LAY SUMMARY

Prednisolone 2.5 mg Gastro-Resistant Tablets
Prednisolone 5 mg Gastro-Resistant Tablets

This is a summary of the Public Assessment Report (PAR) for Prednisolone 2.5 mg and 5 mg Gastro-Resistant Tablets (PL 17907/0553-0556, formerly PL 20620/0098-0101). It explains how the applications for Prednisolone 2.5 mg and 5 mg Gastro-Resistant Tablets were assessed and their authorisations recommended, as well as the conditions of use. It is not intended to provide practical advice on how to use Prednisolone 2.5 mg and 5 mg Gastro-Resistant Tablets.

For practical information about using Prednisolone 2.5 mg and 5 mg Gastro-Resistant Tablets, patients should read the package leaflets or contact their doctor or pharmacist.

The products may be referred to as Prednisolone Tablets in this report.

What are Prednisolone Tablets and what are they used for?
These medicines are the same as Dilacort 2.5 mg and 5 mg Gastro-Resistant Tablets (PL 17507/0186-0187) held by Auden McKenzie (Pharma Division) Limited, which are already authorised in the UK. The licence holder (Auden McKenzie (Pharma Division) Ltd) for Dilacort 2.5 mg and 5 mg Gastro-Resistant Tablets has agreed that its own scientific data can be used as a basis for the grant of an identical licences for Prednisolone 2.5 mg and 5 mg Gastro-Resistant Tablets.(informed consent).

Prednisolone Tablets are used in a wide range of inflammatory and auto-immune conditions including:
- allergies, including severe allergic reactions
- inflammation affecting the:
  - lungs, including asthma
  - blood vessels and heart
  - bowel or kidneys
  - muscles and joints, including rheumatoid arthritis
  - eye or nervous system
- skin conditions
- some infections
- some cancers, including leukaemia, lymphoma and myeloma
- to prevent organ rejection after a transplant.

Prednisolone Tablets are also used to:
- boost steroid levels when the body is not making enough natural steroid on its own
- treat high calcium levels.

How do Prednisolone Tablets work?
Prednisolone Tablets contain the active ingredient, prednisolone, which belongs to a group of medicines called steroids. Their full name is corticosteroids. These corticosteroids occur naturally in the body, and help to maintain health and well-being. Boosting your body with extra corticosteroid (such as prednisolone) is an effective way to treat various illnesses involving inflammation in the body. Prednisolone reduces this inflammation, which could otherwise go on making your condition worse. To get maximum benefit from Prednisolone Tablets, the patient must take the tablets regularly.

How are Prednisolone Tablets used?
Prednisolone Tablets are available as gastro-resistant tablets and are taken by mouth. Prednisolone Tablets should always be taken exactly as advised by the patient’s doctor or pharmacist.
Adults:
Depending on the patient's illness, the daily dose of Prednisolone Tablets may be between 5 mg and 60 mg. In some cases, the patient may be instructed to take the tablets every other day. The doctor will decide when and how to treat the patient with Prednisolone Tablets.

Elderly:
When steroids are taken by elderly patients some of the unwanted side effects can be more serious especially brittle bone disease, diabetes, high blood pressure, infections and thinning of the skin.

Children:
The use of steroids can slow down normal growth of children and adolescents. In order to lessen this effect the tablets are often taken in a single dose every other day.

Please read section 3 of the package leaflet for detailed information on dosing recommendations, the route of administration, and the duration of treatment.

Prednisolone Tablets can only be obtained with a prescription.

What benefits of Prednisolone Tablets haves been shown in studies?
The applications for Prednisolone Tablets are considered to be identical to the previously authorised licences for Dilacort 2.5 mg and 5 mg Gastro-Resistant Tablets (Auden McKenzie (Pharma Division) Limited), with the same benefits and risks. So, no new studies have been provided for Prednisolone Tablets. However, reference is made to the studies for Dilacort 2.5 mg and 5 mg Gastro-Resistant Tablets (Auden McKenzie (Pharma Division) Limited).

What are the possible side effects from Prednisolone Tablets?
Like all medicines, Prednisolone Tablets can cause side effects, although not everybody gets them.

For the full list of all side effects reported with Prednisolone Tablets, see section 4 of the package leaflet.

