



# Clobetasol propionate

## Dermovate<sup>®</sup>

### 500mcg/mL Solution for Scalp Application

#### PRODUCT DESCRIPTION

Clobetasol propionate (*Dermovate*<sup>®</sup>) scalp application is a transparent, slightly gelled solution containing 500 mcg (0.05% w/w) clobetasol propionate.

#### PHARMACOLOGIC PROPERTIES

##### Pharmacodynamics

##### ATC code

D07AD Corticosteroids, very potent (group IV)

##### 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.

##### Pre-clinical Safety Data

##### 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 ( $\geq 100$  micrograms/kg/day), rats (400 micrograms/kg/day) or rabbits (1 to 10 micrograms/kg/day) during pregnancy produced foetal abnormalities including cleft palate.

In the rat study, where some animals were allowed to litter, developmental delay was observed in the F1 generation at  $\geq 100$  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.

#### INDICATIONS

Steroid responsive dermatoses of the scalp such as:

- Psoriasis
- Recalcitrant dermatoses.

#### DOSAGE AND ADMINISTRATION

A small quantity of Clobetasol propionate (*Dermovate*<sup>®</sup>) should be applied to the scalp night and morning until improvement is noticeable. It may then be possible to sustain improvement by applying once a day, or less frequently.

Due to the flammable nature of Clobetasol propionate (*Dermovate*<sup>®</sup>), 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.

### **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.

## **CONTRAINDICATIONS**

The following conditions should not be treated with Clobetasol propionate (*Dermovate*®)

- Infections of the scalp

Clobetasol propionate (*Dermovate*®) is contraindicated in dermatoses in children under one year of age, including dermatitis.

## **WARNINGS AND PRECAUTIONS**

Clobetasol propionate (*Dermovate*®) 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 Adverse 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 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.

### **Children**

In infants and children under 12 years of age, long-term continuous topical corticosteroid therapy should be avoided where possible, as adrenal suppression can occur.

Children are more susceptible to develop atrophic changes with the use of topical corticosteroids. If Clobetasol propionate (*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.

### **Effects on Ability to Drive and Use Machines**

There have been no studies to investigate the effect of Clobetasol propionate (*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 Clobetasol propionate (*Dermovate*®).

## **DRUG INTERACTIONS**

Co-administered drugs that can inhibit CYP3A4 (eg 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.

## **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 Non-clinical Information).

### **Pregnancy**

There are limited data from the use of Clobetasol propionate (*Dermovate*®) in pregnant women.

Topical administration of corticosteroids to pregnant animals can cause abnormalities of foetal development (*see Pre-clinical Information*)

The relevance of this finding to humans has not been established. Administration of Clobetasol propionate (*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 Clobetasol propionate (*Dermovate*®) during lactation should only be considered if the expected benefit to the mother outweighs the risk to the infant.

## **ADVERSE EFFECTS**

### **Adverse Reactions**

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                      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, glaucoma, hyperglycaemia/glucosuria, cataract, hypertension, increased weight/obesity, decreased endogenous cortisol levels, alopecia, trichorrhexis

#### **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.

## **OVERDOSAGE AND TREATMENT**

### **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 Effects*).

### **Treatment**

In the event of overdose, Clobetasol propionate (*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.

## **STORAGE CONDITION**

Store below 25°C.

Keep container tightly closed when not in use. Contents are flammable. Keep away from fire, flame or heat. Do not leave Clobetasol propionate (*Dermovate*®) Solution for Scalp Application in direct sunlight.

## **INSTRUCTIONS FOR USE AND HANDLING**

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

## **AVAILABILITY**

Clobetasol propionate (*Dermovate*®) Solution for Scalp application is available in 25mL plastic bottle.

## **CAUTION**

Foods, Drugs, Devices and Cosmetics Act prohibits dispensing without prescription.  
Keep all medicines out of reach of children.

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