SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Univir 5% Cream

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each gram of Univir 5% Cream contains 10 mg of acyclovir.

For full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Cream.

A White Smooth cream.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Acyclovir 5% Cream is indicated for the treatment of immunocompetent patients with localised skin infections caused by the Herpes simplex virus including initial and recurring herpes genitalis and herpes labialis.

4.2 Posology and method of administration

Cutaneous use.

Aciclovir 5% Cream should be applied to affected parts of the skin five times daily at intervals of approximately four hours, omitting the night time application.

Aciclovir 5% Cream should be applied to the lesion or the impending lesion as early as possible after the start of an infection.

Treatment should be continued for five days. If healing is not complete, treatment may be continued for up to an additional five days.

4.3 Contraindications

Aciclovir 5% Cream is contra-indicated in patients known to be hypersensitive to aciclovir, valaciclovir, propylene glycol or one of the other ingredients of the cream base.

4.4 Special warnings and precautions for use

Aciclovir 5% Cream is not recommended for application to mucous membranes, such as in the mouth, eye or vagina, as it may cause irritation. The cream contains propylene glycol (see section 6.1). Particular care should be taken to avoid accidental application to the eye. PL 00289/1605 Version 2 Aciclovir5%CreamPL00289/1605V2

In severely immuno compromised patients (e.g. AIDS patients or bone marrow transplant recipients) oral administration of aciclovir should be considered. Such patients should be advised to consult a physician concerning the treatment of any infection. Patients with genitalis herpes should abstain from sexual activity for as long as lesions are visible to avoid transmission of infection to their partners. The gravity of recurrent infections varies dependent on the immune status of the patient, the frequency and duration of the episodes, to what extent the skin is affected and whether or not there are any systemic reactions. These factors are to be considered during treatment. Treatment could consist of advice and symptomatic support or a causal therapy. Physical, emotional and psycho-social problems, brought on by herpes infections, differ per patient. Therefore the choice of therapy depends on the situation of the individual patient. In case of severe disease or frequent recurrences, systemic treatment should be considered.

The excipient propylene glycol can cause skin irritations and cetyl alcohol, has been associated with allergic delayed-type hypersensitivity reactions in patients with stasis dermatitis. Cross-sensitisation with cetostearyl alcohol, lanolin, and stearyl alcohol has also been reported. It has been suggested that hypersensitivity may be caused by impurities in commercial grades of cetyl alcohol since highly refined cetyl alcohol (99.5%) has not been associated with hypersensitivity reactions.

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4.5 Interaction with other medicinal products and other forms of interaction

Interactions of aciclovir with other medicinal products at local application are not known.

4.6 Pregnancy and lactation

Pregnancy

Data on a large number of orally exposed pregnancies do not show harmful effects on the foetus or neonate. After dermal application aciclovir was not detected in the plasma (see section 5.2). For information regarding reproductive toxicity please refer to section 5.3. The potential human risk is unknown but probably small. 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.

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 rabbits, rats 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. PL 00289/1605 Version 2 Aciclovir5%CreamPL00289/1605V2

Lactation

Limited pharmacokinetic data indicate that aciclovir can be detected in breast milk after systemic administration. However, the dosage received by a nursing infant following maternal use of aciclovir cream or ophthalmic ointment would be insignificant. Aciclovir was not detected in the plasma after dermal application. Therefore, breast-feeding can be continued after local application of aciclovir.

4.7 Effects on ability to drive and use machines

It is not known whether Aciclovir 5% Cream may interfere with the ability to drive and use machines.

However, an adverse effect on these activities is unlikely.

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, not known (cannot be estimated from the available data).

Immune system disorders:

Very Rare: Immediate hypersensitivity reactions including angioedema and urticaria.

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.

4.9 Overdose

No untoward effects would be expected if the entire contents of the tube containing 500 mg of aciclovir (cream) were ingested orally.

Oral doses of one tablet of 800 mg five times daily for the duration of 7 days are indicated for the treatment of shingles.