For the full list of restrictions, see the package leaflet.

Why are Prednisolone Tablets approved?
No new or unexpected safety concerns arose from these applications. The MHRA, therefore, considered that the benefits of Prednisolone Tablets outweigh their risks; and the grant of Marketing Authorisations was recommended.

What measures are being taken to ensure the safe and effective use of Prednisolone Tablets?
A Risk Management Plan has been developed to ensure that Prednisolone Tablets are used as safely as possible. Based on this plan, safety information has been included in the Summaries of Product Characteristics and the package leaflet for Prednisolone Tablets, 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/reviewed continuously.

Other information about Prednisolone Tablets.
Marketing Authorisations were granted in the UK to Lime Pharma Limited on 11 May 2015.

Subsequent to Change of Ownership procedures, the Marketing Authorisations Prednisolone 2.5 mg and 5 mg Gastro-Resistant Tablets (PL 17907/0553-0556) were granted to Bristol Pharmaceuticals Limited on 18 June 2015.
The full PAR for Prednisolone Tablets follows this summary.

For more information about treatment with Prednisolone Tablets, read the package leaflet, or contact your doctor or pharmacist.

This summary was last updated in July 2015.
Prednisolone 2.5 mg Gastro-Resistant Tablets
Prednisolone 5 mg Gastro-Resistant Tablets

PL 17907/0553-0556

SCIENTIFIC DISCUSSION

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INTRODUCTION

The Medicines and Healthcare products Regulatory Agency (MHRA) granted Lime Pharma Limited Marketing Authorisations for the medicinal products Prednisolone 2.5 mg and 5 mg Gastro-Resistant Tablets (PL 20620/0098-0101) on 11 May 2015. These are prescription-only medicines (POM) indicated for the following:

- **Allergy and anaphylaxis**: bronchial asthma, drug hypersensitivity reactions, serum sickness, angioneurotic oedema, anaphylaxis.
- **Arteritis/collagenosis**: giant cell arteritis/polymyalgia rheumatica, mixed connective tissue disease, polyarteritis nodosa, polymyositis.
- **Blood disorders**: haemolytic anaemia (auto-immune), leukaemia (acute and chronic lymphocytic), lymphoma, multiple myeloma, idiopathic thrombo-cytopenic purpura.
- **Cardiovascular disorders**: post-myocardial infarction syndrome, rheumatic fever with severe carditis.
- **Endocrine disorders**: primary and secondary adrenal insufficiency, congenital adrenal hyperplasia.
- **Gastro-intestinal disorders**: Crohn’s disease, ulcerative colitis, persistent coeliac disease (coeliac disease unresponsive to gluten withdrawal), auto-immune chronic active hepatitis, multisystem disease affecting liver, biliary peritonitis.
- **Hypercalcaemia**: sarcoidosis, vitamin D excess.
- **Infections (with appropriate chemotherapy)**: helminthic infestations, Herxheimer reaction, infectious mononucleosis, miliary tuberculosis, mumps orchitis (adult), tuberculous meningitis, rickettsial disease.
- **Muscular disorders**: polymyositis, dermatomyositis.
- **Neurological disorders**: infantile spasms, Shy-Drager syndrome, sub-acute demyelinating polyneuropathy.
- **Ocular disease**: scleritis, posterior uveitis, retinal vasculitis, pseudo-tumours of the orbit, giant cell arteritis, malignant ophthalmic Graves disease.
- **Renal disorders**: lupus nephritis, acute interstitial nephritis, minimal change glomerulonephritis.
- **Respiratory disease**: allergic pneumonitis, asthma, occupational asthma, pulmonary aspergillosis, pulmonary fibrosis, pulmonary alveolitis, aspiration of foreign body, aspiration of stomach contents, pulmonary sarcoïd, drug induced lung disease, adult respiratory distress syndrome, spasmodic croup.
- **Rheumatic disorders**: rheumatoid arthritis, polymyalgia rheumatica, juvenile chronic arthritis, systemic lupus erythematosus, dermatomyositis, mixed connective tissue disease.
- **Skin disorders**: pemphigus vulgaris, bullous pemphigoid, systemic lupus erythematosus, pyoderma gangrenosum.
- **Miscellaneous**: sarcoidosis, hyperpyrexia, Behçets disease, immuno-suppression in organ transplantation.

