

Public Assessment Report

UKPAR

Betamethasone Valerate 0.1% w/w Ointment
Betamethasone Valerate 0.025% w/w Cream
Betamethasone Valerate 0.025% w/w Ointment
(Betamethasone valerate).

UK Licence No: PL 17507/0232-0234

Auden Mckenzie (Pharma Division) Ltd.

LAY SUMMARY

Betamethasone Valerate 0.1% w/w Ointment
Betamethasone Valerate 0.025% w/w Cream
Betamethasone Valerate 0.025% w/w Ointment

(Betamethasone valerate, cream or ointment, 0.025% w/w and 0.1% w/w)

This is a summary of the Public Assessment Report (PAR) for Betamethasone Valerate 0.1% w/w Ointment (PL 17507/0232), Betamethasone Valerate 0.025% w/w Cream (PL 17507/0233) and Betamethasone Valerate 0.025% w/w Ointment (PL 17507/0234). It explains how Betamethasone Valerate 0.1% w/w Ointment, Betamethasone Valerate 0.025% w/w Cream and Betamethasone Valerate 0.025% 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 Betamethasone Valerate 0.1% w/w Ointment, Betamethasone Valerate 0.025% w/w Cream and Betamethasone Valerate 0.025% w/w Ointment.

The products will be collectively referred to as Betamethasone Valerate Cream/Ointment throughout the remainder of this public assessment report.

For practical information about using Betamethasone Valerate Cream/Ointment patients should read the package leaflet or contact their doctor or pharmacist.

What is Betamethasone Valerate Cream/Ointment and what are they used for?

Betamethasone Valerate Cream/Ointment contains the active ingredient betamethasone valerate which is used to help reduce the redness and itchiness of certain skin problems. These skin problems include eczema, psoriasis and dermatitis.

Betamethasone Valerate 0.025% w/w preparations contains less active ingredient than Betamethasone Valerate 0.1% preparation and are used for milder skin problems or to keep the patient's skin problem under control after Betamethasone Valerate 0.1% w/w has improved it.

This medicine is identical to Audavate 0.1% w/w Ointment (PL 17507/0113), Audavate RD 0.025% w/w Cream (PL 17507/0115) and Audavate RD 0.025% w/w Ointment (PL 17507/0116) which were first granted Marketing Authorisations on 18 September 2012.

How are Betamethasone Valerate 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 Betamethasone Valerate Cream/Ointment 1 to 3 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) unless their doctor tells them too.

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.

Betamethasone Valerate Cream/Ointment can be obtained only with a prescription.

For further information on how Betamethasone Valerate Cream/Ointment is used, refer to the package leaflets and Summaries of Product Characteristics available on the Medicines and Healthcare products Regulatory Agency (MHRA) website.

How does Betamethasone Valerate Cream/Ointment work?

The active ingredient, betamethasone valerate, belongs to a group of medicines called steroids. It helps to reduce swelling and irritation.

What benefits of Betamethasone Valerate Cream/Ointment have been shown in studies?

The applications for Betamethasone Valerate Cream/Ointment are considered to be identical to the previously authorised applications for Audavate 0.1% w/w Ointment (PL 17507/0113), Audavate RD 0.025% w/w Cream (PL 17507/0115) and Audavate RD 0.025% w/w Ointment (PL 17507/0116), with the same benefits and risks, so, no new studies have been provided for Betamethasone Valerate Cream/Ointment. However, reference is made to the studies for Audavate 0.1% w/w Ointment (PL 17507/0113), Audavate RD 0.025% w/w Cream (PL 17507/0115) and Audavate RD 0.025% w/w Ointment (PL 17507/0116).

The company (Auden Mckenzie (Pharma Division) Ltd) referred to the data it provided for the grant of the licences for Audavate 0.1% w/w Ointment (PL 17507/0113), Audavate RD 0.025% w/w Cream (PL 17507/0115) and Audavate RD 0.025% w/w Ointment (PL 17507/0116) as a basis for the grant of identical licences for Betamethasone Valerate Cream/Ointment (PL 17507/0232-0234).

