

NEW ZEALAND DATA SHEET

1. PRODUCT NAME

EUMOVATE clobetasone 17-butyrate 0.05% w/w cream

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Clobetasone 17-Butyrate cream 0.05% w/w

Excipients with known effect:

Cetostearyl alcohol

Chlorocresol

For full list of excipients, see section 6.1 List of excipients.

3. PHARMACEUTICAL FORM

Cream

EUMOVATE cream is white in appearance. The emollient cream is water-miscible.

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

EUMOVATE is suitable for treating atopic eczema, photodermatitis, otitis externa, primary irritant and allergic dermatitis, prurigo nodularis, seborrhoeic dermatitis, and other steroid responsive skin conditions which do not require the use of a more active topical corticosteroid in children and adults. In the more resistant dermatoses, EUMOVATE may be used as maintenance therapy between courses of one of the more active topical steroids.

4.2 Dose and method of administration

Dose

Adults and Children

Crems are especially appropriate for moist or weeping surfaces.

Atopic dermatitis (eczema)

Apply thinly and gently rub in using only enough to cover the entire affected area once or twice a day until improvement occurs, then reduce the frequency of application or change the treatment to a less potent preparation. Allow adequate time for absorption after each application before applying an emollient.

If the condition worsens or does not improve within four weeks, treatment and diagnosis should be re-evaluated.

Therapy with topical corticosteroids should be gradually discontinued once control is achieved and an emollient continued as maintenance therapy.

Rebound of pre-existing dermatoses can occur with abrupt discontinuation of topical corticosteroids especially with potent preparations.

Children

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 clobetasone to ensure the amount applied is the minimum that provides therapeutic benefit.

Special populations

Elderly population

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

The following conditions should not be treated with clobetasone:

- Untreated cutaneous infections
- Rosacea
- Acne vulgaris
- Pruritus without inflammation

4.4 Special warnings and precautions for use

Clobetasone should be used with caution in patients with a history of local hypersensitivity to corticosteroids or to any of the excipients in the preparation. Local hypersensitivity reactions (see section 4.8 Undesirable effects) may resemble symptoms of the condition under treatment.

Manifestations of hypercortisolism (Cushing's syndrome) and reversible hypothalamic-pituitary adrenal (HPA) axis suppression, leading to glucocorticosteroid insufficiency can occur in some individuals as a result of increased systemic absorption of topical steroids. If either of the above are observed, withdraw the drug gradually by reducing the frequency of application or by substituting a less potent corticosteroid. Abrupt withdrawal of treatment may result in glucocorticosteroid insufficiency (see Adverse Effects).

Risk factors for increased systemic effects are:

- Potency and formulation of topical steroid
- Duration of exposure

- Application to a large surface area
- Use on occluded areas of skin e.g. on intertriginous areas or under occlusive dressings
- Increasing hydration of the stratum corneum
- Use on thin skin areas such as the face
- Use on broken skin or other conditions where the skin barrier may be impaired
- In comparison with adults, children 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.

Visual disturbance has been reported by patients using systemic and/or topical corticosteroids. If a patient has blurred vision or other visual disturbances, consider evaluation of possible causes which may include cataract, glaucoma or central serous chorioretinopathy.

Children

In children under 12 years of age, long-term continuous topical corticosteroid therapy should be avoided where possible, as adrenal suppression is more likely to occur.

Infection risk with occlusion

Bacterial infection is encouraged by the warm, moist conditions within skin folds or caused by occlusive dressings. When using occlusive dressings, the skin should be cleansed before a fresh dressing is applied.

Application to the face

Prolonged application to the face is undesirable as this area is more susceptible to atrophic changes.

Application to the eyelids

If applied to the eyelids, care is needed to ensure that the preparation does not enter the eye, as cataract and glaucoma might result from repeated exposure.

Concomitant 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.

Chronic leg ulcers

Topical corticosteroids are sometimes used to treat the dermatitis around chronic leg ulcers. However, this use may be associated with a higher occurrence of local hypersensitivity reactions and an increased risk of local infection.

Accidental ingestion

For external use only. This and all medication should be kept out of the reach of children. In case of accidental ingestion, professional assistance should be sought or a national poison control centre contacted immediately (see section 4.9 Overdose).

4.5 Interaction with other medicines and other forms of interaction

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 inhibitor.

4.6 Fertility, pregnancy and lactation

Pregnancy

There are limited data from the use of clobetasone in pregnant women.

Topical administration of corticosteroids to pregnant animals can cause abnormalities of foetal development. 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.

