Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Viralief 50 mg/g Cream

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each gram of cream contains 50 mg aciclovir.

Excipient(s) with known effect
Each gram of cream contains 150 mg propylene glycol (E1520) and 15 mg cetyl alcohol.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Cream.
White to off-white cream

4 CLINICAL PARTICULARS

Treatment of cold sores caused by herpes simplex virus.

4.1 Therapeutic Indications

Treatment of cold sores caused by herpes simplex virus.

4.2 Posology and method of administration

Viralief 50 mg/g cream should be applied to infected lips 5 times daily at approximately 4 hourly intervals, omitting the night time application.

Viralief 50 mg/g cream should be applied to the lesions or impending lesions as early as possible after the start of an infection.

Treatment should be continued for 5 days. If, after 5 days, healing is not complete then treatment can be continued for up to an additional 5 days.

4.3 Contraindications

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

4.4 Special warnings and precautions for use

Aciclovir cream is not recommended for application to mucous membranes, such as in the mouth, eye or vagina, as it may be irritant. Particular care should be taken to avoid accidental introduction into the eye.

In severely immune-compromised patients (e.g. 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.

Excipients
The excipient cetyl alcohol may cause local skin reactions (e.g. contact dermatitis).

4.5 Interaction with other medicinal products and other forms of interactions

No clinically significant interactions have been identified.

4.6 Fertility, pregnancy and lactation

Pregnancy
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.

Animal studies have revealed harmful effects of the active ingredient, aciclovir.

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 significance of these findings is uncertain.

Breast-feeding
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

No studies on the effects on the ability to drive and use machines have been performed. However, an adverse effect on these activities is unlikely.

4.8 Undesirable effects

Adverse reactions have been ranked under the headings of frequency using the following 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).

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

Skin and subcutaneous tissue disorders
Uncommon: Transient burning or stinging sensation on the application site, mild form of dry skin or flaking, itching.
Rare: Erythema, contact dermatitis after administration. The results of hypersensitivity tests carried out have shown that the reactive substances were mostly the components of the cream and not aciclovir itself.

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

No untoward effects would be expected if the entire contents of a for example 10 g cream tube containing 500 mg of aciclovir were ingested orally.
Oral doses of 800 mg 5 times daily have been administerd for 7 days without adverse effects in the treatment of shingles. Single intravenous doses of up to 80 mg/kg have been inadvertently administered without adverse effects.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacodynamic group: Antibiotics and chemotherapeutics for dermatological use
ATC Code: D 06 BB 03

Aciclovir itself is a pharmacodynamically inactive compound. After penetrating cells infected with herpes simplex virus (HSV), aciclovir is converted to antivirally-active aciclovir triphosphate. This conversion is catalysed by viral HSV thymidine kinase, an enzyme essential for viral replication. HSV thus synthesises its own antiviral agent. The affinity of aciclovir for viral DNA polymerase is 10-20 times greater than its affinity for cellular DNA polymerase. Aciclovir thus selectively inhibits viral enzyme activity. Viral DNA polymerase incorporates aciclovir into viral DNA. As aciclovir is devoid of a 3'-hydroxyl group, no more nucleotides can be added by the formation of 3'-5' bonds, causing chain termination and hence effective reduction of viral replication. Both herpes simplex virus types 1 and 2 are highly sensitive to aciclovir.

In severely immunocompromised patients, prolonged or repeated aciclovir therapy may result in the selection of viral strains with reduced sensitivity. These patients, therefore, will no longer respond to aciclovir.

5.2 Pharmacokinetic properties

Aciclovir penetrates the skin. Intradermal levels are higher than the minimum inhibitory concentration in tissue at steady state. It has not been possible to detect aciclovir in the blood following topical application to the skin. The data reported below are therefore based on oral or intravenous administration.

The main metabolite is 9-carboxy(methoxy)methylguanine. It accounts for about 10-15 % of the renally excreted drug. Most of an aciclovir dose reaching the plasma is eliminated as unchanged drug via the kidneys (by both glomerular filtration and tubular excretion).

The plasma half-life of aciclovir in patients with normal kidney function is about 3 hours. Plasma protein binding is relatively low (9-33 %). Interactions due to displacement from plasma protein binding sites are, therefore, unlikely.

5.3 Preclinical safety data

A large number of *in vitro* tests show that, at very high concentrations, chromosomal damage may occur. During *in vivo* studies, no chromosomal damage has been observed. Aciclovir was not found to be carcinogenic in long-term studies in the rat and the mouse. Systemic administration of aciclovir in internationally accepted standard tests did not produce embryotoxic or teratogenic effects in several species. In a non-standard test in rats, no effects on the foetus were observed, except at high doses, that also produced maternal toxicity.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Macrogol stearate
Dimeticone
Cetyl alcohol
Liquid paraffin
White soft paraffin
Propylene glycol
Purified water.

6.2 Incompatibilities

The cream must not be mixed with other substances.

6.3 Shelf life

3 years

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

Aluminium tube with polyethylene cap.
Each tube contains 2g, 3g or 5g.

Not all pack sizes may be marketed.

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

Clonmel Healthcare Ltd
Clonmel
Co. Tipperary
Ireland

8 MARKETING AUTHORISATION NUMBER

PA0126/201/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 27th November 1998
Date of last renewal: 25th November 2006

10 DATE OF REVISION OF THE TEXT

February 2020