What are the possible side effects from Betamethasone Valerate Cream/Ointment?

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Betamethasone Valerate Cream/Ointment (PL 17507/0232-0234) are considered to be identical to the previously authorised applications for Audavate 0.1% w/w Ointment (PL 17507/0113), Audavate RD 0.025% w/w Cream (PL 17507/0115) and Audavate RD 0.025% w/w Ointment (PL 17507/0116) with the same benefits and risks.

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

Why is Betamethasone Valerate Cream/Ointment approved?

No new or unexpected safety concerns arose from these applications. The MHRA, therefore, considered that the benefits of Betamethasone Valerate 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 Betamethasone Valerate Cream/Ointment?

A Risk Management Plan has been developed to ensure that Betamethasone Valerate Cream/Ointment is used as safely as possible. Based on this plan, safety information has been included in the Summaries of Product Characteristics and the package leaflets for Betamethasone Valerate 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 Betamethasone Valerate Cream/Ointment

Marketing Authorisations were granted in the UK on 12 June 2015.

The full PAR for Betamethasone Valerate Cream/Ointment follows this summary.

For more information about treatment with Betamethasone Valerate Cream/Ointment read the package leaflet, or contact your doctor or pharmacist.

This summary was last updated in July 2015.

TABLE OF CONTENTS

I	Introduction	Page 6
II	Quality aspects	Page 7
III	Non-clinical aspects	Page 9
IV	Clinical aspects	Page 9
V	User consultation	Page 10
VI	Overall conclusion, benefit/risk assessment and recommendation	Page 10

I INTRODUCTION

The Medicines and Healthcare products Regulatory Agency (MHRA) granted Auden Mckenzie (Pharma Division) Ltd Marketing Authorisations for the medicinal products Betamethasone Valerate Cream/Ointment (PL 17507/0232-0234) on 12 June 2015. The products are prescription-only medicines (POM).

Betamethasone Valerate preparations are indicated for the treatment of: eczema in children over 1 year elderly and adults; including atopic and discoid eczemas; prurigo nodularis; psoriasis (excluding widespread plaque psoriasis); neurodermatoses, including lichen simplex, lichen planus; seborrhoeic dermatitis; contact sensitivity reactions; discoid lupus erythematosus and they may be used as an adjunct to systemic steroid therapy in generalised erythroderma.

Betamethasone Valerate 0.025% preparations are indicated for maintenance treatment when control has been achieved with Betamethasone Valerate 0.1%.

In general, ointment preparations are particularly appropriate for dry, lichenified or scaly skin conditions whereas a cream preparation may be more suitable in the case of moist or weeping lesions.

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

The applications cross-refer to Audavate 0.1% w/w Ointment (PL 17507/0113), Audavate RD 0.025% w/w Cream (PL 17507/0115) and Audavate RD 0.025% w/w Ointment (PL 17507/0116) which were first authorised to Auden Mckenzie (Pharma Division) Ltd on 18 September 2012.

Bethamethasone is a corticosteroid with topical anti-inflammatory activity antipruritic, and vasoconstrictive properties.

Topical corticosteroids act as anti-inflammatory agents via multiple mechanisms to inhibit late phase allergic reactions including decreasing the density of mast cells, decreasing chemotaxis and activation of eosinophils, decreasing cytokine production by lymphocytes, monocytes, mast cells and eosinophils, and inhibiting the metabolism of arachidonic acid.

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 Betamethasone Valerate Cream/Ointment (PL 17507/0232-0234) submitted under Article 10c of Directive 2001/83/EC, as amended.

The applications cross-refer to Audavate 0.1% w/w Ointment (PL 17507/0113), Audavate RD 0.025% w/w Cream (PL 17507/0115) and Audavate RD 0.025% w/w Ointment (PL 17507/0116) which were first authorised to Auden Mckenzie (Pharma Division) Ltd on 18 September 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 Betamethasone Valerate 0.1% w/w Ointment (PL 17507/0232), Betamethasone Valerate 0.025% w/w Cream (PL 17507/0233) and Betamethasone Valerate 0.025% w/w Ointment (PL 17507/0234). 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 0.25 mg of betamethasone (0.025% w/w) or 1 mg of betamethasone (0.1% w/w) as betamethasone valerate.

