Medicines & Healthcare products Regulatory Agency

MHRA

Public Assessment Report

National Procedure

Prednisolone 10mg/ml Oral Solution

(prednisolone sodium phosphate)

PLGB 46918/0004

Aerona Clinical Limited

LAY SUMMARY

Prednisolone 10mg/ml Oral Solution (prednisolone sodium phosphate)

This is a summary of the Public Assessment Report (PAR) for Prednisolone 10mg/ml Oral Solution. It explains how this product was assessed and its authorisation recommended, as well as its conditions of use. It is not intended to provide practical advice on how to use this product.

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

For practical information about using Prednisolone Oral Solution, patients should read the Patient Information Leaflet (PIL) or contact their doctor or pharmacist.

What is Prednisolone Oral Solution and what is it used for?

This application 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.

The application was originally submitted as Prednisolone 10mg/ml Oral Solution (PL 46918/0001) for a marketing authorisation (MA) for the United Kingdom (UK) and was subsequently withdrawn and converted to product licence PLGB 46918/0004 (authorised in Great Britain).

Prednisolone Oral Solution can be used:

- to treat breathing difficulties associated with asthma;
- to treat severe allergic reactions;
- to treat illnesses which cause inflammation of the skin, small and medium sized arteries, muscles and joints (including rheumatoid arthritis);
- to treat problems with the immune system, where the immune system attacks the cells in your body;
- to treat certain kidney problems;
- to treat certain illnesses resulting in inflammation of the bowels e.g. ulcerative colitis or Crohn’s disease;
- to treat inflammation of the heart;
- to treat problems with the blood including haemolytic anaemia (a disorder which breaks down red blood cells) and leukaemia;
- to prevent rejection following an organ transplant.

How does Prednisolone Oral Solution work?

Prednisolone Oral Solution contains the active ingredient prednisolone which belongs to a group of medicines called steroids (the full name is corticosteroids).

Corticosteroids occur naturally in the body and help to maintain health and wellbeing. Boosting the body with extra corticosteroid (such as prednisolone) is an effective way to treat various illnesses involving inflammation in the body.

Prednisolone Oral Solution reduces this inflammation, which could otherwise go on making the patient's condition worse. The patient must take this medicine regularly to get the maximum benefit.

How is Prednisolone Oral Solution used?
The pharmaceutical form of this medicine is an oral solution and the route of administration is oral (via the mouth).

The patient's doctor will decide on the most appropriate dose to treat them or their child.

The recommended dose is:
Adults

- The usual starting dose is 1ml to 10ml per day
- The patient's doctor may reduce the dose, after a few days or weeks, depending on how well their condition is responding to the treatment.

For Rheumatoid Arthritis

- The usual starting dose is between 0.75ml and 1ml per day.

Use in children and adolescents

- The patient's doctor will decide the most appropriate dose to treat their child.

If Prednisolone Oral Solution has been prescribed for a child, for the treatment of acute asthma attacks the following dosing regime may be given for up to three days:

- For children over 5 years of age, 3 to 4ml may be prescribed;
- For children aged 2-5 years of age, 2ml may be prescribed;
- For children aged under 2 years, 1ml may be prescribed if the child is being treated in a hospital.

Important: If the patient is unsure how much medicine to take, they should contact their doctor or pharmacist for advice.

For further information on how Prednisolone Oral Solution is used, refer to the PIL 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 Oral Solution have been shown in studies?
Prednisolone Oral Solution is a generic medicine that fulfils criteria meaning that no additional studies are required. Prednisolone Oral Solution has 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 Oral Solution?
For the full list of all side effects reported with this medicine, see Section 4 of the PIL 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 Oral Solution is a generic medicine, its benefits and possible side effects are considered to be the same as for the reference medicine.

Why was Prednisolone Oral Solution approved?
It was concluded that, Prednisolone Oral Solution has 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 Oral Solution?
A Risk Management Plan (RMP) has been developed to ensure that Prednisolone Oral Solution is used as safely as possible. Based on this plan, safety information has been included in the SmPC and the PIL, including the appropriate precautions to be followed by healthcare professionals and patients.

Known side effects are continuously monitored. Furthermore, new safety signals reported by patients/healthcare professionals will be monitored and reviewed continuously.

Other information about Prednisolone Oral Solution
A Marketing Authorisation for Prednisolone Oral Solution was granted in Great Britain (GB, consisting of England, Scotland and Wales) on 14 July 2021.

The full PAR for Prednisolone Oral Solution follows this summary.

This summary was last updated in September 2021.

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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 10mg/ml Oral Solution (PLGB 46918/0004) could be approved.

The product is approved for the following indications:
A wide variety of diseases may sometimes require corticosteroid therapy. Some of the principal indications are:

- 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, 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;
- immunosuppression in transplantation.

