Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Solaraze 3% gel

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each gram contains 30 mg diclofenac sodium (3% w/w).

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Gel
Product imported from the United Kingdom:
A clear, transparent, colourless or pale yellow gel.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

For the treatment of actinic keratoses

4.2 Posology and method of administration

Use in Adults: Solaraze is applied locally to the skin 2 times daily and smoothed into the skin gently. The amount needed depends on the size of the lesion. Normally 0.5 grams (the size of a pea) of the gel is used on a 5 cm x 5 cm lesion site. The usual duration of therapy is from 60 to 90 days. Maximum efficacy has been observed with treatment duration towards the upper end of this range. Complete healing of the lesion(s) or optimal therapeutic effect may not be evident for up to 30 days following cessation of therapy. A maximum of 8 grams daily should not be exceeded. Long term efficacy has not been established.

Use in the Elderly: The usual adult dose may be used.

Use in Children: Dosage recommendations and indications for the use of Solaraze have not been established for use in children.

4.3 Contraindications

Solaraze is contraindicated in patients with a known hypersensitivity to diclofenac, benzyl alcohol, macrogol monomethyl ether 350 and/ or sodium hyaluronate.

Because of cross-reactions, the gel should not be used by patients who have experienced hypersensitivity reactions such as symptoms of asthma, allergic rhinitis or urticaria, to acetylsalicylic acid or other non-steroidal anti-inflammatory agents.

The use of Solaraze is contraindicated during the last trimester of pregnancy *(see Section 4.6).*

4.4 Special warnings and precautions for use

The likelihood of systemic side effects occurring following the topical application of Solaraze is very small compared to the frequency of side effects with oral diclofenac, owing to low systemic absorption with Solaraze.

This product should be used with caution in patients with a history of and/or active gastrointestinal ulceration or bleeding, or reduced heart, liver or renal function, since isolated cases of systemic adverse reactions consisting of renal affection, has been reported with topically administered antiphlogistics.

It is known that NSAIDs can interfere with platelet function. Although the likelihood of systemic side effects is very low, caution should be used in patients with intracranial haemorrhage and bleeding diathesis.

Direct sunlight, including solarium, should be avoided during treatment. If sensitivity skin reactions occur, discontinue use.

Solaraze should not be applied to skin wounds, infections or exfoliative dermatitis. It should not be allowed to come into contact with the eyes or mucous membranes.

4.5 Interaction with other medicinal products and other forms of interaction

No drug interactions during treatment with Solaraze have been reported. After topical administration, systemic absorption is limited. Drug interactions applied to orally administered NSAIDs are improbable.

4.6 Fertility, pregnancy and lactation

Use in pregnancy: Solaraze is contraindicated during the last trimester of pregnancy (see section 4.3) and should not be used during the first two trimesters of pregnancy unless clearly necessary. If used during pregnancy, Solaraze must not be applied to a large area of the skin (>30% of the body surface) and must not be used for long-term treatment (>3 weeks).
There are no adequate data from the use of diclofenac in pregnant women. Animal studies have shown reproductive toxicity *(see section 5.3).* The potential risk for humans is unknown.

The use of prostaglandin synthetase inhibitors in the second and third trimesters of pregnancy may result in:

- Functional renal injury in the foetus. From the 12th week: oligohydramnios (usually reversible after the end of treatment), or anamnios (particularly with prolonged exposure). After birth: kidney failure may persist (particularly with late or prolonged exposure).
- Pulmonary and cardiac toxicity in the foetus (pulmonary hypertension with preterm closing of the ductus arteriosus). This risk exists from the beginning of the 6th month and increases if administration is close to full term.
- Inhibition of uterine contractions.
- Prolongation of pregnancy and labour.
- Increased risk of bleeding in the mother and child.
- Increased risk of oedema formation in the mother.

Use during lactation: It is not expected that any measurable amount of diclofenac sodium would occur in breast milk following topical application. Solaraze can be used at the recommended therapeutic dose. However, Solaraze should not be applied to the breast area of nursing mothers.

4.7 Effects on ability to drive and use machines

Not applicable.

4.8 Undesirable effects

Most frequently reported reactions include skin reactions such as contact dermatitis, erythema and rash or application site reactions such as inflammation, irritation, pain and blistering. In studies there appeared to be no age specific increase or pattern of reactions.

Organ system	**Common (›1/100, <1/10)**	**Uncommon (>1/1000, <1/100)**	**Rare (>1/10000, <1/1000)**	**Very rare <1/10000**
Eye Disorders	Conjunctivitis	Eye pain, Lacrimation Disorder		
Gastrointestinal Disorders		Abdominal pain, diarrhoea, nausea		Gastrointestinal haemorrhage
General Disorders and Administration Site Conditions	Application site reactions (including inflammation, irritation, pain and tingling or blistering at the treatment site)			
Immune System Disorders	Topical application of large amounts may result in systemic effects including hypersensitivity			
Nervous System	Hyperesthesia, hypertonia, localised paraesthesia			
Renal and Urinary System Disorders				Renal failure
Skin and Subcutaneous Tissue Disorders	Contact dermatitis, dry skin, erythema, oedema, pruritus, rash, scaly rash, skin hypertrophy, skin ulcer, vesiculobullous rash	Alopecia, face oedema, maculopapular rash, photosensitivity reaction, seborrhoea		
Vascular Disorders		Haemorrhage		

Temporary hair discolouration at the application site has been reported. This is usually reversed on stopping treatment.

