SCHEDULING STATUS **S4**

1. NAME OF THE MEDICINE

DOVOBET® calcipotriol 50 µg and betamethasone 0,5 mg per gram. Ointment

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each gram contains calcipotriol 50 µg (as monohydrate 52,2 µg) and betamethasone 0,5 mg (as dipropionate 0,643 mg).

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Ointment.

Off-white to yellow.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Treatment of psoriasis vulgaris.

4.2 Posology and method of administration

Adults

DOVOBET should be applied to the affected area once daily. The recommended treatment period is 4 weeks.

There is experience with repeated courses of DOVOBET up to 52 weeks. If it is necessary to continue or restart treatment after 4 weeks, treatment should be continued under medical review and under regular medical supervision.

The maximum daily dose should not exceed 15 g, and the maximum weekly dose should not exceed 100 g. The treated area should not be more than 30 % of the body surface.

Children

There is no experience of use in children and adolescents below the age of 18 years.

Method of administration

DOVOBET ointment should be applied to the affected area. In order to achieve optimal effect, it is not recommended to take a shower or bath immediately after application of DOVOBET ointment.

4.3 Contraindications

- Known hypersensitivity to calcipotriol, betamethasone or to any of the excipients listed in section 6.1.
- DOVOBET is contraindicated in erythrodermic, exfoliative and pustular psoriasis.
- DOVOBET is contraindicated in patients with known disorders of calcium metabolism due to the content of calcipotriol (see section 4.4).
- Due to the content of corticosteroid, DOVOBET is contraindicated in the following conditions: viral (e.g., herpes or varicella) lesions of the skin, fungal or bacterial skin infections, parasitic infections, skin manifestations in relation to tuberculosis, perioral dermatitis, atrophic skin, striae atrophicae, fragility of skin veins, ichthyosis, acne vulgaris, acne rosacea, rosacea, ulcers and wounds (see section 4.4).
- DOVOBET is contraindicated in patients with severe hepatic disorders or severe renal insufficiency.
- Safe use of DOVOBET during human pregnancy and lactation has not been established. Corticosteroids have been shown to be teratogenic in animals following dermal application. As these agents are absorbed percutaneously, teratogenicity following topical application cannot be excluded. Therefore, DOVOBET should not be used during pregnancy, (see section 4.6).

4.4 Special warnings and precautions for use

Effects on endocrine system

DOVOBET ointment contains a potent group III steroid and concurrent treatment with other steroids must

be avoided. Adverse reactions found in connection with systemic corticosteroid treatment, such as adrenocortical suppression or impact on the metabolic control of diabetes mellitus may occur also during topical corticosteroid treatment due to systemic absorption.

Application under occlusive dressings should be avoided since it increases the systemic absorption of corticosteroids. Application on large areas of damaged skin, or on mucous membranes or in skin folds should be avoided since it increases the systemic absorption of corticosteroids (see section 4.8).

A borderline decrease in cortisol response to adrenocorticotropic hormone (ACTH) challenge after 4 weeks of treatment was reported in patients with both extensive scalp and extensive body psoriasis using a combination of high doses of DOVOBET gel (scalp application) and high doses of DOVOBET ointment (body application).

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 a 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.

Effects on calcium metabolism

Due to the calcipotriol content of DOVOBET, hypercalcaemia may occur if the maximum weekly dose (15 g) is exceeded. Serum calcium is normalised when treatment is discontinued. The risk of hypercalcaemia is minimal when the recommendations relevant to calcipotriol are followed. Treatment of more than 30 % of the body surface should be avoided (see section 4.2).

Local adverse reactions

DOVOBET contains a potent group III-steroid and concurrent treatment with other steroids on the same

treatment area must be avoided. Skin of the face and genitals are very sensitive to corticosteroids. DOVOBET should not be used in these areas. The patient must be instructed in correct use of DOVOBET to avoid application and accidental transfer to the face, scalp, mouth or eyes. Hands must be washed after each application to avoid accidental transfer to these areas.

