EU Risk Management Plan for Levosol, 60 mg / ml, oral drops, solution (Levodropropizine)

RMP version to be assessed as part of this application:

RMP Version number: 0.2

Data lock point for this RMP: 15.12.2023

Date of final sign-off: 18.12.2023

QPPV name: Anna Serefko

QPPV signature:

Table of content

Part I: Product(s) Overview

Table Part I.1 – Product(s) Overview

Active substance(s) (INN or common name)	Levodropropizine
Pharmacotherapeutic group(s) (ATC Code)	ATC code: R05DB27; Cough and Cold Preparations, Cough Suppressants
Marketing Authorisation Applicant	Solinea Sp. z o.o. Sp.K..
Medicinal products to which this RMP refers	1
Invented name(s) in the European Economic Area (EEA)	Levosol, 60 mg / ml, oral drops, solution
Marketing authorisation procedure	National
Brief description of the product	Chemical class: Levodropropizine is a non-opioid peripherally acting antitussive drug that is used as an alternative to opioids
	Summary of mode of action: Levodropropizine exerts its antitussive effect through an inhibitory action at the level of the airway sensory nerves and it has been shown to be able to inhibit in vitro the release of neuropeptides from C-fibers. In addition, in anaesthetized cats, it markedly reduces the activation of C-fibres and abolishes the associated reflexes.
	Important information about its composition: Not applicable
Hyperlink to the Product Information	SmPC Levosol 60mg/ml PIL Levosol 60mg/ml
Indication(s) in the EEA	Current: Symptomatic treatment of cough.
	Proposed (if applicable): Not applicable
Dosage in the EEA	Current: 20 drops (corresponding to 60 mg) up to 3 times a day at intervals of at least 6 hours, unless your doctor tells you otherwise.
	Proposed (if applicable): Not applicable
Pharmaceutical form(s) and strengths	Current (if applicable): 60 mg / ml, oral drops, solution
	Proposed (if applicable):Not applicable
Is/will the product be subject to additional monitoring in the EU?	No

Part II: Safety specification

Part II: Module SI - Epidemiology of the indication(s) and target population(s)

According to the Guideline on Good Pharmacovigilance Practices (GVP) Module V – Risk management system (Rev2) EMA/838713/2011, for initial application, which falls under Article 10(1) of Directive 2001/83/EC, module SI is not required.

Part II: Module SII - Non-clinical part of the safety specification

According to the Guideline on Good Pharmacovigilance Practices (GVP) Module V – Risk management system (Rev2) EMA/838713/2011, for initial application, which falls under Article 10(1) of Directive 2001/83/EC, module SII is not required.

Part II: Module SIII - Clinical trial exposure

According to the Guideline on Good Pharmacovigilance Practices (GVP) Module V – Risk management system (Rev2) EMA/838713/2011, for initial application, which falls under Article 10(1) of Directive 2001/83/EC, module SIII is not required.

Part II: Module SIV - Populations not studied in clinical trials

SIV.1 Exclusion criteria in pivotal clinical studies within the development programme

According to the Guideline on Good Pharmacovigilance Practices (GVP) Module V – Risk management system (Rev2) EMA/838713/2011, for initial application, which falls under Article 10(1) of Directive 2001/83/EC, module SIV.1 is not required.

SIV.2 Limitations to detect adverse reactions in clinical trial development programmes

According to the Guideline on Good Pharmacovigilance Practices (GVP) Module V – Risk management system (Rev2) EMA/838713/2011, for initial application, which falls under Article 10(1) of Directive 2001/83/EC, module SIV.2 is not required.

SIV.3 Limitations in respect to populations typically under-represented in clinical trial development programmes

According to the Guideline on Good Pharmacovigilance Practices (GVP) Module V – Risk management system (Rev2) EMA/838713/2011, for initial application, which falls under Article 10(1) of Directive 2001/83/EC, module SIV.3 is not required.