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 as Prednisolone 10mg/ml Oral Solution (PL 46918/0001) under 51B (application of a UKMA (UK)) of The Human Medicines Regulation 2012, as amended (previously Article 10(1) of Directive 2001/83/EC, as amended). PL 46918/0001 was subsequently withdrawn and converted to product licence PLGB 46918/0004 (UKMA(GB) authorised in Great Britain) and approved under Regulation 51A of The Human Medicines Regulation 2012, as amended (previously Article 10(1) of Directive 2001/83/EC, as amended).

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 Great Britain on 14 July 2021.

II QUALITY ASPECTS

II.1 Introduction

Each 1ml of solution contains 10mg of prednisolone (as prednisolone sodium phosphate).

In addition to prednisolone sodium phosphate, this product also contain the excipients glycerol (99%), xylitol, sucralose, sodium dihydrogen phosphate dihydrate, disodium phosphate dihydrate, orange flavour, vanilla cream flavour, sodium methyl parahydroxybenzoate (E219), sodium propyl parahydroxybenzoate (E217), disodium edetate, sodium hydroxide and/or hydrochloric acid (pH adjusters) and purified water.
Water Purified.

The finished product is packaged in Amber (Ph. Eur. Type III) glass bottles containing 30 ml of oral solution, with tamper-evident plastic (HDPE/PPH) screw cap and a 5 ml graduated syringe.

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

II.2 ACTIVE SUBSTANCE

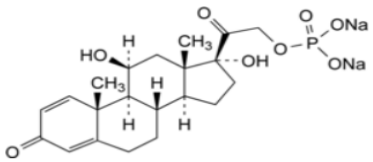
rINN: Prednisolone sodium phosphate

Chemical Name: 11β,17-Dihydroxy-3,20-dioxopregna-1,4-dien-21-yl disodium phosphate.

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

Chemical Structure:

(Ph. Eur. monograph 0735)



Molecular Weight: 484.4

Appearance: White or almost white, hygroscopic, crystalline powder.

Solubility: Freely soluble in water, very slightly soluble in ethanol (96 per cent).

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

Synthesis of the active substance from the designated starting materials has been adequately described and appropriate in-process controls and intermediate specifications are applied. Satisfactory specifications are in place for all starting materials and reagents, and these are supported by relevant Certificates of Analysis.

Appropriate proof-of-structure data have been supplied for the active substance. All potential known impurities have been identified and characterised.

An appropriate specification is provided for the active substance. Analytical methods have been appropriately validated and are satisfactory for ensuring compliance with the relevant specification. Batch analysis data are provided and comply with the proposed specification. Satisfactory Certificates of Analysis have been provided for all working standards.

Suitable specifications have been provided for all packaging used. The primary packaging complies with the current regulations concerning materials in contact with food.

Appropriate stability data have been generated supporting a suitable retest period when stored in the proposed packaging.

II.3 DRUG PRODUCT

Pharmaceutical development

A satisfactory account of the pharmaceutical development has been provided.

Comparative *in vitro* 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 products.

This product does 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 2 years for the unopened bottle, with the storage conditions ‘Store in a refrigerator (2°C – 8°C). Keep the container in the outer carton in order to protect from light’, is acceptable. The in-use shelf life once the bottle is opened is use within 3 months.

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 sodium phosphate 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 sodium phosphate is well-known. According to the regulatory requirements, the applicant has provided a suitable biowaiver and a bioequivalence study is not required for this product. 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 an RMP, in accordance with the requirements of Regulation 182 of The Human Medicines Regulation 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.

