Zovirax™ Cream

Aciclovir

To the Medical and Pharmaceutical Professions

Presentations

Cream containing aciclovir 5% w/w BP. (See list of excipients)

Indications

ZOVIRAX Cream is indicated for the treatment of Herpes simplex virus infections of the skin including initial and recurrent genital herpes and herpes labialis.
Route of administration: topical.
Do not use in eyes.

Dosage and Administration

Adults and Children:

ZOVIRAX Cream should be applied five times daily at approximately four hourly intervals omitting the night time application.
ZOVIRAX Cream should be applied to the lesions or impending lesions as soon as possible, preferably during the earliest stages (prodrome or erythema). Treatment can also be started during the later (papule or blister) stages.
Treatment should be continued for 4 days. If healing has not occurred treatment may be continued for up to an additional 5 days.
Use in the elderly: No special comment

Contra-indications

ZOVIRAX Cream is contra-indicated in patients known to be hypersensitive to aciclovir, valaciclovir, propylene glycol or any of the excipients of *ZOVIRAX* Cream.

Precautions and Warnings

ZOVIRAX 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 (eg AIDS patients or bone marrow transplant recipients) oral *ZOVIRAX* dosing should be considered. Such patients should be encouraged to consult a physician concerning the treatment of any infection.

Drug Interactions

No clinically significant interactions have been identified.

Pregnancy and Lactation

A post-marketing aciclovir pregnancy registry has documented pregnancy outcomes in women exposed to any formulation of *ZOVIRAX*. The registry findings have not shown an increase in the number of birth defects amongst *ZOVIRAX* exposed subjects compared with the general population, and any birth defects showed no uniqueness or consistent pattern to suggest a common cause.
The use of *ZOVIRAX* Cream should be considered only when the potential benefits outweigh the possibility of unknown risks.
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.
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 *ZOVIRAX* Cream would be insignificant.

Adverse Reactions

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 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.

Overdosage

No untoward effects would be expected if the entire contents of a 10 gram tube of *ZOVIRAX* cream containing 500 mg of aciclovir were ingested orally.

Pharmacodynamic Properties

Mode of action:

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 viral-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 Cream significantly reduced episode healing time ($p<0.02$) and time to pain resolution ($p<0.03$) compared with placebo cream in two large double-blind, randomised clinical studies involving 1, 385 subjects with recurrent herpes labialis. Overall, approximately 80% of patients started treatment at an early lesion stage (prodrome or erythema) and 40% at a late lesion stage (papule or blister).

Pharmacokinetic Properties

Pharmacology studies have shown only minimal systemic absorption of aciclovir following repeated topical administration of *ZOVIRAX* Cream.

Further Information

Preclinical Safety Data

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.
Aciclovir 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 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.

Pharmaceutical Precautions and Recommendations

Do not store above 25°C.
Do not refrigerate

Shelf Life

The expiry date is indicated on the packaging.

List of Excipients

Poloxamer 407
Cetostearyl alcohol
Sodium lauryl sulphate
White soft paraffin
Liquid paraffin
Propylene glycol
Purified water
Arlacel 165 (containing glycerol monostearate and polyoxyethylene stearate)
Dimeticone 20

Instructions for Use/Handling

Dilution:

ZOVIRAX Cream contains a specially formulated base and should not be diluted or used as a base for incorporation of other medicaments.

THIS IS A MEDICAMENT

Medicament is a product which affects your health and its consumption contrary to instructions is dangerous for you.
Follow strictly the doctor's prescription, the method of use and the instructions of the pharmacist who sold the medicament.
- The doctor and the pharmacist are the experts in medicines, their benefits and risks.
- Do not by yourself interrupt the period of treatment prescribed.
- Do not repeat the same prescription without consulting your doctor.
- Keep all medicaments out of the reach of children.

Council of Arab Health Ministers, Union of Arab Pharmacists.

Manufactured by:
Glaxo Operations UK Limited*, Barnard Castle, UK
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