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 (0.1% w/w ointment only) or 100g tubes (all presentations).

Not all pack sizes may be marketed.

The proposed shelf life of the unopened product is 3 years for Betamethasone Valerate 0.025% w/w and 0.1% w/w Ointment and 21 months for Betamethasone Valerate 0.025% w/w Cream with the storage condition 'Do not store above 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, Audavate 0.1% w/w Ointment (PL 17507/0113), Audavate RD 0.025% w/w Cream (PL 17507/0115) and Audavate RD 0.025% w/w Ointment (PL 17507/0116).

Expert Report

The applicant cross-refers to the data for Audavate 0.1% w/w Ointment (PL 17507/0113), Audavate RD 0.025% w/w Cream (PL 17507/0115) and Audavate RD 0.025% w/w Ointment (PL 17507/0116) 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 Betamethasone Valerate 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:

Important identified risks	Hypersensitivity to the preparation
	Local skin reactions e.g. contact dermatitis, allergic reactions
	The product should not be used in Rosacea, Acne vulgaris, Perioral dermatitis, Perianal and genital pruritus, Primary cutaneous viral infections (e.g. herpes simplex, chickenpox).
	Use for treatment of dermatosis in children under 1 year old and primary infected skin lesions caused by fungi or bacteria.
	Adrenal suppression – long term continuous therapy particularly in children.
	Thinning of the skin during prolonged treatment while treating psoriasis, discoid lupus erythematosus and severe eczema.
	Use in psoriasis – risk of 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.
	Spread of infections; Bacterial infection is encouraged by the warm, moist conditions induced by occlusive (airtight) dressing.
	Hypercortisolism
Important potential risks	Use in pregnancy and lactation.
	Glaucoma – if applied to eyelids
	Cataracts
	Features of Cushing's syndrome (more likely in infants and children) and dilatation of the superficial blood vessels may occur if occlusive dressings are used

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 Betamethasone Valerate 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 Audavate 0.1% w/w Ointment (PL 17507/0113), Audavate RD 0.025% w/w Cream (PL 17507/0115) and Audavate RD 0.025% w/w Ointment (PL 17507/0116) as the 'parent PIL'.

