IPAR

Public Assessment Report for a
Medicinal Product for Human Use

Scientific Discussion

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 Trazodone Hydrochloride 50mg/5ml Oral Solution, from Key Pharmaceuticals Ltd. on 7th June 2019 for relief of symptoms in all types of depression including depression accompanied by anxiety. Symptoms of depression likely to respond in the first week of treatment include depressed mood, insomnia, anxiety, somatic symptoms and hypochondriasis.

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	Trazodone Hydrochloride 50mg/5ml Oral Solution
Name(s) of the active substance(s) (INN)	TRAZODONE HYDROCHLORIDE
Pharmacotherapeutic classification (ATC code)	N06AX05
Pharmaceutical form and strength(s)	50mg/5ml Oral Solution
Marketing Authorisation Number(s) in Ireland (PA)	PA0343/007/001
Marketing Authorisation Holder	Key Pharmaceuticals Ltd

II. QUALITY ASPECTS

II.1. Introduction

This application is for Trazodone Hydrochloride 50mg/5ml Oral Solution.

II.2 Drug substance

The active substance is trazodone hydrochloride, an established active substance, 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

The medicinal product is an oral solution and contains 50 mg of trazodone hydrochloride per 5 ml of solution.
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.

P.3 Manufacture of the Product

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

The manufacturing process has been validated according to relevant European guidelines.

P.4 Control of Other Substances (Excipients)

All ingredients comply with the 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 liquid preparations for oral use, 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 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 Trazodone Hydrochloride 50mg/5ml Oral Solution.

III. NON-CLINICAL ASPECTS

III.1 Introduction

This active substance is a generic formulation of Molipaxin Liquid 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 Ecotoxicity/environmental risk assessment

As the product is intended for generic substitution no increased environmental exposure is expected and an environmental risk assessment has not been performed. This is acceptable.

III.3 Discussion on the non-clinical aspects

As this is a generic application, additional non-clinical data is not necessary for this application. The active substance Trazodone hydrochloride is well known and its preclinical effects are well documented. Relevant preclinical aspects are outlined in section 5.3 of the SmPC.

IV. CLINICAL ASPECTS

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

This medicinal product is the same as Molipaxin Liquid on the European market. Because the active substance is an aqueous solution comparative bioavailability studies to Molipaxin Liquid are not required and have not been carried out.

The content of the SmPC approved during the national procedure is in accordance with that accepted for the reference product Molipaxin Liquid marketed by Zentiva.

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.

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 reactions reports in the EU from a Third Country

Risk Management Plan
The Applicant submitted a risk management plan to support this application. The following table outlines the approved summary of safety concerns.

Table 1: Safety specification

Summary of safety concerns	
Important identified risks	Hypersensitivity reactions; Hypotension; Cardiac arrhythmias; QT prolongation; Hepatotoxicity; Worsening of symptoms in patients with schizophrenia or other psychotic disorders; Priapism; Suicidal ideation and behaviours; Drug-drug-interactions
Important potential risks	Overdose
Missing information	Use during pregnancy and lactation

Routine risk minimisation and routine pharmacovigilance activities are proposed to address the safety concerns outlines above and this is considered acceptable.

The Applicant should submit Periodic Safety Update Reports (PSUR) 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

Trazodone Hydrochloride 50mg/5ml Oral Solution is a generic form of Molipaxin Liquid. Molipaxin Liquid is a well-known medicinal product with a proven chemical-pharmaceutical quality and an established favourable efficacy and safety profile.

Because of the pharmaceutical form bioequivalence with the reference product can be assumed. 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 Trazodone Hydrochloride 50mg/5ml Oral Solution was the same as the reference product and therefore granted a marketing authorisation.

VI. REVISION DATE

March 2021

VII. UPDATES

SCOPE	PROCEDURE NUMBER	PRODUCT INFORMATION AFFECTED	DATE OF START OF PROCEDURE	DATE OF END OF PROCEDURE
MAH transfer	CRN00C5GJ	SmPC section 7, 8, 10 Package Leaflet New MA Holder: Lexon Pharmaceuticals (Ireland) Limited New PA number: PA23176/005/001	12/03/2021	12/03/2021