Topical application of clobetasone to rats at doses of 0.5 or 5 mg/kg/day, and subcutaneous administration to mice at doses ≥ 3 mg/kg/day or rabbits at doses ≥ 30 $\mu\text{g}/\text{kg}/\text{day}$ during pregnancy resulted in foetal abnormalities including cleft palate.

Breast-feeding

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.

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

Fertility

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

The effect on fertility of topical clobetasone has not been evaluated in animals.

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 Undesirable effects

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

Post-marketing data

Infections and Infestations

Very rare: Opportunistic infection

Immune System Disorders

Very rare: Hypersensitivity

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

Very rare: Allergic contact dermatitis, urticaria, skin atrophy*, pigmentation changes*, exacerbation of underlying symptoms, local skin burning, hypertrichosis, rash, pruritus, erythema

*Skin features secondary to local and/or systemic effects of hypothalamic –pituitary adrenal (HPA) axis suppression.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions via: <https://nzphvc.otago.ac.nz/reporting/>

4.9 Overdose

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 Undesirable effects).

Treatment

In the event of overdose, clobetasone should be withdrawn gradually by reducing the frequency of application or by substituting a less potent corticosteroid because of the risk of glucocorticosteroid insufficiency.

Further management should be as clinically indicated or as recommended by the national poisons centre, where available.

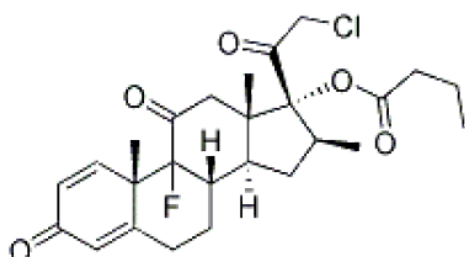
The least potent corticosteroid which will control the disease should be selected. Eumovate preparations do not contain lanolin or parabens.

For advice on the management of overdose please contact the National Poisons Centre on 0800 POISON (0800 764 766).

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Corticosteroids, moderately potent (group II), ATC code: D07AB



Mechanism of action

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.

Pharmacodynamic effects

Topical corticosteroids have anti-inflammatory, antipruritic, and vasoconstrictive properties.

5.2 Pharmacokinetic properties

Absorption

Topical corticosteroids can be systematically absorbed from intact healthy skin. The extent of percutaneous absorption of topical corticosteroids is determined by many factors, including the vehicle and the integrity of the epidermal barrier. Occlusion, inflammation and/or other disease processes in the skin may also increase percutaneous absorption.

Distribution

The use of pharmacodynamic endpoints for assessing the systemic exposure of topical corticosteroids is necessary due to the fact that circulating levels are well below the level of detection.

Biotransformation

Once absorbed through the skin, topical corticosteroids are handled through pharmacokinetic pathways similar to systemically administered corticosteroids. They are metabolised, primarily in the liver.

Elimination

Topical corticosteroids are excreted by the kidneys. In addition, some corticosteroids and their metabolites are also excreted in the bile.

5.3 Preclinical safety data

Carcinogenesis and Genotoxicity

Long-term animal studies have not been performed to evaluate the carcinogenic potential of topical clobetasone. Clobetasone was not mutagenic *in vitro* or *in vivo*.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

glycerol
glycerol monostearate
cetostearyl alcohol
beeswax substitute 6621
arlacel 165
dimethicone 20
chlorocresol
sodium citrate
citric acid monohydrate
water-purified

6.2 Incompatibilities

No incompatibilities have been identified.

6.3 Shelf life

3 years

6.4 Special precautions for storage

Store below 25°C, out of direct sunlight.

6.5 Nature and contents of container

Tubes of 30 g and 100 g.

6.6 Special precautions for disposal and otherhandling

There are no special requirements for use or handling of this product.

7. MEDICINE SCHEDULE

Prescription Medicine

8. SPONSOR

GlaxoSmithKline NZ Limited
Private Bag 106600
Downtown
Auckland
New Zealand

Telephone (09) 367 2900
Facsimile (09) 367 2910

9. DATE OF FIRST APPROVAL

Date of publication in the New Zealand Gazette of consent to distribute the medicine:
14 April 1976

10. DATE OF REVISION OF THE TEXT

27 August 2018

Summary table of changes:

| Section changed | Summary of new information |
|-----------------|--|
| All | Data Sheet re-format |
| 2. | Included excipients of known effect |
| 4.4 | Update to include visual disturbance safety information |
| 4.8 | Added adverse reaction contact information |
| 4.9 | Added information regarding advice on the management of overdose |
| 5.1 | Added Pharmacotherapeutic group, ATC code and Pharmacodynamic effect information |
| 6.1 | Included excipient information |
| 6.2 | Included incompatibility information |
| 6.3 | Included shelf life information |
| 9 | Added date of first approval |

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