VI Overall conclusion, benefit/risk assessment and recommendation

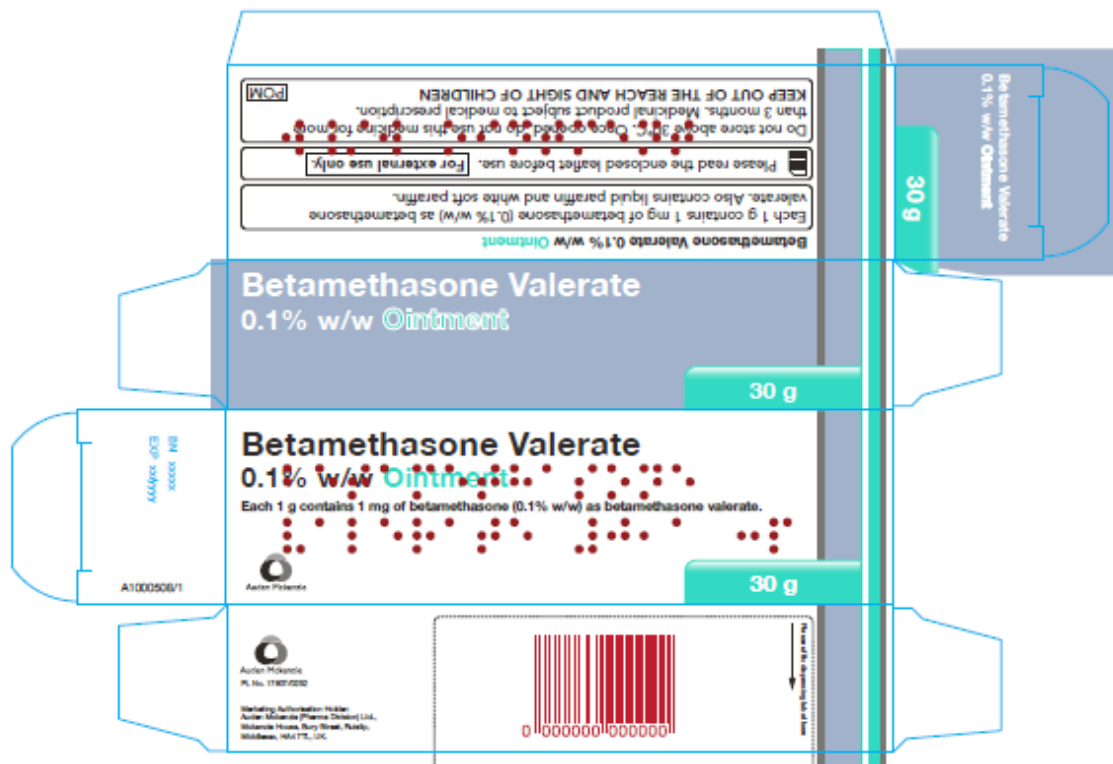
The quality of the products is acceptable, and no new non-clinical or clinical safety concerns have been identified. The applicant's products are identical to the cross-reference products. Extensive clinical experience with betamethasone valerate is considered to have demonstrated the therapeutic value 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.

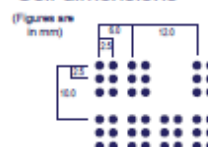
The approved labelling for Betamethasone Valerate Cream/Ointment is presented below:



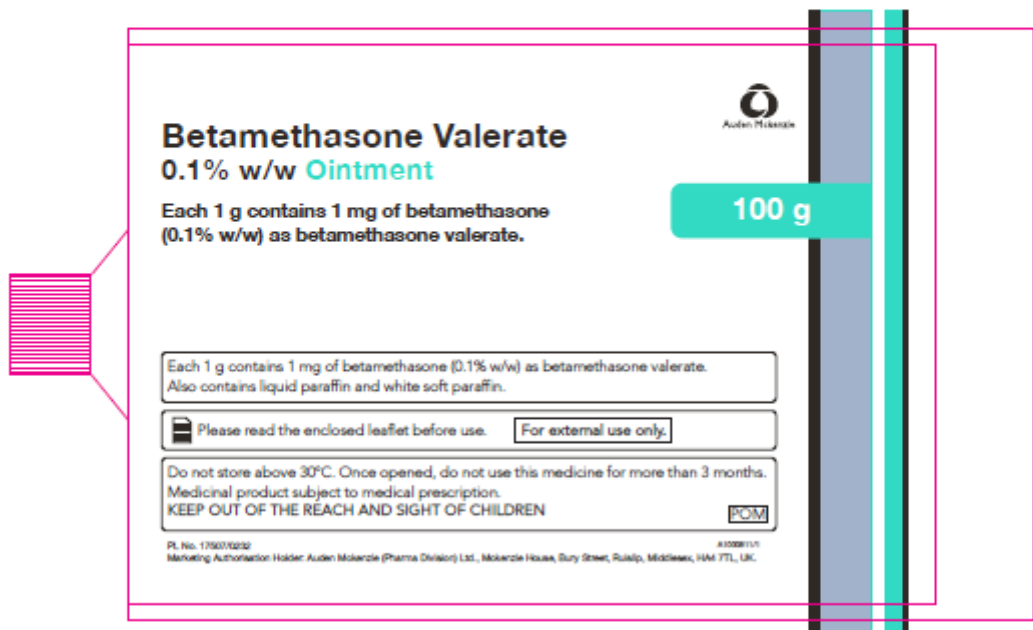
Braille text reads as follows:

betamethasone
valerate 0.1 %
w/w ointment

Braille text complies
with Marburg Medium.
Cell dimensions -



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

Betamethasone Valerate
0.1% w/w Ointment

Each 1 g contains 1 mg of betamethasone
(0.1% w/w) as betamethasone valerate.

