AUSTRALIAN PRODUCT INFORMATION

EUMOVATE (clobetasone butyrate) cream

1 NAME OF THE MEDICINE

Clobetasone butyrate

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

EUMOVATE cream contains 0.05% w/w clobetasone butyrate as the active ingredient.

For the full list of excipients, see Section 6.1 LIST OF EXCIPIENTS.

3 PHARMACEUTICAL FORM

Cream

White cream for topical use

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

Short-term (up to 7 days) treatment of milder forms of eczema, dermatitis and other steroid responsive skin conditions.

4.2 DOSE AND METHOD OF ADMINISTRATION

Adults and children 12 years and over
Apply a thin film and gently rub in, using only enough to cover the affected area twice daily for up to 7 days.

If the condition resolves within 7 days, treatment with EUMOVATE cream should be stopped.

If the condition does not improve within the first 7 days or becomes worse, the patient should see a doctor.

If after 7 days of treatment, improvement is seen but further treatment is required, the patient should see a doctor.

After application, the hands should be washed unless they are the site being treated.

Patients advised by their doctors to use this cream for prolonged periods should be advised to tell subsequent doctors about this use.

All patients should be warned against prolonged used on one area of skin, or use of excessive quantities.

All patients should also be informed that the preparation is prescribed only for a specific condition occurring in a specific individual.

Children
Use in children under 12 years only on the advice of a doctor. Children are more likely to develop local and systemic adverse reactions of topical corticosteroids and, in general, require shorter courses and less potent agents than adults.

Care should be taken when using EUMOVATE cream to ensure the amount applied is the minimum that provided therapeutic benefit.

Elderly
Clinical studies have not identified differences in responses between the elderly and younger patients. The greater frequency of decreased hepatic or renal function in the elderly may delay elimination if systemic absorption occurs. Therefore the minimum quantity should be used for the shortest duration to achieve the desired clinical benefit.

Renal/Hepatic Impairment
In case of systemic absorption (when application is over a large surface area for a prolonged period) metabolism and elimination may be delayed therefore increasing the risk of systemic toxicity. Therefore the minimum quantity should be used for the shortest duration to achieve the desired clinical benefit.

4.3 CONTRAINDICATIONS

EUMOVATE cream should not be used in patients with a history of hypersensitivity to clobetasone butyrate or to any of the excipients in the product.

The following conditions should not be treated with EUMOVATE cream:

- Rosacea, acne, pruritus without rash, perioral dermatitis.
- Untreated bacterial infections such as cellulitis, folliculitis, furunculosis or impetigo.
- Fungal infections such as those associated with tinea (eg athletes foot, jock itch).
- Viral infections including cold sores (herpes simplex), chicken pox or shingles (Varicella zoster) or vaccinia.
- Parasitic infestations such as scabies.

Do not use on broken or infected skin or on inflamed skin near chronic ulcers.

Topical corticosteroids inhibit wound healing processes and are contraindicated in skin ulcers, cuts and abrasions.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Manifestations of hypercortolism (Cushing's syndrome) can occur in some individuals, due to prolonged duration of use, extensive application to the skin, or because of increased systemic absorption due to use of occlusive dressings or application to broken or thin skin.

The management of eczema and dermatitis in adults and children usually requires the supervision of a doctor.

Visual disturbances have been reported with the use of systemic and topical corticosteroids as a result of increased systemic availability and direct contact with the eyes.

Consequently, if a patient presents with symptoms such as blurred vision or other visual disturbances, the patient should be considered for referral to an ophthalmologist for evaluation as possible causes may include cataract, glaucoma or rare diseases such as central serous chorioretinopathy (CSCR)

EUMOVATE cream should not be used for the treatment of psoriasis as this condition needs to be managed by a doctor.

EUMOVATE cream should not be used concomitantly with other corticosteroids (by systemic or topical routes), as this may increase the risk of unwanted effects.

For external use only. This and all medication should be kept out of the reach of children. In the case of accidental ingestion, professional assistance should be sought or the Poisons Information Centre contacted immediately (see Section 4.9 OVERDOSE).

Systemic Absorption
EUMOVATE cream treatment for more than a few days may lead to significant systemic absorption.

The systemic absorption of clobetasone would be expected to increase if:

- large amounts of EUMOVATE cream are used;
- large areas of skin are treated;
- treated skin is damaged or diseased;
- thin skin (such as on the face) or skin in intertrigenous regions is treated;
- the treated area is occluded.

In comparison with adults, children and infants may absorb proportionally larger amounts of topical corticosteroids and thus be more susceptible to systemic adverse effects. This is because children have an immature skin barrier and a greater surface area to body weight ratio compared with adults.

Infection
Topical corticosteroid therapy may predispose to local infection. Appropriate antimicrobial therapy should be used whenever treating inflammatory lesions which have become infected. Any spread of infection requires withdrawal of topical corticosteroid therapy and administration of appropriate antimicrobial therapy.

