SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT
PSODERM 0.05% Ointment

2. QUALITATIVE AND QUANTITATIVE COMPOSITION:
Each 1 g ointment contains:
Active substances:
Clobetasol 17-propionate 0.5 mg
Excipient(s) with known effect:
Propylene glycol 60 mg
For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM
Ointment.

4. CLINICAL PARTICULARS
4.1 Therapeutic indications
PSODERM is a very potent corticosteroid and is used for the treatment of psoriasis (excluding widespread plaque psoriasis), recalcitrant dermatoses, lichen planus, discoid lupus erythematosus and other conditions that do not respond satisfactorily to less active steroids.

4.2 Posology and method of administration
Posology/frequency and duration of administration
PSODERM ointment is appropriate for dry, lichenified or scaly lesions. It should be applied to the diseased area once or twice a day until healing occurs. Once control is achieved, the treatment should be terminated. Treatment should not be continued for more than 4 weeks until the patient's condition is reassessed. Short-term treatment with PSODERM can be repeated to control disease exacerbation. If long-term steroid therapy is required, a less active preparation should be used. Adequate time should be allowed for absorption after each application before applying an emollient.

Since children are more likely to develop local and systemic side effects of corticosteroids, use in children over 12 years of age should be limited to 5 days, and large amounts or long-term applications should be avoided.

Method of administration
It is applied as a thin layer to cover the affected area. In lesions that are more resistant, especially where there is hyperkeratosis, the anti-inflammatory effect of PSODERM 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. After PSODERM application, you should wash your hands unless your hands are the treated area.

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 treatment is necessary, a less potent preparation should be used.

The maximum weekly dose should not exceed 50 g.

Atopic dermatitis (eczema)
Therapy with clobetasol 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 clobetasol.

Recalcitrant dermatoses: patients who frequently relapse
Once an acute episode has been treated effectively with a continuous course of topical corticosteroid, intermittent dosing (once daily, 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 regimen 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.

Additional information on special populations
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.

Pediatric population
It should not be used for more than 5 days in children over 12 years of age and the skin should not be covered after the application. It should be used in the lowest amount and for the shortest time possible in children. PSODERM is not recommended to be used in the childhood age group unless it is mandatory.

Geriatric population
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.

4.3 Contraindications
It is contraindicated for use in rosacea, acne vulgaris and perioral dermatitis, perianal and genital pruritus, primary viral infections of the skin (e.g. herpes simplex, chicken pox), untreated cutaneous infections, hypersensitivity to the preparation, pruritus without inflammation, primary infected skin lesions caused by fungi or bacteria.

4.4 Special warnings and precautions for use
Clobetasol should be used with caution in patients with a history of local hypersensitivity to other 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 because of increased systemic absorption of topical steroids. If any 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.

Risk factors for increased systemic effects are:
- Potency and formulation of topical steroids
- 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
- Due to the higher absorption rate in children compared to adults, the sensitivity to systemic effects may be higher. This is because children have an immature skin barrier and a greater surface area compared with adults.

Care should be taken not to get the preparation in contact with the eyes. In case of contact with the eyes, the eyes should be washed with plenty of water.

Children are more susceptible to atrophic effects of topical corticosteroids. If PSODERM is required to be used in children aged 12 years and older, it is recommended that treatment be limited to 5 days and reviewed weekly.

Treatment should not exceed 5 days and occlusion should not be applied when applied to children aged 12 and over or when applied on the face.

If applied to the eyelids, care is needed to ensure that the preparation does not enter the eye, as cataract and glaucoma might occur. If it enters the eye, the affected eye should be bathed in copious amounts of water.

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 5 days.

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.

Topical steroids should be used with caution in psoriasis as rebound relapses, development of tolerances, risk of generalized 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 supervision for patient is important.

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.

Appropriate antimicrobial therapy should be applied when treating infected inflammatory lesions with local corticosteroids. If any spread of infection is seen, corticosteroid therapy should be

discontinued immediately and systemic antimicrobial agents should be given. 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.

The drug contains propylene glycol, which may cause skin irritation.

4.5 Interaction with other medicinal products and other forms of interaction

Co-administered medicines 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.

Additional information on special populations
Not reported.

Pediatric population
Not reported.

4.6 Fertility, pregnancy and lactation

General recommendation
Pregnancy category is C.

Women of childbearing potential/Contraception
No special contraception is required for use in women of childbearing potential. It should not be used extensively, in high doses and for a long time in women who are planning a pregnancy.

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

Topical administration of corticosteroids to pregnant animals can cause abnormalities of fetal development. 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 fetus. The minimum quantity should be used for the minimum duration.

Lactation
The safe use of topical steroids during lactation has not been established.

It is not known whether the topical administration of steroids 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.

Reproduction ability/Fertility
Animal studies have shown reproductive toxicity. Potential risk to humans is unknown. 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.

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

The frequency classification is as follows:

Very common	: (≥1/10)
Common	: (≥1/100 to <1/10)
Uncommon	: (≥1/1,000 to <1/100)
Rare	: (≥1/10,000 to <1/1,000)
Very rare	: (< 1/10,000)
Not known	: (cannot be estimated from the available data).

Post-marketing data

Infections and infestations

Very rare*:* Opportunistic infections

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, hyperglycemia/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*, telangiectasis*
Very rare: Skin thinning*, skin wrinkling*, skin dryness*, pigmentation changes*, hypertrichosis, exacerbation of underlying symptoms, allergic contact dermatitis, pustular psoriasis, erythema, rash, urticaria, acne

* Due to local and systemic effects of hypothalamic-pituitary adrenal (HPA) axis suppression.

General disorders and administration site conditions

Very rare: Application site irritation/pain

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorization 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 in accordance with local requirements.

4.9 Overdose

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. 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.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Very potent corticosteroids (topical dermatological) (group IV)
ATC code: D07AD01

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.

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

5.2 Pharmacokinetic properties

General 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

Mean peak plasma clobetasol propionate concentrations of 0.63 nanograms/mL occurred in one study 8 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 nanograms/mL and 4.6 nanograms/mL occurred respectively in patients with psoriasis and eczema 3 hours after a single application of 25 g clobetasol propionate 0.05 % ointment.

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

Biotransformation

Once absorbed through the skin, topical corticosteroids are handled through metabolic pathways similar to systemically administered corticosteroids. They are metabolized primarily in the liver and excreted by the kidneys.

Elimination

Topical corticosteroids are excreted by the kidneys. In addition, some metabolites are also excreted in the bile.

5.3 Preclinical safety data

Long-term animal studies have not been performed to evaluate the carcinogenic potential of clobetasol propionate.

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

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 fetal abnormalities including cleft palate.

In the rat study, where some animals were allowed to litter, developmental delay was observed in the F1 generation at ≥ 100 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
Sorbitan sesquioleate
White petrolatum

6.2 Incompatibilities

Not applicable.

6.3. Shelf life

36 months.

6.4 Special precautions for storage

Store at room temperature below 30ºC.

6.5 Nature and contents of container

Supplied in aluminum tubes of 50 g, in a cardboard box.

6.6 Special precautions for disposal

Any unused product or waste material should be disposed according to local requirements.

7. MARKETING AUTHORIZATION HOLDER

DEVA Holding A.Ş.
Halkalı Merkez Mah. Basın Ekspres Cad. No:1
34303 Küçükçekmece – ISTANBUL/TURKEY

8. MARKETING AUTHORIZATION NUMBER

237/69

9. DATE OF FIRST AUTHORIZATION/RENEWAL OF THE AUTHORIZATION

Date of first authorization : 07.12.2011
Date of last renewal :

10. REVISION DATE OF TEXT