Medicines & Healthcare products Regulatory Agency

MHRA

Public Assessment Report

National Procedure

Prednisolone 5 mg Soluble Tablets (prednisolone sodium phosphate)

PL 52914/0004

Acium Limited

LAY SUMMARY

Prednisolone 5 mg Soluble Tablets
(prednisolone sodium phosphate)

This is a summary of the Public Assessment Report (PAR) for Prednisolone 5 mg Soluble Tablets. It explains how this product was assessed and its authorisation recommended, as well as it conditions of use. It is not intended to provide practical advice on how to use this products.

This product will be referred to as Prednisolone soluble tablets in this lay summary for ease of reading.

For practical information about using Prednisolone soluble tablets, patients should read the package leaflet or contact their doctor or pharmacist.

What are Prednisolone soluble tablets and what are they used for?
This application is for Prednisolone 5 mg soluble tablets is for a generic medicine. This means that this medicine is the same as, and considered interchangeable with, a reference medicine already authorised in the United Kingdom (UK) called Prednesol 5 mg Tablets.

Prednisolone soluble tablets are used to treat a variety of inflammatory diseases including severe asthma, rheumatoid arthritis, allergic reactions, bowel diseases, severe skin conditions, kidney disorders and some blood disorders.

How do Prednisolone soluble tablets work?
This medicine contains the active ingredient prednisolone (as prednisolone sodium phosphate), which belongs to a group of medicines called corticosteroids or “steroids”. These corticosteroids occur naturally in the body, and help to maintain health and well-being. Boosting the body with extra corticosteroid (such as Prednisolone soluble tablets) is an effective way to treat various illnesses involving inflammation in the body. The patient must take this medicine regularly to get maximum benefit from it.

Steroids work by reducing inflammation and lowering the body’s immune response.

How are Prednisolone Soluble Tablets used?
The pharmaceutical form of this medicine is a soluble tablet and the route of administration is oral (taken by mouth).

Method of administration:
Prednisolone soluble tablets are best taken dissolved in a glass of water and taken as a drink, but can be swallowed whole with a glass of water. The patient should take the tablets as a single dose each morning unless their doctor has instructed otherwise.

The patient should take care to not leave their drink where someone else may take it as the patient’s medicine could harm them.

The recommended dose is:
Adults:
The dose will depend on the condition the patient is being treated for and can vary between 10 mg and 100 mg daily. The patient’s doctor will always reduce the dose to the smallest dose that works for the patient.

Use in children and adolescents:
To treat asthma attacks:
Children above 2 years - the doctor will decide the most appropriate dose to treat the child.

Children under 2 years - may be treated in the hospital.
Treatment for up to three days is usually enough, but may be longer.

Method of administration:
The tablets can be swallowed whole, but they are best taken as a drink after dissolving them in a glass of water. The patient should take their tablets as a single dose each morning, unless their doctor has told them otherwise.

For further information on how Prednisolone soluble tablets are used, refer to the package leaflet and Summary of Product Characteristics (SmPC) available on the Medicines and Healthcare products Regulatory Agency (MHRA) website.

This medicine can only be obtained with a prescription.

The patient should always take this medicine exactly as their doctor/pharmacist has told them. The patient should check with their doctor or pharmacist if they are not sure.

What benefits of Prednisolone soluble tablets have been shown in studies?
Prednisolone soluble tablets are a generic medicine that fulfils criteria, meaning that no additional studies are required. Prednisolone soluble tablets have been considered a generic medicine of the reference medicine, based on a comparison of their physical and chemical characteristics.

What are the possible side effects of Prednisolone soluble tablets?
For the full list of all side effects reported with this medicine, see Section 4 of the package leaflet or the SmPC available on the MHRA website.

If a patient gets any side effects, they should talk to their doctor, pharmacist or nurse. This includes any possible side effects not listed in the product information or the PIL that comes with the medicine. Patients can also report suspected side effects themselves, or a report can be made on behalf of someone else they care for, directly via the Yellow Card scheme at www.mhra.gov.uk/yellowcard or search for 'MHRA Yellow Card' online. By reporting side effects, patients can help provide more information on the safety of this medicine.

