## 1.3.1.1 Package Insert for DOVOBET GEL

**SCHEDULING STATUS: S4**

**PROPRIETARY NAME AND DOSAGE FORM:**

**Dovobet Gel**

**COMPOSITION:**

Each one gram of **Dovobet Gel** contains:

- 50 µg (microgram) of calcipotriol monohydrate.
- 0,5 mg of betamethasone as the dipropionate.

**Inactive ingredients:**

All-rac-alpha-tocopherol, butylhydroxytoluene, castor oil, liquid paraffin, polyoxypropylene stearyl ether.

**PHARMACOLOGICAL CLASSIFICATION**

A 13.9.1 Preparations for psoriasis.

**PHARMACOLOGICAL ACTION:**

**Pharmacokinetic properties:**

***Absorption:***

Clinical studies with radio-labelled ointment also applicable to the gel indicate that the systemic absorption of calcipotriol and betamethasone from Dovobet ointment formulation is less than 1 % of the dose (2,5 g) when applied to normal skin (625 $cm^2$) for 12 hours. Application to psoriasis plaques and under occlusive dressings may increase the absorption of topical corticosteroids. Absorption through damaged skin is approximately 24 %.

***Metabolism, distribution and elimination:***

Following systemic exposure, both calcipotriol and betamethasone dipropionate are extensively metabolised. Plasma elimination half-life after intravenous application is 5-6 hours. Due to the formation of a depot in the skin, elimination after dermal application is in order of days. Betamethasone is metabolised especially in the liver, but also in the kidneys to glucuronide and sulphate esters. Protein binding is approximately 64 %.

Calcipotriol and betamethasone dipropionate were below the lower limit of quantification in all blood samples of 34 patients treated for 4 or 8 weeks with **Dovobet Gel** for extensive psoriasis involving the body and scalp. One metabolite of calcipotriol and one metabolite of betamethasone dipropionate were quantifiable in some of the patients.

## INDICATIONS

**Dovobet Gel** is indicated for the topical treatment of:

- Scalp psoriasis in adults.
- Mild to moderate psoriasis vulgaris plaques on non-scalp regions of the body in adults.

## CONTRAINDICATIONS

**Dovobet Gel** is contraindicated in:

- Patients with a known hypersensitivity to the active substances or to any of the excipients of **Dovobet Gel** (see **COMPOSITION**).
- Patients who suffer from erythrodermic, exfoliative and pustular psoriasis.
- Patients with known disorders of calcium metabolism (due to the calcipotriol content in **Dovobet Gel**).

- Patients who suffer from 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 or syphilis, perioral dermatitis, atrophic skin, striae atrophicae, fragility of skin veins, ichthyosis, acne vulgaris, acne rosacea, rosacea, ulcers, wounds, perianal and genital pruritus- (due to the betamethasone content in **Dovobet Gel**).
- Pregnancy and lactation.

**WARNINGS AND SPECIAL PRECAUTIONS**

**Effects on endocrine system:**

**Dovobet Gel** contains a potent group III steroid and concurrent treatment with other steroids must be avoided. Adverse reactions which may occur due to systemic corticosteroid treatment, such as adrenocortical suppression or worsening on the metabolic control of diabetes mellitus, may also occur during topical corticosteroid treatment due to systemic absorption (see **SIDE EFFECTS**).

**Application under occlusive dressings should be avoided since it increases the systemic absorption of corticosteroids (see SIDE EFFECTS).**

**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 SIDE EFFECTS).**

In a study in patients with both extensive scalp and extensive body psoriasis using a combination of high doses of **Dovobet Gel** (body application) and high doses of Dovobet ointment (scalp application), 5 of 32 patients showed a decrease in cortisol response to adrenocorticotropic hormone (ACTH) challenge after 4 weeks of treatment.

**Effects of Dovobet Gel on calcium metabolism:**

Hypercalcaemia may occur if the maximum daily dose of 15 g is exceeded. This occurs due to the calcipotriol component in **Dovobet Gel** (see **SIDE EFFECTS**). However, when treatment is discontinued, serum calcium is normalised.

The risk of hypercalcaemia can be minimised when the recommendations relevant to calcipotriol are followed. Treatment of more than 30 % of the body surface should be avoided (see **DOSAGE AND DIRECTIONS FOR USE**).

**Local adverse reactions:**

**Dovobet Gel** 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 Gel** should not be used in these areas. The patient must be instructed in correct use of the **Dovobet Gel** to avoid application and accidental transfer to the face, mouth and 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 appropriate antimicrobial therapy. However, if infection worsens, treatment with **Dovobet Gel** should be stopped since it contains corticosteroids.

**Discontinuation of treatment:**

When treating psoriasis with topical corticosteroids as contained in **Dovobet Gel**, there may be a

risk of generalised pustular psoriasis or of rebound effects when treatment is discontinued. Medical supervision should therefore continue in the post-treatment period. Gradual withdrawal may be required.

**Long-term use:**

With long-term use the patient may suffer from an increased risk of local and systemic corticosteroid induced adverse reactions. The treatment should be discontinued in case of adverse reactions which are related to long-term use of corticosteroid (see **SIDE EFFECTS**).

**Unevaluated use:**

There is no experience for the use of **Dovobet Gel** in guttate psoriasis.