Part II: Module SV - Post-authorisation experience

According to the Guideline on Good Pharmacovigilance Practices (GVP) Module V – Risk management system (Rev2) EMA/838713/2011, for initial application, which falls under Article 10(1) of Directive 2001/83/EC, module SV is not required.

Part II: Module SVI - Additional EU requirements for the safety specification

According to the Guideline on Good Pharmacovigilance Practices (GVP) Module V – Risk management

system (Rev2) EMA/838713/2011, for initial application, which falls under Article 10(1) of Directive 2001/83/EC, module SVI is not required.

Part II: Module SVII - Identified and potential risks

According to the algorithm harmonisation RMP domain for active substances for which there is no innovator or the innovator has no RMP, only those safety concerns should be listed that either:

1. have ongoing additional pharmacovigilance activity, or
2. have ongoing additional risk minimisation measure, or
3. have essential targeted questionnaires in place.

None of the above steps are required and the safety concerns are well defined.

SVII.1 Identification of safety concerns in the initial RMP submission

SVII.1.1. Risks not considered important for inclusion in the list of safety concerns in the RMP

Reason for not including an identified or potential risk in the list of safety concerns in the RMP:

Risks with minimal clinical impact on patients (in relation to the severity of the indication treated):

Vomiting, diarrhoea, epigastric pain, rash, urticaria, rash acneform, neuropathy, headache, palmar-plantar erythrodysesthesia.

Adverse reactions with clinical consequences, even serious, but occurring with a low frequency and considered to be acceptable in relation to the severity of the indication treated:

Anaphylactic reactions, angioedema.

SVII.1.2. Risks considered important for inclusion in the list of safety concerns in the RMP

Not applicable.

SVII.2 New safety concerns and reclassification with a submission of an updated RMP

Not applicable.

SVII.3 Details of important identified risks, important potential risks, and missing information

Not applicable.

Part II: Module SVIII - Summary of the safety concerns

Table SVIII.1: Summary of safety concerns

Summary of safety concerns	
Important identified risks	None
Important potential risks	None
Missing information	None

Part III: Pharmacovigilance Plan (including post-authorisation safety studies)

III.1 Routine pharmacovigilance activities

The safety concerns are well defined. Where there are well-characterized safety concerns, routine pharmacovigilance may be sufficient.

III.2 Additional pharmacovigilance activities

Not applicable.

III.3 Summary Table of additional Pharmacovigilance activities

MAH neither has on-going or planned nor completed additional pharmacovigilance studies/activities in the Pharmacovigilance Plan.

Part IV: Plans for post-authorisation efficacy studies

Not applicable. MAH does not plan post-authorisation efficacy studies.

Part V: Risk minimisation measures (including evaluation of the effectiveness of risk minimisation activities)

Risk Minimisation Plan

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

V.1. Routine Risk Minimisation Measures

Not applicable.

V.2. Additional Risk Minimisation Measures

Not applicable.

V.3 Summary of risk minimisation measures

Not applicable.

Part VI: Summary of the risk management plan

Summary of risk management plan for Levosol, 60 mg / ml, oral drops, solution (Levodropropizine)

This is a summary of the risk management plan (RMP) for Levosol, 60 mg / ml, oral drops, solution. The RMP details important risks of Levosol and how more information will be obtained about Levosol's risks and uncertainties (missing information).

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

Important new concerns or changes to the current ones will be included in updates of Levosol's RMP.

I. The medicine and what it is used for

Levosol is authorised for symptomatic treatment of cough (see SmPC for the full indication). It contains Levodropropizine as the active substance and it is given orally.

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

Important risks of Levosol together with measures to minimise such risks and the proposed studies for learning more about Levosol'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 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 Levosol 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 Levosol. 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	None
Important potential risks	None
Missing information	None

II.B Summary of important risks

The safety information in the proposed Product Information is aligned to the reference medicinal product.

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 Levosol.

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

There are no studies required for Levosol.

Part VII: Annexes

Table of contents