
SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Calcipotriol Sandoz 0,05 mg/ml, oplossing voor cutaan gebruik

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml of cutaneous solution contains 0.05 mg (is equal to 50 micrograms) of calcipotriol.

Excipients with known effect:

Each ml of cutaneous solution contains 30 mg of propylene glycol.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Cutaneous solution.

Clear, colourless solution with an odour of menthol.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

[Nationally completed name] is indicated for the topical treatment of mild to moderate scalp psoriasis (psoriasis vulgaris).

4.2 Posology and method of administration

Posology

Adults

[Nationally completed name] should be applied to the affected areas twice daily (morning and evening).

The maximum weekly dose should not exceed 60 ml. If this solution is used together with cream or ointment containing calcipotriol, the total weekly dose of calcipotriol should not exceed 5 mg (for example 60 ml of [Nationally completed name] plus 40 g of cream or ointment, or 40 ml of [Nationally completed name] plus 60 g of cream or ointment).

Duration of treatment should be decided by the physician, but should normally not be for longer than 22 weeks.

Renal/hepatic impairment

Patients with known severe renal or liver impairment should not be treated with calcipotriol (see section 4.3).

Children and adolescents (under 18 years of age)

[Nationally completed name] is not recommended for use in children and adolescents below 18 years due to a lack of data on safety and efficacy.

4.3 Contraindications

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

- Patients with severe renal or liver impairment
- Known disorders of calcium metabolism or treatment with other medicinal products which increase serum calcium level.
- Hypercalcaemia

4.4 Special warnings and precautions for use

Effects on calcium metabolism

Due to the content of calcipotriol, hypercalcaemia may occur if the maximum weekly dose is exceeded (see section 4.2).

Serum calcium is normalised when treatment is discontinued.

The risk of hypercalcaemia is minimal when the dose recommendations are followed.

Local adverse reactions

Calcipotriol should not be used on the face, as it may cause skin irritation. The patient must be instructed in correct use of the product to avoid accidental transfer to the face and eyes. Hands must be washed after each application to avoid accidental transfer to these areas.

Calcipotriol should be used with caution in skin folds as this may increase the risk of side effects (see section 4.8).

UV exposure

During treatment with calcipotriol, physicians are recommended to advise patients to limit or avoid excessive exposure to either natural or artificial sunlight. Calcipotriol should be used with UV radiation only if the physician and patient consider that the potential benefits outweigh the potential risks (see section 5.3).

Unevaluated use

Due to lack of data, Calcipotriol should be avoided in guttate, erythrodermic and pustular psoriasis.

Due to lack of data, calcipotriol should be avoided in patients with severe liver and kidney disease (see section 4.3).

[Nationally completed name] contains 30 mg propylene glycol per ml of solution. Propylene glycol may cause skin irritation.

Paediatric population

The efficacy and long term safety of this ointment in children and adolescents has not been established. Therefore its use in this population cannot be recommended.

4.5 Interaction with other medicinal products and other forms of interaction

Concomitant use with systemic vitamin D products, calcium supplements, or other agents that can increase serum calcium concentrations such as thiazide diuretics, estrogens, anabolic steroids, and parathyroid hormone or parathyroid hormone analogs may increase the risk of clinically significant hypercalcaemia.

There is no experience of concomitant therapy with other antipsoriatic products applied to the same area of skin at the same time.

4.6 Fertility, pregnancy and lactation

Pregnancy:

The safety of the use of calcipotriol during human pregnancy has not been established. Studies in animals have shown reproductive toxicity when calcipotriol was administered orally (see section 5.3). Topically applied calcipotriol is slightly systemically absorbed, but a disruption of calcium homeostasis is not expected. As a precautionary measure, it is preferable to avoid the use of <product name> in pregnancy.

Lactation:

It is unknown whether calcipotriol is excreted in breast milk. Short-term use on small surfaces is not expected to lead to a relevant systemic absorption and no effects on the breastfed child are anticipated. Under these conditions, calcipotriol can be used during breastfeeding. Calcipotriol should not be applied to the breast during breastfeeding. For long-term treatment and/or treatment of larger surfaces with calcipotriol, breastfeeding is not recommended.

Fertility

There are no data on the effect of calcipotriol therapy on human fertility.

4.7 Effects on ability to drive and use machines

Calcipotriol 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.

Systemic reactions (hypercalcaemia and hypercalciuria) have been reported. The risk of developing such reactions increases if the recommended total dose is exceeded (see section 4.4).

The undesirable effects are listed by MedDra SOC and the individual undesirable effects are listed starting with the most frequently reported.

Frequency of adverse reactions is defined as:

Very common ($\geq 1/10$),

Common ($\geq 1/100$ to $< 1/10$),

Uncommon ($\geq 1/1,000$ to $< 1/100$),

Rare ($\geq 1/10,000$ to $< 1/1,000$),

Very rare ($< 1/10,000$),

Not known (cannot be estimated from the available data).

