Silkis®
calcitriol
OINTMENT

1. NAME OF THE MEDICINAL PRODUCT
Silkis 3 µg/g ointment

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
One gram of ointment contains 3 µg of calcitriol (INN). For the full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM
Ointment
White, translucent ointment

4.CLINICAL PARTICULARS

4.1. Therapeutic indications
Silkis is indicated in topical treatment of mild to moderately severe plaque psoriasis (psoriasis vulgaris) with up to 35% of body surface area involvement.

4.2. Posology and method of administration
Posology
Silkis Ointment should be applied to the psoriasis affected areas twice per day, once in the morning and once in the evening before retiring and after washing.
It is recommended that not more than 35% of the body surface be exposed to daily treatment. Not more than 30 g of ointment should be used per day. There is limited clinical experience available for the use of this dosage regimen of more than 6 weeks.
Paediatric population
There is no experience of the use of Silkis in children (see 4.4. Special warnings and precautions for use).
Special population
Patients with kidney or liver dysfunction should not use Silkis (see also 4.3. Contra-indications).

4.3. Contra-indications
Hypersensitivity to the active substance(s) or to any of the excipients listed in section 6.1.
Patients on systemic treatment of calcium homeostasis.
Patients with kidney or liver dysfunction.
Patients with hypercalcaemia and patients known to suffer from abnormal calcium metabolism.

4.4. Special warnings and precautions for use
The ointment can be applied to the face with caution, as there is an increased risk of irritation in this area. Contact with the eyes should be avoided. The hands should be washed after applying the ointment in order to avoid unintentional application to non lesional areas. Not more than 35% of the body surface should be exposed to daily treatment. Not more than 30g of ointment should be used per day.
Due to potential effects on calcium metabolism, substances which stimulate absorption must not be added to the ointment, and the ointment must not be covered with an occlusive dressing.
In case of severe irritation or contact allergy, the treatment with Silkis should be discontinued and the patient should obtain medical advice. If contact allergy is demonstrated this discontinuation is definitive.
Although no clinically significant hypercalcaemia was observed in clinical studies with a dosage under 30 g/day of Silkis ointment, some absorption of calcitriol through the skin does occur and excessive use of the ointment can lead to systemic side-effects, such as an increase in urine and serum calcium levels, which is a known class effect for calcitriol.
There is no information about the use of Silkis in other clinical forms of psoriasis (other than plaque psoriasis) i.e. Psoriasis guttata acuta, pustular psoriasis, psoriasis erythrodermica and rapid progressive plaque psoriasis.
Paediatric population
In view of the particular sensitivity of neonates versus adult rodents to the toxic effects of calcitriol, exposure of children to calcitriol ointment should be avoided (see also 4.2. Posology and method of administration).

4.5. Interaction with other medicinal products and other forms of interaction
Silkis must be used with caution in patients receiving medications known to increase the serum calcium level, such as thiazide diuretics, or medications with pharmacological effects impacted by a change in calcium levels, such as digoxin. Caution must also be exercised in patients receiving calcium supplements or high doses of vitamin D. There is no experience of the concurrent use of calcitriol and other medications for the treatment of psoriasis.
Information on interaction of systemic medications after the use of calcitriol ointment is limited.
Silkis Ointment has a slight irritant potential, and therefore, it is possible that concomitant use of peeling agents, astringents or irritants products may produce additive irritant effects.

4.6. Fertility, pregnancy and lactation
Pregnancy:
There are no or limited amount of data from the use of Calcitriol in pregnant women. Studies in animals have shown developmental toxicity at doses which caused maternal toxicity (see section 5.3). The potential risk for humans is unknown.
Silkis should only be used during pregnancy in restricted amounts when clearly necessary. Calcium levels should be monitored.
Breast-feeding:
Calcitriol has been found in milk of lactating dams. Due to the lack of human data, it should not be used during breastfeeding.

4.7. Effects on ability to drive and use machines
Silkis has no or negligible influence on the ability to drive and use machines.