Concomitant skin infections

When lesions become secondarily infected, they should be treated with antimicrobiological therapy. However, if infection worsens, treatment with DOVOBET should be stopped (see section 4.3).

Discontinuation of treatment

When treating psoriasis with topical corticosteroids, such as contained in DOVOBET, there may be a risk of generalised pustular psoriasis or of rebound effects when discontinuing treatment. Medical supervision should therefore continue in the post-treatment period.

Long-term use

With long-term use there is an increased risk of local and systemic corticosteroid adverse reactions. The treatment should be discontinued in case of adverse reactions related to long-term use of corticosteroid (see section 4.8).

Unevaluated use

There is no experience with the use of DOVOBET in guttate psoriasis.

Concurrent treatment and UV exposure

There is limited experience for the use of this medicine on the scalp. DOVOBET ointment for body psoriasis lesions has been used in combination with DOVOBET gel for scalp psoriasis lesions, but there is limited experience of combination of DOVOBET with other topical anti-psoriatic products at the same treatment area, other anti-psoriatic medicines administered systemically or with phototherapy.

During DOVOBET treatment, patients should limit or avoid excessive exposure to either natural or artificial sunlight.

4.5 Interaction with other medicines and other forms of interaction

No interaction studies have been performed with DOVOBET.

4.6 Fertility, pregnancy and lactation

Safety and efficacy in pregnancy and lactation have not been established (see section 4.3)

Pregnancy

DOVOBET is contraindicated in pregnancy (see section 4.3). The potential risk for use of DOVOBET during pregnancy is uncertain.

Breastfeeding

Caution should be exercised when prescribing DOVOBET to women who are breastfeeding. The patient should also be instructed to not use DOVOBET on the breast whilst breastfeeding.

4.7 Effects on ability to drive and use machines

DOVOBET has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

The most frequently reported adverse reactions during treatment are various skin reactions, like pruritus and skin exfoliation.

Pustular psoriasis and hypercalcaemia have been reported.

Adverse reactions are listed by MedDRA SOC and the individual adverse reactions are listed starting with the most frequently reported.

Infections and infestations	
Less frequent	Skin infection*, folliculitis, furuncle
Blood and lymphatic system disorders	
Less frequent	Ecchymosis
Immune system disorders	
Less frequent	Hypersensitivity
Endocrine disorders	
Less frequent	Hirsutism, cushings syndrome
Metabolism and nutrition disorders	
Less frequent	Hypercalcaemia, hypokalaemic syndrome
Nervous system disorders	
Less frequent	Hyperaesthesia, numbness in fingers
Eye disorders	
Not known	Blurred vision****, Posterior subscapular cataracts
Vascular disorders	
Less frequent	Hypertension
Gastrointestinal disorder	
Less frequent	Gastric ulcer
Skin and subcutaneous tissue disorders	
Frequent	Skin exfoliation, pruritus, rash**, burning sensation of the skin
Less frequent	Skin atrophy, exacerbation of psoriasis, dermatitis, erythema, purpura or ecchymosis, skin irritation, pustular psoriasis, skin striae, photosensitivity reaction, acne, dry skin

Musculoskeletal and connective tissue disorders	
Less frequent	Protein depletion
General disorders and administration site conditions	
Less frequent	Application site pigmentation changes, application site pain***, rebound effect, Oedema

*Skin infections including bacterial, fungal and viral skin infections have been reported.

**Various types of rash reactions such as exfoliative rash, rash papular and rash pustular have been reported.

***Application site burning is included in application site pain.

****See section 4.4.

Paediatric population

The safety of DOVOBET ointment in children below 18 years have not been established.

Calcipotriol

Adverse reactions include application site reactions, pruritus, skin irritation, burning and stinging sensation, dry skin, erythema, rash, dermatitis, eczema, aggravated psoriasis, photosensitivity and hypersensitivity reactions including less frequent cases of angioedema and facial oedema.

Systemic effects after topical use may appear less frequently causing hypercalcaemia or hypercalciuria, (see section 4.4).

