Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Dermovate 0.05% w/w Ointment

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each gram of ointment contains 0.5 mg of clobetasol propionate (equivalent to 0.05% w/w).

Excipients with known effect:
Each gram of ointment contains 50 mg of propylene glycol (equivalent to 5% w/w)

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Ointment
A white to off-white, translucent, homogeneous ointment.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Dermovate is a very potent topical corticosteroid for adults, elderly and children over 1 year for the relief of the inflammatory and pruritic manifestations of steroid responsive dermatoses.

These include the following:
- Psoriasis (excluding widespread plaque psoriasis)
- Recalcitrant dermatoses
- Lichen planus
- Discoid lupus erythematosus
- Other skin conditions which do not respond satisfactorily to less potent steroids

4.2 Posology and method of administration

Clobetasol propionate belongs to the most potent class of topical corticosteroids (Group IV) and prolonged use may result in serious undesirable effects (see section 4.4). If treatment with a local corticosteroid is clinically justified beyond 4 weeks, a less potent corticosteroid preparation should be considered. Repeated but short courses of clobetasol propionate may be used to control exacerbations (see details below).

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

Posology
Apply thinly and gently rub in using only enough to cover the entire affected area once or twice a day or up to 4 weeks 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.

Repeated short courses of Dermovate may be used to control exacerbations.

In more 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.

If the condition worsens or does not improve within 2-4 weeks, treatment and diagnosis should be re-evaluated.

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

The maximum weekly dose should not exceed 50 g/week

Atopic dermatitis (eczema)
Therapy with Dermovate 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 Dermovate.

Recalcitrant dermatoses
Patients who frequently relapse
Once an acute episode has been treated effectively with a continuous course of topical corticosteroid, intermittent dosing (applying once a day, twice weekly, without occlusion) may be considered. This has been shown to be helpful in reducing the frequency of relapse.

Application should be continued to all previously affected sites or to known sites of potential relapse. This regime should be combined with routine daily use of emollients. The condition and the benefits and risks of continued treatment must be re-evaluated on a regular basis.

Paediatric population
Dermovate is contraindicated in children under one year of age.

Children are more likely to develop local and systemic side effects of topical corticosteroids and, in general require shorter courses and less potent agents that adults (please refer to section 4.4 for further information).

Courses should be limited if possible to few days and reviewed weekly.

Care should be taken when using this medicinal product 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 the 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

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

The following conditions should not be treated with Dermovate:

- Unresolved cutaneous viral, bacterial or fungal infections
- Rosacea
- Acne vulgaris
- Pruritus without inflammation
- Perianal and genital pruritus
- Perioral dermatitis
- Widespread plaque psoriasis, except single lesions

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

4.4 Special warnings and precautions for use

Cases of osteonecrosis serious infections (including necrotizing fasciitis) and systemic immunosuppression (sometimes resulting in reversible Kaposi's sarcoma lesions) have been reported with long-term use of clobetasol propionate beyond the recommended doses (see section 4.2). In some cases patients used concomitantly other potent oral/topical corticosteroids or immunosuppressors (e.g. methotrexate, mycophenolate mofetil). If treatment with local corticosteroids is clinically justified beyond 4 weeks, a less potent corticosteroid preparation should be considered.

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 section 4.8) 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 section 4.8). The risk with topical corticosteroids is reduced but potentially still exists.

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.

Paediatric population
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 tolerences, 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 lesion 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.

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 a few 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.

There have been a few reports in the literature of the development of cataracts in patients who have been using corticosteroids for prolonged periods of time. Although it is not possible to rule out systemic corticosteroids as a known factor, prescribers should be aware of the possible role of corticosteroids in cataract development.

Visual disturbance
Visual disturbance may be reported with systemic and topical corticosteroid use. If a patient presents with symptoms such as blurred vision or other visual disturbances, the patient should be considered for referral to an ophthalmologist for evaluation of possible causes which may include cataract, glaucoma or rare diseases such as central serous chorioretinopathy (CSCR) which have been reported after use of systemic and topical corticosteroids.

Excipients – Important Information
Dermovate Ointment contains propylene glycol which may cause skin irritation.

4.5 Interaction with other medicinal products and other forms of 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.

The interaction is relevant for all routes of administration, however, it is more relevant to routes of administration that generate the highest systemic exposure.

4.6 Fertility, pregnancy and lactation

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

Topical administration of corticosteroids to pregnant animals can cause abnormalities of foetal development (see section 5.3). The relevance of this finding to humans has not been established. Administration of clobetasol 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.

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

If used during lactation clobetasol 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.

Clobetasol administered subcutaneously to rats had no effect upon mating performance; however, fertility was decreased at the highest dose (see section 5.3).

4.7 Effects on ability to drive and use machines

There have been no studies to investigate the effect of clobetasol 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.

4.8 Undesirable effects

Adverse reactions are listed below by MedDRA system organ class and frequency. Frequencies are defined as: very common (≥1/10), common (≥1/100 to <1/10), uncommon (≥1/1000 to <1/100), rare (≥1/10,000 to <1/1000) 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.

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

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

General Disorders and Administration Site Conditions
Very rare Application site irritation/pain

Eye disorders
Very Rare Cataract, central serous chorioretinopathy, glaucoma

Not known: Vision, blurred (see also section 4.4)

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via HPRA Pharmacovigilance, Website: www.hpra.ie.

4.9 Overdose

Symptoms
Topically applied clobetasol 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).

Management
In the event of overdose, clobetasol 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.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Corticosteroids, very potent (group IV)
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.

5.2 Pharmacokinetic properties

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 ng/ml occurred in one study eight hours after the second application (13 hours 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 hours after application. In a separate study, mean peak plasma concentrations of approximately 2.3 ng/ml and 4.6 ng/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.

5.3 Preclinical 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.

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.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Propylene glycol
White soft paraffin
Sorbitan sesquioleate

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years.

6.4 Special precautions for storage

Do not store above 30°C.

6.5 Nature and contents of container

Dermovate Ointment is supplied in 30g and 100g collapsible aluminium tubes.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

Patients should be advised to wash their hands after applying Dermovate, unless it is the hands that are being treated.

7 MARKETING AUTHORISATION HOLDER

GlaxoSmithKline (Ireland) Limited
12 Riverwalk
Citywest Business Campus
Dublin 24
Ireland

8 MARKETING AUTHORISATION NUMBER

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 27 October 1983

Date of last renewal: 27 October 2008

10 DATE OF REVISION OF THE TEXT

July 2021