Because Prednisolone soluble tablets are a generic medicine, their possible side effects are considered to be the same as for the reference medicine.

Why were Prednisolone soluble tablets approved?
It was concluded that, Prednisolone soluble tablets have been shown to be comparable to the reference medicine. Therefore, the MHRA decided that, as for the reference medicine, the benefits are greater than the risks and recommended that it can be approved for use.

What measures are being taken to ensure the safe and effective use of Prednisolone soluble tablets?
As for all newly-authorised medicines, a Risk Management Plan (RMP) has been developed for Prednisolone soluble tablets The RMP details the important risks of Prednisolone soluble tablets, how these risks can be minimised, any uncertainties about Prednisolone soluble tablets (missing information), and how more information will be obtained about the

important risks and uncertainties.

The following safety concerns have been recognised for Prednisolone 5 mg soluble tablets:

Important identified risks	• Hypersensitivity to prednisolone sodium phosphate or any excipients. • Psychiatric disorders (psychosis, depression, mania without known history, activation of previous psychiatric disorders) • Increase in susceptibility and severity of infections • Metabolism disorders • Growth inhibition in paediatric population • Cushing like symptoms
Important potential risks	• Use in pregnancy
Important missing information	• Use in lactating mothers

The information included in the SmPC and the PIL is compiled based on the available quality, non-clinical and clinical data, and includes appropriate precautions to be followed by healthcare professionals and patients. Side effects of Prednisolone soluble tablets are continuously monitored and reviewed including all reports of suspected side-effects from patients, their carers, and healthcare professionals.

A RMP and a summary of the pharmacovigilance system have been provided with this application and are satisfactory.

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Other information about Prednisolone soluble tablets

A Marketing Authorisation for Prednisolone soluble tablets was granted in the UK on 05 January 2022.

The full PAR for Prednisolone soluble tablets follows this summary.

This summary was last updated in March 2022.

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I INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the Medicines and Healthcare products Regulatory Agency (MHRA) considered that the application for Prednisolone 5 mg soluble tablets (PL 52914/0004) could be approved.

The product is approved for the following indications in adults and children:
The treatment of:

- bronchial asthma, severe hypersensitivity reactions, anaphylaxis; rheumatoid arthritis, systemic lupus erythematosus, dermatomyositis, mixed connective tissue disease (excluding systemic sclerosis), polyarteritis nodosa;
- inflammatory skin disorders, including pemphigus vulgaris, bullous pemphigoid and pyoderma gangrenosum;
- minimal change nephrotic syndrome and acute interstitial nephritis;
- ulcerative colitis, Crohn's disease; sarcoidosis;
- rheumatic carditis;
- haemolytic anaemia (autoimmune), acute lymphoblastic and chronic lymphocytic leukaemia, malignant lymphoma, multiple myeloma, idiopathic thrombocytopenic purpura;
- immmunosuppression in transplantation.

The active substance prednisolone (as 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.

This application was submitted under Article 10(1) of Directive 2001/83/EC, as amended (equivalent to Regulation 51B of The Human Medicines Regulations 2012, as amended) as a generic medicine of a suitable originator medicinal product, Prednesol 5 mg Tablets, that has been licensed within the United Kingdom (UK) for a suitable time, in line with the legal requirements.
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No new non-clinical studies were conducted, which is acceptable given that the application is for a generic medicinal product of a suitable reference product.

A biowaiver was submitted with this application, which was accepted. No bioequivalence study was required and no new clinical studies were provided with this application.

The MHRA has been assured that acceptable standards of Good Manufacturing Practice (GMP) are in place for this product at all sites responsible for the manufacture, assembly and batch release of this product.

A Risk Management Plan (RMP) and a summary of the pharmacovigilance system have been provided with this application and are satisfactory.

A national Marketing Authorisation was granted in the UK on 05 January 2022.

II QUALITY ASPECTS

II.1 Introduction

This product contain 5 mg of prednisolone (as prednisolone sodium phosphate) in each soluble tablet.

