IPAR

Public Assessment Report for a
Medicinal Product for Human Use

Scientific Discussion

Zopiclone Pinewood 3.75 mg film coated tablet
Zopiclone
PA0281/257/002

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 Zopiclone Pinewood 3.75 mg film coated tablets from Pinewood Laboratories Limited on 5th January 2024 for the short-term treatment of insomnia in adults.

The applicant applied for a marketing authorisation via a decentralised procedure with Ireland acting as Reference Member State. There was no Concerned Member State involved. It was an application for a change to an existing marketing authorisation leading to an extension as referred to in Annex I of Regulations (EC) No 1234/2008, i.e., the addition of a new strength (line extension) to the existing marketing authorisation granted to Pinewood Laboratories Limited for Zopiclone Pinewood 7.5mg film coated tablets (PA 281/257/1) on 08/07/2022 during IE/H/1190/001/DC.

The application for Zopiclone Pinewood 3.75 mg film coated tablets was submitted in accordance with Article 10(1) of Directive 2001/83/EC, the same legal basis as the application for Zopiclone Pinewood 7.5 mg film coated tablets.

The European reference product (ERP) is Imovane 7.5 mg film coated tablets (9514) by Sanofi Oy, registered since 22/07/87 in Finland. Zimovane 7.5 mg film coated tablets (PA 2010/57/1), MAH Mylan IRE Healthcare Limited, is the innovator authorised in the RMS, registered since 18/08/2006.

Zopiclone is a hypnotic agent, and a member of the cyclopyrrolone group of compounds. It rapidly initiates and sustains sleep without reduction of total REM sleep and with preservation of slow wave sleep. It is not considered a new active substance.

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

Name of the product:	Zopiclone Pinewood 3.75 mg film coated tablets
Name(s) of the active substance(s) (INN):	Zopiclone
Pharmacotherapeutic classification (ATC code):	N05CF01
Pharmaceutical form and strength:	3.75 mg film coated tablets
Marketing Authorisation Number(s) in Ireland:	PA0281/257/002
Marketing Authorisation Holder:	Pinewood Laboratories Limited
MRP/DCP No. :	IE/H/1190/002/DC
Reference Member State:	IE
Concerned Member State:	None

II. QUALITY ASPECTS

II.1. Introduction

This application is for Zopiclone Pinewood 3.75 mg film coated tablets.

II.2 Drug substance

The active substance is Zopiclone, 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 have been provided.

II.3 Medicinal product

P.1 Composition

Each film-coated tablet contains 3.75 mg of zopiclone. 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.

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 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 Ph. Eur. and 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 Zopiclone Pinewood 3.75 mg film coated tablets.

III. NON-CLINICAL ASPECTS

III.1 Introduction

This active substance is a generic formulation of Zopiclone 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

Since Zopiclone Pinewood is a generic product, it will not lead to an increased exposure to the environment. Additional environmental risk assessment studies are therefore not deemed necessary.

III.6 Discussion on the non-clinical aspects

Pharmacodynamic, pharmacokinetic and toxicological properties of Zopiclone Pinewood are well known. As Zopiclone is a widely used, well-known active substance, the applicant has not provided additional studies and further studies are not required. A nonclinical overview based on literature review was provided and is acceptable for this type of generic application. Nonclinical sections of the SmPC are in line with the originator which is acceptable.

IV. CLINICAL ASPECTS

IV.1 Introduction

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

This generic application was submitted as a line extension to the applicant's previously authorised higher strength tablet, Zopiclone Pinewood 7.5 mg film coated tablet (PA0281/257/001), which was approved on 08/07/2022 in the decentralised procedure IE/H/1190/001/DC.

