PRODUCT INFORMATION

ZOVIRAX™ OPHTHALMIC OINTMENT

Name of the Medicine: Aciclovir

Description:

Aciclovir is a synthetic acyclic purine nucleoside analogue. Its chemical name is 9-((2-hydroxyethoxy)methyl)guanine. It is a white crystalline powder. Each gram of Zovirax Ophthalmic Ointment contains 30 mg of aciclovir in white soft paraffin base (aciclovir 3 per cent).

Pharmacology:

Microbiology:
Aciclovir is an antiviral agent which is active *in vitro* against *Herpes simplex* virus (HSV) types I and II. However, the relationship between *in vitro* sensitivity of herpes viruses to aciclovir and clinical response to therapy has yet to be established. Aciclovir needs to be phosphorylated to the active compound, aciclovir triphosphate, in order to become active against the virus. Such conversion is very limited in normal cells and in addition cellular DNA polymerase is not very sensitive to the active compound. However, in infected cells HSV or VZV-coded thymidine kinase facilitates the conversion of aciclovir to aciclovir monophosphate which is then converted to aciclovir triphosphate by cellular enzymes. Aciclovir triphosphate acts as an inhibitor of, and substrate for, the herpes-specified DNA polymerase, preventing further viral DNA synthesis.

Pharmacokinetics:
Aciclovir is absorbed through the corneal epithelium and superficial ocular tissues, and achieves significant concentrations in aqueous humour. Small quantities (2-16% of the applied dose) appear in the urine. In animal studies low levels of aciclovir could be detected in blood after topical application to the eye.

Indications:

Treatment of *Herpes simplex* keratitis.

Contraindications:

Patients with known hypersensitivity to aciclovir or valaciclovir.

Precautions:

Patients should be informed that transient mild stinging immediately following application may occur.

Patients should avoid wearing contact lenses when using Zovirax Ophthalmic Ointment.

Resistant strains have been isolated *in vitro* and in animals following treatment with aciclovir. HSV strains resistant *in vitro* to aciclovir have also been isolated from immunecompromised as well as immuno-competent patients receiving aciclovir for *Herpes simplex* infections. Therefore the potential for the development of resistant HSV strains in patients treated with

aciclovir should be borne in mind. The relationship between *in vitro* sensitivity of herpes viruses to aciclovir and clinical response to therapy has yet to be established.

Use in Pregnancy: (Category B3)
Animal studies show that aciclovir crosses the placenta readily. Aciclovir was not teratogenic in the mouse (450 mg/kg/day po), rabbit (50 mg/kg/day, sc and iv) or rat (50 mg/kg/day, sc) when dosed throughout the period of major organogenesis. In additional studies in which rats were given 3 sc doses of 100 mg/kg aciclovir on gestation day 10, fetal abnormalities, such as head and tail anomalies, were reported).

There have been no adequate and well controlled studies concerning the safety of aciclovir in pregnant women. Only small amounts are absorbed following application to the eye. It should not be used during pregnancy unless the benefits to the patient clearly outweigh the potential risks to the foetus.

Use in Lactation:
Limited human data show that aciclovir does pass into breast milk. Aciclovir should only be administered to nursing mothers if the benefits to the mother outweigh the potential risks to the baby.

Effects on Fertility:
There is no information on the effect of Zovirax on human female fertility. In a study of 20 male patients with normal sperm count, oral aciclovir administered at doses of up to 1g per day for up to six months has been shown to have no clinically significant effect on sperm count, motility or morphology.

Adverse Effects:

Transient mild stinging immediately following administration occurs in a proportion of patients. Superficial punctate keratopathy occurs somewhat more frequently but healing has occurred, without apparent sequelae, following the completion of a course of treatment of dendritic ulcers. Blepharitis has been reported in patients on Zovirax opthalmic ointment.

Sensitivity reactions have been reported but are uncommon.

The following have also been reported but may be disease-related: mild hyperaemia, discharge, lid oedema and erythema, epithelial microcysts and conjunctivitis.

Post-marketing:
There have been very rare reports of immediate hypersensitivity reactions including angiodema with topical aciclovir

Dosage & Administration:

Adults: 1 cm ribbon of ointment should be placed inside the lower conjunctival sac five times a day at approximately four hourly intervals. Treatment should be continued for 14 days or at least 3 days after healing is completed, whichever is shorter.

Children: As for adults.

Overdosage:

No untoward effects are likely to occur if the entire contents of a tube containing 135 mg of aciclovir were ingested orally.

Presentation and Storage Conditions:

White to pale yellow *sterile* ointment containing 3 per cent w/w aciclovir in a white soft paraffin base: 4.5 g tube.
Store below 25°C.
Discard one month after opening.

Name and Address of Sponsor:

GlaxoSmithKline Australia Pty Ltd.
1061 Mountain Highway
Boronia Victoria 3155

Poison Schedule: S4

Date of Approval:

TGA Approval Date: 27 September 2007

Version 1.0