DERMOVATE Cream and Ointment
Clobetasol propionate

QUALITATIVE AND QUANTITATIVE COMPOSITION
DERMOVATE Cream and Ointment contains Clobetasol propionate 0.05% w/w.

CLINICAL INFORMATION
Indications
DERMOVATE is a very active topical corticosteroid which is of particular value when used in short courses for the treatment of the more resistant dermatoses such as psoriasis (excluding widespread plaque psoriasis), recalcitrant eczema, lichen planus, discoid lupus erythematosus and other conditions which do not respond satisfactorily to less active steroids.

Dosage and Administration
Pharmaceutical form
Cream and Ointment.

Ointment
Ointments are especially appropriate for dry, lichenified or scaly lesions.

Cream
Creams are especially appropriate for moist or weeping surfaces.

Adults, elderly and children over 1 year
Apply sparingly to the affected area once or twice daily until improvement occurs and discontinue when control is achieved. In the more responsive conditions this may be within a few days. Treatment should not be continued for more than four weeks without the patient's condition being reviewed. Repeated short courses of *DERMOVATE* may be used to control exacerbations. If continuous steroid treatment is necessary, a less potent preparation should be used.

In very resistant lesions, especially where there is hyperkeratosis, the effect of *DERMOVATE* can be enhanced, if necessary, by occluding the treatment area with polythene film.

Overnight occlusion only is usually adequate to bring about a satisfactory response. Thereafter improvement can usually be maintained by application without occlusion.

Contraindications
The following conditions should not be treated with *DERMOVATE:*
- Untreated cutaneous infections
- Rosacea
- Acne vulgaris
- Pruritus without inflammation
- Perianal and genital pruritus
- Perioral dermatitis.

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 or to any of the excipients in the preparation. Local hypersensitivity reactions (*see Adverse Reactions*) 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 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 (in infants the nappy may act as an occlusive dressing))
- 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
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 *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.

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

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.

Cream and ointment
DERMOVATE cream and ointment contain paraffin. Instruct patients not to smoke or go near naked flames due to the risk of severe burns. Fabric (clothing, bedding, dressings etc) that has been in contact with these products burns more easily and is a serious fire hazard. Washing clothing and bedding may reduce product build-up but not totally remove it.

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.

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 *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.

If used during lactation *DERMOVATE* should not be applied to the breasts to avoid accidental ingestion by 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 *DERMOVATE* 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

D07AD Corticosteroids, very potent (group IV).

Mechanism of action

Topical corticosteroids act as antiinflammatory 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 antiinflammatory, 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.

Mean peak plasma clobetasol propionate concentrations of 0.63 nanograms/mL occurred in one study eight hours after the second application (13 h after an initial application) of 30 g clobetasol propionate 0.05% ointment to normal individuals with healthy skin. Following the application of a second dose of 30 g clobetasol propionate cream 0.05%, mean peak plasma concentrations were slightly higher than the ointment and occurred 10 h 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 clobetasol propionate 0.05% ointment.

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.

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 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
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 about some of these excipients see Warnings and Precautions.

Shelf Life
The expiry date is indicated on the packaging.

Storage
The storage conditions are detailed on the packaging.

Nature and Contents of Container
Cream
Collapsible aluminium tube with epoxy phenolic internal coating and carton.

Ointment
Collapsible aluminium tube with epoxy phenolic internal coating and carton.

Not all presentations are available in every country.

Incompatibilities
No incompatibilities have been identified.

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

Package Quantities and Registration Number

DERMOVATE Cream, 5 g tube	Reg. No. DKL9232000429A1
DERMOVATE Cream, 10 g tube	Reg. No. DKL9232000429A1
DERMOVATE Ointment, 10 g tube	Reg. No. DKL9232000330A1

HARUS DENGAN RESEP DOKTER

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