The applications were submitted as abridged applications according to Article 10c of Directive 2001/83/EC, as amended, cross-referring to Dilacort 2.5 mg and 5 mg Gastro-Resistant Tablets (PL 17507/0186-187; Auden McKenzie (Pharma Division) Limited), which were authorised on 28 December 2012 as generic applications under Article 10(1) of Directive 2001/83/EC as amended. Dilacort 2.5 mg and 5 mg Gastro-Resistant Tablets (PL 17507/0186-187; Auden McKenzie (Pharma Division) Limited) cross-refer to Deltacortril 2.5mg and 5mg Gastro-resistant Tablets (PL 16853/0092-0093), which are currently marketed by Alliance Pharmaceuticals Limited).

Prednisolone 2.5 mg and 5 mg Gastro-Resistant Tablets contain the active ingredient prednisolone, which is a synthetic glucocorticoid that is used clinically for its anti-inflammatory and immune-suppressive properties. It has low mineralocorticoid activity making the drug of choice for all conditions in which routine systemic corticosteroid therapy is indicated.
Prednisolone is the active metabolite of prednisone, with a predominant glucocorticoid and low mineralocorticoid activity, making it useful for the treatment of a wide range of inflammatory and auto-immune conditions.

No new data were submitted nor were necessary to be submitted for these applications, as the data are identical to that of the previously granted cross-reference products.

Subsequent to Change of Ownership procedures, the Marketing Authorisations Prednisolone 2.5 mg and 5 mg Gastro-Resistant Tablets (PL 17907/0553-0556) were granted to Bristol Pharmaceuticals Limited on 18 June 2015.
PHARMACEUTICAL ASSESSMENT

LICENCE NO: PL 17907/0553-0556 (formerly PL 20620/0098-0101)
PROPRIETARY NAME(S): Prednisolone 2.5 mg and 5 mg Gastro-Resistant Tablets
ACTIVE(S): Prednisolone
COMPANY NAME: Bristol Laboratories Limited
E.C. ARTICLE: Article 10c of Directive 2001/83/EC, as amended
LEGAL STATUS: POM

1. INTRODUCTION
These are abridged applications for the products Prednisolone 2.5 mg and 5 mg Gastro-Resistant Tablets (PL 17907/0553-0556, formerly PL 20620/0098-0101) submitted under Article 10c of Directive 2001/83/EC, as amended.

The applications cross-refer to Dilacort 2.5 mg and 5 mg Gastro-Resistant Tablets (PL 17507/0186-0187; Auden McKenzie (Pharma Division) Limited), which were granted Marketing Authorisations in the UK on 28 December 2012. Dilacort 2.5 mg and 5 mg Gastro-Resistant Tablets (PL 17507/0186-187; Auden McKenzie (Pharma Division) Limited) cross-refer to Deltacortril 2.5 mg and 5 mg Gastro-resistant Tablets (PL 16853/0092-0093), which are currently marketed by Alliance Pharmaceuticals Limited). The applications are considered valid.

2. MARKETING AUTHORISATION APPLICATION FORM
2.1. Name
The proposed names of the products are Prednisolone 2.5 mg and 5 mg Gastro-Resistant Tablets (PL 17507/0553-0556 formerly PL 20620/0098-0101). The products have been named in line with current requirements.

2.2. Strength, pharmaceutical form, route of administration, container and pack sizes
Each gastro-resistant tablet contains 2.5 mg or 5 mg of prednisolone.

The products are packaged in polyvinylchloride/ polyvinylidene chloride /aluminium (PVC/PVdC/Al) blisters, in a pack size of 28 tablets.

The proposed shelf life for the products is 36 months, with the special storage conditions ‘Store below30°C’. The packaging, proposed shelf-life and storage conditions are consistent with the details registered for the respective cross reference products.

2.3. Legal status
On approval, the products will be available as a Prescription Only Medicines (POM).

2.4. Marketing Authorisation Holder/Contact Persons/Company
Bristol Laboratories Limited, Unit 3, Canalside, Northbridge Road, Berkhamsted, Hertfordshire, HP4 1EG, United Kingdom.

