SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Skinoren 20% Cream.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

1 g of Skinoren Cream contains 200 mg (20% w/w) azelaic acid.
For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Cream.
White, opaque cream.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Topical treatment of acne vulgaris.

4.2 Posology and method of administration

Skinoren Cream should be applied to the affected areas of skin twice daily (mornings and evenings), and rubbed in gently. As a guide 2.5 cm (approx. 0.5 g) of cream is sufficient for the entire facial area. If other areas of acne, in addition to the face require treatment, for example the chest and back, the amount of cream should be adjusted accordingly.
Patients with sensitive skin should be advised to use Skinoren only once a day (in the evening) for the first week of treatment and then proceed to twice daily applications.
Before Skinoren Cream is applied, the skin should be thoroughly cleaned with plain water and dried. A mild skin-cleansing agent may be used.
The duration of use of Skinoren Cream can vary from patient to patient and also depends on the severity of the acne. In general, a distinct improvement becomes apparent after about 4 weeks. To obtain the best results, Skinoren

Cream should be used continuously over a period of several months (see Section 5.1 Pharmacodynamic properties).
It is important to continue to use Skinoren Cream regularly over the entire period of treatment. However, in the event of intolerable skin irritation (see Section 4.8 Undesirable effects), the amount of cream per application should be reduced or the frequency of use of Skinoren Cream should be reduced to once a day until the irritation ceases. If required, treatment might have to be temporarily interrupted for a few days.
Paediatric population
Use in adolescents (12 - 18 years of age): dose adjustment is not required when Skinoren Cream is administered to adolescents aged 12 - 18 years.
The safety and efficacy of Skinoren Cream in children below the age of 12 years have not been established.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

For external use only.
Care must be taken when using Skinoren Cream to avoid contact with the eyes, mouth and other mucous membranes, and patients should be instructed accordingly (see Section 5.3 Preclinical safety data). In the event of accidental contact, the eyes, mouth and/or affected mucous membranes should be washed with large amounts of water. If eye irritation persists, patients should consult a physician. The hands should be washed after each application of Skinoren Cream.
Worsening of asthma in patients treated with azelaic acid has been reported rarely during post-marketing surveillance.
Skinoren contains a small amount of benzoic acid, which is mildly irritating to the skin, eyes and mucous membranes.
Skinoren also contains propylene glycol, which may cause skin irritation.

4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies have been performed. The composition of
Skinoren Cream gives no indication of any undesired interactions of the single components that could adversely affect the safety of the product. No drug-specific interactions were noted during any of the controlled clinical trials.

4.6 Fertility, pregnancy and lactation

Pregnancy
There are no adequate and well-controlled studies of topically administered azelaic acid in pregnant women.
Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonal/foetal development, parturition or postnatal development (see Section 5.3 Preclinical safety data).
Caution should be exercised when prescribing azelaic acid to pregnant women.

Lactation
Infants must not come into contact with treated skin/breast.
It is not known if azelaic acid is passed into breast milk in vivo. Due to low percutaneous absorption and since azelaic acid is not concentrated in milk, the amount of azelaic acid reaching the infant via mother's milk is approximately 0.01%. This corresponds to less than 200 µg per day following administration of the maximum recommended dose of 5 g Skinoren 20% Cream twice daily.
Caution should be exercised when Skinoren Cream is administered to a nursing mother.

4.7 Effects on ability to drive and use machines

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

4.8 Undesirable effects

From clinical studies and post-marketing surveillance, the most frequently observed side-effects included application site burning, application site pruritus and application site erythema.
Frequencies of side-effects observed in clinical studies and post-marketing surveillance and given in the table below are defined according to the MedDRA frequency convention:
Very common (≥1/10),
Common (≥1/100 to <1/10),
Uncommon (≥1/1,000 to <1/100),
Rare (≥1/10,000 to <1/1,000),
Very rare (<1/10,000),
Not known (cannot be estimated from the available data).

System Organ Class	Very Common	Common	Uncommon	Rare
Skin and subcutaneous tissue disorders			seborrhoea, acne, skin depigmentation	cheilitis
General	application	application site	application site	application site

disorders and administration site conditions	site burning, application site pruritus, application site erythema	exfoliation, application site pain, application site dryness, application site discolouration, application site irritation	paraesthesia, application site dermatitis, application site discomfort, application site oedema	vesicles, application site eczema, application site warmth, application site ulcer, application site rash
Immune system disorders				drug hypersensitivity, worsening of asthma (see section 4.4)

Generally, local skin irritation regresses in the course of treatment.
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 the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard.

4.9 Overdose

No known cases of azelaic acid overdosage resulting from topical administration of Skinoren Cream have been reported. Results from acute toxicity studies do not indicate that any risk of acute intoxication is to be expected following a single dermal application of an overdose (application over a large area under conditions favourable to absorption) or inadvertent oral ingestion. Due to the very low local and systemic toxicity of azelaic acid intoxication is unlikely.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: other anti-acne preparations for topical use.
ATC Code: D10AX03

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

Clinically, a significant reduction of the colonization density of *Propionibacterium acnes* and a significant reduction of 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 normalizes the disturbed terminal epidermal differentiation processes in acne. In the rabbit ear model, azelaic acid accelerates the comedolysis of tetradecane-induced comedones.

There is clinical experience for a continuous application time period of up to one year.

5.2 Pharmacokinetic properties

After dermal administration of the cream, azelaic acid penetrates into all layers of human skin. The penetration is more rapid into damaged skin than into intact skin. A total of 3.6% of the administered dose was absorbed percutaneously after a single topical administration of 1 g azelaic acid (5 g cream).
A portion of the azelaic acid which is absorbed through the skin is eliminated unchanged with the urine. The remaining portion is metabolized through beta-oxidation into short-chained dicarboxylic acids (C_7, C_5 carboxylic acids) which have likewise been found in the urine.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, contact hypersensitivity, genotoxicity and toxicity to reproduction and development. In studies of embryo-fetal development in rats, rabbits and monkeys, azelaic acid was not teratogenic but showed embryolethal effects associated with maternal toxicity only at oral doses sufficiently in excess of the maximum human exposure to indicate little relevance to clinical use.
If azelaic acid came into contact with the eyes of monkeys and rabbits, signs of moderate to severe irritation became evident. Therefore, contact with the eyes should be avoided.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

• Arlatone 983S (polyoxyethylene fatty acid ester)

• Cutina CBS (mixture of mono-diglycerides, fatty alcohols, triglycerides and wax
esters)
• Cetearyl octanoate
• Propylene glycol
• Glycerol 85% (E422)
• Benzoic acid (E210)
• Purified water.

6.2 Incompatibilities

None known.

6.3 Shelf life

3 years.
After first opening of the container, the in-use shelf life is 6 months

6.4 Special precautions for storage

Do not store above 30°C.

6.5 Nature and contents of container

Tubes containing 20, 30 or 50 g. Not all pack sizes are marketed.
Aluminium tube with internal epoxide coating and polyethylene screw cap.

6.6 Special precautions for disposal

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Bayer plc
Bayer House
Strawberry Hill
Newbury
Berkshire RG14 1JA
United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)

PL 00010/0649

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 12 December 1989
Date of latest renewal: 24 November 2005

10 DATE OF REVISION OF THE TEXT

08/04/2016