Dermovate

Version GDSv16/IPIv09

Dermovate

Clobetasol propionate

Qualitative and Quantitative Composition

DERMOVATE Cream and ointment contains clobetasol propionate 0.05% w/w.

Clinical Information

Directions

DERMOVATE is a very potent topical corticosteroid indicated for adults, the elderly and children over 1 year of age for the relief of inflammatory and pruritic manifestations of corticosteroid-sensitive dermatoses.

These include:

- psoriasis (excluding disseminated plaque psoriasis)
- Recalcitrant dermatosis
- lichen planus
- discoid lupus erythematosus
- orafter skin conditions that do not respond satisfactorily to less active corticosteroids

Dosage and Administration

Pharmaceutical form: cream and ointment

Ointment

Ointments are especially appropriate for dry, lichenized or scaly lesions.

Cream

The creams are especially suitable for wet or oozing surfaces.

Adults, Seniors and Children Over 1 Year

Apply a thin film and rub in gently, using just enough to cover the entire affected area, once or twice a day for no more than 4 weeks, until there is improvement, and then reduce the frequency of application or switch to a less potent preparation. Allow adequate time for absorption after each application, before applying an emollient.

Repeated short courses of ***DERMOVATE*** can be performed to control exacerbations.

In more resistant lesions, especially where hyperkeratosis is present, the effect of ***DERMOVATE*** can be increased, if necessary, by occlusion of the treatment area with a polyethylene film.

Usually, occlusion only at night is adequate to produce a satisfactory response. Thereafter, improvement can usually be maintained by application without occlusion.

If the condition worsens or does not improve in 2 to 4 weeks, treatment and diagnosis should be reevaluated.

Treatment should not be continued for more than 4 weeks. If continuous treatment is necessary, a less potent preparation should be used.

The maximum weekly dose should not exceed 50 g/week.

Atopic dermatitis (eczema)

Treatment with ***DERMOVATE*** cream and ointment should be gradually reduced after achieving control and an emollient should be continued as maintenance treatment.

Recurrence of pre-existing dermatoses may occur with sudden discontinuation of ***DERMOVATE***.

Recalcitrant dermatosis

Patients Who Relapse Frequently

Once an acute episode has been effectively treated with continuous topical corticosteroid therapy, intermittent administration (once daily, twice weekly, without occlusion) may be considered. This has been shown to be helpful in reducing the frequency of recurrence.

Application should be continued in all previously affected areas or in areas that are sites of possible relapse. This regimen should be combined with routine daily use of emollients. The condition and the benefits and risks of continued treatment should be reassessed regularly.

Children

DERMOVATE is contraindicated in children under 1 year of age.

In children, local and systemic side effects of topical corticosteroids are more likely and generally require shorter courses and less potent agents than adults.

When using ***DERMOVATE***, care should be taken to ensure that the amount applied is the minimum that provides therapeutic benefits.

Elderly

In clinical studies, no differences in responses have been identified between elderly and younger patients. The increased frequency of decreased liver or kidney function in the elderly may slow elimination if systemic absorption occurs. Therefore, the minimum amount should be used for the shortest possible time to achieve the desired clinical benefit.

Renal/hepatic dysfunction

In case of systemic absorption (when the application is over a large surface area for a prolonged period), metabolism and elimination may be delayed, thus increasing the risk of systemic toxic effects. Therefore, the minimum amount should be used for the shortest possible time to achieve the desired clinical benefit.

Contraindications

The following conditions should not be treated with ***DERMOVATE***:

- untreated skin infections;
- rosacea;
- acne vulgaris;
- itching without inflammation;
- perianal and genital pruritus;
- perioral dermatitis.

DERMOVATE is contraindicated for dermatoses, including dermatitis, in children under 1 year of age.

Warnings and Precautions

DERMOVATE should be used with caution in patients with a history of local hypersensitivity to corticosteroids or any of the excipients in the preparation. Local hypersensitivity reactions (see ADVERSE REACTIONS) may resemble symptoms of the condition being treated.

In some individuals, hypercortisolism (Cushing's syndrome) and reversible inhibition of the hypothalamic-pituitary-adrenal (HHS) axis, leading to glucocorticoid insufficiency, may occur as a result of increased systemic absorption of topical corticosteroids. If any of these manifestations are observed, gradually withdraw the drug by reducing the frequency of its application or replacing it with another less potent corticosteroid. Sudden discontinuation of treatment may result in glucocorticoid insufficiency (see ADVERSE REACTIONS).