The Qualified Person (QP) responsible for pharmacovigilance is stated and a satisfactory CV has been provided.

2.5 Manufacturers
The proposed manufacturing sites are consistent with those registered for the cross-reference products and evidence of Good Manufacturing Practice (GMP) compliance has been provided.

2.6. Qualitative and quantitative composition
The proposed compositions are consistent with the details registered for the respective cross-reference products.
2.7. Manufacturing process
The proposed manufacturing processes are consistent with the details registered for the cross-reference products and the maximum batch sizes are stated.

2.8. Finished product/shelf-life specification
The proposed finished product specifications are consistent with the details registered for the cross-reference products.

2.9. Drug substance specification
The proposed drug substance specification is consistent with the details registered for the cross-reference products.

2.10. TSE Compliance
With the exception of lactose monohydrate, none of the excipients contain materials of animal or human origin. The supplier of lactose monohydrate has confirmed that the milk used in the production of lactose monohydrate is sourced from healthy animals under the same conditions as that intended for human consumption. In addition, the supplier has confirmed that no ruminant material other than calf rennet is used during the production of lactose monohydrate. This is consistent with the cross-reference products.

2.11. Bioequivalence
No bioequivalence data are required to support these simple abridged application because the proposed products are manufactured to the same formulae and utilises the same processes as the reference products to Dilacort 2.5 mg and 5 mg gastro-resistant tablets (PL 17507/0186-0187; Auden McKenzie (Pharma Division) Limited).

3. EXPERT REPORT
The applicant cross-refers to the data for to Dilacort 2.5 mg and 5 mg gastro-resistant tablets (PL 17507/0186-0187; Auden McKenzie (Pharma Division) Limited), to which these applications are claimed to be identical. This is acceptable.

4. PRODUCT NAME & APPEARANCE
See Section 2.1 for details of the proposed product names. The appearance of each product is identical to the respective cross-reference product.

5. SUMMARIES OF PRODUCT CHARACTERISTICS (SmPCs)
The proposed SmPCs are consistent with the details registered for the respective cross-reference products.

6. PATIENT INFORMATION LEAFLET (PIL) AND LABELLING
PIL
The PIL has been prepared in line with the details registered for the cross-reference products.

Carton and label
The proposed text is consistent with that for the cross-reference products. The Marketing Authorisation holder has committed to submitting mock-ups to the relevant regulatory authorities for approval before marketing the products.

7. CONCLUSION
The data submitted with the applications are acceptable. The grant of Marketing Authorisations is recommended.
NON-CLINICAL ASSESSMENT

As these are abridged applications submitted under Article 10c of Directive 2001/83/EC, as amended, no new non-clinical data have been supplied and none are required.

Suitable justification has been provided for non-submission of an Environmental Risk Assessment. As the applications are identical versions of already authorised products, it is not expected that environmental exposure will increase following approval of the Marketing Authorisations for the proposed products.

The grant of Marketing Authorisations is recommended.
CLINICAL ASSESSMENT

As these are abridged applications submitted under Article 10c of Directive 2001/83/EC, as amended, no new clinical data have been supplied and none are required.

The Marketing Authorisation Holder has provided details of a suitable pharmacovigilance system that fulfils the requirements and provides adequate evidence that they have the services of a qualified person responsible for pharmacovigilance, and have the necessary means for the notification of any adverse reaction suspected of occurring either in the Community or in a third country.

An acceptable Risk Management Plan (RMP) has been submitted. Routine risk minimisation is provided through the Summaries of Product Characteristics and the Patient Information Leaflet and this is sufficient.

The grant of Marketing Authorisations is recommended.
OVERALL CONCLUSION AND BENEFIT/RISK ASSESSMENT

QUALITY
The data for the applications are consistent with those previously assessed for the cross-reference products and as such have been judged to be satisfactory.

NON-CLINICAL
No new non-clinical data were submitted and none are required for applications of this type.

EFFICACY
The applications are identical to the previously granted licences for Dilacort 2.5 mg and 5 mg Gastro-Resistant Tablets (PL 17507/0186-0187; Auden McKenzie (Pharma Division) Limited.