Betamethasone (as dipropionate)

Local reactions can occur after topical use, especially during prolonged application, including skin atrophy, telangiectasia, striae, folliculitis, hypertrichosis, perioral dermatitis, allergic contact dermatitis, depigmentation and colloid milia.

When treating psoriasis with topical corticosteroids, there may be a risk of generalised pustular psoriasis.

Systemic reactions due to topical use of corticosteroids are less frequent in adults, however they can be severe.

Adrenocortical suppression, cataract, infections, impact on the metabolic control of diabetes mellitus and increase of intra-ocular pressure can occur, especially after long term treatment. Systemic reactions occur more frequently when applied under occlusion (plastic, skin folds), when applied on large areas and during long term treatment (see section 4.4).

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare providers are asked to report any suspected adverse reactions to SAHPRA via the "**6.04 Adverse Drug Reactions Reporting Form**", found online under SAHPRA's publications:

https://www.sahpra.org.za/Publications/Index/8.

Additionally, suspected adverse reactions can be reported to the Holder of Certificate of Registration via Adcock.AEReports@adcock.com.

4.9 Overdose

Use of above the recommended dose may cause elevated serum calcium which subsides when treatment is discontinued. The symptoms of hypercalcaemia include polyuria, constipation, muscle weakness, confusion and coma.

Excessive prolonged use of topical corticosteroids, as contained in DOVOBET, may suppress the pituitary-adrenal functions, resulting in secondary adrenal insufficiency which is usually reversible.

Treatment is symptomatic and supportive.

In cases of toxicity due to chronic use, DOVOBET treatment must be discontinued gradually.

It has been reported that due to misuse one patient with extensive erythrodermic psoriasis treated with 240 g of DOVOBET ointment weekly (corresponding to a daily dose of approximately 34 g) for 5 months (maximum recommended dose 15 g daily) developed Cushing's syndrome during treatment and then pustular psoriasis after abruptly stopping treatment.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

A 13.8.1 Preparations for psoriasis.

Pharmacotherapeutic group: Antipsoriatics. Other antipsoriatics for topical use, Calcipotriol, combinations. ATC Code:D05AX52

Calcipotriol is a vitamin D analogue. It is suggested that calcipotriol induces differentiation and suppresses proliferation of keratinocytes. This is the proposed basis for its effect in psoriasis.

The dipropionate ester of betamethasone is a glucocorticoid exhibiting the general properties of corticosteroids. In pharmacological doses, corticosteroids are used primarily for their anti-inflammatory and/or immunosuppressive effects. The exact mechanism of the action of corticosteroids in psoriasis is uncertain.

5.2 Pharmacokinetic properties

The human transdermal absorption of calcipotriol and betamethasone has been shown to be less than 1 % of the administered dose for both substances. The systemic absorption under normal conditions of use is not expected to have any influence on systemic parameters. The presence of the two active constituents does not influence the pharmacokinetic behaviour of each other.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Liquid paraffin

Polyoxypropylene stearyl ether

All-rac-α-tocopherol

White soft paraffin

6.2 Incompatibilities

In the absence of compatibility studies, this medicine must not be mixed with other medicines.

6.3 Shelf life

2 years

After first opening: 12 months

6.4 Special precautions for storage

Store at or below 25 °C. Keep well closed.

6.5 Nature and contents of container

Aluminium tubes with polyethylene screw caps:

Tube size: 15, 30, 60, 100 and 120 g.

Polyethylene-aluminium laminate tubes with polyethylene screw cap:

Tube size: 15, 30, 60, 100 and 120 g.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Adcock Ingram Limited

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Erand Gardens,

Midrand, 1685

Customer Care: 0860 ADCOCK/ 232625

Under licence from

Leo Pharma A/S

Industriparken 55, 2750 Ballerup, Denmark

8. REGISTRATION NUMBER(S)

37/13.9.1/0241

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

8 June 2007

10. DATE OF REVISION OF THE TEXT

28 July 2023

Namibia: NS2 10/13.9.1/0489

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