IPAR

Public Assessment Report for a
Medicinal Product for Human Use

Scientific Discussion

Paralief Sinus Tablets Paracetamol 500 mg Pseudoephedrine hydrochloride 30 mg
Paracetamol
PSEUDOEPHEDRINE HYDROCHLORIDE
PA0126/339/001

The Public Assessment Report reflects the scientific conclusion reached by the Health Products Regulatory Authority (HPRA) at the end of the evaluation process and provides a summary of the grounds for approval of a marketing authorisation for a specific medicinal product for human use. It is made available by the HPRA for information to the public, after deletion of commercially sensitive information. The legal basis for its creation and availability is contained in Article 21 of Directive 2001/83/EC, as amended. It is a concise document which highlights the main parts of the documentation submitted by the applicant and the scientific evaluation carried out by the HPRA leading to the approval of the medicinal product for marketing in Ireland.

CONTENTS

I. INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the HPRA has granted a marketing authorisation for Paralief Sinus Tablets, from Chanelle Medical on 27th January 2017 *the short term symptomatic treatment of nasal and sinus congestion associated with the symptoms of cold and flu, such as mild pain, headache and/or fever. Paralief Sinus Tablets are indicated in adults and adolescents aged 15 years and over*.

This application for a marketing authorisation was submitted as a decentralised procedure application in accordance with Article 10a of Directive 2001/83/EC and is referred to as a well-established use application. The RMS is IE, withBE, DE, ES, FR, and PT CMS'.

This is a non-prescription medicine which may be supplied through pharmacies only.

The Summary of Product Characteristics for (SmPC) for this medicinal product is available on the HPRA's website at www.hpra.ie.

Name of the product	Paralief Sinus Tablets
Name(s) of the active substance(s) (INN)	Paracetamol/Pseudoephedrine Hydrochloride
Pharmacotherapeutic classification (ATC code)	N02BE01 Analgesics and antipyretics R01BA02 Sympathomimetics
Pharmaceutical form and strength(s)	500/30 mg Tablets
DCP No.	IE/H/458/001/DC
Reference Member State	IE
Concerned Member State	BE DE ES FR PT
Marketing Authorisation Holder	Chanelle Medical

II. QUALITY ASPECTS

II.1. Introduction

This application is for Paralief Sinus Tablets

II.2 Drug substance

The active substances are paracetamol and pseudoephedrine hydrochloride, established active substances described in the European Pharmacopoeia, and are manufactured in accordance with the principles of Good Manufacturing Practice (GMP)

The active substance specification is considered adequate to control the quality and meets current pharmacopoeial requirements. Batch analytical data demonstrating compliance with this specification has been provided.

II.3 Medicinal product

P.1 Composition

Each tablet contains 500mg of paracetamol, and 30mg of pseudoephedrine hydrochloride.
The excipients in the medicinal product are listed in section 6.1 of the SmPC.
A visual description of the product is included in section 3 of the SmPC.

P.2 Pharmaceutical Development

The product is an established pharmaceutical form and its development is adequately described in accordance with the relevant European guidelines.

P.3 Manufacture of the Product

The product is manufactured in accordance with the principles of good manufacturing practice (GMP) at suitably qualified manufacturing sites.

The manufacturing process has been validated according to relevant European/ICH guidelines and the process is considered to be sufficiently validated.

P.4 Control of Other Substances (Excipients)

All ingredients comply with Ph. Eur. and are adequately controlled by the manufacturer's specifications.

P.5 Control of Finished Product

The Finished Product Specification is based on the pharmacopoeial monograph for tablets, and the tests and control limits are considered appropriate for this type of product.

The analytical methods used are described in sufficient detail and are supported by validation data.

Batch analytical data for a number of batches from the proposed production site(s) have been provided, and demonstrate the ability of the manufacturer to produce batches of finished product of consistent quality.

P.6 Packaging material

The approved packaging for this product is described in section 6.5 of the SmPC.

Evidence has been provided that the packaging complies with EU legislation for use with foodstuffs requirements.

P.7 Stability of the Finished Product

Stability data on the finished product in the proposed packaging have been provided in accordance with EU guidelines and support the shelf-life and storage conditions listed in sections 6.3 and 6.4 of the SmPC.

II.4 Discussion on Chemical, Pharmaceutical and Biological Aspects

The important quality characteristics of the product are well-defined and controlled. Satisfactory chemical and pharmaceutical documentation has been provided, assuring consistent quality of Paralief Sinus Tablets.

III. NON-CLINICAL ASPECTS

III.1 Introduction

The pharmacodynamic, pharmacokinetic and toxicological properties of Paralief Sinus Tablets are well known. As Paralief Sinus Tablets are widely used, well-known active substances, the applicant has not provided additional studies and further studies are not required.

A non-clinical overview based on literature review was provided. GLP standards cannot be established for literature references, this is acceptable for this type of application.

III.2 Pharmacology

N/A

III.3 Pharmacokinetics

N/A

III.4 Toxicology

N/A

III.5 Ecotoxicity/environmental risk assessment

A justification for the absence of specific study data in the environmental risk assessment was provided and the introduction of Paralief Sinus Tablets to the market will not lead to an increase in environmental exposure.

III.6 Discussion on the non-clinical aspects

The use of Paralief Sinus Tablets are well established. As Paralief Sinus Tablets are widely used, well-known active substances, the applicant has not provided additional non-clinical studies and further repetitive tests on animals and humans are not required.

IV. CLINICAL ASPECTS

IV.1 Introduction

This application is based on well-established use and therefore the clinical dossier is based upon published literature.

