Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Dermovate Scalp Application 0.05% w/v Cutaneous Solution

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 10 ml of cutaneous solution contains 5 mg of clobetasol propionate (equivalent to 0.05% w/v).

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Cutaneous solution
A colourless, clear to slightly hazy, slightly viscous solution.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Dermovate Scalp Application is a very potent corticosteroid indicated for adults, elderly and children over 1 year for the relief of the inflammatory and pruritic manifestations of steroid responsive dermatoses of the scalp such as:
- Psoriasis
- Recalcitrant dermatoses

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).

Posology
A small quantity of Dermovate Scalp Application 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.

As with other highly potent 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.

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.

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.

Use in the presence of unresolved bacterial, viral, tuberculosis or fungal infections of the scalp.

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.

<u>Paediatric population</u>
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 psoriases 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.

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.

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.

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.

Atrophic changes may occur on the face and to a lesser degree in other parts of the body after prolonged treatment with potent topical steroids.

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 clobetasol propionate 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.

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

Carbomer
Isopropyl alcohol
Sodium hydroxide (for pH adjustment only)
Purified water

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years.

6.4 Special precautions for storage

Do not store above 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 scalp application in direct sunlight.

6.5 Nature and contents of container

HDPE, squeeze bottle with an elongate nozzle containing a colourless, clear to slightly hazy, slightly viscous liquid.

Pack size: 100 ml

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.

7 MARKETING AUTHORISATION HOLDER

GlaxoSmithKline (Ireland) Limited
12 Riverwalk
Citywest Business Campus

Dublin 24
Ireland

8 MARKETING AUTHORISATION NUMBER

PA1077/005/003

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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Date of last renewal: 27 October 2008

10 DATE OF REVISION OF THE TEXT

July 2021