Risk factors for increased systemic effects are:

- potency and formulation of topical corticosteroid;
- duration of exposure;
- application over a large surface area;
- use on occluded areas of skin, e.g. in intertriginous areas or under occlusive dressings (in infants the diaper may act as an occlusive dressing);
- increased hydration of the stratum corneum;
- use on areas of thin skin, such as the face;
- use on denuded skin or other conditions where there is impaired skin barrier function;
- Compared to adults, children and infants may absorb proportionately larger amounts of topical corticosteroids and therefore be more susceptible to systemic adverse effects. This is because children have immaturity of skin barrier function and ratio of surface area to body weight greater than adults.

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

Children

In infants and children younger than 12 years of age, continued long-term topical corticosteroid treatment should be avoided whenever possible, as adrenal suppression may occur.

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

Risk of Infection with Occlusion

Bacterial infections are facilitated by hot and humid conditions in skin folds or due to occlusive dressings. When occlusive dressings are used, the skin should be cleaned before applying a new dressing.

Use in Psoriasis

Topical corticosteroids should be used with caution in patients with psoriasis, as recurrence, tolerance development, risk of generalized pustular psoriasis, and development of local or systemic toxicity have been reported in some cases due to impaired barrier skin function. If used in patients with psoriasis, it is important to carefully monitor the patient.

Concomitant infection

Appropriate antimicrobial treatment should be used whenever inflammatory lesions that have become infected are treated. If the infection spreads, it is necessary to discontinue treatment with topical corticosteroid and administer appropriate antimicrobial therapy.

Chronic Leg Ulcers

Topical corticosteroids are sometimes used to treat dermatitis around chronic leg ulcers. However, such use could be associated with an increase in the occurrence of local hypersensitivity reactions and increased risk of local infection.

Application on the Face

Application on the face is inadvisable, as this area is more susceptible to atrophic changes. If used on the face, treatment should be limited to only a few days.

Application on the Eyelids

If applied to the eyelids, it is necessary to take care to prevent the preparation from entering the eyes, as repeated exposure could lead to cataracts and glaucoma.

Cream and Ointment

DERMOVATE cream and ointment contain paraffin. Instruct patients not to smoke or go near exposed flames because of the risk of severe burns. Fabrics (clothing, bedding, bandages, etc.) that have been in contact with this product burn more easily and pose a serious fire hazard. Washing clothes and bedding can reduce product buildup, but not completely remove it.

Interactions

Concomitantly administered drugs that may inhibit CYP3A4 (e.g., ritonavir or itraconazole) have been shown to inhibit corticosteroid metabolism and lead to increased systemic corticosteroid exposure. The extent to which this interaction is clinically important depends on the dose and route of administration of corticosteroids and the potency of the CYP3A4 inhibitor.

Pregnancy and Lactation

Fertility

There are no human data to assess the effect of topical corticosteroids on fertility. Clobetasol administered subcutaneously to rats had no effect on mating performance; however, at the higher dose, fertility decreased (see Preclinical Information).

Pregnancy

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

Topical administration of corticosteroids to pregnant females may cause abnormalities in fetal development (see Preclinical Information).

The importance of this data in 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 fetus. The minimum amount should be used for the shortest possible time.

Nursing

The safe use of topical corticosteroids during breastfeeding has not been established.

It is unknown whether topical administration of corticosteroids could result in sufficient systemic absorption to produce detectable amounts in human milk. Administration of ***DERMOVATE*** during lactation should only be considered if the expected benefit to the mother outweighs the risk to the infant.

If used during breastfeeding, ***DERMOVATE*** should not be applied to the breast area, to prevent accidental ingestion by the baby.

Effects on the Ability to Drive Vehicles and the Use of Machinery

No studies have been conducted to investigate the effect of ***DERMOVATE*** on driving performance or the ability to operate machinery. No harmful effect is expected to occur in such activities, from the adverse reaction profile of topical application of ***DERMOVATE.***

Adverse Reactions

Adverse drug reactions (ADRs) are listed below according to the MedDRA dictionary class of organ systems and their frequency. Their frequency is defined as very common (≥1/10), common (≥1/100 and <1/10), uncommon (≥1/1000 and <1/100), uncommon (≥1/10000 and <1/1000) and very uncommon (<1/10000), including isolated reports.

