IPAR

Public Assessment Report for a
Medicinal Product for Human Use

Scientific Discussion

Aripiprazole Pinewood 1 mg/ml Oral Solution
Aripiprazole
PA0281/274/001

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

II. QUALITY ASPECTS

III. NON-CLINICAL ASPECTS

IV. CLINICAL ASPECTS

V. OVERALL CONCLUSION AND BENEFIT-RISK ASSESSMENT

VI. REVISION DATE

VII. UPDATE

I. INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the HPRA has granted a marketing authorisation for Aripiprazole Pinewood 1 mg/ml Oral Solution, from Pinewood Laboratories Ltd on 19/09/2025 for treatment of schizophrenia in adults and in adolescents aged 15 years and older, treatment of moderate to severe manic episodes in Bipolar I Disorder and for the prevention of a new manic episode in adults who experienced predominantly manic episodes and whose manic episodes responded to aripiprazole treatment and for the treatment up to 12 weeks of moderate to severe manic episodes in Bipolar I Disorder in adolescents aged 13 years and older.

This application for a marketing authorisation was submitted in accordance with Article 10(1) of Directive 2001/83/EC and is referred to as a 'generic' application. It was submitted as a national authorisation in Ireland.

The reference medicinal product is Abilify oral solution by Otsuka Pharmaceutical Netherlands BV, authorised in the European Union (EU/1/04/276/034) since 04/06/2004.

The legal status for this marketing authorisation is subject to medical prescription, which may not be renewed.
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	Aripiprazole Pinewood 1 mg/ml Oral Solution
Name(s) of the active substance(s) (INN)	Aripiprazole
Pharmacotherapeutic classification (ATC Code)	N05AX12
Pharmaceutical form and strength(s)	1 mg/ml Oral Solution
Marketing Authorisation Number(s) in Ireland (PA)	PA0281/274/001
Marketing Authorisation Holder	Pinewood Laboratories Ltd Ballymacarbry Clonmel Co. Tipperary Ireland

II. QUALITY ASPECTS

II.1. Introduction

This application is for Aripiprazole Pinewood 1 mg/ml Oral Solution.

II.2 Drug substance

The active substance is aripiprazole, 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

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 guidelines and the process is considered to be sufficiently validated.

P.4 Control of Other Substances (Excipients)

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 oral solutions, 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.

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 Aripiprazole Pinewood 1 mg/ml Oral Solution.

III. NON-CLINICAL ASPECTS

III.1 Introduction

This active substance is a generic formulation of Abilify 1mg/ml oral solution on the European market. No new preclinical data have been submitted. This is acceptable for this type of application.

The pharmacodynamic, pharmacokinetic and toxicological properties of aripiprazole are well known.

III.2 Pharmacology

N/A

III.3 Pharmacokinetics

N/A

III.4 Toxicology

N/A

III.5 Ecotoxicity/environmental risk assessment

Since Aripiprazole 1mg/ml oral solution is intended for generic substitution, this will not lead to an increased exposure to the environment. Additional studies on environmental risk assessment are therefore not deemed necessary.

III.6 Discussion on the non-clinical aspects

The pharmacodynamic, pharmacokinetic and toxicological properties of aripiprazole are well known. As aripiprazole 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. Non-clinical findings are adequately represented in the appropriate sections of the SmPC.

IV. CLINICAL ASPECTS

IV.1 Introduction

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

The content of the SmPC approved during the national procedure is in accordance with that accepted for the reference product Abilify oral solution marketed by Otsuka Pharmaceutical Netherlands BV.

The HPRA has been assured that GCP standards were followed in an appropriate manner in the study conducted.

IV.2 Pharmacokinetics

For this generic application, the applicant has submitted one bioequivalence study in which the pharmacokinetic profile of the test product Aripiprazole Pinewood 1 mg/ml Oral Solution is compared with the pharmacokinetic profile of the reference product Abilify oral solution.

A comparative randomised, single-dose, two-treatment, two-period, two-sequence crossover open label study to determine the bioequivalence of Chanelle Medical Aripiprazole 1 mg/ml oral solution (1 mg/ml Aripiprazole Oral Solution) and Otsuka Pharmaceutical Europe Ltd. ABILIFY 1 mg/ml oral solution (1 mg/ml Aripiprazole Oral Solution) following an oral administration of 5 ml aripiprazole to healthy adults under fasting conditions.

A summary of the pharmacokinetic parameters is presented in the table below:

Treatment	**AUC_{0-72}** **xg/ml/h**	**C_{max}** **ng/ml**
Test	688.98 ± 172.85	20.246 ± 4.65
Reference	715.83 ± 181.01	20.271 ± 4.40
***Ratio (90% CI)**	96.56 % (93.29 – 99.95 %)	99.58 % (94.06 – 105.43 %)

**ln-transformed values*

In accordance with the regulatory requirements, the test/reference ratios and their 90 % confidence intervals calculated for AUC_{0-72h} and C_{max} were inside the normal range of acceptability (80.00 – 125.00 %) to show bioequivalence between the test and reference product. Based on the pharmacokinetic parameters of the active substance, the reference product Abilify oral solution and test product Aripiprazole Pinewood 1 mg/ml Oral Solution are bioequivalent with extent to the rate and extent of absorption and fulfil the bioequivalence requirements outlined in the relevant CHMP Note for 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

The safety of aripiprazole is described in the clinical overview and is well known. With the exception of the safety data generated during the bioequivalence study, no new safety data were submitted, and none are required for this type of application.

The safety data from the bioequivalence study showed that the test and reference products were equally well tolerated. No new or unexpected safety issues were raised from this study

Risk Management Plan:

Risk Management Plan version 0.1, with date of final sign off 03 Sep 2024 is considered acceptable. The approved summary of safety concerns is outlined below:

Summary of Safety concerns

Important identified risks	Extrapyramidal symptoms, including tardive dyskinesia
Important potential risks	Orthostatic hypotension
Missing information	Use in Pregnancy and Lactation

Routine pharmacovigilance and routine risk minimisation measures are proposed, and this is considered acceptable.

Periodic Safety Update Report (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

Aripiprazole Pinewood 1 mg/ml Oral Solution has a proven chemical-pharmaceutical quality and is a generic form of a suitable approved reference product (Abilify). Abilify 1 mg/ml oral solution is a well-known medicinal product with an established favourable efficacy and safety profile. Bioequivalence has been shown between Aripiprazole Pinewood 1 mg/ml Oral Solution and the reference product.

V. OVERALL CONCLUSIONS

Aripiprazole Pinewood 1 mg/ml Oral Solution is a generic form of Abilify 1 mg/ml oral solution. Abilify 1 mg/ml oral solution 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. 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 Aripiprazole Pinewood 1 mg/ml Oral Solution 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

SCOPE	PROCEDURE NUMBER	PRODUCT INFORMATION AFFECTED	DATE OF START OF PROCEDURE	DATE OF END OF PROCEDURE
New National	CRN00DXGY	SmPC, IPAR and PIL	19th September 2025	18th September 2030