The estimation of the frequency of adverse reactions is based on pooled analysis of data from clinical studies and spontaneous reporting.

Infections and infestations

Uncommon	Folliculitis
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Immune system disorders

Uncommon	Hypersensitivity reactions
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Metabolism and nutrition disorders

Uncommon	Hypercalcaemia
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Skin and subcutaneous tissue disorders

Very common:	Skin irritation
Common	pruritus, skin burning sensation, erythema, bullous reactions, worsening of psoriasis, (contact) dermatitis, skin exfoliation, skin rash*
Uncommon	Eczema, dry skin, morbilliform, papular, and pustular), skin oedema, seborrheic dermatitis, photosensitivity reaction
Rare	Urticaria

Renal and urinary disorders

Uncommon	Hypercalciuria
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General disorders and administration site conditions

Common	Application site pain
Uncommon	Application site pigmentation changes (hyper and depigmentation)

* Various types of rashes such as rash erythematous, rash maculo-papular, rash morbilliform, rash papular and rash pustular have been reported.

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 the national reporting system listed in Appendix V.

4.9 Overdose

Use above the recommended dose may cause elevated serum calcium which quickly subsides when treatment is discontinued.

The symptoms of hypercalcemia include polyuria, constipation, muscle weakness, confusion and coma..

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antipsoriatics, antipsoriatics for topical use, ATC code: D05AX02

Calcipotriol is a vitamin D derivative. *In vitro* data suggest that calcipotriol induces differentiation and suppresses proliferation of keratinocytes. The effect of calcipotriol in psoriasis is ascribed mainly to this.

An effect, first of all on the desquamation, then on the infiltration and finally on the erythema, is seen after two to four weeks of treatment. The maximum effect is usually achieved after six weeks.

5.2 Pharmacokinetic properties

No data are available on the absorption of calcipotriol following use of the scalp solution.

Data from a single study containing 5 evaluable patients with psoriasis treated with 0.3 – 1.7 g of a 50 micrograms/g tritium labelled calcipotriol ointment suggested that less than 1% of the dose was absorbed. However, total recovery of the tritium label over a 96 hour period ranged from 6.7 to 32.6%, figures maximised by uncorrected chemiluminescence. There were no data on ³H tissue distribution or excretion from the lungs.

5.3 Preclinical safety data

The effect on calcium metabolism is approximately 100 times less than that of the hormonally active form of vitamin D₃.

A dermal carcinogenicity study in mice revealed no special hazards for humans.

Calcipotriol has shown maternal and foetal toxicity in rats and rabbits when given by the oral route at doses of 54 µg/kg/day and 12 µg/kg/day, respectively. The foetal abnormalities observed with concomitant maternal toxicity included signs indicative of skeletal immaturity (incomplete ossification of the pubic bones and forelimb phalanges, and enlarged fontanelles) and an increased incidence of supernumerary ribs.

The significance for humans is unknown.

In another study where albino hairless mice were repeatedly exposed to both ultraviolet (UV) radiation and topically applied calcipotriol for 40 weeks at doses which correspond to 9, 30 and 90 µg/m²/day (equivalent to 0.25, 0.84 and 2.5 times the maximum recommended daily dose for a 60 kg adult, respectively), a reduction in the time required for UV radiation to induce the formation of skin tumours was observed (statistically significant in males only), suggesting that calcipotriol may enhance the effect of UV radiation to induce skin tumours. The clinical relevance of these findings is unknown.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium citrate
Hypromellose
Propylene glycol
Isopropyl alcohol
Levomenthol
Water, purified

6.2 Incompatibilities

Not applicable

6.3 Shelf life

2 years

After first opening: 3 months

6.4 Special precautions for storage

Do not store above 25°C.
Do not refrigerate or freeze.
Keep the bottle in the outer carton in order to protect from light.

Keep the cutaneous solution away from fire or flames (the alcohol base is inflammable).

6.5 Nature and contents of container

Polyethylene bottle fitted with polyethylene nozzle and closed with polypropylene screw cap.
Packsizes: 30 ml, 60 ml, 100 ml and 120 ml.

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.

7. HOUDER VAN DE VERGUNNING VOOR HET IN DE HANDEL BRENGEN

Sandoz B.V.
Hospitaaldreef 29
1315 RC Almere
Nederland

8. NUMMER(S) VAN DE VERGUNNING VOOR HET IN DE HANDEL BRENGEN

RVG 101240

9. DATUM VAN EERSTE VERLENING VAN DE VERGUNNING/VERLENING VAN DE VERGUNNING

Datum van eerste verlening van de vergunning: 3 februari 2009.
Datum van laatste verlenging: 30 september 2010.

10. DATUM VAN HERZIENING VAN DE TEKST

Laatste gedeeltelijke wijziging betreft rubriek 7: 8 februari 2024.