DERMOVATE

Clobetasol propionate

QUALITATIVE AND QUANTITATIVE COMPOSITION

DERMOVATE Scalp Application contains clobetasol propionate 0.05 % w/w.

CLINICAL INFORMATION

Indications

Steroid responsive dermatoses of the scalp such as:

- Psoriasis
- Recalcitrant eczemas

Dosage and Administration

Pharmaceutical form: Scalp Application

Apply sparingly to the scalp night and morning until improvement occurs. As with other highly-active topical steroid preparations, therapy should be discontinued when control is achieved. Repeated short courses of *DERMOVATE* Scalp Application may be used to control exacerbations. If continuous steroid treatment is necessary, a less potent preparation should be used.

Avoid contact with the eyes. Hands should be washed after application.

Due to the flammable nature of *DERMOVATE* Scalp Application, patients should avoid smoking or being near an open flame during application and immediately after use.

Children

Children are more likely to develop local and systemic side effects of topical corticosteroids and, in general, require shorter courses and less potent agents than adults.

Care should be taken when using clobetasol propionate to ensure the amount applied is the minimum that provides therapeutic benefit.

Clobetasol propionate is contraindicated in children under 1 year of age.

Elderly

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.

Contraindications

The following conditions should not be treated with *DERMOVATE*

- Hypersensitivity to clobetasol, or to any of the excipients in the preparation
- Infections of the scalp

DERMOVATE is contraindicated in dermatoses in children under one year of age, including dermatitis.

Warnings and Precautions

DERMOVATE should be used with caution in patients with a history of local hypersensitivity to corticosteroids. Local hypersensitivity reactions (*see Adverse Reactions*) may resemble symptoms of the condition under treatment.

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

If signs of hypersensitivity appear, application should be stopped immediately.

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 Reactions*).

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 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.

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

Long-term continuous topical therapy should be avoided where possible, particularly in infants and children, as adrenal suppression can occur even without occlusion.

Children are more susceptible to develop atrophic changes with the use of topical corticosteroids. If *DERMOVATE* is required for use in children, it is recommended that the treatment should be limited to only a few days and reviewed weekly.

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.

Use in psoriasis

Topical corticosteroids should be used with caution in psoriasis as rebound relapses, development of tolerances, risk of generalised pustular psoriasis and development of local or systemic toxicity due to impaired barrier function of the skin have been reported in some cases. If used in psoriasis, careful patient supervision is important.

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.

Interactions

Co-administered drugs that can inhibit CYP3A4 (e.g. ritonavir and 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.

Fertility, Pregnancy and Lactation

Fertility

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

Clobetasol administered subcutaneously to rats had no effect upon mating performance; however, fertility was decreased at the highest dose (*see Pre-Clinical Safety Data*).

Pregnancy

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

Topical administration of corticosteroids to pregnant animals can cause abnormalities of foetal development (*see Non-Clinical Information*).

The relevance of this finding to humans has not been established. Administration of *DERMOVATE* 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.

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 *DERMOVATE* during lactation should only be considered if the expected benefit to the mother outweighs the risk to the infant.

Effects on Ability to Drive and Use Machines

There have been no studies to investigate the effect of *DERMOVATE* 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 *DERMOVATE*.

Adverse Reactions

Adverse 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 (≥1/1,000 and <1/100), rare (≥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	Local 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, hyperglycaemia/glucosuria, hypertension, increased weight/obesity, decreased endogenous cortisol levels, alopecia, trichorrhexis

Eye Disorders

Very rare	Cataract, central serous chorioretinopathy, glaucoma

Skin and Subcutaneous Tissue Disorders

Common	Pruritus, local skin burning /skin pain
Uncommon	Skin atrophy*, striae*, telangiectasias*
Very rare	Skin thinning*, skin wrinkling*, skin dryness*, pigmentation changes*, hypertrichosis, exacerbation of underlying symptoms, allergic contact dermatitis/dermatitis, pustular psoriasis, erythema, rash, urticaria, acne

General Disorders and Administration Site Conditions

Very rare	Application site irritation/pain

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

Overdose

Symptoms and signs

Topically applied clobetasol propionate 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 Adverse Reactions*).

Treatment

In the event of overdose, *DERMOVATE* 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.

PHARMACOLOGICAL PROPERTIES

Pharmacodynamics

ATC code

D07AD01

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.

Pharmacokinetics

Absorption

Topical corticosteroids can be systemically 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.

Metabolism

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.

Non-Clinical Information

Carcinogenesis / Mutagenesis

Carcinogenesis

Long-term animal studies have not been performed to evaluate the carcinogenic potential of clobetasol propionate.

Genotoxicity

Clobetasol propionate was not mutagenic in a range of *in vitro* bacterial cell assays.

Fertility

In fertility studies, subcutaneous administration of clobetasol propionate to rats at doses of 6.25 to 50 micrograms/kg/day produced no effects on mating, and fertility was only decreased at 50 micrograms/kg/day.

Pregnancy

Subcutaneous administration of clobetasol propionate to mice (≥100 micrograms/kg/day), rats (400 micrograms/kg/day) or rabbits (1 to 10 micrograms/kg/day) during pregnancy produced foetal abnormalities including cleft palate and intrauterine growth retardation.

In the rat study, where some animals were allowed to litter, developmental delay was observed in the F1 generation at ≥100 micrograms/kg/day and survival was reduced at

400 micrograms/kg/day. No treatment-related effects were observed in F1 reproductive performance or in the F2 generation.

PHARMACEUTICAL INFORMATION

List of Excipients

Carbomer
Isopropyl alcohol
Sodium hydroxide
Purified water

Shelf Life

The expiry date is indicated on the packaging.

Storage

The storage conditions are detailed on the packaging.

Keep container tightly closed when not in use. Contents are flammable. Keep away from fire, flame or heat. Do not leave *DERMOVATE* Scalp Application in direct sunlight.

Nature and Contents of Container

White opaque polyethylene squeeze bottle with an elongated nozzle and a polyethylene cap.

Incompatibilities

No incompatibilities have been identified.

Use and Handling

DERMOVATE scalp application is flammable. Keep away from heat sources (e.g., naked flames, lit cigarettes) during and immediately after using it. Not all presentations are available in every country.

Product Registrant

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