

Part II

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Silkis micrograms per g ointment

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

One gram of ointment contains 3 micrograms of calcitriol (INN).

For excipients, see 6.1.

3 PHARMACEUTICAL FORM

Ointment

White, translucent ointment.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

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

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.

There is no experience of the use of Silkis in children (see 4.4. Special Warnings and Precautions for Use). Patients with kidney or liver dysfunction should not use Silkis (see also 4.3. Contra-indications).

4.3 Contraindications

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.

Silkis must not be used in patients known to be hypersensitive to the active substance or to any of the excipients.

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.

In view of the particular sensitivity of neonatal 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).

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.

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.

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. 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 of interaction of systemic medications after the use of calcitriol ointment is limited. As no relevant elevation of plasma level is seen after the use of calcitriol on the skin, interaction with systemic medication is unlikely.

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 Pregnancy and lactation

Use during Pregnancy:

There are no adequate data from the use of Silkis 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.

Use during Lactation:

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

No effects on ability to drive and use machines have been observed.

4.8 Undesirable effects

Skin irritation (reddening, itching) usually temporary, has been reported. 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.

During clinical studies, no clinically significant hypercalcaemia was observed at the maximal dose of 30 g of ointment per day.

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

ATC code: D 05AX03.

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

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

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).

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
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 the method of administration provided above (Section 4.2), and should not be mixed with other medicinal products.

6.3 Shelf Life

3 years.

6.4 Special precautions for storage

No special precautions for storage.

6.5 Nature and contents of container

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

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

None.

7 MARKETING AUTHORISATION HOLDER

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8 MARKETING AUTHORISATION NUMBER

PA 590/16/1

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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