In addition to prednisolone, this product also contains the excipients sodium hydrogen

carbonate, sodium acid citrate, saccharin sodium, povidone, erthyrosine lake (E127) and sodium benzoate (E211)

The finished product is packaged in oriented polyamide/aluminium/polyvinylchloride/ aluminium (OPA/Al/PVC/Al) blisters, in a pack size of 30 soluble tablets.

Satisfactory specifications and Certificates of Analysis have been provided for all packaging components. All primary packaging complies with the current European regulations concerning materials in contact with food.

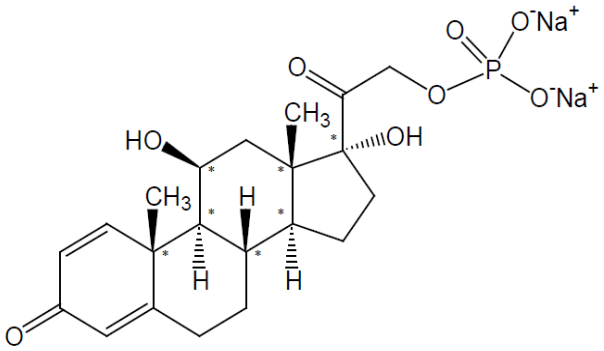
II.2 ACTIVE SUBSTANCE

rINN: Prednisolone sodium phosphate

Chemical Name: 11β,17-dihydroxy-3,20-dioxpregna-1,4-dien-21-yl disodium phosphate

Molecular Formula: $C_{21}H_{27}Na_2O_8P$

Chemical Structure:



Molecular Weight: 484.4 g/mol

Appearance: White or slightly yellow, friable hygroscopic granules or powder

Solubility: The drug substance is freely soluble in water, soluble in methanol, slightly soluble in alcohol and in chloroform; very slightly soluble in acetone and in dioxane.

Prednisolone sodium phosphate is the subject of a European Pharmacopoeia monograph.

All aspects of the manufacture and control of the active substance are covered by a European Directorate for the Quality of Medicines and Healthcare (EDQM) Certificate of Suitability

II.3 DRUG PRODUCT

Pharmaceutical development

A satisfactory account of the pharmaceutical development has been provided.

Comparative *in vitro* dissolution and impurity profiles have been provided for the proposed and reference products.

All excipients comply with either their respective European/national monographs, or a suitable in-house specification. Satisfactory Certificates of Analysis have been provided for all excipients.

No excipients of animal or human origin are used in the final product.

This product do not contain or consist of genetically modified organisms (GMO).

Manufacture of the product
A description and flow-chart of the manufacturing method has been provided.

Satisfactory batch formulation data have been provided for the manufacture of the product, along with an appropriate account of the manufacturing process. The manufacturing process has been validated and has shown satisfactory results.

Finished Product Specifications
The finished product specifications at release and shelf-life are satisfactory. The test methods have been described and adequately validated. Batch data have been provided that comply with the release specifications. Certificates of Analysis have been provided for any working standards used.

Stability
Finished product stability studies have been conducted in accordance with current guidelines, using batches of the finished product stored in the packaging proposed for marketing. Based on the results, a shelf-life of 18 months, with the storage conditions 'Store below 25°C. Store in the original package.', is acceptable.

Suitable post approval stability commitments have been provided to continue stability testing on batches of finished product.

II.4 Discussion on chemical, pharmaceutical and biological aspects
The grant of a Marketing Authorisation is recommended.

III NON-CLINICAL ASPECTS

III.1 Introduction
As the pharmacodynamic, pharmacokinetic and toxicological properties of prednisolone are well-known, no new non-clinical studies are required, and none have been provided. An overview based on the literature review is, thus, appropriate.

III.2 Pharmacology
No new pharmacology data were provided and none were required for this application.

III.3 Pharmacokinetics
No new pharmacokinetic data were provided and none were required for this application.

III.4 Toxicology
No new toxicology data were provided and none were required for this application.

