SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Calcipotriol 0,05 mg/g, zalf

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each gram of ointment contains 0.05 mg (is equal to 50 micrograms) of calcipotriol.

Excipients with known effect:
Each gram of ointment contains 10 mg of propylene glycol.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Ointment.
White to off-white ointment.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

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

4.2 Posology and method of administration

Posology

Adults
As monotherapy
[Nationally completed name] should be applied to the affected skin on limbs or trunk once or twice daily. At the beginning of treatment, twice daily (morning and evening) application is recommended. For maintenance therapy, the frequency of application may be decreased to once daily, depending on the response.

Ointment has to be applied as a thin layer to affected skin with gentle rubbing to cover the affected area until most of the ointment disappears.

The maximum amount of ointment applied should not exceed 100 grams per week. If it is used together with cream or solution containing calcipotriol, the total weekly dose of calcipotriol should not exceed 5 mg (for example 40 ml scalp solution plus 60 g of cream or ointment) due to the risk of hypercalcaemia (see section 4.4).

The duration of therapy depends on the clinical appearance. A pronounced therapeutic effect is generally seen after a maximum of 4-8 weeks. Therapy can be repeated.

As combination therapy
Once daily application in combination with topical corticosteroids (e.g. administration of [Nationally completed name] in the morning and steroid in the evening) is effective and well tolerated.

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)
There is limited experience with the use of calcipotriol ointment in children and adolescents. The efficacy and long-term safety of above mentioned dose (under adults) has not been established in children and adolescents. Therefore its use in this population cannot be recommended (see section 4.4).

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.

In view of a possible effect on calcium metabolism, the addition of penetration-promoting substances (such as salicylic acid) to the ointment is not permitted. Occlusion is undesirable for the same reason.

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 10 mg propylene glycol per gram of ointment. 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 hypercalcemia.

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 (≥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).

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

Immune system disorders

Uncommon	Hypersensitivity reactions

Metabolism and nutrition disorders

Uncommon	Hypercalcaemia

Skin and subcutaneous tissue disorders

Very common	Skin irritation
Common	pruritus, skin burning sensation, erythema, bullous reactions, worsening psoriasis, (contact) dermatitis, skin exfoliation, skin rash*
Uncommon	Eczema, Dry skin, photosensitivity reaction, skin oedema, seborrheic dermatitis
Rare	Urticaria, ,

Renal and urinary disorders

Uncommon	Hypercalciuria

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 show 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

Data from a single study containing 5 evaluable patients with psoriasis treated with 0.3 – 1.7g 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 ^{3}H 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 D_3.

A dermal carcinogenicity study in mice showed no indications of increased carcinogenic risks.

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/m^2/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

Macrogol stearyl ether
Disodium edetate
Disodium phosphate dihydrate
α-Tocopheryl acetate
Propylene glycol (E490)
Paraffin, light liquid
Water, purified
Paraffin, white soft

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.
Store in the original package.

6.5 Nature and contents of container

The ointment comes in an aluminium tube with polypropylene screw cap of 30 grams.

The ointment comes in an aluminium tube with polyethylene screw cap of 30 grams, 60 grams, 100 grams and 120 grams.

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 33409

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

Datum van eerste verlening van de vergunning: 1 mei 2007.
Datum van laatste verlenging: 31 juli 2010.

10. DATUM VAN HERZIENING VAN DE TEKST

Laatste gedeeltelijke wijziging betreft rubriek 7: 8 februari 2024.