SAFETY
No new safety data were supplied or required for these applications. Prednisolone has a well-established safety profile. No new or unexpected safety concerns arose from these applications.

PRODUCT LITERATURE
The SmPCs and PIL are satisfactory, and consistent with those for the cross-reference products. The labelling text complies with statutory requirements and is satisfactory.

BENEFIT/RISK ASSESSMENT
The quality of the products is acceptable, and no new non-clinical or clinical safety concerns have been identified. The applicant’s products are identical to the cross-reference products. Extensive clinical experience with prednisolone is considered to have demonstrated the therapeutic value of the compounds. The benefit/risk assessment is, therefore, considered to be positive.
Prednisolone 2.5 mg Gastro-Resistant Tablets
Prednisolone 5 mg Gastro-Resistant Tablets

PL 17907/0553-0556

STEPS TAKEN FOR ASSESSMENT

1 The MHRA received the Marketing Authorisation applications (PL 20620/0098-0101) on 27 June 2014.

2 Following standard checks and communication with the applicant the MHRA considered the applications valid on 21 August 2014.

3 Following assessment of the application the MHRA requested further information relating to the dossier on 19 November 2014 and 16 March 2015.

4 The applicant responded to the MHRA’s request, providing further information on the 22 January 2015 and 18 March 2015.

5 The applications were granted on 11 May 2015.
**Prednisolone 2.5 mg Gastro-Resistant Tablets**
**Prednisolone 5 mg Gastro-Resistant Tablets**

**PL 17907/0553-0556**

**STEPS TAKEN AFTER AUTHORISATION - SUMMARY**

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SUMMARY OF PRODUCT CHARACTERISTICS

In accordance with Directive 2010/84/EU, the Summaries of Product Characteristics (SmPCs) for products granted Marketing Authorisations at a national level are available on the MHRA website.
PATIENT INFORMATION LEAFLET

In accordance with Directive 2010/84/EU, the Patient Information Leaflets (PILs) for products granted Marketing Authorisations at a national level are available on the MHRA website.
LABELLING
The Marketing Authorisation Holder has submitted a text version only and has committed to submitting mock-up livery to the relevant regulatory authorities for approval before packs are marketed.
1. NAME OF THE MEDICINAL PRODUCT

Prednisolone 2.5 mg Gastro-Resistant Tablets
Prednisolone 5 mg Gastro-Resistant Tablets

2. STATEMENT OF ACTIVE SUBSTANCES

Prednisolone 2.5 mg Tablets: Each tablet contains 2.5 mg prednisolone.
Prednisolone 5 mg Tablets: Each tablet contains 5 mg prednisolone.

3. LIST OF EXCIPIENTS

Prednisolone 2.5 mg Tablets: Also contains lactose monohydrate. See leaflet for further information.
Prednisolone 5 mg Tablets: Also contains lactose monohydrate, sunset yellow FCF (E110) & ponceau 4R red (E124). See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Gastro-Resistant Tablets: 28 tablets

5. METHOD AND ROUTES OF ADMINISTRATION

For oral use

Please read the enclosed package leaflet before use.

6. SPECIAL WARNINGS THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE REACH AND SIGHT OF CHILDREN

Keep medicines out of the reach and sight of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

-

8. EXPIRY DATE

Exp: MM/ YYYY

9. SPECIAL STORAGE CONDITIONS

Store below 30 °C.

10. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Bristol Laboratories Ltd.,
Berkhamsted, Herts, HP4 1EG, UK

11. MARKETING AUTHORISATION NUMBER
UKPAR Prednisolone 2.5 mg and 5 mg Gastro-Resistant Tablets

12. MANUFACTURERS BATCH NUMBER

BN: XXXX

13. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.
POM

14. OTHER

Swallow the tablets whole. Do not crush or chew.

15. INSTRUCTIONS FOR USE

- 

Label Text - Blister

1. NAME OF THE MEDICINAL PRODUCT

Prednisolone 2.5 mg Gastro-Resistant Tablets
Prednisolone 5 mg Gastro-Resistant Tablets

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Bristol Laboratories Ltd.

3. EXPIRY DATE

Exp: MM/YYYY

4. BATCH NUMBER

BN: XXXX