Post-Market Data

Infections and Infestations

Very rareOpportunistic infection

Immune System Disorders

Very uncommonLocal hypersensitivity

Endocrine Disorders

Very uncommonHypothalamic-pituitary-adrenal (HHS) axis suppression: Cushingoid traits: (e.g., moon face, central obesity), delayed weight/growth gain in children, osteoporosis, hyperglycemia/glycosuria, hypertension, weight gain/obesity, decreased endogenous cortisol levels, alopecia, tricorrhoxys.

Eye Disorders

Very uncommon Cataract, central serous chorioretinopathy, glaucoma

Skin and Subcutaneous Tissue Disorders

CommonPruritus, burning skin/localized skin pain.

UncommonSkin atrophy*, stretch marks*, telangiectasias*.

Very uncommonThinning of the skin*, wrinkling of the skin*, dryness of the skin*, changes in pigmentation*, hypertrichosis, exacerbation of underlying symptoms, dermatitis/allergic contact dermatitis, pustular psoriasis, erythema, rash, urticaria, acne.

General Disorders and Conditions of the Place of Administration

Very uncommon Pain/irritation at the application site
*Skin characteristics secondary to local and/or systemic effects of inhibition of the hypothalamic-pituitary-adrenal (HHS) axis.

Overdose

Symptoms and signs

DERMOVATE applied topically may be absorbed in sufficient amounts to produce systemic effects. Although acute overdose is very unlikely, features of hypercortisolism may occur in the case of chronic overdose or abuse (see ADVERSE REACTIONS).

Treatment

In case of overdose, ***DERMOVATE*** should be withdrawn gradually by reducing the frequency of its application or replacing it with a less potent corticosteroid, due to the risk of glucocorticoid insufficiency.

Further management should be as clinically indicated or recommended by the national poison center in countries where it exists.

Pharmacological properties

Pharmacodynamics

ATC Code

D07AD Corticosteroids, very potent (group IV)

Mechanism of Action

Topical corticosteroids act as anti-inflammatory agents through multiple mechanisms to inhibit late-phase allergic reactions, including decreasing mast cell density, decreasing chemotaxy and eosinophil activation, decreasing cytokine production in lymphocytes, monocytes, mast cells, and eosinophils, and inhibiting arachidonic acid metabolism.

Pharmacodynamic effects

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

Pharmacokinetics

Absorption

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

In one study, mean peak plasma concentrations of clobetasol propionate of 0.63 nanograms/ml occurred eight hours after the second application (13 hours after an initial application) of 30 g of 0.05% clobetasol propionate ointment to normal people with healthy skin. Following the application of a second dose of 30 g of 0.05% clobetasol propionate cream, mean peak plasma concentrations were slightly higher than those of the ointment and occurred 10 hours after application. In a separate study, mean peak plasma concentrations of approximately 2.3 nanograms/mL and 4.6 nanograms/mL occurred respectively in patients with psoriasis and eczema three hours after a single application of 25 g of 0.05% clobetasol propionate ointment.

Distribution

The use of pharmacodynamic endpoints is necessary to assess systemic exposure of topical corticosteroids because circulating levels are well below the detection level.

Metabolism

Once absorbed through the skin, topical corticosteroids are managed through pharmacokinetic pathways similar to systemically administered corticosteroids. They are metabolized mainly in the liver.

Elimination

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

Preclinical Information

Carcinogenesis/Mutagenesis

Carcinogenesis

No long-term animal studies have been conducted to evaluate the carcinogenic potential of clobetasol propionate.

Genotoxicity

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

Reproductive toxicology

Fertility

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

Pregnancy

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

In the rat study, where some animals were allowed to breed, developmental delay in F1 generation was observed at doses of ≥100 micrograms/kg/day and survival was reduced at doses of 400 micrograms/kg/day. No treatment-related effects on F1 reproductive performance or F2 generation were observed.Pharmaceutical Information

List of excipients

Cream

Glyceryl monostearate

Cetostearyl alcohol

Chlorocresol

Sodium citrate

Citric acid (monohydrate)

Purified water

Arlacel 165

Beeswax substitute 6621

Propylene glycol

Ointment

Propylene glycol

White soft paraffin

Sorbitan sesquioleate

For important information on some of these excipients, see Warnings and Precautions.

Life

The expiry date is indicated on the packaging.

Storage

Storage conditions are detailed on the packaging.

Nature and Content of the Container

Cream

Collapsible aluminum tubes, internally coated with a lacquer with an epoxy resin base and closed with a lid.

Ointment

Collapsible aluminum tubes, internally coated with a lacquer with an epoxy resin base and closed with a lid.

Incompatibilities

No incompatibilities have been identified.

Use/Handling

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

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