Patch testing of previously treated patients indicate a 2.18% probability of allergic contact dermatitis sensitisation (type IV) to diclofenac with as yet unknown clinical relevance.
Cross-reactivity to other NSAIDs is not likely. Serum testing more than 100 patients indicated no presence of type I anti-diclofenac antibodies.

4.9 Overdose

Due to the low systemic absorption of Solaraze, overdosage is extremely unlikely as a result of topical use. However, the skin should be rinsed with water. There have been no clinical cases of ingestion of Solaraze inducing overdosage.

In the event of accidental ingestion resulting in significant systemic side effects, general therapeutic measures normally adopted to treat poisoning with non-steroidal antiinflammatories should be used.

Supporting and symptomatic treatment should be given for complications such as renal failure, convulsions, gastrointestinal irritation and respiratory depression. Specific therapies such as forced diuresis and dialysis will probably not be therapeutic in eliminating NSAIDs due to their high rate of protein binding.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

ATC-Code: D11 A X 18
Other Dermatologicals

Mechanisms of action:

Diclofenac is a non-steroidal anti-inflammatory drug. The mechanism of action of diclofenac in actinic keratosis is not known but may be related to the inhibition of the cycloxygenase pathway leading to reduced prostaglandin E2 (PGE2) synthesis. Efficacy of the treatment has only been demonstrated in placebo-controlled studies. Comparative studies with topical 5-fluorouracil have not been conducted. The long term beneficial effects of Solaraze has not been proven.

Pharmacodynamic Effects:

Solaraze has been shown to clear AK lesions with maximum therapeutic effect seen 30 days after cessation of drug therapy.

5.2 Pharmacokinetic properties

Absorption: Mean absorption through the skin varies between <1-12% with large interindividual variability. Absorption is dependant on the amount of the topical dose applied and the site of application.

Distribution: Diclofenac binds highly to serum albumin.

Biotransformation: Biotransformation of diclofenac involves partly conjugation of the intact molecule, but mainly single and multiple hydroxylations resulting in several phenolic metabolites, most of which are converted to glucuronide conjuguates. Two of these phenolic metabolites are biologically active, however to a much lesser extent than diclofenac.
Metabolism of diclofenac following percutaneous and oral administration is similar.

Elimination: Diclofenac and its metabolites are excreted mainly in the urine. Systemic clearance of diclofenac from plasma is 263 ± 56 ml/min (mean value ± SD) following oral administration. Terminal plasma half-life is short (1-2 hours). For the metabolites also have short terminal half-lives of 1-3 hours.

Pharmacokinetics in special patient populations: After topical application, the absorption of diclofenac in normal and compromised epidermis are comparable although there is a large inter-individual variation. Systemic absorption of diclofenac is approximately 12% of the administered dose for compromised skin and 9% for intact skin.

5.3 Preclinical safety data

Published animal studies have shown that when given orally, the principal adverse effect is on the gastrointestinal tract. Diclofenac inhibited ovulation in the rabbit and impaired implantation, as well as early embryonic development in the rat. The embryo/foeto-toxic potential of diclofenac was evaluated in three animal species (rat, mouse and rabbit). Foetal death and growth retardation occurred at maternal toxic doses, however, on the basis of the available data, diclofenac is not considered to be teratogenic. The gestation period and the duration of parturition were extended by diclofenac. Doses lower than maternal toxic ones did not affect the postnatal development. Results from extensive genotoxicity and carcinogenicity testing suggest that it is unlikely that diclofenac would pose a significant carcinogenic hazard to humans.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium hyaluronate
Benzyl alcohol
Macrogol monomethyl ether 350
Purified water

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

The shelf-life expiry date of this product shall the date stated on the container and outer carton of the product on the market in the country of origin.

Shelf life after opening: 6 months

6.4 Special precautions for storage

Do not store above 25˚C.

6.5 Nature and contents of container

The product is supplied in an epoxy-phenolic lined sealed aluminium tube with a white polypropylene screw on cap with a pierced tip,in 50g size.

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 PARALLEL PRODUCT AUTHORISATION HOLDER

Primecrown 2010 Limited
4/5 Northolt Trading Estate
Belvue Road
Northolt
Middlesex UB5 5QS
United Kingdom

8 PARALLEL PRODUCT AUTHORISATION NUMBER

PPA1633/015/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 30th September 2011

10 DATE OF REVISION OF THE TEXT