" • PL sections "Warnings and precautions, "How the product is given", "Side effects" • Legal status: Prescription only medicine (POM) • Used only by well-qualified health care professional in a monitored setting Additional risk minimisation measures: • No risk minimisation measures.

Important identified risk 3: Cardiac arrest	
Evidence for linking the risk to the medicine	Cardiac arrest has been reported from clinical trials and post-marketing surveillance for landiolol treatment and were mainly associated with elderly patients or with patients having hypertension or cardiac diseases as complications. Close monitoring of the heart rate, ECG and blood pressure and dosage adjustment or discontinuation, if required, is recommended.
Risk factors and risk groups	Elderly patients, patients having hypertension or cardiac diseases.
Risk minimisation measures	Routine risk minimisation measures: • SmPC sections "Posology and method of administration", "Contraindications", "Warnings and precautions, "Interactions", "Undesirable effects", "Overdose" • PL sections "Warnings and precautions, "How the product is given", "Side effects" • Legal status: Prescription only medicine (POM) • Used only by well-qualified health care professional in a monitored setting Additional risk minimisation measures: • No risk minimisation measures.

Missing information 1: Use in paediatric population (<18 years old)	
Evidence for linking the risk to the medicine	The safety and efficacy of landiolol HCl in children aged 0 to 18 years have not yet been established. Rapibloc Conc is not foreseen to be used in the paediatric population, due to its high ethanol content.
Risk factors and risk groups	Paediatric population
Risk minimisation measures	Routine risk minimisation measures: • SmPC sections "Posology and method of administration", "Warnings and precautions", • PL section "How the product is given", • Legal status: Prescription only medicine (POM) • Used only by well-qualified health care professional in a monitored setting Additional risk minimisation measures: • No risk minimisation measures.

Missing information 2: Use in pregnancy and breastfeeding	
Evidence for linking the risk to the medicine	There are no adequate data from the use of landiolol HCl in pregnant/breastfeeding women. Based on the pharmacological action of beta-blocking agents, in the later period of pregnancy, side effects on the foetus and neonate (especially hypoglycaemia, hypotension and bradycardia) should be taken into account. If the treatment with landiolol HCl is considered necessary, the uteroplacental blood flow and foetal growth should be monitored. The new-born must be closely monitored. A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from landiolol HCl therapy taking into account the benefit of breast feeding for the child and the benefit of therapy for the woman.
Risk factors and risk groups	Population of child-bearing potential
Risk minimisation measures	Routine risk minimisation measures: • SmPC section "Warnings and precautions", "Fertility, pregnancy and lactation" • PL section "Fertility, pregnancy and lactation" • Legal status: Prescription only medicine (POM) • Used only by well-qualified health care professional in a monitored setting Additional risk minimisation measures: • No risk minimisation measures.

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 Rapibloc 300 mg powder for solution for infusion.

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

There are no studies required for Rapibloc 300 mg powder for solution for infusion.