Public Assessment Report

UKPAR

Clobetasone butyrate 0.05% w/w Ointment

(Clobetasone butyrate).

UK Licence No: PL 17507/0237

Auden Mckenzie (Pharma Division) Ltd.
LAY SUMMARY

Clobetasone butyrate 0.05% w/w Ointment
(Clobetasone butyrate, ointment, 0.05% w/w)

This is a summary of the Public Assessment Report (PAR) for Clobetasone butyrate 0.05% w/w Ointment (PL 17507/0237). It explains how Clobetasone butyrate 0.05% w/w Ointment 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 Clobetasone butyrate 0.05% w/w Ointment.

The product will be referred to as Clobetasone butyrate Ointment throughout the remainder of this public assessment report.

For practical information about using Clobetasone butyrate Ointment patients should read the package leaflet or contact their doctor or pharmacist.

What is Clobetasone butyrate Ointment and what is it used for?
Clobetasone butyrate Ointment contains the active ingredient clobetasone butyrate which is used to help reduce the redness and itchiness of certain skin problems. It is used for mild skin problems or to keep the patient’s skin problems under control. These skin problems include eczema, dermatitis or insect bites. It is also used to help reduce inflammation of the outer ear.

This medicine is identical to Clobavate 0.05% w/w ointment (PL 17507/0118) which was first granted a Marketing Authorisation on 18 January 2013.

How is Clobetasone butyrate Ointment used?
The pharmaceutical form of this medicine is an 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 Clobetasone butyrate Ointment up to 2 times a day. This may be reduced as the patient’s skin begins to get better.

The 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) unless their doctor tells them to.

If the patient is using an emollient (moisturising) preparation, they must allow time for the ointment to be absorbed after each application before applying the emollient.

If the patient’s skin problem does not improve, 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.

Clobetasone butyrate Ointment can be obtained only with a prescription.
For further information on how Clobetasone butyrate Ointment is used, refer to the package leaflet and Summary of Product Characteristics available on the Medicines and Healthcare products Regulatory Agency (MHRA) website.

**How does Clobetasone butyrate Ointment work?**
The active ingredient, clobetasone butyrate, belongs to a group of medicines called steroids. It helps to reduce swelling and irritation.

**What benefits of Clobetasone butyrate Ointment have been shown in studies?**
The application for Clobetasone butyrate Ointment is considered to be identical to the previously authorised application for Clobavate 0.05% w/w ointment (PL 17507/0118), with the same benefits and risks, so, no new studies have been provided for Clobetasone butyrate Ointment. However, reference is made to the studies for Clobavate 0.05% w/w ointment (PL 17507/0118).

The company (Auden Mckenzie (Pharma Division) Ltd) referred to the data it provided for the grant of the licence for Clobavate 0.05% w/w ointment (PL 17507/0118) as a basis for the grant of an identical licence for Clobetasone butyrate Ointment (PL 17507/0237).

**What are the possible side effects from Clobetasone butyrate Ointment?**
Like all medicines, this medicine can cause side effects, although not everybody gets them.

Clobetasone butyrate Ointment (PL 17507/0237) is considered to be identical to the previously authorised application for Clobavate 0.05% w/w ointment (PL 17507/0118) with the same benefits and risks.

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

**Why is Clobetasone butyrate Ointment approved?**
No new or unexpected safety concerns arose from this application. The MHRA, therefore, considered that the benefits of Clobetasone butyrate Ointment outweigh their risks; and the grant of a Marketing Authorisation (licence) was recommended.

**What measures are being taken to ensure the safe and effective use of Clobetasone butyrate Ointment?**
A Risk Management Plan has been developed to ensure that Clobetasone butyrate Ointment is used as safely as possible. Based on this plan, safety information has been included in the Summary of Product Characteristics and the package leaflet for Clobetasone butyrate 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 Clobetasone butyrate Ointment**
A Marketing Authorisation was granted in the UK on 02 June 2015.

The full PAR for Clobetasone butyrate Ointment follows this summary.

For more information about treatment with Clobetasone butyrate 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 a Marketing Authorisation for the medicinal product Clobetasone butyrate Ointment (PL 17507/0237) on 02 June 2015. The product is a prescription-only medicine (POM).

Clobetasone butyrate Ointment is suitable for the treatment of corticosteroid sensitive dermatoses, including atopic eczema, photodermatitis, otitis externa, primary irritant and allergic dermatitis (including napkin rash), intertrigo, prurigo nodularis, seborrhoeic dermatitis and insect bite reactions.

This application was submitted as an abridged application according to Article 10c of Directive 2001/83/EC, as amended.

The application cross-refers to Clobavate 0.05% w/w ointment (PL 17507/0118) which was first authorised to Auden Mckenzie (Pharma Division) Ltd on 18 January 2013 via the decentralised procedure with the UK as reference member state (RMS).

