IPAR

Public Assessment Report for a
Medicinal Product for Human Use

Scientific Discussion

Prednisolone 5 mg soluble tablets
Prednisolone sodium phosphate
PA1567/003/001

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.

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I. INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the HPRA has granted a marketing authorisation for Prednisolone 5 mg soluble tablets, from Activase Pharmaceuticals Limited on 21st March 2025 for the treatment of several inflammatory and immunological disorders and neoplasms,.

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

Ireland was the Reference Member State (RMS) and the only Concerned Member State (CMS) was France.

This is a prescription-only medicinal product.

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	Prednisolone 5 mg soluble tablets
Name(s) of the active substance(s) (INN)	Prednisolone sodium phosphate
Pharmacotherapeutic classification (ATC code)	H02AB06
Pharmaceutical form and strength(s)	5 mg, soluble tablet
Marketing Authorisation Number(s) in Ireland	PA1567/003/001
Marketing Authorisation Holder	Activase Pharmaceuticals Limited
DCP No.	IE/H/1286/001/DC
Reference Member State	IE
Concerned Member State	FR

II. QUALITY ASPECTS

II.1. Introduction

This application is for Prednisolone 5 mg soluble tablets.

II.2 Drug substance

The active substance is prednisolone sodium phosphate, 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 finished product is a pink, round tablet, marked with 'PD' on one side and scored with a break line on the other side containing 5 mg pf prednisolone (as prednisolone sodium phosphate).

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 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./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 Prednisolone 5 mg soluble tablets.

III. NON-CLINICAL ASPECTS

III.1 Introduction

This active substance, prednisolone, is the same as that present in Prednesol 5 mg tabletson on the European market since 1978. No new preclinical data have been submitted.

The pharmacodynamic, pharmacokinetic and toxicological properties of prednisolone are well known. As prednisolone is a widely used, well-known active substances, and this is a generic application, the applicant has not provided additional nonclinical studies and further studies are not required. The overview provided based on literature review is thus appropriate.

III.2 Ecotoxicity/environmental risk assessment

The applicant has not provided a full environmental risk assessment (ERA) in accordance with the guideline (CHMP/SWP/4447/00). Instead, justification for the absence of a full ERA is supplied. Since Prednisolone 5 mg soluble tablets is intended for generic substitution, this will not lead to an increased exposure to the environment. Further environmental risk assessment studies are therefore not deemed necessary.

III.3 Discussion on the non-clinical aspects

The pharmacodynamic, pharmacokinetic and toxicological properties of prednisolone are well known. The non-clinical overview on the pre-clinical pharmacology, pharmacokinetics and toxicology provided is adequate. As prednisolone is a widely used, well-known active substance, the applicant has not provided additional studies and further studies are not required. Non-clinical findings are adequately represented in the appropriate sections of the SmPC.

IV. CLINICAL ASPECTS

IV.1 Introduction

Prednisolone sodium phopshate 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 Prednesol marketed by MAH.

For this generic application, the applicant has submitted a BCS biowaiver which has been adequately justified and is accepted.

IV.2 Pharmacokinetics

Absorption
Prednisolone is readily absorbed from the gastrointestinal tract with peak plasma concentrations achieved by 1-2 hours after an oral dose. Plasma prednisolone is mainly protein bound (70-90%), with binding to albumin and corticosteroid-binding globulin. The plasma half-life of prednisolone, after a single dose, is between 2.5-3.5 hours.

Distribution
The volume of distribution and clearance of total and unbound prednisolone are concentration dependent and this has been attributed to saturable protein binding over the therapeutic plasma concentration range.

Biotransformation
Prednisolone is extensively metabolised, mainly in the liver, but the metabolic pathways are not clearly defined.

Elimination
Over 90% of the prednisolone dose is excreted in the urine, with 7-30% as free prednisolone and the remainder being recovered as a variety of metabolites.

IV.3 Pharmacodynamics

Prednisolone sodium phosphate is a synthetic glucocorticoid with the same general properties as prednisolone itself and other compounds classified as corticosteroids. Prednisolone is four times as active as hydrocortisone on a weight for weight basis. Prednisolone irreversibly binds with glucocorticoid receptors found in virtually all tissues so that prednisolone can activate and influence biochemical behaviour of most cells. The steroid/receptor complexes interact with cellular DNA in the nucleus, binding to steroid-response elements and modifying gene transcription. They both induce synthesis of some genes and, therefore, some proteins, and inhibit synthesis of others.

IV.4 Clinical Efficacy

No additional efficacy clinical studies to demonstrate efficacy have been included in the application. This is appropriate for this type of application.

IV.5 Clinical Safety

The overall safety profile of prednisolone is established and generally known. No additional safety clinical studies to demonstrate safety have been included in the application and none are required.

Risk Management Plan

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, characterise, prevent, or minimise risks relating to Prednisolone 5 mg Soluble Tablets.

Safety specification
The initial RMP (v0.2; date of final sign-off 08/11/2023) submitted with this application proposed the following list of safety concerns:

Summary of safety concerns	
Important identified risks	None
Important potential risks	None
Missing information	None

Pharmacovigilance Plan

Routine pharmacovigilance is suggested, and no additional pharmacovigilance activities are proposed by the applicant, which is endorsed.

Risk minimisation measures

Routine risk minimisation is suggested, and no additional risk minimisation activities are proposed by the applicant, which is endorsed.
The MAH shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the Marketing Authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:

- At the request of the RMS;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

If the dates for submission of a PSUR and the update of a RMP coincide, they can be submitted at the same time, but via different procedures.

Periodic Safety Update Report (PSUR)

Active substance is currently listed in the published EURD list

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

This is a generic application, the application dossier has been submitted in accordance with the Directive 2001/83/EC, as amended as a generic 10(1) application.

The reference product is well established in the EU being authorised since 1978. Prednisolone has demonstrated efficacy and has a well-established documented safety profile.

This is a generic application, therefore additional clinical studies are not required. A satisfactory BCS biowaiver has been submitted, which has been accepted to support the claim of bioequivalence with the reference product.

V. OVERALL CONCLUSIONS

Prednisolone 5 mg soluble tablets is a generic form of Prednesol. Prednesol is a well-known medicinal product with a proven chemical-pharmaceutical quality and an established favourable efficacy and safety profile.

A satisfactory BSC biowaiver has been submitted with supports bioequivalence with the reference product 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 Prednisolone 5 mg soluble tablets demonstrated bioequivalence with the reference product as well as a satisfactory risk/benefit profile and therefore granted a marketing authorisation.

VI. REVISION DATE

19.02.2030