Public Assessment Report

UKPAR

Clobetasol Propionate 0.05% w/w Cream
Clobetasol Propionate 0.05% w/w Ointment

(Clobetasol propionate).

UK Licence No: PL 17507/0235-0236

Auden Mckenzie (Pharma Division) Ltd.
LAY SUMMARY

Clobetasol Propionate 0.05% w/w Cream/Ointment
(Clobetasol propionate, cream or ointment, 0.05% w/w)

This is a summary of the Public Assessment Report (PAR) for Clobetasol Propionate 0.05% w/w Cream (PL 17507/0235) and Clobetasol Propionate 0.05% w/w Ointment (PL 17507/00236). It explains how Clobetasol Propionate 0.05% w/w Cream and Clobetasol Propionate 0.05% w/w Ointment were assessed and their authorisation recommended, as well as their conditions of use. It is not intended to provide practical advice on how to use Clobetasol Propionate 0.05% w/w Cream and Clobetasol Propionate 0.05% w/w Ointment.

The products will be collectively referred to as Clobetasol Propionate Cream & Ointment throughout the remainder of this public assessment report.

For practical information about using Clobetasol Propionate Cream & Ointment patients should read the package leaflet or contact their doctor or pharmacist.

What are Clobetasol Propionate Cream & Ointment and what are they used for?
Clobetasol Propionate Cream & Ointment contain the active ingredient clobetasol propionate which is used to help reduce the redness and itchiness of certain skin problems. These skin problems include eczema, psoriasis and dermatitis that have not responded to milder steroid creams or ointments.

This medicine is identical to ClobaDerm 0.05% w/w Cream (PL 17507/0109) and ClobaDerm 0.05% w/w Ointment (PL 17507/0110) which was first granted Marketing Authorisations on 21 June 2012.

How are Clobetasol Propionate Cream & Ointment used?
The pharmaceutical form of this medicine is a cream or ointment and the route of administration is for use on the skin (topical).

The patient should always use this medicine exactly as the patient’s doctor or pharmacist has told them. The patient should check with their doctor or pharmacist if they are not sure.

The patient will usually apply a thin layer of Clobetasol Propionate Cream or Ointment 1 or 2 times a day. This may be reduced as the patient’s skin begins to get better, or stopped when it is better.

The cream or ointment is for use on the skin only.

The patient must not use this medicine on large areas of the body for a long time (such as every day for many weeks or months). If the patient needs treatment for a long time, their doctor may decide the patient needs to use a milder cream or ointment.

The germs that cause infections like warm and moist conditions under dressings so always clean the skin before a fresh dressing is put on. If you are applying the cream or ointment on someone else make sure you wash your hands after use or wear disposable plastic gloves.

If the patient’s skin problem does not improve in 2 to 4 weeks, they should talk to their doctor.

Please refer to section 3 of the package leaflet for information on how to use and apply this medicine.
Clobetasol Propionate Cream & Ointment can be obtained only with a prescription.

For further information on how Clobetasol Propionate Cream & Ointment are used, refer to the package leaflet and Summary of Product Characteristics available on the Medicines and Healthcare products Regulatory Agency (MHRA) website.

How do Clobetasol Propionate Cream & Ointment work?
The active ingredient, clobetasol propionate, belongs to a group of medicines called steroids. It helps to reduce swelling and irritation.

What benefits of Clobetasol Propionate Cream & Ointment have been shown in studies?
The applications for Clobetasol Propionate Cream & Ointment are considered to be identical to the previously authorised applications for ClobaDerm 0.05% w/w Cream (PL 17507/0109) and ClobaDerm 0.05% w/w Ointment (PL 17507/0110), with the same benefits and risks, so, no new studies have been provided for Clobetasol Propionate Cream & Ointment. However, reference is made to the studies for ClobaDerm 0.05% w/w Cream (PL 17507/0109) and ClobaDerm 0.05% w/w Ointment (PL 17507/0110).

The company (Auden Mckenzie (Pharma Division) Ltd) referred to the data it provided for the grant of the licences for ClobaDerm 0.05% w/w Cream (PL 17507/0109) and ClobaDerm 0.05% w/w Ointment (PL 17507/0110) as a basis for the grant of identical licences for Clobetasol Propionate Cream & Ointment (PL 17507/0235-0236).

What are the possible side effects from Clobetasol Propionate Cream & Ointment?
Like all medicines, this medicine can cause side effects, although not everybody gets them.

