Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Soothelip Aciclovir Cream 5% For Cold Sores

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Aciclovir 5% w/w
Also contains propylene glycol, cetyl alcohol and sorbic acid.

For a full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Cream
White to off white-cream.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Treatment of cold sore infection.

4.2 Posology and method of administration

Soothelip should be applied to the lesion or impending lesion as early as possible after the start of an infection. It is particularly important to start treatment of recurrent episodes during the prodromal period or when lesions first appear.

Adults (including elderly): Soothelip should be applied five times daily at approximately four hourly intervals, omitting the night time application. Treatment should be continued for five days. If, after five days, healing is not complete then treatment can be continued for up to an additional five days.

4.3 Contraindications

Soothelip is contraindicated in patients known to be hypersensitive to aciclovir, valaciclovir, propylene glycol or any of the excipients of Soothelip (listed in section 6.1); do not use in eyes.

4.4 Special warnings and precautions for use

In severely immune-compromised patients (*eg* AIDS patients or bone marrow transplant recipients) oral aciclovir dosing should be considered. Such patients should be encouraged to consult a physician concerning the treatment of any infection.
Soothelip is not recommended for application to mucous membranes such as in the mouth, eye or vagina, as it may be an irritant.
Particular care should be taken to avoid accidental introduction into the eye. The results of a wide range of mutagenicity tests *in vitro* and *in vivo* indicate that Soothelip does not pose a genetic risk to man. Soothelip was not found to be carcinogenic in long term studies in the rat and the mouse.
Largely reversible adverse effects on spermatogenesis in association with overall toxicity in rats and dogs have been reported only at doses of Soothelip greatly in excess of those employed therapeutically. There has been no experience of the effect of Soothelip on human fertility. Two generation studies in mice did not reveal any effect of (orally administered) Soothelip on fertility.
Aciclovir Tablets have been shown to have no definite effect upon sperm count, morphology or motility in man.

The excipient propylene glycol can cause skin irritations. The excipients cetyl alcohol and sorbic acid can cause local skin reactions (e.g. contact dermatitis).

4.5 Interaction with other medicinal products and other forms of interaction

Probenecid increases the mean half-life and area under the plasma concentration curve of systemically administered Soothelip.
However, this is likely to be of little relevance to the topical application of Soothelip.
No clinically significant interactions have been identified.

4.6 Fertility, pregnancy and lactation

Pregnancy
A post-marketing aciclovir pregnancy registry has documented pregnancy outcomes in women exposed to any formulation of aciclovir. The registry findings have not shown an increase in the number of birth defects amongst aciclovir exposed subjects compared with the general population, and any birth defects showed no uniqueness or consistent pattern to suggest a common cause.

Systemic administration of aciclovir in internationally accepted standard tests did not produce embryotoxic or teratogenic effects in rats, rabbits or mice.

In a non-standard test in rats, foetal abnormalities were observed, but only following such high subcutaneous doses that maternal toxicity was produced. The clinical relevance of these findings is uncertain.

Experience in humans is limited, so the use of aciclovir should be considered only when the potential benefits outweigh the possibility of unknown risks however the systemic exposure to aciclovir from topical application of aciclovir cream is very low.

Lactation
Limited human data show that the drug does pass into breast milk following systemic administration. However, the dosage received by a nursing infant following maternal use of aciclovir cream would be insignificant.

4.7 Effects on ability to drive and use machines

None known.

4.8 Undesirable effects

The following convention has been used for the classification of undesirable effects in terms of frequency: very common ≥1/10, common ≥1/100 and <1/10, uncommon ≥1/1000 and <1/100, rare ≥1/10,000 and <1/1000, very rare <1/10,000.

Clinical trial data have been used to assign frequency categories to adverse reactions observed during clinical trials with aciclovir 3% ophthalmic ointment. Due to the nature of the adverse events observed, it is not possible to determine unequivocally which events were related to the administration of the drug and which were related to the disease. Spontaneous reporting data has been used as a basis for allocating frequency for those events observed postmarketing.

Skin and subcutaneous tissue disorders
Uncommon: Transient burning or stinging following application of aciclovir cream.
Mild drying or flaking of the skin.
Itching.

Rare: Erythema. Contact dermatitis following application.
Where sensitivity tests have been conducted, the reactive substances have most often been shown to be components of

the cream rather than aciclovir.

Immune system disorders
Very rare: Immediate hypersensitivity reactions including angioedema and urticaria.

4.9 Overdose

No untoward effects would be expected if the entire contents of a Soothelip 10g tube containing 500mg of Aciclovir were ingested orally. Oral doses of 800mg five times daily (4g/daily), have been administered for seven days without adverse effects. Single intravenous doses of up to 80mg/kg have been inadvertently administered without adverse effects. Soothelip is dialysable.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

ATC Code: D06BB03 (aciclovir for topical use)
Aciclovir is an antiviral agent which is highly active *in vitro* against herpes simplex virus (HSV) types I and II and varicella zoster virus. Toxicity to mammalian host cells is low.

Aciclovir is phosphorylated after entry into herpes infected cells to the active compound Aciclovir triphosphate. The first step in this process is dependent on the presence of the HSV-coded thymidine kinase. Aciclovir triphosphate acts as an inhibitor of, and substrate for, the herpes-specified DNA polymerase, preventing further viral DNA synthesis without affecting the normal cellular processes.

5.2 Pharmacokinetic properties

Aciclovir is excreted through the kidney by both glomerular filtration and tubular secretion. The terminal or beta-phase half-life is reported to be about 2 to 3 hours for adults without renal impairment. In chronic renal failure this value is increased and may be up to 19.5 hours in anuric patients. During haemodialysis the half-life is reduced to 5.7 hours, with 60% of a dose of aciclovir being removed in 6 hours. Faecal excretion may account for about 2% of a dose. There is a wide distribution to various tissues, including the CSF where concentrations achieved are about 50% of those achieved in plasma. Protein binding is reported to range from 9% to 33%. Aciclovir crosses the placenta and is excreted in breast milk in concentrations approximately 3 times higher than those in maternal serum. Absorption of aciclovir is usually slight following topical application to intact skin, although it may be increased by changes in formulation.

5.3 Preclinical safety data

Not applicable.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Cetyl Alcohol
Dimeticone
Heavy Liquid Paraffin
Polyethylene Glycol-5 Glyceryl Stearate
Propylene Glycol
Sorbic Acid
White Soft Paraffin
Purified water

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Do not store above 25^{o}C.
Do not refrigerate or freeze.

6.5 Nature and contents of container

The product is supplied in aluminium tubes with screw caps in cartons.

Carton: White backed folding board.
Tube: Manufactured from 99.5% pure aluminium lacquered internally.
Cap: polythene or polypropylene.

Pack size: 2g

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

8 MARKETING AUTHORISATION NUMBER

PA 21/87/1

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