100 g

Each 1 g contains 1 mg of betamethasone (0.1% w/w) as betamethasone valerate.
Also contains liquid paraffin and white soft paraffin.

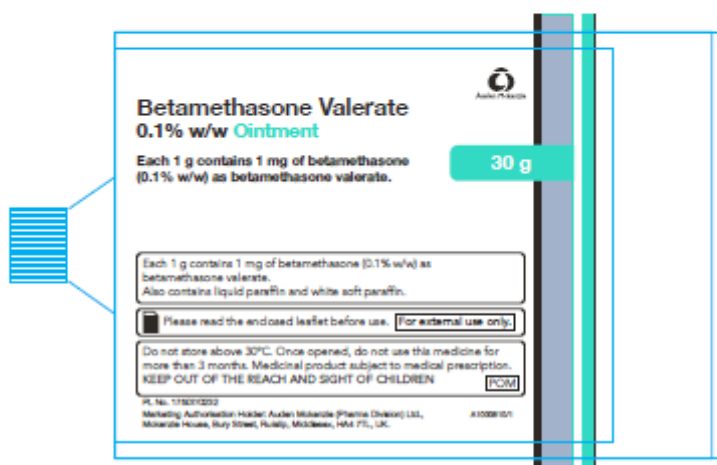
 Please read the enclosed leaflet before use. **For external use only.**

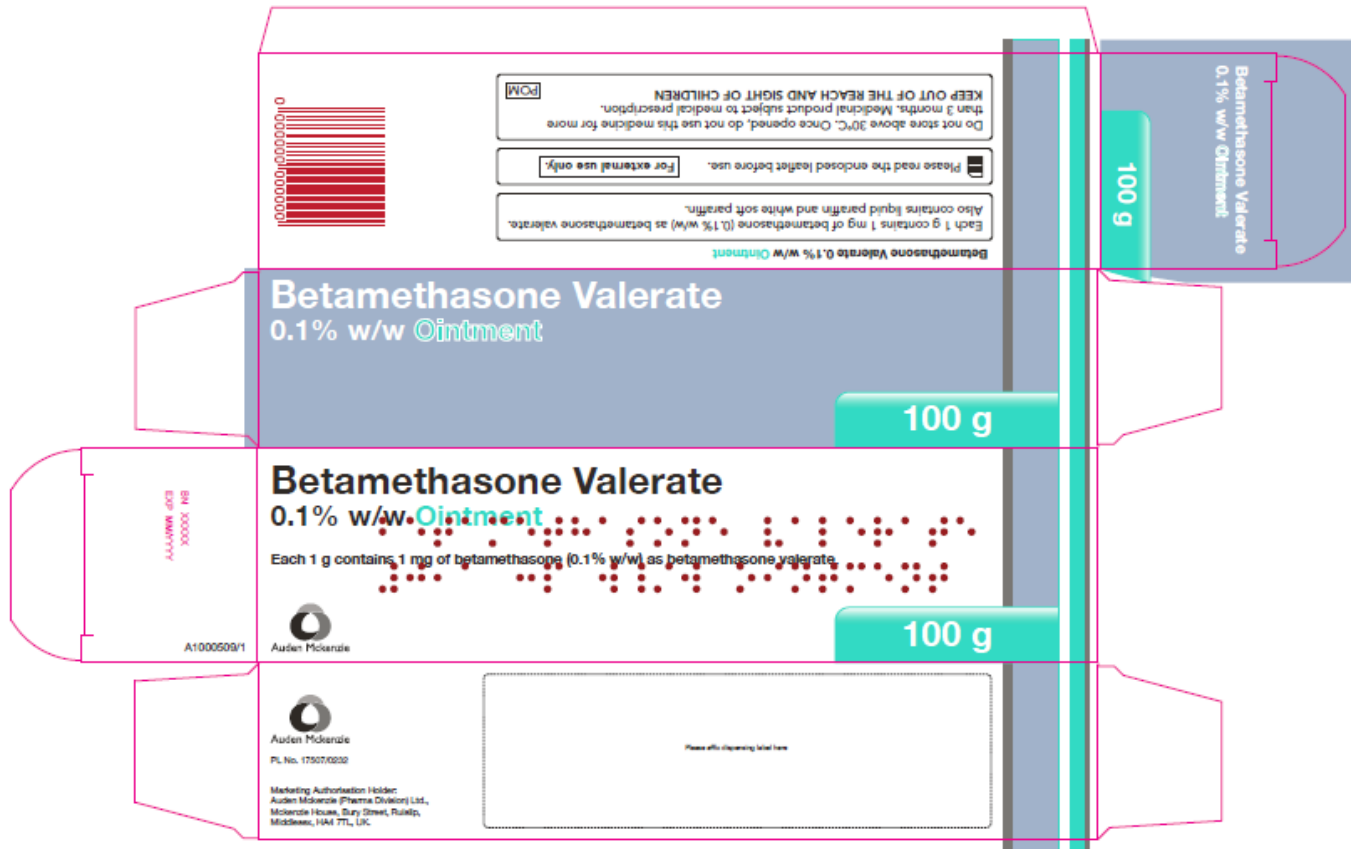
Do not store above 30°C. Once opened, do not use this medicine for more than 3 months.
Medicinal product subject to medical prescription.
KEEP OUT OF THE REACH AND SIGHT OF CHILDREN

