**IPAR**

**Public Assessment Report for a**
**Medicinal Product for Human Use**

Scientific Discussion

Lacosamide Ascend 10 mg/ml syrup
Lacosamide
PA23429/001/001

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 Lacosamide Ascend 10 mg/ml Syrup, from Ascend GmbH, for the treatment of epilepsy in adults, adolescents and children from 2 years of age. Lacosamide is indicated as adjunctive therapy

- in the treatment of partial-onset seizures with or without secondary generalisation in adults, adolescents and children from 2 years of age with epilepsy.
- in the treatment of primary generalised tonic-clonic seizures in adults, adolescents and children from 4 years of age with idiopathic generalised epilepsy.

This is a generic application submitted under Article 10(1) of Directive 2001/83/EC authorised via a decentralised procedure (DCP) IE/H/1250/001/DC with Ireland (HPRA) as RMS and Germany the only CMS.
This medicinal product will be subject to prescription.

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** | Lacosamide Ascend 10 mg/ml syrup |
| **Name(s) of the active substance(s) (INN)** | Lacosamide |
| **Pharmacotherapeutic classification (ATC Code)** | N03AX18 |
| **Pharmaceutical form and strength(s)** | 10mg/mlSyrup |
| **Marketing Authorisation Number(s) in Ireland (PA)** | PA23429/001/001 |
| **Marketing Authorisation Holder** | Ascend GmbH |
| **MRP/DCP No.** | IE/H/1250/001 |
| **Reference Member State** | Ireland |
| **Concerned Member State(s)** | DE |

## II. QUALITY ASPECTS

### II.1. Introduction
This application is for Lacosamide Ascend 10mg/ml Syrup.

### II.2 Drug substance
The active substance is Lacosamide, an established active substance described in the European Pharmacopoeia, and is 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 ml of syrup contains 10 mg lacosamide.

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/*Ancillary Substances*)

All ingredients comply with Ph. Eur. or 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 the dosage form, 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 Ph. Eur./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 Lacosamide Ascend 10 mg/ml syrup.

## III. NON-CLINICAL ASPECTS

**III.1 Introduction**

This active substance is a generic formulation of is Vimpat 10 mg/ml Syrup 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.

**III.2 Pharmacology**

N/A

**III.3 Pharmacokinetics**

N/A

**III.4 Toxicology**

N/A

**III.5 Ecotoxicity/environmental risk assessment**

N/A

**III.6 Discussion on the non-clinical aspects**

Since Lacosamide Ascend is a generic product, an increase in environmental exposure to the active substance is not anticipated. Environmental risk assessment studies are therefore not deemed necessary.

## IV. CLINICAL ASPECTS

Lacosamide is a well-known active substance with established efficacy and tolerability.

The content of the SmPC approved during the decentralised procedure is in accordance with that accepted for the reference product Vimpat 10 mg/ml Syrup marketed by MAH USB Pharma S.A., Belgium.
No bioequivalence studies were performed and a biowaiver was applied for. The conditions for a biowaiver were met as per the requirements of the EMA 'Guideline on the Investigation of Bioequivalence' CPMP/EWP/QWP/1401/98 and no further clinical studies are considered necessary to confirm the bioequivalence of Lacosamide 10 mg/ml Syrup.

### IV.2 Pharmacokinetics
Oral bioavailability of Lacosamide tablets is approximately 100%. 95 % of the dose is excreted in the urine as Lacosamide and metabolites. The elimination half-life of Lacosamide is approximately 13 hours. Following twice daily dosing, steady state plasma concentrations are achieved after a 3 day period.

### IV.3 Pharmacodynamics
The precise mechanism by which lacosamide exerts its antiepileptic effect in humans remains to be fully elucidated. In vitro electrophysiological studies have shown that lacosamide selectively enhances slow inactivation of voltage-gated sodium channels, resulting in stabilization of hyperexcitable neuronal membranes.

### IV.4 Clinical Efficacy
As Lacosamide is a well-known active substance, the applicant has not provided additional studies and further studies are not required. The clinical overview on the efficacy is thus, appropriate for this generic application submitted under Article 10(1) of Directive 2001/83/EC.

### IV.5 Clinical Safety
As Lacosamide is a well-known active substance, the applicant has not provided additional studies and further studies are not required. The clinical overview on the safety is thus, appropriate for this generic application submitted under Article 10(1) of Directive 2001/83/EC.

Please see the accompanying product information for full prescribing details including safety information on contraindications, warnings, interactions and possible side effects.

A risk management plan was submitted, in accordance with the requirements of Directive 2001/83/EC as amended, describing the pharmacovigilance activities and interventions designed to identify, characterise, prevent or minimise risks relating to Lacosamide Ascend 10mg/ml Syrup. The submitted Risk Management Plan is considered acceptable.

Periodic safety update reports (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.

### IV.6 Discussion on the clinical aspects
Abridged (generic) applications submitted under Article 10(1) of Directive 2001/83/EC avoid the need for repetitive tests on humans. For these applications the bioequivalence studies are pivotal, however, in this case Lacosamide Ascend 10 mg/ml Syrup meets the conditions for a biowaiver as per the EMA 'Guideline on the Investigation of Bioequivalence' CPMP/EWP/QWP/1401/98 and no further clinical studies are considered necessary to confirm the bioequivalence with the reference product Vimpat 10 mg/ml Syrup (EU/1/08/470/018) of UCB Pharma S.A., Belgium.
The content of the SmPC approved during the decentralised procedure is in accordance with that accepted for the reference product, Vimpat 10 mg/ml Syrup (EU/1/08/470/018) marketed by UCB Pharma S.A., Belgium.

## V. OVERALL CONCLUSIONS

Lacosamide Ascend 10 mg/ml syrup is a generic form of Vimpat 10 mg/ml Syrup. Vimpat 10 mg/ml Syrup is a well-known medicinal product with a proven chemical-pharmaceutical quality and an established favourable efficacy and safety profile.

Bioequivalence has been shown to be in compliance with the CHMP guidance documents. The SmPC is consistent with that of the reference product.

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 Lacosamide Ascend 10 mg/ml Syrup demonstrated bioequivalence with the reference product as well as a satisfactory risk/benefit profile and therefore granted a marketing authorisation.

**VI. REVISION DATE**

**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 |
|---|---|---|---|---|
| New DCP as RMS | IE/H/1250/001/DC | SmPC, PIL, Label | 10th May 2024 | 9th May 2024 |