III.5 Ecotoxicity/Environmental Risk Assessment
Suitable justification has been provided for non-submission of an Environmental Risk Assessment. As the application is for a generic version of an already authorised product, an increase in environmental exposure is not anticipated following approval of the Marketing Authorisation for the proposed product.

III.6 Discussion on the non-clinical aspects
The grant of a Marketing Authorisation is recommended.

IV CLINICAL ASPECTS

IV.1 Introduction

The clinical pharmacology, efficacy and safety of prednisolone are well-known. According to the regulatory requirements, the applicant has provided a suitable biowaiver and a bioequivalence study is not required for these products. An overview based on a literature review is, thus, satisfactory.

IV. 2 Pharmacokinetics

No new pharmacokinetic data have been submitted for this application and none were required.

IV.3 Pharmacodynamics

No new pharmacodynamic data have been submitted for this application and none were required.

IV.4 Clinical efficacy

No new efficacy data were submitted with this application and none were required.

IV.5 Clinical safety

No new safety data were submitted with this application and none were required. The safety profile for this product is considered to be the same as Prednesol 5 mg Tablets.

IV.6 Risk Management Plan (RMP)

The applicant has submitted a RMP, in accordance with the requirements of Regulation 182 of The Human Medicines Regulations 2012, as amended. The applicant proposes only routine pharmacovigilance and routine risk minimisation measures for all safety concerns. This is acceptable.

IV.7 Discussion on the clinical aspects

The grant of a Marketing Authorisation is recommended for this application.

V USER CONSULTATION

A full colour mock-up of the Patient Information Leaflet (PIL) has been provided with the application in accordance with legal requirements.

The PIL has been evaluated via a user consultation study in accordance with legal requirements. The results show that the PIL meets the criteria for readability as set out in the guideline on the readability of the label and package leaflet of medicinal products for human use.

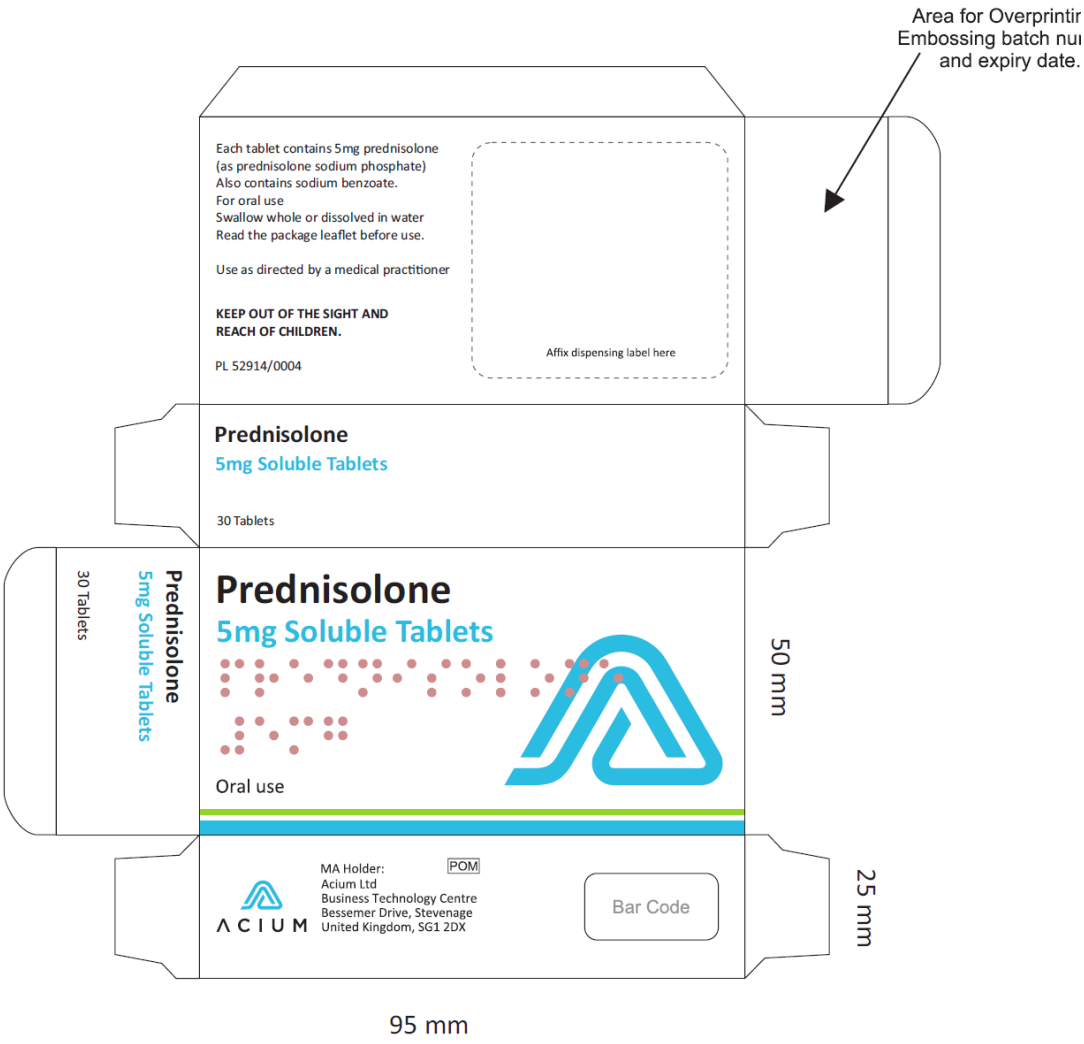
VI OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

