SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Silkis 3 micrograms per g ointment

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

One gram of ointment contains 3 micrograms 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
The safety and efficacy of Silkis in children less than 18 years have not been established. Currently available data are described in sections 4.4, 5.1 and 5.3 but no recommendation on a posology can be made.

Special population
Patients with kidney or liver dysfunction should not use Silkis (see also 4.3. Contraindications).

4.3 Contraindications

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

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.

Instruct patients not to smoke or go near naked flames - risk of severe burns. Fabric (clothing, bedding, dressings etc.) that has been in contact with this product burns more easily and is a serious fire hazard. Washing clothing and bedding may reduce product build-up but not totally remove it.

Paediatric population

There is limited amount of clinical data supporting the use of Silkis in the paediatric population (See section 5.1).

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 section 5.3).

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 nor or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

Between 10% and 20% of patients can be expected to experience adverse reactions. Adverse reactions are usually localised 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.		
MedDRA 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 Yellow Card Scheme
Website: www.mhra.gov.uk/yellowcard.

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.

Paediatric population

Very limited efficacy data of Calcitriol in the paediatric population are available from a 8-week randomized, vehicle-controlled study (18132) in children aged 2 to 12 years with plaque psoriasis (n= 19; 8 on active, 11 on vehicle), and a 26-weeks open-label, uncontrolled, multicenter long-term safety and efficacy study (18131) in children aged 2 to 17 years (n=54). Calcitriol 3µg/g was applied twice daily excluding the face and scalp. However, due to slow enrolment, both studies were closed prematurely. The safety and efficacy of Calcitriol ointment in children less than 18 years have not been established (see section 4.2).

In Study 18132 the primary endpoint was the success rate, defined as the percentage of subjects with an Investigator Global Assessment score of 0 (clear) or 1 (almost clear) and at least a 2-grade improvement from baseline. The success rate was not statistically significantly different (p=0.370) for the Calcitriol 3 µg/g ointment group compared with the Vehicle group, with 3 subjects (37.5%) of the Calcitriol 3 µg/g ointment group achieving success and 7 subjects (63.6%) of the Vehicle group. Due to the very small sample size, any observed numerical difference in treatment groups is most likely due to chance. Local irritations were the most reported adverse events.

In Study 18131 the primary endpoint was the percentage of subjects with an IGA score of 0 (clear) or 1 (almost clear); and the secondary endpoint change from baseline in pruritus. The study was completed by 76% of the subjects. The majority of subjects improved the IGA score from baseline to week 26, with 24.1% having at least a 2-grade improvement. At the end of the study, 37% of the subjects had an IGA of clear/almost clear. For the secondary endpoint, 37% of subjects had no pruritus at Week 26 and 20.4% of subjects achieved at least 2-grade improvement from baseline. Due to the uncontrolled study design, no conclusion can be drawn regarding efficacy in paediatric patients. Most common AE’s were infections and skin reactions, there were no changes in parameters of calcium homeostasis. However, the safety data are considered limited. See also section 5.3.

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.

In rats, intra muscular injections of Calcitriol for 2 weeks induced calcification in soft tissues. However, the neonatal rats seem to be more sensitive than the adults, as calcification occurred in all dose groups (0.13, 0.38 and 1.28 µg/kg/day) whereas it was observed only in the adult high dose group (0.03, 0.13 and 0.64 µg/kg/day).

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

3 years

Shelf life after first opening: 8 weeks

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 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.

7 MARKETING AUTHORISATION HOLDER

Galderma (UK) Limited
Evergreen House North
Grafton Place
London
NW1 2DX
United Kingdom

8 MARKETING AUTHORISATION NUMBER

PL 10590/0047

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

12/12/2001 / 09/02/2009

10 DATE OF REVISION OF THE TEXT

25/10/2022