POM

PL No. 17507/0232
Marketing Authorisation Holder: Auden Molerle (Pharma Division) Ltd., Molerle House, Bury Street, Ruislip, Middlesex, HA4 7TL, UK.

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



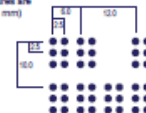


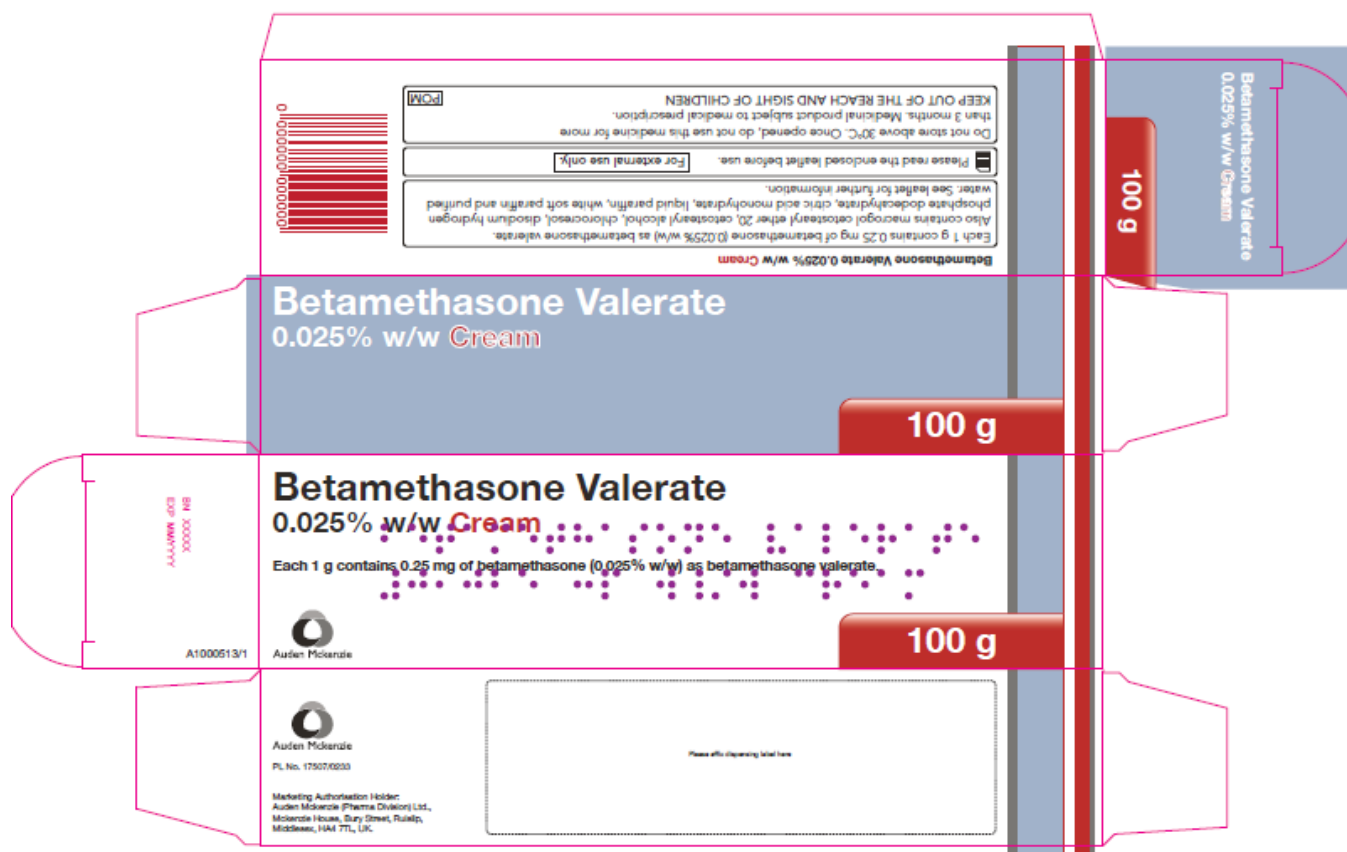
Braille text reads as follows:

