Bayer HealthCare

APPROVED PACKAGE INSERT

SCHEDULING STATUS: S1

PROPRIETARY NAME AND DOSAGE FORM:

SKINOREN GEL
Gel

COMPOSITION:

1 g SKINOREN GEL contains 150 mg azelaic acid. Excipients: propylene glycol, polysorbate 80, lecithin, carbopol 980, triglycerides: medium chain, sodium hydroxide, disodium edetate, benzoic acid and purified water.

PHARMACOLOGICAL CLASSIFICATION:

A 13.12 Acne preparations

PHARMACOLOGICAL ACTION:

Pharmacodynamic properties:

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

Clinically, a significant reduction in the colonisation density of *Propionibacterium acnes* and a significant reduction in the fraction of free fatty acids in the skin surface lipids is observed.

In vitro and *in vivo*, azelaic acid inhibits the proliferation of keratinocytes and normalises the disturbed terminal epidermal differentiation processes in acne. In the rabbit ear model azelaic acid accelerates the comedolysis of tetradecane-induced comedones.

The mechanism by which azelaic acid interferes with the pathogenic events in rosacea is unknown. Several *in vitro* and *ex vivo* investigations indicate that azelaic acid may exert an anti-inflammatory effect by reducing the formation of pro-inflammatory, reactive oxygen species.

Pharmacokinetic properties:

Azelaic acid penetrates into all layers of the skin after topical application of the gel. Penetration is faster into damaged skin than into intact skin. A total of 3,6 % of the dose applied is absorbed percutaneously after a single topical application of 1 g azelaic acid (5 g Skinoren Acne Cream). Clinical investigations in acne patients indicated similar absorption rates of azelaic acid from SKINOREN GEL and cream.

A portion of the azelaic acid absorbed through the skin is excreted in unchanged form with the urine. The remaining portion is broken down by β-oxidation into dicarboxylic acids with shorter chain length (C_7, C_5) which have likewise been found in the urine.

Steady-state plasma levels of azelaic acid in rosacea patients after 8 weeks twice daily treatment with SKINOREN GEL were double those seen in control patients. However the plasma levels were within the range also observed in volunteers and acne patients on normal diets. This indicates that the extent of percutaneous absorption of azelaic acid following twice daily application of SKINOREN GEL does not alter the systemic burden of azelaic acid derived from dietary and endogenous sources.

INDICATIONS:

Treatment of mild to moderate acne vulgaris.
Treatment of mild to moderate (papulopustular) rosacea.

CONTRA-INDICATIONS:

Hypersensitivity to the active substance or to any excipients of the gel.

WARNINGS:

For external use only

Care must be taken when using SKINOREN GEL to avoid from contact with the eyes, mouth and other mucous membrane and patients should be instructed accordingly. In the event of accidental contact, the eyes, mouth and/or affected mucous membrane should be washed with large amounts of water. If eye irritation persists, patients should consult a medical practitioner. The hands should be washed after each application of the SKINOREN GEL.

It is advisable to avoid alcoholic cleansers, tinctures and astringents, abrasives and peeling agents when using SKINOREN GEL for treatment of papulopustular rosacea.

Benzoic acid is mildly irritant to the skin, eyes and mucous membranes. Propylene glycol may cause skin irritation.

INTERACTIONS:

None are known.

PREGNANCY AND LACTATION:

Safety of SKINOREN GEL in pregnancy and lactation has not been established.

DOSAGE AND DIRECTIONS FOR USE:

SKINOREN GEL should be applied to the affected areas of the skin twice a day (morning and evening) and rubbed in gently. Approximately 0,5 g = 2,5 cm of gel is sufficient for the entire facial area.

Before SKINOREN GEL is applied, the skin should be thoroughly cleaned with plain water, and dried. A mild skin-cleansing agent may be used.

It is important to use SKINOREN GEL continuously over the entire period of treatment.

The duration of use of SKINOREN GEL can vary from person to person and also depends on the severity of the skin disorder. In general, an improvement becomes apparent after about 4 weeks. To obtain the best results, however, SKINOREN GEL should be used continuously over several months.

In the event of intolerable skin irritation (see “Side-effects“), the amount of gel per application should be reduced or the frequency of use of SKINOREN GEL should be reduced to once a day until the irritation ceases. If required, the treatment should be temporarily interrupted for a few days.

Paediatric population:

Used in adolescents (12 to 18 years of age) for the treatment of acne vulgaris. Dose adjustment is not required when SKINOREN GEL is administered to adolescents aged (12 to 18 years).

The safety and efficacy of SKINOREN GEL for the treatment acne vulgaris in children below the age of 12 years have not been established.

The safety and efficacy of SKINOREN GEL for the treatment of papulopustular rosacea in children below the age of 18 years have not been established.

SIDE EFFECTS AND SPECIAL PRECAUTIONS:

Side effects:

Only cutaneous treatment-related adverse events were reported in clinical studies.

In clinical studies, most frequently observed side effects included, application site pruritus, application site burning and application site pain.

Frequencies of side effects observed in clinical studies and given in the table below are defined according to MedDRA frequency convention: very common (≥ 1/10); common (≥ 1/100, < 1/10); uncommon (≥ 1/1000, < 1/100); rare (≥ 1/10 000, < 1/1000).

Acne:

System Organ Class	Very common	Common	Uncommon
Skin and subcutaneous tissue disorder			Contact dermatitis
General disorders and administration site conditions	Application site pruritus, application site burning, application site pain	Application site dryness, application site rash, application site paraesthesia	Application site erythema, application site exfoliation, application site warmth, application site discolouration

Rosacea:

System Organ Class	Very common	Common	Uncommon
Skin and subcutaneous tissue disorders			Acne, contact dermatitis
General disorders and administration site conditions	Application site burning, application site pain, application site pruritus	Application site paraesthesia, application site dryness, application site rash, application site oedema	Application site discomfort, application site erythema, application site urticaria

Hypersensitivity and rash has been reported in post-marketing surveillance.
Worsening of asthma in patients treated with azelaic acid has been reported during post-marketing surveillance.

Paediatric population:

Treatment of acne vulgaris in adolescents 12 to 18 years of age: in 4 clinical phase II and II/III studies involving adolescents 12 to 17 years of age (120/383; 31 %), overall incidence of adverse events for SKINOREN GEL was similar for the groups aged 12 to 17 years (40 %), aged ≥ 18 years (37 %) and for the entire patient population (38 %). This similarity also applied to the group aged 12 to 20 years (40 %).

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:

Treatment is supportive and symptomatic.

IDENTIFICATION:

White to yellowish white opaque hydrogel.

PRESENTATION:

Standard tubes with membrane closures and screw caps (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) containing 5, 30 or 50 g.

STORAGE INSTRUCTIONS:

Keep well closed. Store at or below 25 °C. Keep out of reach of children.

REGISTRATION NUMBER:

South Africa: 36/13.12/0028
Namibia: (NS1) 04/13.12/1439

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION:

Bayer (Pty) Ltd
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DATE OF PUBLICATION OF THE PACKAGE INSERT:

Date on the registration certificate of the medicine: 20 September 2002
Date on the most recently revised package insert as approved by Council: 03 October 2014