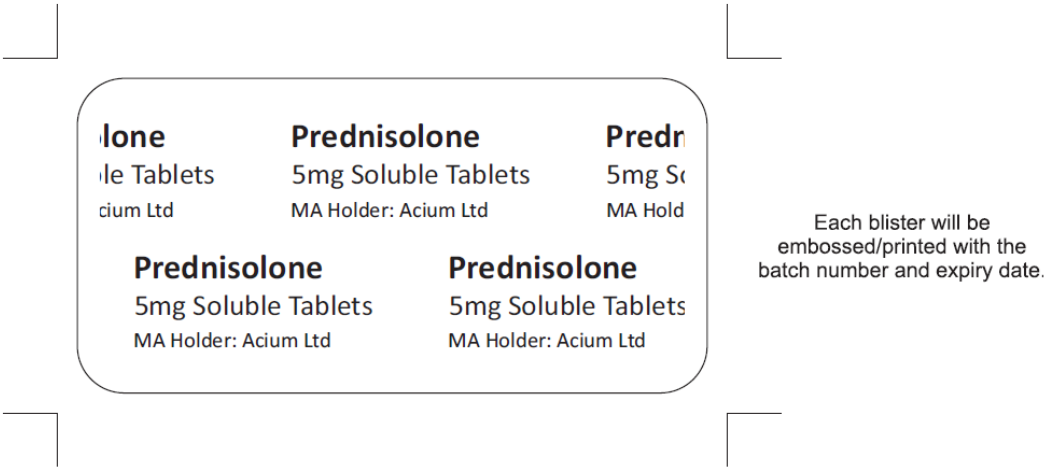
The quality of the product is acceptable, and no new non-clinical or clinical safety concerns have been identified. Extensive clinical experience with prednisolone is considered to have demonstrated the therapeutic value of the compound. The benefit/risk is, therefore, considered to be positive.

The Summary of Product Characteristics (SmPC), PIL and labelling are satisfactory, in line with current guidelines and consistent with the reference products.

In accordance with legal requirements, the current approved UK versions of the SmPC and PIL for this product are available on the MHRA website.

Representative copies of the labels at the time of UK licensing are provided below:





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Steps taken after the initial procedure with an influence on the Public Assessment Report (non-safety variations of clinical significance)

Please note that only non-safety variations of clinical significance are recorded below and in the annexes to this PAR. The assessment of safety variations where significant changes are made are recorded on the MHRA website or European Medicines Agency (EMA) website. Minor changes to the Marketing Authorisation are recorded in the current SmPC and/or PIL available on the MHRA website.

Application type	**Scope**	**Product information affected**	**Date of grant**	**Outcome**	**Assessment report attached Y/N**