Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Zovirax Cold Sore 5% w/w Cream

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

5% w/w aciclovir

Excipients with known effects: contains 40 %w/w propylene glycol (E 1520), 6.75%w/w Cetostearyl alcohol and 0.75 %w/w sodium laurilsulfate

For a full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Cream.

A smooth white to off white cream.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Zovirax Cold Sore Cream is indicated for the treatment of Herpes simplex virus infections of the skin, lips and face (recurrent herpes labialis).

4.2 Posology and method of administration

Adults:
Zovirax Cold Sore Cream should be applied five times daily at approximately four hourly intervals omitting the night time application. Treatment should be continued for at least 4 days. If healing has not occurred, treatment may be continued for up to 10 days. If lesions are still present after 10 days users should be advised to consult a doctor.

Zovirax cold sore cream should be applied as soon as possible, preferably during the earliest stages (prodome or erythema). Treatment can also be started during the later (papule or blister) stages.

Children:
Children should use the adult dose.

4.3 Contraindications

Hypersensitivity to aciclovir, valaciclovir, propylene glycol or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Zovirax Cold Sore Cream should only be used on cold sores on the lips and face. It is not recommended for application to mucous membranes, such as in the mouth or eye. Particular care should be taken to avoid contact with the eye.

In severely immunocompromised patients (e.g. AIDS patients or bone marrow transplant recipients) oral dosing should be considered. Such patients should be encouraged to consult a physician concerning the treatment of any infection.

People with particular severe recurrent herpes labialis should be encouraged to seek medical advice.

Cetostearyl alcohol may cause local skin reactions (e.g. contact dermatitis).

Zovirax Cold Sore Cream contains 200 mg propylene glycol in each daily dose which is equivalent to 400 mg/g.

Zovirax Cold Sore Cream contains 3,75 mg sodium laurilsulfate in each daily dose which is equivalent to 7.5 mg/g. Sodium laurilsulfate may cause local skin reactions (such as stinging or burning sensation) or increase skin reactions caused by other products when applied on the same area.

4.5 Interaction with other medicinal products and other forms of interaction

No clinically significant interactions have been identified.

4.6 Fertility, pregnancy and lactation

Fertility

See clinical studies in section 5.3.

Pregnancy

The use of aciclovir cream 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 subjects exposed to aciclovir compared with the general population and any birth defects showed no uniqueness or consistent pattern to suggest a common cause. Systemic exposure to aciclovir from topical application of aciclovir cream is very low.

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.

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

Not applicable.

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.

Skin and subcutaneous tissue disorders

Uncommon

- Transient burning or stinging following application of Zovirax Cold Sore 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.

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, website: www.hpra.ie.

4.9 Overdose

No untoward effects would be expected if the entire contents of a 2 g content of Zovirax Cold Sore Cream containing 100 mg of aciclovir were ingested orally.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

ATC Code: D06 BB 03

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 normal cellular processes.

Zovirax Cold Sore Cream significantly reduced episode healing time ($p<0.02$) and time to pain resolution ($p<0.03$) compared with placebo cream in two multicentre, double-blind, randomised clinical studies involving 1,385 subjects treated over 4 days for recurrent herpes labialis, Zovirax Cold Sore Cream 5% was compared to vehicle cream.

Based on the pooled dataset from the two studies the mean time from clinician-assessed start of treatment to healing (episode duration) was 4.6 days using Zovirax Cold Sore Cream and 5.0 days using vehicle cream ($p<0.001$). The median clinician-assessed episode duration was 4.0 days using aciclovir cream (25%-ile=3.0 days, 75%-ile=6.0 days) and 4.3 days using vehicle cream (25%-ile=3.1 days, 75%-ile=6.6 days), with a corresponding hazard ratio of 1.22 ($p<0.001$).

The median duration of subject-assessed pain was 2.9 days using aciclovir cream and 3.0 days using vehicle cream, with a corresponding hazard ratio of 1.21 ($p<0.001$).

Overall approximately 60% of subjects started treatment at an earlier lesion stage (prodome or erythema) and 40% at a late lesion stage (papule or vesicle).

5.2 Pharmacokinetic properties

Limited pharmacology studies have shown only minimal systemic absorption of aciclovir following repeated topical administration of Zovirax Cold Sore cream.

5.3 Preclinical safety data

There is no experience on the effect of Zovirax Cold Sore Cream on human female fertility. In patients with normal sperm count, chronically administered oral aciclovir has been shown to have no clinically significant effect on sperm count, motility or morphology.

NON-CLINICAL INFORMATION

- **Mutagenicity**

The results of a wide range of mutagenicity tests *in vitro* and *in vivo* indicate that aciclovir does not pose a genetic risk to man.

- **Carcinogenicity**

Aciclovir was not found to be carcinogenic in long-term studies in the rat and the mouse.

- **Fertility**

Largely reversible adverse effects on spermatogenesis in association with overall toxicity in rats and dogs have been reported only at systemic doses of aciclovir greatly in excess of those employed therapeutically. Two-generation studies in mice did not reveal any effect of orally administered aciclovir on fertility.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Cetostearyl alcohol
Liquid paraffin
Poloxamer 407
Propylene glycol (E1520)
Purified water
Sodium laurilsulfate
White soft paraffin
Dimeticone
Glycerol Monostearate
Macrogol Stearate

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years in aluminium tubes.
2 years in pump container.

6.4 Special precautions for storage

Do not store above 25°C. Do not refrigerate.

6.5 Nature and contents of container

Zovirax Cold Sore Cream is stored in two types of containers:

Aluminium tube - Collapsable lacquered aluminium tubes with polyethylene plastic screw caps. The tubes contain a latex end-seal at the crimped end and a membrane seal at the nozzle end. A spike is incorporated into the structure of the cap.
Pack size: 2g.

Pump assembly - Polypropylene container with pump assembly and polypropylene cap.
Pack size: 2g.

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

Haleon Ireland Limited
12 Riverwalk
Citywest Business Campus
Dublin 24
Ireland

8 MARKETING AUTHORISATION NUMBER

PA0678/090/002

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 16 July 1993

Date of last renewal: 16 July 2008

10 DATE OF REVISION OF THE TEXT

July 2023