1 SKINOREN® 20% Cream

SKINOREN® 20% Azelaic Acid Cream

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

1 g of white to slightly yellowish opaque cream contains 0.2 g (20%) micronised azelaic acid.

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Topical cream.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Topical treatment of acne vulgaris.

4.2 Dose and method of administration

Before SKINOREN® is applied, the skin should be thoroughly cleaned with clear water or, if applicable, a mild skin-cleansing agent.

SKINOREN® should be applied to the affected areas of skin twice a day (morning and evening) and rubbed gently into the skin. SKINOREN® should not be applied sparingly; however, excessive amounts of cream must be avoided (approximately 2.5 cm of cream is sufficient for the entire facial area).

In the event of excessive irritation of the skin, the amount of cream per application should be reduced or the frequency of use of SKINOREN® should be reduced to once a day until the irritation ceases. Treatment might have to be temporarily interrupted for a few days.

It is important to continue to use SKINOREN® regularly over the entire period of treatment.
The duration of use of SKINOREN® can vary from person to person and also depends on the severity of the skin disorder.

In acne, a distinct improvement becomes apparent after about 4 weeks. To obtain the best results, however, SKINOREN® should be used regularly over several months.

4.3 Contraindications

Hypersensitivity to the active substance, propylene glycol or any of the other excipients listed in 6.1.

4.4 Special warnings and precautions for use

For external use only.

Local tolerance studies with the formulation in the rabbit eye showed a moderate to high-grade irritative effect; which is ascribed to the active substance. On accidental contamination, the eye should immediately be rinsed with copious amounts of water.

4.5 Interaction with other medicines and other forms of interaction

None so far known.

4.6 Fertility, pregnancy and lactation

Pregnancy

Reproduction-toxicity studies (fertility, embryotoxicity, teratogenicity) in animals have not produced any evidence for a risk on use during pregnancy.

Breast-feeding

The amount of azelaic acid theoretically transferred per day to the baby with the breastmilk is negligible and should not imply any risk, particularly when its extremely low toxicity is considered.

4.7 Effects on ability to drive and use machines

Not known.

4.8 Undesirable effects

Local skin irritation (mostly burning or itching sensations, occasionally reddening and scaling) may occur — usually at the start of treatment. In the majority of cases, irritation symptoms are mild, and generally regress in the course of treatment.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions to https://nzphvc.otago.ac.nz/reporting/

4.9 Overdose

Animal-experimental studies of the systemic and local tolerance failed to show any systemic or local organotoxic effects after administration of either the active substance itself or the cream formulation in amounts up to the maximum that can be applied. Intoxication is therefore unlikely.

For advice on the management of overdose please contact the National Poisons Centre on 0800 POISON (0800 764766).

5 PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Other Anti-Acne Preparations for Topical Use

ATC code: D10AX03

5.1 Pharmacodynamic properties

The antimicrobial property of azelaic acid and a direct influence on follicular hyperkeratosis are assumed to be the basis for the therapeutic efficacy of SKINOREN® in acne.

A significant reduction of the colonisation density of *Propionibacterium acnes* and a significant reduction of the fraction of free fatty acids in the skin surface lipids are observed under treatment with SKINOREN®.

Azelaic acid inhibits the proliferation of cultivated keratinocytes (suppression of DNA synthesis) and accelerates the comedolysis of tetradecane-induced comedones in the rabbit ear model. Electronmicroscopic and immuno-histochemical analyses of skin biopsies taken after treatment with SKINOREN® reveal ultrastructural changes, in particular of the keratohyaline granules and of filaggrin, an important factor in keratinisation. These findings suggest that, under clinical conditions, SKINOREN® affects the keratinocytes and the pattern of keratinisation.

5.2 Pharmacokinetic properties

Azelaic acid penetrates into all layers of human skin after dermal application of the cream. Penetration is faster into damaged skin than into intact skin. A total of 3.6% of the dose applied was absorbed percutaneously after a single topical application of 1 g azelaic acid (5 g cream). Calculated on this basis, the application of 5 g cream twice-daily results in a systemic substance load of 1–1.5 mg/kg body weight. Azaleic acid is bound to plasma proteins to the extent of 43%. A portion of the azelaic acid absorbed through the skin is excreted, unchanged, in urine. The remaining portion is broken down by β-oxidation into dicarboxylic acids with shorter chains (C7 and C5 carboxylic acids) which have likewise been detected in urine.

5.3 Preclinical safety data

Animal-experimental studies of the systemic and local tolerance failed to show any systemic or local organotoxic effects after administration of both the active substance itself and the cream formulation in amounts up to the maximum that can be applied. Intoxication is therefore unlikely even after oral ingestion of large amounts of the formulation. *In vitro* and *in vivo* studies with the active substance produced no evidence for genotoxic effects on germinal and somatic cells. No signs that the active substance has sensitising properties were found in the maximisation test in the guinea pig.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Arlatone 983 S (polyoxyethylene fatty acid ester)
Cutina CBS (mixture of mono-diglycerides, fatty alcohols, triglycerides and wax esters)
Cetearyl octanoate
Propylene glycol
Glycerol 85%
Benzoic acid
Purified water

6.2 Incompatibilities

None known.

6.3 Shelf life

Shelf life: 3 years

6.4 Special precautions for storage

Do not store above 30°C.

Store all drugs properly and keep them out of reach of children.

6.5 Nature and contents of container

Tubes containing 30 g.
Standard tube with membrane closure and screw cap (tube material aluminium, internal coating done with epoxide, end seal band made of polyamide-based compound, external coating made of polyester, screw cap made of high-density polyethylene).

6.6 Special precautions for disposal

None

7 MEDICINE SCHEDULE

Pharmacy Medicine

8 SPONSOR

LEO Pharma Limited

Auckland

New Zealand

Toll Free No.: 0800 497 456

9 DATE OF FIRST APPROVAL

27 May 1993

10 DATE OF REVISION OF THE TEXT

March 2020

SUMMARY TABLE OF CHANGES

Section affected	**Summary of new information**
Section 8	Updated 'SPONSOR' details
Section 10	Updated 'DATE OF REVISION OF THE TEXT'