Clobetasone butyrate is a topically active corticosteroid of moderate potency (UK Class II - 2-25 times as potent as hydrocortisone). Clobetasone butyrate has little effect on hypothalamo-pituitary-adrenal function, even when applied to adults in large amounts under whole body occlusion. It is less potent than other available corticosteroid preparations and has been shown not to suppress the hypothalamo-pituitary-adrenal axis in patients treated for psoriasis or eczema.

Pharmacological studies in man and animals have shown that clobetasone butyrate has a relatively high level of topical activity accompanied by a low level of systemic activity.

No new data were submitted nor were necessary to be submitted for this application, as the data are identical to that of the previously granted cross-referenced product.
II QUALITY ASPECTS

II.1 Introduction
This is an abridged application for Clobetasone butyrate Ointment (PL 17507/0237) submitted under Article 10c of Directive 2001/83/EC, as amended.

The application cross-refers to Clobavate 0.05% w/w ointment (PL 17507/0118) which was first authorised to Auden Mckenzie (Pharma Division) Ltd on 18 January 2013. The application is considered valid.

II.2 Drug Substance

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

II.3 Medicinal Product

Name
The proposed product name for this application is Clobetasone butyrate 0.05% w/w Ointment (PL 17507/0237). The product has been named in line with current requirements.

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

The finished product is 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 36 months with the storage condition ‘Store in the original package in order to protect from light.’ 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 product will be available as a prescription-only medicine (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 product and evidence of Good Manufacturing Practice (GMP) compliance has been provided.

Qualitative and quantitative composition
The proposed composition is consistent with the details registered for the cross-reference product.

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

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

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

Bioequivalence
No bioequivalence data are required to support this simple abridged application because the proposed product is manufactured to the same formula utilising the same processes as the cross-reference product, Clobavate 0.05% w/w ointment (PL 17507/0118).

Expert Report
The applicant cross-refers to the data for Clobavate 0.05% w/w ointment (PL 17507/0118) to which this application is 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 application is acceptable. The grant of a Marketing Authorisation is recommended.
III NON-CLINICAL ASPECTS
Introduction
As this is an abridged application 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 application is an identical version of an already authorised product, it is not expected that environmental exposure will increase following approval of the Marketing Authorisation for the proposed product.

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

IV CLINICAL ASPECTS
Introduction
As this is an abridged application 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 Clobetasone butyrate 0.05% w/w Ointment.

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

Summary table of safety concerns:

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<thead>
<tr>
<th>Important identified risks</th>
<th>Hypersensitivity</th>
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<tr>
<td></td>
<td>Use in acne vulgaris, rosacea or in perioral dermatoses.</td>
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<td></td>
<td>Use in the presence of untreated infections of bacterial, tuberculous, treponemal, viral or fungal origin.</td>
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<td>Adrenal suppression and growth retardation – continuous treatment longer than 3 weeks particularly in children under the age of 3 years.</td>
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<td>Cushingoid (a hormone disorder which can cause symptoms including gaining weight quickly, especially on the trunk and face, thinning of the skin and sweating) features (moon face, hirsutism (excess body hair), buffalo hump, flushing, ecchymoses (bruising), striae (stretch marks) &amp; acne)</td>
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<td>Use in psoriasis - topical corticosteroids may be hazardous in psoriasis for a number of reasons including rebound relapses, development of tolerance, risk of generalised pustular psoriasis and development of local or systemic toxicity due to impaired barrier function of the skin.</td>
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<tr>
<th>Important potential risks</th>
<th>Glaucoma – if applied to eyelids</th>
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<td>Co-administration of antivirals and antifungals</td>
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<th>Important missing information</th>
<th>Use in pregnancy</th>
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<td>Use in lactation</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 a Marketing Authorisation is recommended.

**V User consultation**
User-testing of the PIL for Clobetasone butyrate 0.05% w/w Ointment has been accepted based on the bridging report provided by the applicant making reference to the successful user-testing of the PIL for Clobavate 0.05% w/w ointment (PL 17507/0118) as the ‘parent PIL’.

**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. The applicant’s product is identical to the cross-reference product. Extensive clinical experience with clobetasone butyrate 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 Summary 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 Clobetasone butyrate 0.05% w/w Ointment is presented below:
PAR Clobetasone butyrate 0.05% w/w Ointment

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

Clobetasone Butyrate 0.05% w/w Ointment
Each 1 g of ointment contains 3.5 mg of clobetasone butyrate.

Please read the enclosed leaflet before use.
Not for external use only.

KEEP OUT OF THE REACH AND SIGHT OF CHILDREN
This medicine should be disposed of 3 months after first opening.
Store in the original packaging in order to protect from light.
Medicinal product subject to medical prescription.

30g