

SUMMARY OF PRODUCT CHARACTERISTICS (SPC)

SILKADERM

0.05% cream

1.1 TRADE NAME – Silkaderm

1.2 INTERNATIONAL NON-PROPERTY NAME - Tretinoin

2. COMPOSITION

Each gram of SILKADERM 0.05% cream contains:

active ingredient: tretinoin - 0.5 mg.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

A yellowish cream.

Cream for application to the skin.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Silkaderm is indicated for topical application in the treatment of acne vulgaris.

4.2 Dosage and Administration

Use in adolescents and adults

Silkaderm cream is applied thinly once or twice a day after thoroughly cleaning the affected areas of skin. The affected areas of skin are thoroughly cleaned and degreased with warm water using a non-irritating detergent. Silkaderm cream is then applied thinly.

The frequency of application depends on the type and severity of the disease and the skin reaction. Silkaderm cream is generally applied twice a day. For light, sensitive skin or more severe skin reactions, it is recommended that the product be applied only once a day (in the evening) or every other day. Hands should be washed carefully after applying Silkaderm cream.

Use in children

Silkaderm cream must not be used on prepubertal children.

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
- Silkaderm cream must not be used in the following conditions: acute skin infections, acute eczema, rosacea, rosacea-like dermatitis, hyperpigmentation, acne vulgaris in prepubertal children.
- Pregnancy (see section 4.6)
- Women planning a pregnancy

4.4 Special warnings and precautions for use

Cream contains cetostearyl alcohol which may cause local skin reactions (e.g. contact dermatitis).

Cream contains methylparaben which may cause allergic reactions (possibly delayed).

Cream contains propylparaben which may cause allergic reactions (possibly delayed).

Cream contains butylated hydroxytoluene may cause local skin reactions (e.g. contact dermatitis), or irritation to the eyes and mucous membranes.

Cream contains propylene glycol, which at threshold 50 mg/kg/day may cause skin irritation.

Do not use Silkaderm cream on mucous membranes or in the area of the mouth, nose and corners of the eyes.

Since Silkaderm cream can increase photosensitivity, exposure to sunlight, solariums or UV radiation should be avoided or reduced to a minimum during treatment. In the event of "sunburn", treatment must be temporarily stopped.

If direct sunlight cannot be avoided, covering treated skin areas with clothing and using a sun protection product is recommended.

If X-rays are used in addition to using Silkaderm cream, skin irritation may become more severe.

4.5 Interaction with other medicinal products and other forms of interaction

Concomitant therapy with other locally applied acne therapeutics, soap or cleansing milk with a peeling effect, soap and cosmetics with a strong drying effect, products with a high alcohol and/or astringent content should be used with caution, as skin irritation may increase. Particular caution is required when using peeling preparations (e.g. containing benzoyl peroxide).

4.6 Fertility, pregnancy and breast-feeding

Oral use of retinoids causes congenital malformations. When used as directed, topically administered retinoids are generally assumed to result in low systemic exposure due to minimal dermal absorption. However, there may be individual factors (e.g. compromised skin barrier, excessive use) that may contribute to increased systemic exposure.

Pregnancy

Silkaderm cream is contraindicated during pregnancy and in women planning to become pregnant (see section 4.3). If the drug is used during pregnancy or if the patient becomes pregnant while using this drug, treatment must be discontinued.

Breast-feeding

To avoid direct contact of the infant with the active ingredient, Silkaderm cream must not be used on the breast area during breastfeeding.

Fertility

No data available.

4.7 Effects on ability to drive and use machines

Silkaderm Cream has no influence on the ability to drive and use machines.

4.8 Undesirable effects

Side effects when used as intended

The following frequencies are used to assess side effects:

Very common ($\geq 1/10$)

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

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

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

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

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

Diseases of the skin and subcutaneous tissue Occasionally (0.1 – 1%), skin intolerance reactions may occur after using Silkaderm cream. Skin irritation, hypopigmentation and increased permeability of the skin to other locally applied medications may also occur.

Drying, burning, stinging, pruritus, erythema or flaking of the skin may also occur. These side effects usually decrease over the course of therapy. If excessive skin irritation occurs, treatment should be interrupted and continued as soon as the reactions have subsided. If skin irritation persists, treatment should be discontinued.

