Singapore proposed PI_clean

ZOVIRAX ™ Cream

QUALITATIVE AND QUANTITATIVE COMPOSITION

Cream containing 5% w/w acyclovir

PHARMACEUTICAL FORM

Cream

CLINICAL PARTICULARS

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.*

Dosage and Administration

Adults and children:-

ZOVIRAX Cream should be applied five times daily at approximately 4-hourly intervals omitting the night time dose.

ZOVIRAX Cream should be applied to the lesions or impending lesions 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 the lesions first appear.

Treatment should be continued for 5 days. If healing has not occurred treatment may be continued for up to 10 days.

Contra-indications

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

Special Warnings and Special Precautions for Use

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 (e.g. 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.

Use in Pregnancy and Lactation

A post-marketing acyclovir 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 acyclovir 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.

Effects on Ability to Drive and Use Machines

No data.

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 acyclovir.

Immune system disorders:-

Very rare
- Immediate hypersensitivity reactions including angioedema

Overdose

No untoward effects would be expected if the entire contents of a 10 gram tube of Zovirax Cream containing 500 mg of acyclovir were ingested orally. Doses of 800 mg five times a day (4 g/day) have been administered for 7 days without adverse effects.

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

Acyclovir is dialysable.

Pharmacodynamic Properties

Acyclovir 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.

Acyclovir is phosphorylated after entry into herpes infected cells to the active compound acyclovir triphosphate. The first step in this process is dependent on the presence of the viral-coded thymidine kinase.

Acyclovir triphosphate acts as an inhibitor of and substrate for the herpes specified DNA polymerase preventing further viral DNA synthesis without affecting normal cellular processes.

Pharmacokinetic Properties

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

Clinical Studies

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

Preclinical Safety Data

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

Acyclovir 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 acyclovir greatly in excess of those employed therapeutically. Two-generation studies in mice did not reveal any effect of orally administered acyclovir on fertility.

PHARMACEUTICAL PARTICULARS

List of Excipients

Propylene Glycol
White Soft Paraffin
Cetostearyl Alcohol
Liquid Paraffin
Arlacel 165
Poloxamer 407
Dimeticone 20
Sodium Laurilsulfate
Purified Water

Special Precautions for Storage

Store below 25°C. Do not refrigerate.

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

Version number: GDS17/IPI03(SI)

Date of issue: 13 September 2006

Manufactured by Glaxo Wellcome Operations, UK

ZOVIRAX is a trademark of the GlaxoSmithKline group of companies.