

ZOVIRAX™ Ophthalmic Ointment

Aciclovir

QUALITATIVE AND QUANTITATIVE COMPOSITION

Ophthalmic ointment containing 3% w/w aciclovir.

PHARMACEUTICAL FORM

Ophthalmic ointment.

CLINICAL PARTICULARS

Indications

ZOVIRAX ophthalmic ointment is indicated for the treatment of *herpes simplex* keratitis.

Dosage and Administration

The dosage for all age groups is the same.

A 10mm ribbon of the ointment should be placed inside the lower conjunctival sac five times a day at approximately four hourly intervals.

Treatment should continue for at least 3 days after healing.

Contraindications

ZOVIRAX ophthalmic ointment is contra-indicated in patients known to be hypersensitive to aciclovir or valaciclovir.

Warnings and 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.

Interactions

No clinically significant interactions have been identified.

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 aciclovir 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* ophthalmic ointment 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* ophthalmic ointment would be insignificant.

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 $\geq 1/10$, common $\geq 1/100$ and $< 1/10$, uncommon $\geq 1/1000$ and $< 1/100$, rare $\geq 1/10,000$ and $< 1/1000$, very rare $< 1/10,000$.

Clinical trial data have been used to assign frequency categories to adverse reactions observed during clinical trials with aciclovir 3% ophthalmic ointment. Due to the nature of the adverse events observed, it is not possible to determine unequivocally which events were related to the administration of the drug and which were related to the disease. Spontaneous reporting data has been used as a basis for allocating frequency for those events observed post-marketing.

Immune system disorders

Very rare: Immediate hypersensitivity reactions including angioedema

Eye disorders

Very common: Superficial punctate keratopathy

This did not necessitate an early termination of therapy and healed without apparent sequelae.

Common: Transient mild stinging of the eye occurring immediately following application, conjunctivitis.

Rare: Blepharitis

Local irritation and inflammation such as blepharitis and conjunctivitis have been reported in patients receiving *ZOVIRAX* ophthalmic ointment.

Overdose

No untoward effects would be expected if the entire contents of the tube containing 135mg aciclovir were ingested orally.

PHARMACOLOGICAL PROPERTIES

Pharmacodynamic Properties

Mechanism of Action:

Aciclovir is an antiviral which is highly active *in vitro* against herpes simplex (HSV) types I and II and *varicella zoster* viruses. Toxicity to mammalian cells is low.

Aciclovir is phosphorylated to the active compound acyclovir triphosphate after entry into a herpes infected cell. The first step in this process requires 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.

Pharmacokinetic Properties

Aciclovir is rapidly absorbed from the ophthalmic ointment through the corneal epithelium and superficial ocular tissues with the result that viral toxic concentrations are achieved in the aqueous humor. It has not been possible to detect aciclovir in the blood by existing methods after topical application of *ZOVIRAX* ophthalmic ointment, but trace quantities are detectable in the urine. These levels, however, are not therapeutically significant.

Clinical Studies

There is no information on the effect of *ZOVIRAX* ophthalmic ointment 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.

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.

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 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 PARTICULARS

List of Excipients

White petrolatum.

Incompatibilities

No data.

Shelf Life

The expiry date is indicated on the packaging.

Special Precautions for Storage

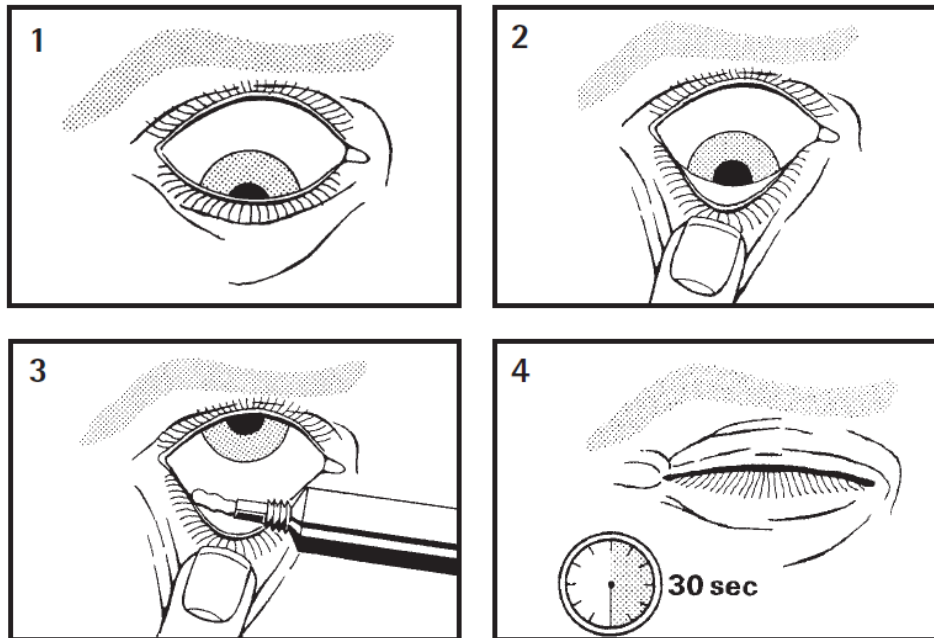
Store below 25°C. An opened tube of *ZOVIRAX* ophthalmic ointment should be discarded after one month.

Nature and Contents of Container

Tube with nozzle and screw cap.

Pack size: 4.5g

INSTRUCTIONS FOR USE/HANDLING



Manufactured by:
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