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4.8. Undesirable effects

Between 10% and 20% of patients can be expected to experience adverse reactions. Adverse reactions are usually localized to the application site and mild to moderate in nature.

Very common adverse reactions: Adverse reactions occurring in ≥ 1/10 of patients. Common adverse reactions: Adverse reactions occurring in ≥ 1/100, <1/10 of patients. Uncommon adverse reactions: Adverse reactions occurring in ≥ 1/1000, <1/100 of patients. Rare adverse reactions: Adverse reactions occurring in ≥1/10000; <1/1000 of patients. Very rare adverse reactions: Adverse reactions occurring in <1/10000 of patients Not known: cannot be estimated from the available data. Adverse reactions reported by more than two patients in the clinical studies are included.		
System Organ Class	Frequency	Preferred term
Skin and Subcutaneous disorders	Common	Pruritus, Skin discomfort, Skin irritation, Erythema
	Uncommon	Dry skin, Psoriasis (aggravated)
	Not known*	Skin oedema, Contact dermatitis

*Adverse reactions reported from post marketing surveillance

In case of severe irritation or contact allergy, the treatment with Silkis should be discontinued and the patient should obtain medical advice. If contact allergy is demonstrated this discontinuation is definitive.

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.

4.9. Overdose

The most common symptoms which may occur after accidental administration are anorexia, nausea, vomiting, constipation, hypotonia and depression. Lethargy and coma are occasionally observed. If hypercalcaemia or hypercalciuria occurs, the use of Silkis should be discontinued until the serum or urinary calcium levels have returned to normal.

If the medication is applied excessively no more rapid or better results will be obtained and marked redness, peeling or discomfort may occur.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Pharmacotherapeutic group: Other antipsoriatics for topical use.
ATC code: D 05AX03

Mechanism of action

Calcitriol inhibits the proliferation and stimulates differentiation of keratinocytes. Calcitriol inhibits proliferation of T-cells and normalises the production of various inflammation factors.

Pharmacodynamic effects

Topical administration of Silkis Ointment to patients with plaque psoriasis results in an improvement of the skin lesions. This effect is noted from 4 weeks after the start of treatment.

5.2. Pharmacokinetic properties

Absorption

The mean absorption of calcitriol is estimated at around 10%. Following absorption, both unchanged calcitriol and metabolites have been demonstrated in plasma. The effect of the metabolites on calcium homeostasis is negligible. In most patients, circulating levels of exogenous calcitriol are below the level of detection (2pg/ml).

Distribution

In clinical trials, no relevant increase in plasma calcitriol levels after treatment of large body surface areas of up to 6000 cm2 (35% body surface area) was noted.

5.3. Preclinical safety data

Animal studies show that repeated excessive exposure to calcitriol leads to renal failure and tissue calcification due to hypervitaminosis D associated with hypercalciuria, hypercalcaemia, and hyperphosphataemia.

No indication of teratogenicity was observed in embryofoetal toxicity studies designed to assess the teratogenic potential of calcitriol. Some evidence of developmental toxicity was obtained in a cutaneous rabbit study at doses which caused maternal toxicity. No such effect was found in rats.

Local toxicity studies in animals with calcitriol showed slight skin and eye irritation.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Liquid paraffin, white soft paraffin and alpha-tocopherol.

6.2. Incompatibilities

There are no relevant data on the compatibility of Silkis with other medicinal products. Therefore, Silkis should be used according to the posology and method of administration provided above (Section 4.2). In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3. Shelf life

This medicine should not be used after the expiry date (Exp. Date) shown on the pack.

6.4. Special precautions for storage

Store at a temperature not exceeding 25°C.

6.5. Nature and contents of container

The product is packaged in collapsible aluminium tubes coated internally with an epoxy - phenolic resin and fitted with a white high density polyethylene or polypropylene screw cap. Tubes contain either 15, 30 or 100g of ointment.

Not all pack sizes may be marketed.

6.6. Special precautions for disposal

No special requirements.

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