EU Risk Management Plan for Ibuprofen Gen.Orph 5 mg/mL solution for injection (ibuprofen)

RMP version to be assessed as part of this application:

RMP Version number: 0.1

Data lock point for this RMP: 31-AUG-2022

Date of final sign-off: 17-APR-2023

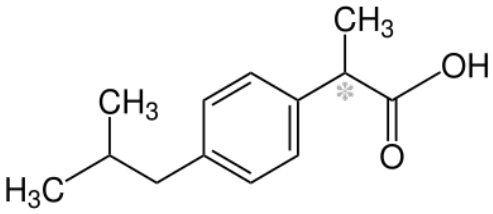
QPPV name: Sandrine BOUCHENOT

QPPV oversight declaration: The content of this RMP has been reviewed and approved by the marketing authorisation applicant´s QPPV. The electronic signature is available on file.

Table of content

Part I: Product(s) Overview

Table Part I.1 – Product(s) Overview

Active substance(s) **(INN or common name)**	Ibuprofen
Pharmacotherapeutic group(s) (ATC Code)	Other cardiac preparations (C01 EB16)
Marketing Authorisation Holder (Applicant)	Gen.Orph
Medicinal products to which this RMP refers	1
Invented name(s) in the European Economic Area (EEA)	Ibuprofen Gen.Orph 5 mg/mL solution for injection
Marketing authorisation procedure	centralised
Brief description of the product	Chemical class Chemical name : 2-[4-(2-methylpropyl)phenyl]propanoic acid Empirical formula : $C_{13}H_{18}O_2$ Molecular weight : 206.28 Structural formula : 
	Summary of mode of action : Ibuprofen is a nonsteroidal antiinflammatory (NSAID) that possesses anti-inflammatory, analgesic and antipyretic activity. Ibuprofen is a racemic mixture of S(+) and R(-) enantiomers. *In vivo* and *in vitro* studies indicate that the S(+) isomer is responsible for the clinical activity. Ibuprofen is a non selective inhibitor of cyclo-oxygenase, leading to reduced synthesis of prostaglandins. Since prostaglandins are involved in the persistence of the *ductus arteriosus* after birth, this effect is believed to be the main mechanism of action of ibuprofen in this indication.

	Important information about its composition Not applicable
Hyperlink to the Product Information	ema-combined-en
Indication(s) in the EEA	Current: Treatment of a haemodynamically significant patent ductus arteriosus in preterm newborn infants less than 34 weeks of gestational age.
	Proposed (if applicable): Not applicable
Dosage in the EEA	Current: Treatment with IBUPROFEN GEN.ORPH should only be carried out in a neonatal intensive care unit under the supervision of an experienced neonatologist. <u>Posology</u> A course of therapy is defined as three intravenous injections of ibuprofen given at 24-hour intervals. The first injection should be given after the first 6 hours of life. The ibuprofen dose is adjusted to the body weight as follows: - 1st injection: 10 mg/kg, - 2nd and 3rd injections: 5 mg/kg. If anuria or manifest oliguria occurs after the first or second dose, the next dose should be withheld until urine output returns to normal levels. If the ductus arteriosus does not close 48 hours after the last injection or if it re-opens, a second course of 3 doses, as above, may be given. If the condition is unchanged after the second course of therapy, surgery of the patent ductus arteriosus may then be necessary.
	Proposed (if applicable): Not applicable
Pharmaceutical form(s) and strengths	Current (if applicable): Pharmaceutical form : solution for injection Strengths : 5 mg/mL
	Proposed (if applicable): Not applicable
Is/will the product be	No

subject to additional monitoring in the EU?	

Part II: Safety specification

Part II: Module SVIII - Summary of the safety concerns

The active substance is well known. The originator product does not have an RMP. The important risk and missing information for Ibuprofen Gen.Orph 5 mg/mL solution for injection are included in the list published on the CMDh website. In conclusion, no safety concern is mentioned in this RMP.

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

No routine pharmacovigilance activities beyond adverse reactions reporting and signal detection are in place for Ibuprofen Gen.Orph 5 mg/mL solution for injection.

III.2 Additional pharmacovigilance activities

No additional pharmacovigilance activities are in place for Ibuprofen Gen.Orph 5 mg/mL solution for injection.

III.3 Summary Table of additional Pharmacovigilance activities

Not applicable

Part IV: Plans for post-authorisation efficacy studies

No post-authorisation efficacy studies have been planned or needed for the generic medicinal product Ibuprofen Gen.Orph 5 mg/mL solution for injection.

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 of Ibuprofen Gen.Orph 5 mg/mL solution for injection is aligned to the reference medicinal product.

V.1. Routine Risk Minimisation Measures

This section is not applicable since no safety concerns are included in this RMP.

V.2. Additional Risk Minimisation Measures

This section is not applicable.

V.3 Summary of risk minimisation measures

This section is not applicable.

Part VI: Summary of the risk management plan

Summary of risk management plan for Ibuprofen Gen.Orph 5 mg/mL solution for injection (ibuprofen)

This is a summary of the risk management plan (RMP) for Ibuprofen Gen.Orph 5 mg/mL solution for injection. The RMP details important risks of Ibuprofen Gen.Orph 5 mg/mL solution for injection, how these risks can be minimised, and how more information will be obtained about Ibuprofen Gen.Orph 5 mg/mL solution for injection's risks and uncertainties (missing information).

Ibuprofen Gen.Orph 5 mg/mL solution for injection's summary of product characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how Ibuprofen Gen.Orph 5 mg/mL solution for injection should be used.

This summary of the RMP for Ibuprofen Gen.Orph 5 mg/mL solution for injection 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 Ibuprofen Gen.Orph 5 mg/mL solution for injection's RMP.

I. The medicine and what it is used for

Ibuprofen Gen.Orph 5 mg/mL solution for injection is authorised for treatment of a haemodynamically significant patent ductus arteriosus in preterm newborn infants less than 34 weeks of gestational age (see SmPC for the full indication). It contains ibuprofen as the active substance and it is given by intravenous route.

Further information about the evaluation of Ibuprofen Gen.Orph 5 mg/mL solution for injection's benefits can be found in Ibuprofen Gen.Orph 5 mg/mL solution for injection's EPAR, including in its plain-language summary, available on the 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 characterise the risks

Important risks of Ibuprofen Gen.Orph 5 mg/mL solution for injection, together with measures to minimise such risks and the proposed studies for learning more about Ibuprofen Gen.Orph 5 mg/mL solution for injection'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 Ibuprofen Gen.Orph 5 mg/mL solution for injection 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 Ibuprofen Gen.Orph 5 mg/mL solution for injection. 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 Ibuprofen Gen.Orph 5 mg/mL solution for injection.

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

There are no studies required for Ibuprofen Gen.Orph 5 mg/mL solution for injection.

Part VII: Annexes

Table of contents

Annex 4 - Specific adverse drug reaction follow-up forms

Not applicable

Annex 6 - Details of proposed additional risk minimisation activities (if applicable)

Not applicable