**Concurrent treatment and Ultraviolet exposure:**

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 Gel** with other topical anti-psoriatic medicines at the same treatment area, other anti-psoriatic medicines administered systemically or with phototherapy.

During **Dovobet Gel** treatment, medical practitioners are to advise patients to limit or avoid excessive exposure to either natural or artificial sunlight.

**Effects on ability to drive and use machines**

**Dovobet Gel** has no influence on the ability to drive and use machines.

**Adverse reactions to excipients:**

**Dovobet Gel** contains butylhydroxytoluene (see **COMPOSITION**), which may cause local skin reactions (e.g. contact dermatitis) or irritation to the eyes and mucous membranes.

## INTERACTIONS

No interaction studies with other medicines or other forms of interaction have been performed on **Dovobet Gel**.

## PREGNANCY AND LACTATION

**Pregnancy:**

**Dovobet Gel** should not be used in pregnancy.

Safety of **Dovobet Gel** use in pregnancy has not been established.

**Lactation:**

Betamethasone in **Dovobet Gel** passes into breast milk.

**Dovobet Gel** should not be used in lactation.

**Fertility:**

**Dovobet Gel** causes no impairment of male and female fertility.

**DOSAGE AND DIRECTIONS FOR USE**

Do not exceed the recommended dose and duration of treatment.

**Adults:**

**Dovobet Gel** should be applied to the affected areas once daily.

The recommended treatment period is 4 weeks for ***scalp*** areas and 8 weeks for ***non-scalp*** areas.

**If it is necessary to continue or restart treatment after this period, treatment should be continued after medical review and under regular medical supervision.**

When using calcipotriol containing medicines, such as **Dovobet Gel**, the maximum daily dose should not exceed 15 g and the weekly dose should not exceed 100 g. The body surface area treated, should not exceed 30 % (see **WARNINGS AND SPECIAL PRECAUTIONS**).

If using on the scalp, all the affected scalp areas may be treated with **Dovobet Gel**. Usually an amount between 1 g and 4 g per day is sufficient for treatment of the scalp (4 g corresponds to one teaspoon full).

**Method of administration:**

**Dovobet Gel:**

- The bottle should be shaken before use.
- The gel should be applied to the affected area.
- **The gel should not be applied directly to the face or eyes.**
- The hands should be washed after each use.

- In order to achieve optimal effect, it is not recommended to take a shower or bath immediately after application of the gel.
- The gel should remain on the skin during the night or during the day.

**Special populations:**

***Renal and hepatic impairment:***

The safety and efficacy of **Dovobet Gel** in patients with severe renal insufficiency or severe hepatic disorders have not been evaluated.

***Paediatric population:***

The safety and efficacy of **Dovobet Gel** in children below 18 years have not been established.

**SIDE EFFECTS:**

**Infections and infestations:**

*Less frequent:* Skin infection (bacterial, fungal and viral), folliculitis.

**Immune system disorders:**

*Less frequent:* Hypersensitivity.

**Eye disorders**

*Less frequent*: Eye irritation.

**Skin and subcutaneous tissue disorders**

*Frequent:* Pruritus.

*Less frequent:* Exacerbation of psoriasis, burning sensation of skin, skin pain or irritation, dermatitis, erythema, acne, dry skin, rash (erythematous and pustular), skin striae, skin exfoliation.

**General disorders and administration site conditions:**

*Less frequent:* Pain (and burning sensation) at application site, rebound effect.

The following adverse reactions are considered to be related to the pharmacological classes of calcipotriol and betamethasone, respectively as contained in **Dovobet Gel**:

**Calcipotriol:**

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

Systemic effects after topical use may appear causing hypercalcaemia or hypercalciuria (see **WARNINGS AND SPECIAL PRECAUTIONS**).

**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, colloid milia and de-pigmentation.

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

Systemic reactions due to topical use of corticosteroids may occur in adults; and 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 **WARNINGS AND SPECIAL PRECAUTIONS**).

**KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT**

Use above the recommended dose may cause elevated serum calcium which should subside when treatment is discontinued. Excessive prolonged use of topical corticosteroids such as contained in **Dovobet Gel**, may suppress the pituitary-adrenal functions, resulting in secondary adrenal insufficiency which is usually reversible. In such cases, symptomatic and supportive treatment is indicated.

In case of chronic toxicity, the corticosteroid treatment must be discontinued gradually.

Cushing syndrome and pustular psoriasis may develop with using dosages in excess of the maximum recommended dose and/or exceeding the recommended duration of treatment. Acute adrenal failure may be precipitated by abruptly stopping treatment.

## IDENTIFICATION

An almost clear, colourless to slightly off-white lipophilic gel. A thin oily layer may occur on the top.

## PRESENTATION

**Dovobet Gel** is packaged in either 30, 60 and 120 ml white high-density polyethylene bottles equipped with a low-density polyethylene nozzle and a high-density polyethylene red screw cap.

The bottles and package insert are contained in an outer unit carton with packaging sizes of 15 g, 30 g, and 60 g.

## STORAGE INSTRUCTIONS

Store at or below 30 °C.

Do not refrigerate.

Keep the bottle well closed.

Keep in the outer carton to protect from light.

Use within 6 months after first opening.

## KEEP OUT OF REACH OF CHILDREN.

## REGISTRATION NUMBER

46/13.9.1/0615

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