Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Batrafen 1% w/w Cream

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Ciclopirox olamine, 1% w/w.
(10mg ciclopirox olamine in 1g Batrafen cream).

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Cream
White to almost white cream with a characteristic odour.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Batrafen cream is indicated in the topical treatment of infections due to superficial dermatophytes, Candida species and other fungi sensitive to the anti-infective.

4.2 Posology and method of administration

Route of administration: Topical.

Adults and Children over 6 years of age: Application 2 to 3 times daily for 2 weeks.

To avoid relapses, treatment should be continued for one to two weeks after disappearance of the symptoms, usually within two weeks.

4.3 Contraindications

Batrafen cream is contraindicated in the following:

- Infants less than one year of age.
- Pregnancy or in women breast feeding infants.
- Patients with known hypersensitivity to any component.

Batrafen cream should not be applied to the eyes or mucosa.

Batrafen cream should not be applied to an open wound.

Batrafen cream contains paraffin which can cause leaking or breaking of latex condoms. Contact between Batrafen cream and latex condoms must therefore be avoided because the protection afforded by the condoms may otherwise be lost.

4.4 Special warnings and precautions for use

All possibly infected areas should be treated at the same time.

Local irritation may develop. If this is severe, treatment should be discontinued.

The duration of application should vary according to individual need.

Sufficient experience is not yet available on the use of Batrafen powder in children under 6 years.

Batrafen Cream contains 10 mg benzyl alcohol per 10g tube.

4.5 Interaction with other medicinal products and other forms of interaction

There is no information available on interactions with Batrafen.

4.6 Fertility, pregnancy and lactation

There is no information in use during pregnancy or lactation. The product should not be used therefore in these situations.

4.7 Effects on ability to drive and use machines

None.

4.8 Undesirable effects

In rare cases, transient local reactions, e.g. pruritus or a burning sensation, may occur as may allergic contact dermatitis.

4.9 Overdose

There is no experience of overdose with ciclopirox preparations. However, no relevant systemic effects would be expected to occur if Batrafen Cream were applied to large areas or used too frequently.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

ATC: D01 AE14

Ciclopirox is a broad-spectrum N-hydroxypyridone antimicrobial agent for topical use that exerts fungistatic and fungicidal potency against pathogenic dermatophytes, yeasts and moulds.

In vitro studies showed that the compound has a high and uniform action on fungi pathogenic to human skin. The dose-response curve for ciclopirox is, in contrast to the azoles, very steep. This indicates fungicidal potential close to the MIC. Ciclopirox exhibits a high penetration into keratinized skin. *In vivo* studies in the model of guinea-pig dermatophytosis demonstrated a high activity and superiority to known compounds.

Ciclopirox has several mechanisms of action including chelation of polyvalent metal cations (e.g. FE^{3+} and Al^{3+}) thus it inhibits the metal dependent enzymes, including those responsible for the degradation of peroxides within the microbial cell. This mode of action of ciclopirox is unique and minimises the risk of cross resistance with other antimicrobial agents.

5.2 Pharmacokinetic properties

Only a limited amount of ciclopirox applied in different formulations is absorbed systemically, even when applied to inflamed skin covering approximately 25% of the body surface area and including highly permeable areas such as the groin.

A comparative cross-over study of the pharmacokinetics of ciclopirox gel 0.77%and ciclopirox olamine cream 1% in 18 healthy males (5g of each product /25cm x 30cm on intact skin on the back) indicated that there were no significant or clinically important differences between ciclopirox gel and ciclopirox olamine cream in a mean maximum serum levels of total ciclopirox or in measures of renal excretion.

5.3 Preclinical safety data

Acute toxicity: The acute toxicity of ciclopirox after a single dose was tested in mice, rats and rabbits after intravenous, subcutaneous, intraperitoneal and oral administration and after dermal application. Generally, acute toxicity of ciclopirox is rather low.

Repeated dose toxicity: Repeated dose oral toxicity studies with ciclopirox olamine were performed in rats and dogs with oral administration and in rabbits, guinea-pigs and dogs using the dermal route. Treatment periods varied between 14 days and 13 weeks. In repeated-dose oral toxicity studies in rats and dogs, the no effect level was 10mg/kg/day.

Dermal reactions were seen in the skin of most vehicle - or drug-treated rabbits, guinea pigs and dogs (varying degrees of hyperkeratosis, parakeratosis, dermal edema and dermal infiltration of mixed inflammatory cells). These changes were completely reversible after discontinuation of the treatment. No systemic toxicity was observed.

Reproduction toxicology: No significant evidence of impaired fertility was observed in rats after oral doses and no peri-/postnatal toxicity was observed in this species.

No fetotoxicity or teratogenicity was shown for ciclopirox olamine in the mouse, rat, rabbit and monkey after oral doses and also after the dermal route of administration in rat and rabbit.

Mutagenicity: The following battery of in vitro genotoxicity tests was conducted with ciclopirox olamine: evaluation of gene mutation in the *Ames Salmonella* and E.coli assays (negative); gene mutation assays in the HGPRT test with V79 Chinese hamster cells (negative); a primary DNA damage assay (i.e. unscheduled DNA synthesis assay in A549 human cells) (negative); in vitro cell transformation assay in BALB/C3T3 cells (negative).

In vitro chromosome aberration assays in V79 Chinese hamster cells were positive due to the chelating properties of ciclopirox olamine. However, in a corresponding *in-vivo* Chinese hamster bone marrow cytogenic assay, ciclopirox was negative for chromosome aberrations up to 5.000 mg/kg and it was demonstrated that ciclopirox was present in higher concentrations in the bone marrow.

Additional *in vivo* micronucleus and dominant lethal test in the mouse were negative.

Neoplastic potential: A carcinogenicity study in female mice dosed by the dermal route twice weekly for 50 weeks followed by a 6 month drug-free observation period prior to necropsy revealed no evidence of tumors at the application site.

Toxicitiy of excipients: All excipients are according to the pharmacopoeia.

Local tolerance: Primary acute dermal irritation studies in rabbits indicated that ciclopirox olamine cream is not a primary skin irritant. Similarly a study in rabbits indicated that ciclopirox olamine cream is not an eye irritant.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Benzyl alcohol
Octyldodecanol
Light liquid paraffin
Stearyl alcohol
Cetyl alcohol
Myristyl alcohol
Polysorbate 60
Sorbitan stearate
(S) - Lactic acid
Purified water

6.2 Incompatibilities

Cosmetics containing multivalent metal ions (e.g. make-up).

6.3 Shelf Life

2 years.

6.4 Special precautions for storage

Do not store above 25°C. Keep the tube in the outer carton in order to protect from light.

6.5 Nature and contents of container

Aluminium tube (epoxyphenoic resin lined) with a HDPE screw cap.
Each tube contains 20g Batrafen cream.

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

sanofi-aventis Ireland Ltd.
Citywest Business Campus
Dublin 24

8 MARKETING AUTHORISATION NUMBER

PA 540/32/1

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 12 November 1984

Date of last renewal: 12 November 2009

10 DATE OF REVISION OF THE TEXT

November 2010