Increased sensitivity to sunlight and UV radiation is possible during treatment with Silkaderm

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 Arpimed “LLC” by going to www.arpimed.com and fill out the appropriate form “Report an adverse reaction or inefficiency of drug”. Hotline number: (+374 55) 05 79 86. And by using Center of Drug and Medical Technology Expertise “SNPO”, going to the site: www.pharm.am in “Report about adverse effect of medicine” section and fill out the “Report of adverse reaction or manufacturing problem of medicinal product”. Hotline numbers: +37410200505; +37496220505.

4.9 Overdose

There have been no reports of acute overdoses of tretinoin when applied locally. Increased use of tretinoin does not improve the treatment outcome and can lead to more severe skin irritations such as erythema, scaling and itching.

If necessary, symptomatic treatment should be carried out.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Acne medications, retinoids for topical use in acne, (tretinoin).

ATC code: D10AD01

5.2 Pharmacokinetic properties

No data available.

5.3 Preclinical data on safety

Mutagenic effects are not to be expected at therapeutic doses.

A toxic threshold dose of 5-50 mg/kg can be specified for oral administration for repeated use in animals, which is approximately 2,000-20,000 times higher than the active ingredient amounts usually applied therapeutically to the skin in humans. In view of the low penetration rate of tretinoin through the skin, the estimated safety margin increases by a further 2 orders of magnitude.

The wide margin of safety is confirmed by studies on the chronic toxicity of a 0.05% tretinoin gel when applied locally to rabbit skin over 13 weeks. The application of a daily amount of gel that is about 200 times greater than that normally used on humans did not cause any systemic intolerance reactions, even when applied to previously damaged (scarified) skin. On intact skin, the same qualitative and quantitative picture developed that can be assessed in the context of the specific pharmacological effect, such as erythema, skin edema and rejection of superficial epidermal layers as well as epithelial proliferation. All local reactions were reversible.

The repeated application of 0.05 and 0.1% tretinoin solution to the rabbit eye did not result in any irritation of the eye beyond the solvent effect.

There are no carcinogenicity studies on animals. Studies on hairless albino mice exposed to strong sunlight indicate that tretinoin may increase the tumorigenic potential of UV rays. Whether these results can be transferred to humans has not been investigated.

Reproductive toxicity

In rats and rabbits, no teratogenic or other embryotoxic findings occurred after topical administration of doses of up to 1 mg/kg/body weight/day when oral intake of the active ingredient by the mother animals was prevented. The plasma levels for tretinoin and active metabolites were in the range of endogenous concentrations and gave no indication of significant percutaneous absorption.

Tretinoin administered systemically (orally, subcutaneously) has caused malformations in all species studied (rats, mice, hamsters, rabbits, monkeys). The lowest teratogenic dose in the most sensitive species (mouse) is between 1-3 mg/day when administered subcutaneously.

There are isolated reports of birth defects in children whose mothers were treated topically with tretinoin during pregnancy. A cohort study of children whose mothers were exposed to topical tretinoin treatment during the first trimester of pregnancy showed no increase in malformations compared to a group of unexposed women. Controlled, prospective studies on pregnant women have not been conducted. The blood levels of tretinoin leading to teratogenic effects are not known.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients:

glyceryl stearate SE
cetareth 12
cetareth 20
liquid paraffin
glycerin
cetostearyl alcohol

methylparaben
propylparaben
diazolidinyl urea
disodium edetate
butylhydroxytoluene
propylene glycol
dimethicone
water purified

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Store out of the reach of children, at a temperature not higher than 25°C in original pack.

6.5 Nature and contents of container

15 g of cream is filled into aluminum tubes (inside package).

The tubes are packed and inserted with the leaflet into cardboard boxes (outer package).

6.6 Special precautions for disposal and other handling

None.

7. MANUFACTURER

“Arpimed” LLC

Bldg. 19, mcr 2nd, Abovyan, 2204, Kotayki Marz, Republic of Armenia

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8. MARKETING AUTHORISATION HOLDER

“Arpimed” LLC

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9. DATE OF FIRST AUTHORISATION

10.02.2003

10. DATE OF REVISION OF THE TEXT