Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Skinoren 20% w/w Cream.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

1 g Skinoren cream contains 200 mg (20 % w/w) micronized azelaic acid.

For excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Cream.

White opaque cream.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

In the treatment of acne vulgaris.

4.2 Posology and method of administration

In general, Skinoren should be applied twice a day (mornings and evenings) as directed.

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

Skinoren should be applied to the affected areas of skin and rubbed well in.

It is important to continue to use Skinoren regularly over the entire period of treatment.

In the event of excessive irritation of the skin (see “Undesirable effects”), the frequency of use of Skinoren should be reduced to once a day until the irritation ceases or the treatment should be temporarily interrupted.

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

4.3 Contraindications

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

4.4 Special warnings and precautions for use

For external use only.

Skinoren Cream contains benzoic acid which is mildly irritant to the skin, eyes and mucous membranes and propylene glycol which may cause skin irritation. Care should be taken to avoid contact with the eyes, mouth and other mucous membranes or open wounds, 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.

Not for use in children.

4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies have been performed. The composition of Skinoren 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
It is not known if azelaic acid is secreted into human milk *in vivo*. However an *in vitro* equilibrium dialysis experiment demonstrated that passage of drug into maternal milk may occur. But the distribution of azelaic acid into maternal milk is not expected to cause a significant change from baseline azelaic acid levels in the milk.
Azelaic acid is not concentrated in milk and less than 4% of topically applied azelaic acid is systemically absorbed, not increasing endogenous azelaic acid exposure above physiological levels. However, caution should be exercised when Skinoren is administered to a nursing woman.
Infants must not come into contact with treated skin/breast.

4.7 Effects on ability to drive and use machines

Skinoren 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 pruritus, application site burning and application site erythrema.

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, <1/10),
Uncommon (≥1/1,000; <1/100),
Rare (≥1/10,000, <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
Immune system disorders				drug hypersensitivity,

				worsening of asthma (see section 4.4)
Skin and subcutaneous tissue disorders			Seborrhea, Skin depigmentation, acne	Cheilitis
General disorders and administration site conditions	Application site burning, Application site pruritus Application site erythema,	Application site pain, Application site exfoliation, Application site dryness, Application site discolouration, Application site irritation,	Application site paraesthesia, Application site dermatitis Application site discomfort, application site oedema	Application site rash, Application site warmth, Application site vesicles Application site eczema Application site ulcer

Generally, local skin irritation regresses in the course of the treatment.

Pediatric population
In clinical studies involving adolescents 12-18 years of age (454/1336; 34%), the local tolerability of Skinoren Cream was similar in pediatric and adult patients.

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 HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; E-mail: medsafety@hpra.ie.

4.9 Overdose

Due to the very low local and systemic toxicity of azelaic acid intoxication is unlikely.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Skinoren exerts an antibacterial and comedolytic effect. Azelaic acid, the active ingredient in Skinoren, inhibits the growth of the propionibacteria involved in the development of inflammatory acne and in the production of acne-promoting fatty acids.

Azelaic acid affects the homification process of the epidermal cells and is therefore able to exert a therapeutic effect on the formation of comedones (blackheads, whiteheads) which occur in acne.

5.2 Pharmacokinetic properties

After dermal administration of the cream, the azelaic acid penetrates all layers of the human skin. The penetration is faster into damaged skin than into intact skin.

That portion retained in the skin is concentrated in the basal epidermal layer. Systemic absorption after topical application is approximately 5%. 43% of the azelaic acid is bound to plasma proteins. Due to the lower percutaneous

absorption, the amount of azelaic acid reaching the infant via the mother's milk is negligible i.e. less than 200 mcg per day which corresponds to 0.01% of the two 5 g doses.

A part of the azelaic acid which is absorbed through the skin is excreted in unchanged form with the urine. The remaining portion is metabolised by ß-oxidation into dicarboxylic acids with shorter chain length 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, genotoxicity and toxicity to reproduction and development.

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

Stearoyl Macroglycerides
Cutina CBS (Glyceryl Stearate, Cetearyl alcohol,
Cetyl Palmitate, Cocoglycerides)
Cetearyloctanoate
Propylene glycol
Glycerol (85 %)
Benzoic acid (E210)
Purified water

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

No special precautions for storage.

6.5 Nature and contents of container

Aluminium tube with internal epoxide coating and a polyethylene screw cap.

Tubes containing 30 g.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Bayer Limited
The Atrium
Blackthorn Road
Dublin 18
Ireland

8 MARKETING AUTHORISATION NUMBER

PA1410/072/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorization: 9th May 1996

Date of last renewal: 9th May 2006

10 DATE OF REVISION OF THE TEXT

January 2015