Skin Damage
Topical corticosteroids cause atrophy of the epidermis and damage to the dermis. This may produce atrophic striae and discolouration, which are usually permanent. These are more likely to occur with prolonged therapy, occlusive dressings, application to intertrigenous areas, application to the face, and in children.

EUMOVATE cream should not be used on the face, groin, genitals or between the toes. As with other topical corticosteroids, it should not be used on skin with impaired circulation, such as stasis ulcers, since it may cause prolonged vasoconstriction.

Occlusive Dressings
Do not use with occlusive dressings, as occlusion increases the possibility of local and systemic side effects. Infants and children are at greater risk than adults.

Use near eyes
Care should be taken to ensure that the cream does not enter the eye, as cataracts and glaucoma might result from repeated exposure.

Use in renal/hepatic impairment
In case of systemic absorption (when application is over a large surface area for a prolonged period) metabolism and elimination may be delayed therefore increasing the risk of systemic toxicity).

Use in the elderly
See Section 4.2 DOSE AND METHOD OF ADMINISTRATION

Paediatric use

In infants and children, long term continuous topical therapy should be avoided, since skin damage and adrenal suppression can occur even without occlusion. The least potent corticosteroid that will control the disease should be selected. In infants, the napkin may act as an occlusive dressing, and increase absorption. Corticosteroids may inhibit linear bone growth and inhibit epiphyseal maturation. Treatment should be minimised and supervised closely.

Effects on laboratory tests

No data available.

4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

None reported. EUMOVATE cream should not be used concomitantly with other topical or systemic corticosteroids, either prescribed or obtained over-the-counter (such as hydrocortisone) as this may increase the likelihood of drug interactions.

Co-administered drugs that can inhibit CYP3A4 (e.g. ritonavir, itraconazole) have been shown to inhibit the metabolism of corticosteroids leading to increased systemic exposure. The extent to which this interaction is clinically relevant depends on the dose and route of administration of the corticosteroids and the potency of the CYP3A4.

4.6 FERTILITY, PREGNANCY AND LACTATION

Effects on fertility

There are no data in humans to evaluate the effect of topical corticosteroids on fertility.

Use in pregnancy

(Pregnancy Category A)

There are limited data from the use of EUMOVATE cream in pregnant women. Topical administration of corticosteroids to pregnant animals can cause abnormalities of foetal development including cleft palate and intra-uterine growth retardation. Studies in mice, rats and rabbits revealed similar findings following administration of clobetasone butyrate. The relevance of this finding to humans has not been established.

Administration of clobetasone during pregnancy should only be considered if the expected benefit to the mother outweighs the risk to the foetus. The minimum quantity should be used for the minimum duration.

Women who are pregnant should consult a doctor before use.

Use in lactation

The safe use of topical corticosteroids during lactation has not been established. It is not known whether the topical administration of corticosteroids could result in sufficient systemic absorption to produce detectable amounts in breast milk. Administration of clobetasone during lactation should only be considered if the expected benefit to the mother outweighs the risk to the infant.

Women who are breast-feeding should seek medical advice before using this product.

If used during lactation, clobetasone should not be applied to the breasts to avoid accidental ingestion by the infant.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

There have been no studies to investigate the effect of clobetasone on driving performance or the ability to operate machinery. A detrimental effect on such activities would not be anticipated from the adverse reaction profile of topical clobetasone.

4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)

Systemic side effects are more likely in children, if large areas of the skin are treated or if large amounts are used, if treatment is prolonged or if treated areas are occluded.

The use of corticosteroids by multiple routes of administration (eg topical and oral or inhaled) may increase the likelihood of adverse reactions occurring.

Adverse events drug reactions (ADRs) are listed below by MedDRA system organ class and by frequency. Frequencies are defined as: very common (≥1/10), common (≥1/100 and <1/10), uncommon (≥1/1000 and <1/100), rare (≥1/10,000 and <1/1000) and very rare (<1/10,000) including isolated reports.

Infections and Infestations

Very rare: Opportunistic infection

Immune System Disorders

Very rare: Hypersensitivity. Local hypersensitivity reactions such as erythema, rash, pruritus, urticaria, local skin burning and allergic contact dermatitis may occur at the site of application and may resemble symptoms of the condition under treatment.

Patients should be advised to stop treatment if signs of hypersensitivity appear.

Endocrine Disorders

Very rare Hypothalamic-pituitary adrenal (HPA) axis suppression:

	Cushingoid features (e.g. moon face, central obesity), delayed weight gain/growth retardation in children, osteoporosis, glaucoma, hyperglycaemia/glucosuria, cataract, hypertension, increased weight/obesity, decreased endogenous cortisol levels.

Skin and Subcutaneous Tissue Disorders

Rare	Hypersensitivity, allergic contact dermatitis, urticaria, skin atrophy*, pigmentation changes*, exacerbation of underlying symptoms, local skin burning, hypertrichosis, rash, pruritus, erythema, hair disorders, bruising, rosacea. Exacerbation of eczema and dermatitis has also been reported.