During the latter procedure, the applicant demonstrated bioequivalence between Zopiclone Pinewood 7.5 mg film coated tablet and the reference medicinal product, Imovane 7.5 mg Film-coated tablets (9514) by Sanofi Oy, by conducting a single-dose, randomised, two-period, two-treatment, two-sequence, crossover bioequivalence study in healthy subjects under fasting conditions. Both test and reference products were considered bioequivalent with extent to the rate and extent of absorption and fulfilled the bioequivalence requirements outlined in the relevant CHMP Note for Guidance.

The results of the bioequivalence study performed with the Zopiclone Pinewood 7.5 mg film coated tablet could be extrapolated to Zopiclone Pinewood 3.75 mg film coated tablet as all general biowaiver criteria specified in the current EMA guidance were met.

IV.2 Pharmacokinetics

No new pharmacokinetic data were submitted as part of this application.

In accordance with current EMA guidance, the applicant successfully applied for a waiver for additional *in vivo* bioequivalence testing. This was based on extrapolation from the demonstration of bioequivalence between the applicant's previously authorised higher tablet strength, Zopiclone Pinewood 7.5 mg film coated tablet (PA0281/257/001), and the reference medicinal product, and fulfilment of the criteria specified in the guidance.

IV.3 Pharmacodynamics

No new pharmacodynamic data were submitted, and none are required for an application of this type.

IV.4 Clinical Efficacy

No new efficacy data were submitted, and none are required for an application of this type.

IV.5 Clinical Safety

No new safety data were submitted, and none are required for an application of this type.

Risk Management Plan (RMP)
The MAH has submitted a risk management plan, in accordance with the requirements of Directive 2001/83/EC as amended, describing the pharmacovigilance activities and interventions designed to identify, characterize, prevent or minimise risks relating to Zopiclone Pinewood 3.75 mg Film coated Tablet.

No safety concerns were proposed by the applicant, which is endorsed.

Routine pharmacovigilance and risk minimisation activities were proposed by the applicant, which is endorsed.

Periodic Safety Update Reports (PSUR)
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.
- In case the active substance will be removed in the future from the EURD list because the MAs have been withdrawn in all but one MS, the MAH shall contact that MS and propose DLP and frequency for further PSUR submissions together with a justification.

IV.6 Discussion on the clinical aspects

Zopiclone 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 Imovane 7.5 mg Film-coated tablets (9514) by Sanofi Oy.

This generic application was submitted as a line extension to the applicant's previously authorised higher strength tablet, Zopiclone Pinewood 7.5 mg film coated tablet (PA0281/257/001), which was approved on 08/07/2022 in the decentralised procedure IE/H/1190/001/DC.

As bioequivalence had been successfully demonstrated (IE/H/1190/001/DC) between the test and reference products at the higher strength (7.5 mg), in accordance with current guidance, no additional in vivo bioequivalence testing was needed to support this application.

V. OVERALL CONCLUSIONS

Zopiclone Pinewood 3.75 mg film coated tablets have been authorised as a line extension (new additional strength) to the existing marketing authorisation granted to Pinewood Laboratories Limited for Zopiclone Pinewood 7.5 mg film coated tablets (PA 281/257/1).

Zopiclone Pinewood 3.75 mg film coated tablets is a lower strength generic form of Imovane 7.5 mg film coated tablets (9514) by Sanofi Oy. Imovane 7.5 mg film coated tablets is a well-known medicinal product with a proven chemical-pharmaceutical quality and an established favourable efficacy and safety profile.

Bioequivalence between Zopiclone Pinewood 7.5 mg film coated tablets and Imovane 7.5 mg film coated tablets had been shown to be in compliance with the CHMP guidance documents in the preceding decentralised procedure, IE/H/1190/001/DC. As bioequivalence had been demonstrated for the higher strength tablet, the need for an in vivo bioequivalence study for the lower strength, Zopiclone Pinewood 3.75 mg film coated tablets, was waived in accordance with current guidance.

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 Zopiclone Pinewood 3.75 mg film coated tablets demonstrated a satisfactory risk/benefit profile and therefore could be granted a marketing authorisation.

VI. REVISION DATE

18.11.2028