Single intravenous doses of up to 80 mg/kg body weight have been inadvertently administered without adverse effects.

Aciclovir may be removed from the body through dialysis.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties PL 00289/1605 Version 2 Aciclovir5%CreamPL00289/1605V2

Pharmacotherapeutic group: chemotherapeutics for topical use.

ATC-code: D 06 BB 03

Aciclovir is an antiviral agent which is highly active *in vitro* against Herpes simplex (HSV) types I and II and Varicella zoster viruses. After entry into a herpes infected cell aciclovir is converted into active aciclovir-triphosphate. The first step in this process requires the presence of the HSV-coded thymidine kinase. Aciclovir-triphosphate acts as an inhibitor of, and substrate for, the herpes-specific DNA polymerase, preventing further viral DNA synthesis without affecting normal cellular processes.

Virology

Exposing Herpes simplex viruses *in vitro* to aciclovir may lead to diminished sensitivity in viruses. These viruses usually show a lack of thymidine kinase; this enzyme is responsible for the activation of aciclovir. However, studies in animals have shown these strains to be less virulent.

Similar viral strains have been observed occasionally during controlled and open studies in a few, largely severely immunodeficient, patients such as bone marrow transplant recipients or patients with congenital, severely combined immunodeficiency.

Manifestation of these viruses did not deteriorate the clinical picture, whilst in some cases the virus disappeared again spontaneously.

When treating such severely immunodeficient patients one should take into account possible manifestation of diminished sensitive viruses. Prolonged clinical experience will have to shed more light, however, on the correlation between *in vitro* virus sensitivity and clinical response to aciclovir therapy.

5.2 Pharmacokinetic properties

Aciclovir penetrates the skin. Intracutaneous levels exceed minimal effective tissue levels in steady state. No plasma level of aciclovir could be determined after local treatment with aciclovir. Therefore, the following data are based on oral or intravenous application.

The most significant metabolite is 9-carboxymethoxymethylguanine and accounts for 10 to 15% of the amount excreted in the urine. Aciclovir taken up in the plasma is excreted mainly unchanged by the kidneys (by glomerular filtration as well as tubular excretion).

In patients with normal renal function the plasma half-life is about 3 hours. Plasma protein binding is relatively low (9-33%). Interactions involving binding site displacement are therefore not anticipated.

5.3 Preclinical safety data

Systemic administration of aciclovir did not produce embryotoxic or teratogenic effects in rabbits, rats or mice. Fetal abnormalities were observed, but only following such high subcutaneous doses that maternal toxicity was produced. The clinical relevance of these findings is uncertain. PL 00289/1605 Version 2 Aciclovir5%CreamPL00289/1605V2

Only at doses well above human therapeutic dose, reversible adverse effects on spermatogenesis were reported in rats and dogs. In two generation studies in mice, aciclovir administered orally had no effect on fertility. Aciclovir has no definite effect upon sperm count, morphology or motility in man. Preclinical data reveal no special hazard for humans based on conventional genotoxicity and carcinogenicity studies.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Propylene glycol

White soft paraffin

Liquid paraffin

Cetostearyl alcohol

Sodium lauryl sulphate

Propylene glycol

Benzyl alcohol

Purified water

6.2 Incompatibilities

Not applicable

6.3 Shelf life

36 months.

6.4 Special precautions for storage

Do not store above 30 °C.

6.5 Nature and contents of container

Aluminium collapsible tubes of 10 g.

6.6 Instructions for use and handling

No special requirements.

7. MARKETING AUTHORISATION HOLDER

UNIVERSAL CORPORATION LIMITED,

CLUB ROAD, PLOT NO. 13777,

P.O. BOX 1748-00902,

KIKUYU - KENYA.

8. MARKETING AUTHORISATION NUMBER

H2002/0046

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

21st February 2001

10 DATE OF REVISION OF THE TEXT

Not Applicable