# IPAR

An tÚdarás Rialála Táirgí Sláinte
Health Products Regulatory Authority

# Public Assessment Report for a Medicinal Product for Human Use

Scientific discussion

Paravance Extra Capsules
Paracetamol 500 mg
Caffeine 65 mg
PA0979/068/001

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

## INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the HPRA has granted a marketing authorisation for Paravance Extra Capsules (Paracetamol 500 mg / Caffeine 65 mg), from Reckitt Benckiser Ireland Ltd. on 12/05/2017 for the relief of symptoms associated with the common cold and influenza, including relief of aches and pains, fever, sore throat, headache, fatigue and drowsiness, and lowering of temperature.

This application for a marketing authorisation was submitted in accordance with Article 10c of Directive 2001/83/EC and is referred to as an 'informed consent' application. This means that the Marketing Authorisation Holder for Lemsip Cold and Flu Capsules with Caffeine, an authorised medicinal product in Europe, has permitted the applicant to refer to their dossier to obtain an authorisation for Paravance Extra Capsules (Paracetamol 500 mg / Caffeine 65 mg). In this case the Applicant and the Marketing Authorisation holder are the same company.

Paravance Extra Capsules (Paracetamol 500 mg / Caffeine 65 mg) has the same qualitative and quantitative composition in terms of actives substances and the same pharmaceutical form as Lemsip Cold and Flu Capsules with Caffeine

The Summary of Product Characteristics for (SmPC) for this medicinal product is available on www.HPRA.ie.

| | |
|---|---|
| Name of the product | Paravance Extra Capsules (Paracetamol 500 mg / Caffeine 65 mg). |
| Name(s) of the active substance(s) (INN) | PARACETAMOL / CAFFEINE |
| Pharmacotherapeutic classification (ATC code) | N02BE51 |
| Pharmaceutical form and strength(s) | 500/65 milligram |
| Marketing Authorisation Number(s) in Ireland (PA) | PA0979/068/001 |
| Marketing Authorisation Holder | Reckitt Benckiser Ireland Ltd |

# II QUALITY ASPECTS

## II.1. Introduction

This application is for Paravance Extra Capsules (Paracetamol 500 mg / Caffeine 65 mg).

This is a duplicate PA - Article 10c (informed consent) Lemsip Cold and Flu Capsules with Caffeine PA 979/24/1. the quality data in support of this product is identical to the up-to-date quality data of the Lemsip Cold and Flu Capsules with Caffeine PA 979/24/1 dossier which has been assessed and approved.

Hence a more detailed quality comment is not required.

## 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 in the Lemsip Cold and Flu Capsules with Caffeine PA 979/24/1 dossier, assuring consistent quality of Paravance Extra Capsules (Paracetamol 500 mg / Caffeine 65 mg).

# III NON-CLINICAL ASPECTS

## III.1 Introduction

This active substance is the same as that present in Lemsip Cold and Flu Capsules with Caffeine PA0979/024/001 on the European market. No new preclinical data have been submitted. As such, no pre-clinical assessment has been made on the application. This is acceptable for this type of application.

# IV CLINICAL ASPECTS

## IV.1 Introduction

This application for a marketing authorisation was submitted in accordance with
Article 10c of Directive 2001/83/EC and is referred to as an 'informed consent' application. This means that the Marketing Authorisation Holder for Lemsip Cold and Flu Capsules with Caffeine PA0979/024/001, an authorised medicinal product in Europe, has permitted the applicant to refer to their dossier to obtain an authorisation for Paracetamol Extra Capsules From The Makers of Disprin. In this case the Applicant and the Marketing Authorisation holder are the same company.

Paracetamol Extra Capsules From The Makers of Disprin has the same qualitative and quantitative composition in terms of actives substances and the same pharmaceutical form as Lemsip Cold and Flu Capsules with Caffeine.

## IV.2 Pharmacokinetics

Paracetamol is absorbed rapidly and completely from the small intestine, producing peak plasma levels after 15-20 minutes following oral dosing. The systemic availability is subject to first-pass metabolism and varies with dose between 70% and 90%. The drug is rapidly and widely distributed throughout the body and is eliminated from plasma with a T½ of approximately 2 hours. The major metabolites are glucuronide and sulphate conjugates (>80%) which are excreted in urine.

Caffeine is absorbed readily after oral, rectal or parenteral administration, but absorption from the gastrointestinal tract may be erratic. There is little evidence of accumulation in any particular tissue. Caffeine passes readily into the central nervous system and into saliva. Concentrations have also been detected in breast milk. It is metabolised almost completely and is excreted in the urine as 1-methyluric acid, 1-methylxanthine and other metabolites with only about 1% unchanged.

## IV.3 Pharmacodynamics

Paracetamol has both analgesic and antipyretic activity which is believed to be mediated principally through its inhibition of prostaglandin synthesis within the central nervous system.

Caffeine is a central nervous system stimulant. It inhibits the enzyme phosphodiesterase and has an antagonistic effect at central adenosine receptors.
Its action on the central nervous system is mainly on the higher centres and it produces a condition of wakefulness and increased mental activity.

## IV.4 Clinical Efficacy

There was no additional clinical trial data submitted in support of this application. This was an informed consent application. Efficacy data was submitted and assessed in support of the application for Lemsip Cold and Flu Capsules with Caffeine which supported the product's efficacy.

## IV.5 Clinical Safety

There was no additional clinical trial data submitted in support of this application. This was an informed consent application. Safety data was submitted and assessed in support of the application for Lemsip Cold and Flu Capsules with Caffeine which supported the product's safety.

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: (RMP)**

An updated RMP has been provided by the applicant.

The updated RMP includes the following agreed Summary of Safety Concerns:

Important identified risks:
- Gastrointestinal disorders – particularly for those patients consuming caffeine with a history of peptic ulceration.
- Hypersensitivity – particularly those patients with allergies to the active or excipient ingredients. May cause rash, swollen face, pruritus, bronchospasm, anaphylaxis and urticaria.
- Overdosage leading to irreversible liver damage – particularly in patients with pre-existing hepatic or renal insufficiency.

Important potential risks:
- Drug interactions – particularly drugs that affect liver function, and anticoagulant drugs such as warfarin, which may be affected by higher doses of paracetamol.

Missing information:
- None.

Routine pharmacovigilance is considered acceptable.

**PSUR cycle:**

The next PSUR should 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.

## V OVERALL CONCLUSIONS

Paracetamol Extra Capsules From the Makers of Disprin, is the same as Lemsip Cold and Flu Capsules with Caffeine (PA0979/024/001). Lemsip Cold and Flu Capsules with Caffeine is a well-known medicinal product with a proven chemical-pharmaceutical quality and an established and favourable efficacy and safety profile.

The HPRA, on the basis of the data submitted considered that Paracetamol Extra Capsules From the Makers of Disprin was the same as Lemsip Cold and Flu Capsules with Caffeine (PA0979/024/001) and therefore granted a marketing authorisation.

## VI REVISION DATE

11/05/2022

## VII UPDATES

This section reflects the significant changes following finalisation of the initial procedure.

| SCOPE | PROCEDURE NUMBER | PRODUCT INFORMATION AFFECTED | DATE OF START OF PROCEDURE | DATE OF END OF PROCEDURE |
|---|---|---|---|---|