Clobetasol Propionate Cream & Ointment (PL 17507/0235-0236) are considered to be identical to the previously authorised applications for ClobaDerm 0.05% w/w Cream (PL 17507/0109) and ClobaDerm 0.05% w/w Ointment (PL 17507/0110) with the same benefits and risks.

For a full list of all the side effects reported with Clobetasol Propionate Cream & Ointment see section 4 of the package leaflet, available on the Medicines and Healthcare products Regulatory Agency (MHRA) website.

Why is Clobetasol Propionate Cream & Ointment approved?
No new or unexpected safety concerns arose from these applications. The MHRA, therefore, considered that the benefits of Clobetasol Propionate Cream & Ointment outweigh their risks; and the grant of Marketing Authorisations (licences) was recommended.

What measures are being taken to ensure the safe and effective use of Clobetasol Propionate Cream & Ointment?
A Risk Management Plan has been developed to ensure that Clobetasol Propionate Cream & Ointment 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 Clobetasol Propionate Cream & Ointment 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 Clobetasol Propionate Cream & Ointment
Marketing Authorisations were granted in the UK on 02 June 2015.
The full PAR for Clobetasol Propionate Cream & Ointment follows this summary.

For more information about treatment with Clobetasol Propionate Cream & Ointment read the package leaflet, or contact your doctor or pharmacist.

This summary was last updated in July 2015.
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I INTRODUCTION
The Medicines and Healthcare products Regulatory Agency (MHRA) granted Auden Mckenzie (Pharma Division) Ltd Marketing Authorisations for the medicinal products Clobetasol Propionate Cream & Ointment (PL 17507/0235-0236) on 02 June 2015. The products are prescription-only medicines (POM).

Clobetasol propionate is a very active topical corticosteroid which is of particular value when used in short courses for the treatment of more resistant dermatoses such as psoriasis (excluding widespread plaque psoriasis), recalcitrant eczemas, lichen planus, discoid lupus erythematosus, and other skin conditions which do not respond satisfactorily to less active steroids.

These applications were submitted as abridged applications according to Article 10c of Directive 2001/83/EC, as amended.

The applications cross-refer to ClobaDerm 0.05% w/w Cream (PL 17507/0109) and ClobaDerm 0.05% w/w Ointment (PL 17507/0110) which were first authorised to Auden Mckenzie (Pharma Division) Ltd on 21 June 2012.

Clobetasol propionate is a highly active corticosteroid with topical anti-inflammatory activity. The major effect of clobetasol propionate on skin is a non-specific anti-inflammatory response, partially due to vasoconstriction and decrease in collagen synthesis.

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.
II QUALITY ASPECTS

II.1 Introduction
These are abridged applications for Clobetasol Propionate Cream & Ointment (PL 17507/0235-0236) submitted under Article 10c of Directive 2001/83/EC, as amended.

The applications cross-refer to ClobaDerm 0.05% w/w Cream (PL 17507/0109) and ClobaDerm 0.05% w/w Ointment (PL 17507/0110) which were first authorised to Auden Mckenzie (Pharma Division) Ltd on 21 June 2012. The applications are considered valid.

II.2 Drug Substance
Drug substance specification
The proposed drug substance specifications are consistent with the details registered for the cross-reference products.

II.3 Medicinal Product
Name
The proposed product names for these applications are Clobetasol Propionate 0.05% w/w Cream (PL 17507/0235) and Clobetasol Propionate 0.05% w/w Ointment (PL17507/00236). The product has been named in line with current requirements.

Strength, pharmaceutical form, route of administration, container and pack sizes
Each gram of cream or ointment contains 0.5 mg of clobetasol propionate (0.05% w/w).

Both pharmaceutical forms of the finished product (cream and ointment) are packed into collapsible aluminium tubes internally coated with an epoxy resin based lacquer and closed with a polypropylene cap in pack sizes of 30 g or 100g tubes.

Not all pack sizes may be marketed.

The proposed shelf life of the unopened product is 2 years with the storage condition ‘Store below 30°C.’ Once opened, the in-use shelf life of the product is 3 months.

The proposed packaging, shelf-life and storage conditions are consistent with the details registered for the cross-reference product.

Legal status
On approval, the products will be available as prescription-only medicines (POM).

Marketing Authorisation Holder/Contact Persons/Company
Auden Mckenzie (Pharma Division) Ltd, McKenzie House, Bury Street, Ruislip, Middlesex, HA4 7TL, UK.

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

Qualitative and quantitative composition
The proposed compositions are consistent with the details registered for the cross-reference products.

Manufacturing process
The proposed manufacturing processes are consistent with the details registered for the cross-reference products and the maximum batch sizes are stated.