Paracetamol and pseudoephedrine are well-known active substances with established efficacy and tolerability both as monotherapies and combined together.

IV.2 Pharmacokinetics

The applicant provided an adequate overview of the pharmacokinetics of both paracetamol and pseudoephedrine.

Paracetamol
Absorption
Peak plasma paracetamol concentration usually occurs between 30 and 90 minutes after oral ingestion.
Distribution
Paracetamol is distributed uniformly throughout most body fluids and is only 15 to 25 per cent bound to plasma proteins. The plasma half-life of paracetamol after therapeutic doses is in the range of 1 to 3 hours.
Renal insufficiency
In cases of renal failure (GFR≤50ml/min), the elimination of paracetamol is slightly delayed, the elimination half-life ranging from 2 to 5.3 hours. For the glucuronide and sulphate conjugates, the elimination rate is 3 times slower in subjects with severe renal impairment than in healthy subjects. Therefore, it is recommended, when giving paracetamol to patients with renal failure (GFR≤50ml/min), to reduce the dose and to increase the minimum interval between each administration to at least 6 hours.

Pseudoephedrine
Absorption
Pseudoephedrine is rapidly and completely absorbed from the gastrointestinal tract after oral administration with no pre-systemic metabolism. Peak plasma levels are achieved after 1-2 hours.

Biotransformation
Pseudoephedrine is partly metabolised in the liver by N-demethylation to norpseudoephedrine, an active metabolite.

Elimination
Pseudoephedrine and its metabolite are excreted in the urine: 55% to 75% of a dose is excreted unchanged. The rate of urinary excretion of pseudoephedrine is accelerated when the urine is acidified. Conversely as the urine pH increases, the rate of urinary excretion is slowed.

IV.3 Pharmacodynamics

The pharmacodynamics of paracetamol and pseudoephedrine have been adequately discussed by the applicant and has been based on published literature.

Paracetamol
Paracetamol has analgesic and antipyretic actions but only weak anti-inflammatory properties. This may be explained by presence of cellular peroxides at sites of inflammation which prevent inhibition of cyclo-oxygenase by paracetamol at other sites associated with low levels of cellular peroxides, e.g. pain, fever, paracetamol can successfully inhibit prostaglandin biosynthesis.

Pseudoephedrine
Pseudoephedrine has direct and indirect sympathomimetic activity and is an effective upper respiratory tract decongestant. Pseudoephedrine is substantially less potent than ephedrine in producing both tachycardia and elevation of systolic blood pressure and considerably less potent in causing stimulation of the central nervous system.

Section 4.5 of the SmPC reflects known interactions with other medicinal products.

IV.4 Clinical Efficacy

The efficacy of paracetamol and pseudoephedrine in the indications proposed are well established and have been adequately described by the applicant.

IV.5 Clinical Safety

The safety data provided by the applicant is based on literature review. The safety profile of paracetamol and pseudoephedrine are well known both as monotherapies and in combination together. The applicant has given an adequate overview of the safety of paracetamol and pseudoephedrine and the Summary of Product Characteristics (SmPC) and Patient Leaflet (PL) contain the relevant safety warnings and are generally in line with other licensed similar products.

Pharmacovigilance System
The marketing authorisation holder (MAH) submitted a summary of the Pharmacovigilance System, including confirmation of the availability of an EU Qualified Person for Pharmacovigilance (EU-QPPV) and the means for notification of adverse reaction reports in the EU or from a Third Country.

Risk Management Plan (usual pharmacovigilance requirements +/- additional requirements)
With regard to PSUR submission, the MAH should take the following into account:
- PSURs shall be submitted in accordance with the requirements set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and published on the European medicines web-portal. Marketing authorisation holders shall continuously check the European medicines web-portal for the DLP and frequency of submission of the next PSUR.
- For medicinal products authorized under the legal basis of Article 10(1) or Article 10a of Directive 2001/83/EC, no routine PSURs need to be submitted, unless otherwise specified in the EURD list.
- For medicinal products that do not fall within the categories waived of the obligation to submit routine PSURs by the revised pharmacovigilance legislation, the MAH should follow the DLP according to the EURD list.

IV.6 Discussion on the clinical aspects

This application is based on well-established use and therefore the clinical dossier is based upon published literature.

Paracetamol and pseudoephedrine are well-known active substances with established efficacy and tolerability when used in combination.

V. OVERALL CONCLUSIONS

The applicant has satisfactorily supported the requested indications and posology with bibliographic data.

The MAH has provided written confirmation that systems and services are in place to ensure compliance with their pharmacovigilance obligations.

The HPRA, on the basis of the data submitted, considered that Paralief Sinus Tablets demonstrated adequate evidence of efficacy for the approved indications as well as a satisfactory risk/benefit profile and therefore granted a marketing authorisation.

Following MRP/DCP procedure:
Discussion in CMD(h), specific obligations, follow-up measures, if applicable

VI. REVISION DATE

August 2021

VII. UPDATES

Scope
A.2.B Change in the (invented) name of the medicinal product

(From: Paracetamol 500mg/Pseudoephedrine hydrochloride 30mg Tablets

To:

Paralief Sinus Tablets
Paracetamol 500 mg
Pseudoephedrine hydrochloride 30 mg)

Procedure number	Product Information affected	Date of start of procedure	Date of end of procedure	Approval/non approval
IE/H/458/001/IB/005	SPC and PIL	08/12/2017	08/01/2018	Approved
CRN009WY5 MA Transfer	SmPC section 7, 8, 10 Package Leaflet New MA Holder: Clonmel Healthcare Ltd. New PA number: PA0126/339/001	N/A	13/08/2021	Approved