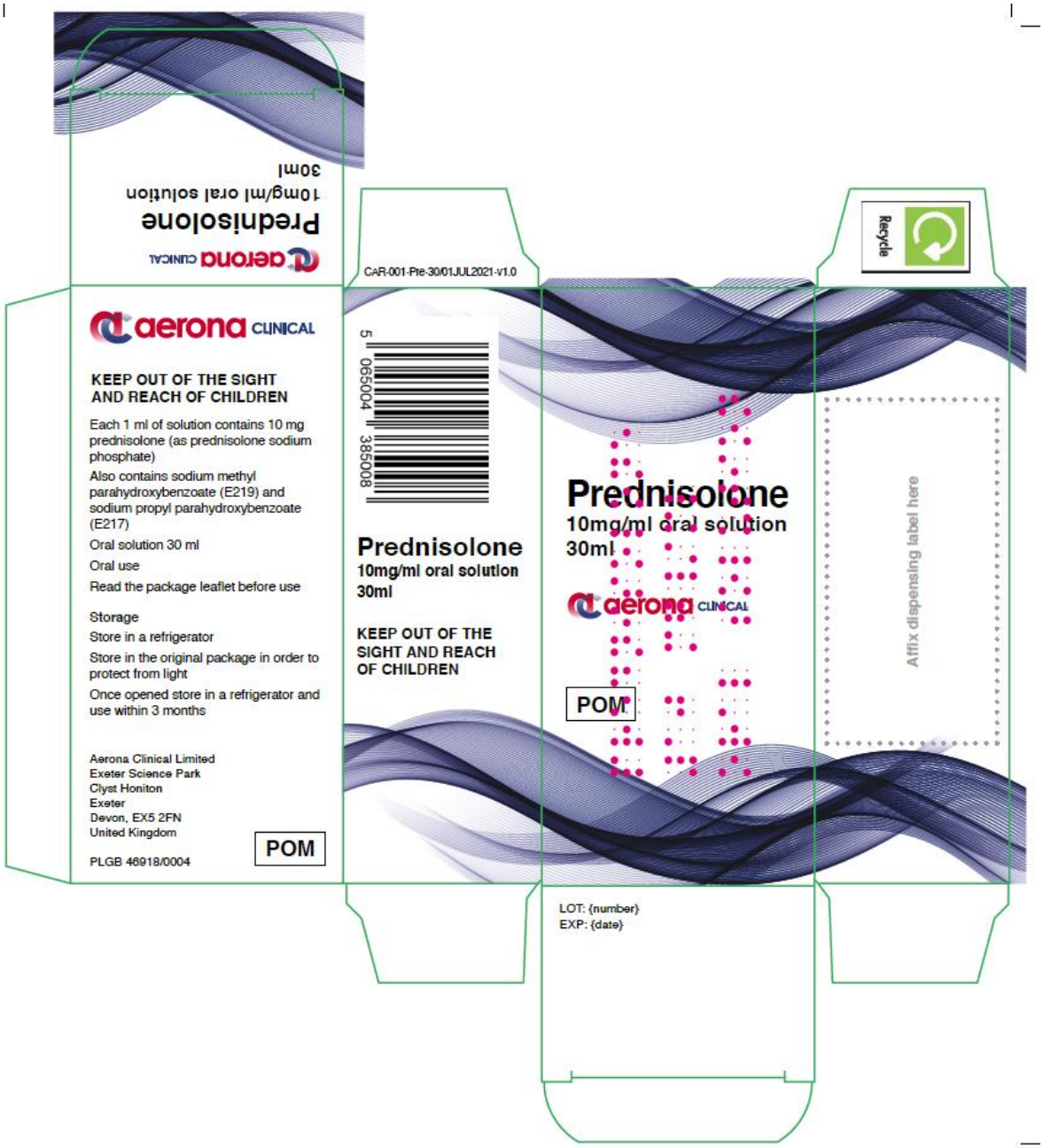
VI OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

The quality of the product is acceptable, and no new non-clinical or clinical safety concerns have been identified. Extensive clinical experience with prednisolone sodium phosphate 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), Patient Information Leaflet (PIL) and labelling are satisfactory, in line with current guidelines and consistent with the reference product.

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

Representative copies of the labels at the time of licensing are provided below.


Prednisolone
10mg/ml oral solution
30ml
aerona CLINICAL
KEEP OUT OF THE SIGHT AND REACH OF CHILDREN
Each 1 ml of solution contains 10 mg prednisolone (as prednisolone sodium phosphate)
Also contains sodium methyl parahydroxybenzoate (E219) and sodium propyl parahydroxybenzoate (E217)
Oral solution 30 ml
Oral use
Read the package leaflet before use
Storage
Store in a refrigerator
Store in the original package in order to protect from light
Once opened store in a refrigerator and use within 3 months
Aerona Clinical Limited
Exeter Science Park
Clyst Honiton
Exeter
Devon, EX5 2FN
United Kingdom
PLGB 46918/0004
POM
CAR-001-Pre-30/01JUL2021-v1.0
5 065004 385008
Prednisolone
10mg/ml oral solution
30ml
KEEP OUT OF THE SIGHT AND REACH OF CHILDREN
Recycle
Prednisolone
10mg/ml oral solution
30ml
aerona CLINICAL
POM
Affix dispensing label here
LOT: {number}
EXP: {date}

Prednisolone
10mg/ml oral solution
30ml

Each 1 ml of solution contains 10 mg prednisolone (as prednisolone sodium phosphate). Also contains sodium methyl parahydroxybenzoate (E219) and sodium propyl parahydroxybenzoate (E217) Oral solution 30 ml.

Storage. Store in a refrigerator. Store in the original package in order to protect from light. Once opened store in a refrigerator and use within 3 months.
KEEP OUT OF THE SIGHT AND REACH OF CHILDREN

Recycle

POM

Aerona Clinical Limited, Exeter Science Park, Clyst Honiton, Exeter, Devon, EX5 2FN, United Kingdom

PLGB 46918/0004
LAB-001-Pre-30/01JUL2021-v1.0

TABLE OF CONTENT OF THE PAR UPDATE

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**