With prolonged treatment, permanent damage (including development of stria and telangiectases) to the dermis may occur.

Patients should be advised to stop treatment if signs of hypersensitivity appear.

Reporting suspected adverse effects

Reporting suspected adverse reactions after registration of the medicinal product is important. It allows continued monitoring of the benefit-risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions at www.tga.gov.au/reporting-problems.

4.9 OVERDOSE

Symptoms and Signs

Topically applied clobetasone may be absorbed in sufficient amounts to produce systemic effects. Acute overdosage is very unlikely to occur. However, in the case of chronic overdosage or misuse, the features of hypercortisolism may occur (see Section 4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS). There is also a risk of skin atrophy with the chronic use of topical steroids.

Treatment

In the event of overdose, clobetasone should be withdrawn gradually under medical supervision because of the risk of glucocorticosteroid insufficiency.

For information on the management of overdose, contact the Poisons Information Centre on 13 11 26 (Australia).

5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Mechanism of action

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.

The anti-inflammatory properties of clobetasone butyrate reduce the erythema and itchiness associated with eczema and dermatitis.

The cream base in EUMOVATE Cream has moisturising properties.

Clinical trials

No data available.

5.2 PHARMACOKINETIC PROPERTIES

Data are lacking on the systemic distribution, metabolism and excretion of clobetasone butyrate in humans.

Although pharmacokinetic studies were not carried out with the cream formulation, plasma clobetasone butyrate levels would be expected to be no greater or even lower, with the cream formulation, as creams are less occlusive than ointments.

Absorption

A single application of 30 g clobetasone butyrate 0.05% ointment to eight patients (3 with eczema and 5 with psoriasis) resulted in a small rise in plasma clobetasone butyrate levels during the first three hours not exceeding 0.6 ng/mL then the levels gradually decreased. The maximum plasma level reached in the first three hours was 0.6 ng/mL. This rise in levels was followed by a more gradual decline with plasma levels of clobetasone butyrate falling below 0.1 ng/mL (the lower limit of the assay) after 72 hours. The normal diurnal variation in plasma cortisol levels was not affected by the application of clobetasone butyrate ointment.

5.3 PRECLINICAL SAFETY DATA

In studies conducted in rats and dogs, histological changes induced by clobetasone butyrate were typical of corticosteroids (thymic involution, adrenal cortex atrophy, fatty replacement of bone marrow, lympholysis of the spleen and lymph nodes, and a reduction or disappearance of eosinophils from the endometrium). However, on a dose-for-dose basis, these findings were of a lesser severity than those associated with other corticosteroids.

Genotoxicity

No data available.

Carcinogenicity

No data available.

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

The excipients are glycerol, glycerol monostearate, cetostearyl alcohol, beeswax substitute 6621, arlacel 165, dimethicone 20, chlorocresol, sodium citrate dihydrate, citric acid monohydrate, water-purified.

6.2 INCOMPATIBILITIES

Incompatibilities were either not assessed or not identified as part of the registration of this medicine.

6.3 SHELF LIFE

In Australia, information on the shelf life can be found on the public summary of the Australian Register of Therapeutic Goods (ARTG). The expiry date can be found on the packaging.

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Store below 25°C.

6.5 NATURE AND CONTENTS OF CONTAINER

Aluminium tubes containing 15 g and 30 g.

A 5 g physician's sample pack is also available.

Not all pack sizes may be distributed in Australia.

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

In Australia, any unused medicine or waste material should be disposed of by taking to your local pharmacy.

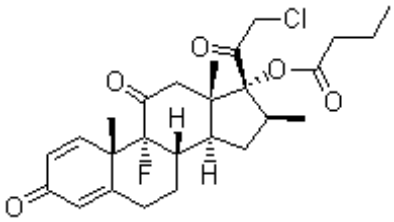
6.7 PHYSICOCHEMICAL PROPERTIES

Clobetasone butyrate is a corticosteroid used topically for its glucocorticoid effects. Its chemical name is 21-chloro-9α-fluoro-17α-hydroxy-16β-methylpregna-1,4-diene-3,11,20-trione 17-butyrate.

Molecular formula: $C_{26}H_{32}ClFO_5$

Molecular weight: 479.0

Chemical structure



CAS number

25122-57-0

7 MEDICINE SCHEDULE (POISONS STANDARD)

Pharmacist Only Medicine

8 SPONSOR

GlaxoSmithKline Australia Pty Ltd

Level 4, 436 Johnston Street,
Abbotsford, Victoria, 3067

9 DATE OF FIRST APPROVAL

2 March 2005

10 DATE OF REVISION

7 November 2018

SUMMARY TABLE OF CHANGES

Section Changed	Summary of new information
All	PI re-format
4.4	Safety update to include visual disturbance

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