The format of this leaflet was determined by the Ministry of Health and its content was checked and approved in June 2014

Zovirax™ Ophthalmic Ointment

SUMMARY OF PRODUCT CHARACTERISTICS

1. Trade Name Of The Medicinal Product

Zovirax Ophthalmic Ointment

2. Qualitative and Quantitative Composition

Aciclovir 3.0% W/W
For the full list of excipients, see section 6.1.

3. Pharmaceutical Form

Ophthalmic Ointment

Clinical Particulars

4.1 Therapeutic Indications

Treatment of herpes simplex keratitis.

4.2 Posology and Method of Administration

Topical administration to the eye.

Adults: 1cm ribbon of ointment should be placed inside the lower conjunctival sac five times a day at approximately four hourly intervals, omitting the night time application. Treatment should continue for at least 3 days after healing is complete.

Children: As for adults

Use in the elderly: As for adults.

4.3 Contra-indications

Zovirax Ophthalmic Ointment is contra-indicated in patients with a known hypersensitivity to aciclovir or valaciclovir, or any of the excipients listed in section 6.1.

4.4 Special Warnings and Precautions for Use

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

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

4.5 Interaction with other Medicaments and other Forms of Interaction

No clinically significant interactions have been identified.

4.6. Fertility, pregnancy and breast-feeding

Pregnancy
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 described amongst Zovirax exposed subjects compared with the general population, and any birth defects showed no uniqueness or consistent pattern to suggest a common cause.

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.

The use of Zovirax Ophthalmic Ointment should be considered only when the potential benefits outweigh the possibility of unknown risks.

Breast-feeding
Limited human data show that the drug does pass into breast milk following systemic administration. However, the dosage received by the nursing infant following maternal use of Zovirax Ophthalmic Ointment would be insignificant.

Fertility
There is no information on the effect of aciclovir 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.

See Clinical Studies in section 5.2.

4.7 Effects on Ability to Drive and Use Machines

Eye ointments can affect visual ability and therefore caution is advised when driving or using machines.

4.8 Undesirable Effects

Adverse reactions are listed below by MedDRA body system organ class and by frequency.

The frequency categories used are:

Very common	≥ 1/10,
Common	≥ 1/100 and < 1/10,
Uncommon	≥ 1/1,000 and <1/100,
Rare	≥ 1/10,000 and <1/1,000,
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 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 and urticaria.

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.

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.

4.9 Overdose

No untoward effects would be expected if the entire contents of the tube containing 135 mg of aciclovir were ingested orally. However, the accidental, repeated overdose of oral aciclovir, over several days, has resulted in gastrointestinal effects (nausea and vomiting) and neurological effects (headache and confusion). Aciclovir is dialysable by haemodialysis.

Pharmacological Properties

5.1 Pharmacodynamic Properties

Aciclovir is an antiviral agent which is highly active *in vitro* against herpes simplex (HSV) types I and II, but its toxicity to mammalian cells is low.

Aciclovir is phosphorylated to the active compound aciclovir triphosphate after entry into a herpes infected cell. The first step in this process requires the presence of the HSV- coded thymidine kinase. Aciclovir triphosphate acts as an inhibitor of, and substrate for, herpes specified DNA polymerase, preventing further viral DNA synthesis without affecting normal cellular processes

5.2 Pharmacokinetic Properties

Aciclovir is rapidly absorbed from the ophthalmic ointment through the corneal epithelium and superficial ocular tissues, achieving antiviral concentrations in the aqueous humor. It has not been possible by existing methods to detect aciclovir in the blood after topical application to the eye. However, trace quantities are detectable in the urine. These levels are not therapeutically significant.

5.3 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.

Systemic administration of aciclovir in internationally accepted standard tests did not produce embryotoxic or teratogenic effects in rats, rabbits 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.

Pharmaceutical Particulars

6.1 List of Excipients

White petrolatum

6.2 Incompatibilities

None known

6.3 Shelf Life

The expiry date of the product is indicated on the label and packaging.

6.4 Special Precautions for Storage

Store below 25^{o}C
Use within one month of first opening tube.

6.5 Nature and Contents of Container

Laminate tube supplied with polyethylene tube head and white high density polyethylene tamper evident screw cap closure.

Pack size: 4.5 G

Administrative Data

7. MANUFACTURER

Jubilant Hollisterstier General Partnership, Quebec, Canada.

8. LICENSE HOLDER AND IMPORTER

GlaxoSmithKline (Israel) Ltd., 25 Basel St., Petach Tikva.

9. LICENSE NUMBER

027-71-21521