beta methasone valerate
0 . 1 % w / w o i n t m e n t

Braille text complies
with Marburg Medium.
Cell dimensions -

(Figures are
in mm)

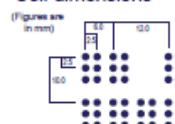




Braille text reads as follows:

betamethasone valerate
0.025% w/w cream

Braille text complies
with Marburg Medium.
Cell dimensions -



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



Betamethasone Valerate
0.025% w/w Cream

Each 1 g contains 0.25 mg of betamethasone
(0.025% w/w) as betamethasone valerate.

100 g

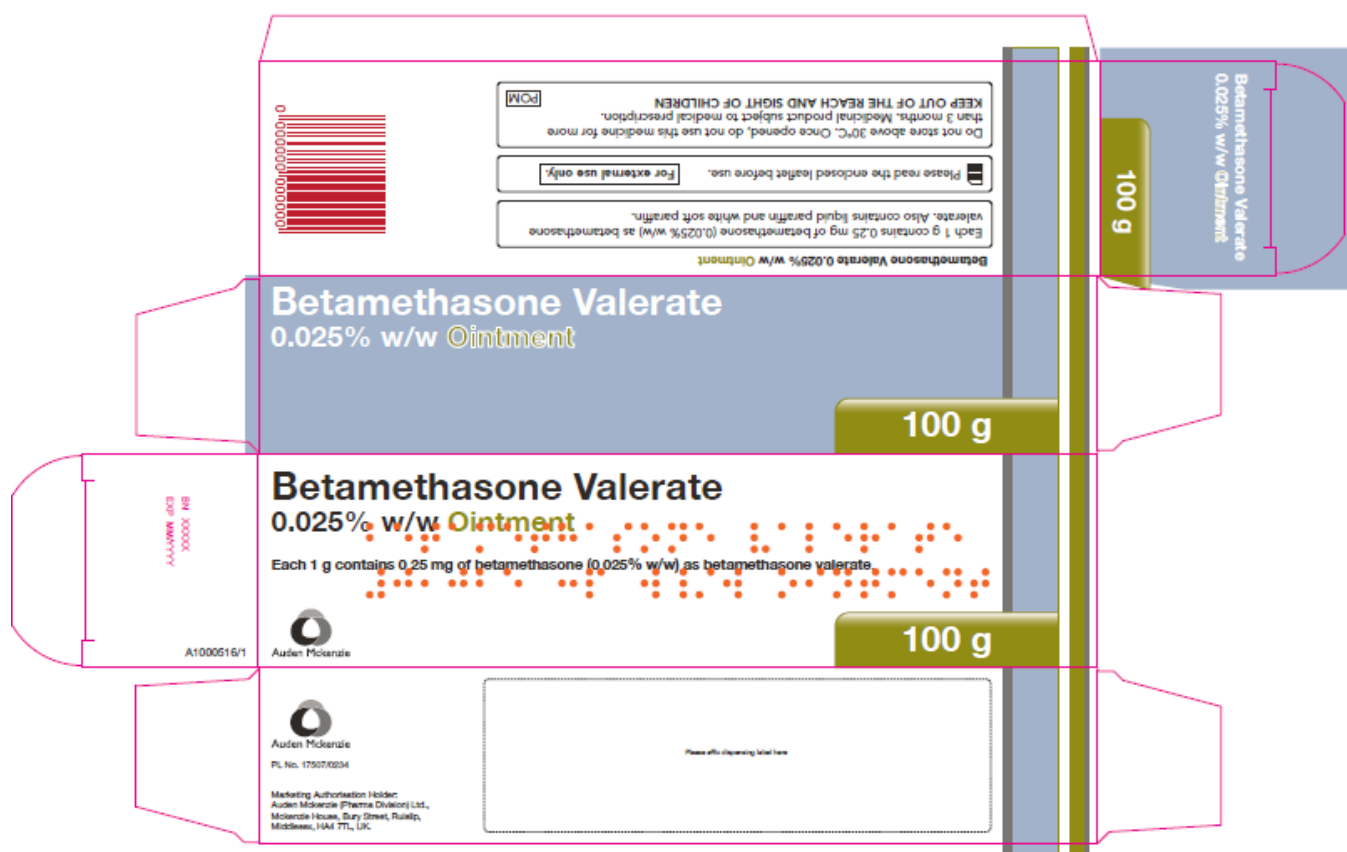
Each 1 g contains 0.25 mg of betamethasone (0.025% w/w) as betamethasone valerate.
Also contains macrogol cetostearyl ether 20, cetostearyl alcohol, chlorocresol, disodium
hydrogen phosphate dodecahydrate, citric acid monohydrate, liquid paraffin, white soft
paraffin and purified water. See leaflet for further information.

 Please read the enclosed leaflet before use. For external use only.

Do not store above 30°C. Once opened, do not use this medicine for more than 3 months.
Medicinal product subject to medical prescription.
KEEP OUT OF THE REACH AND SIGHT OF CHILDREN POM

PL No. 17507/0232
Marketing Authorisation Holder: Aldin Molerzie (Pharma Division) Ltd., Molerzie House, Sany Street, Ruislip, Middlesex, HA4 7TL, UK.

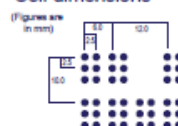
A10000147



Braille text reads as follows:

betamethasone valerate
0 . 0 2 5 % w / w o i n t m e n t

Braille text complies
with Marburg Medium.
Cell dimensions -



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



Betamethasone Valerate
0.025% w/w Ointment

Each 1 g contains 0.25 mg of betamethasone
(0.025% w/w) as betamethasone valerate.


Audeo Molecules

100 g

Each 1 g contains 0.25 mg of betamethasone (0.025% w/w) as betamethasone valerate.
Also contains liquid paraffin and white soft paraffin.

 Please read the enclosed leaflet before use.

For external use only.

Do not store above 30°C. Once opened, do not use this medicine for more than 3 months.
Medicinal product subject to medical prescription.
KEEP OUT OF THE REACH AND SIGHT OF CHILDREN

PL No. 17507/0234
Marketing Authorisation Holder: Audeo Molecules (Pharma Division) Ltd., Molecules House, Sany Street, Ruislip, Middlesex, HA4 7TL, UK.

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