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

TSE Compliance
None of the excipients contain materials of animal or human origin. This is consistent with the cross-reference products.

Bioequivalence
No bioequivalence data are required to support these simple abridged applications because the proposed products are manufactured to the same formula utilising the same processes as the cross-reference products, ClobaDerm 0.05% w/w Cream (PL 17507/0109) and ClobaDerm 0.05% w/w Ointment (PL 17507/0110).

Expert Report
The applicant cross-refers to the data for ClobaDerm 0.05% w/w Cream (PL 17507/0109) and ClobaDerm 0.05% w/w Ointment (PL 17507/0110) to which these applications are claimed to be identical. This is acceptable.

Product Name and Appearance
See Section II.3 ‘Medicinal Product; Name’ for details of the proposed product name. The appearance of each product is identical to that of the cross-reference product.

II.4 Discussion on chemical, pharmaceutical and biological aspects
The data submitted with the applications are acceptable. The grant of Marketing Authorisations is recommended.
III NON-CLINICAL ASPECTS

Introduction
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.

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

Discussion on the non-clinical aspects
The grant of Marketing Authorisations is recommended.

IV CLINICAL ASPECTS

Introduction
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.

Risk Management Plan (RMP)
The marketing authorisation holder (MAH) has submitted a risk management plan (RMP), 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 Clobetasol Propionate Cream & Ointment.

A summary of safety concerns and planned risk minimisation activities, as approved in the RMP, are listed below:

Summary table of safety concerns:

<table>
<thead>
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<th>Important identified risks</th>
<th>Hypersensitivity to the preparation</th>
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<tbody>
<tr>
<td></td>
<td>Local skin reactions e.g. contact dermatitis, allergic reactions</td>
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<td></td>
<td>Use in Rosacea, Acne vulgaris, Perioral dermatitis, Perianal and genital pruritus, Primary cutaneous viral infections (e.g. herpes simplex, chickenpox).</td>
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<tr>
<td></td>
<td>The use of Clobetasol Propionate skin preparations is not indicated in the treatment of primary infected skin lesions caused by infection with fungi (e.g. candidiasis, tinea) or bacteria (e.g. impetigo): or dermatoses in children under one year of age, including dermatitis and napkin eruptions.</td>
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<tr>
<td></td>
<td>Adrenal suppression – long term continuous therapy particularly in children.</td>
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Routine pharmacovigilance and routine risk minimisation are proposed for all safety concerns.

**Discussion on the clinical aspects**
The grant of Marketing Authorisations is recommended.

**V User consultation**
User-testing of the PIL for Clobetasol Propionate Cream & Ointment has been accepted based on the bridging report provided by the applicant making reference to the successful user-testing of the PIL for ClobaDerm 0.05% w/w Cream (PL 17507/0109) and ClobaDerm 0.05% w/w Ointment (PL 17507/0110) as the ‘parent PIL’.

**VI Overall conclusion, benefit/risk assessment and recommendation**
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 clobetasol propionate is considered to have demonstrated the therapeutic value of the compound. The benefit/risk balance is, therefore, considered to be positive.
Summaries of Product Characteristics (SmPC), Patient Information Leaflets (PIL) and Labels

The Summaries of Product Characteristics and Patient Information Leaflet (PIL) are consistent with the details registered for the cross-reference products.

In accordance with Directive 2010/84/EU the Summaries of Product Characteristics (SmPCs) and Patient Information Leaflets (PILs) for products granted Marketing Authorisations at a national level are available on the MHRA website.

The approved labelling for Clobetasol Propionate Cream & Ointment is presented below:
Batch (BN XXXX) / expiry (EXP MM/YYYY) details will be applied to the tube crimp during production.
PAR Clobetasol Propionate 0.05% w/w Cream/Ointment

Batch (BN XXXX) / expiry (EXP MM/YYYY) details will be applied to the tube crimp during production.

Clobetasol Propionate 0.05% w/w Ointment

1 g of ointment contains 0.5 mg of clobetasol propionate (0.05% w/w).

1 g of ointment contains 0.5 mg of clobetasol propionate (0.05% w/w). Excipients: Also contains propylene glycol, sorbitan sesquiostearate and white soft paraffin. See leaflet for further information.

Please read the enclosed leaflet before use. For information, for external use only.

KEEP OUT OF THE REACH AND SIGHT OF CHILDREN
Do not store above 20°C. This medicine should be disposed of 3 months after first opening. Medicinal product subject to medical prescription.

PLA Healthcare