IRISH MEDICINES BOARD ACT 1995

MEDICINAL PRODUCTS(LICENSING AND SALE)REGULATIONS, 1998

(S.I. No.142 of 1998)

PPA1328/067/001
Case No: 2034068

The Irish Medicines Board in exercise of the powers conferred on it by the above mentioned Regulations hereby grants to

B & S Healthcare

Unit 4, Bradfield Road, **Ruislip**, **Middlesex**, **HA4 0NU**, **United Kingdom**

an authorisation, subject to the provisions of the said Regulations, in respect of the product

Zovirax 30 mg/g Eye Ointment

The particulars of which are set out in Part I and Part II of the attached Schedule. The authorisation is also subject to the general conditions as may be specified in the said Regulations as listed on the reverse of this document.

This authorisation, unless previously revoked, shall continue in force from **26/03/2007** until **11/01/2012**.

Signed on behalf of the Irish Medicines Board this

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A person authorised in that behalf by the said Board.

Part II

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Zovirax 30 mg/g Eye Ointment

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each gram of ointment contains 30 mg aciclovir equivalent to 3% w/w aciclovir.
For full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Eye Ointment.

Product imported from Germany:
A soft, homogenous, white to off-white, slightly translucent, unctious ointment.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

In the treatment of Herpes simplex keratitis.

4.2 Posology and method of administration

For ophthalmic administration.
Adults and children: A l cm 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 is complete.

4.3 Contraindications

Zovirax Ophthalmic Ointment is contra-indicated in patients known to be hypersensitive to aciclovir or valaciclovir.

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 medicinal products and other forms of interaction

No clinically significant interactions have been identified.

4.6 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.
Experience in humans is limited, so the use of Zovirax Eye 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.

4.7 Effects on ability to drive and use machines

No specific studies have been conducted, but there is no evidence to suggest that aciclovir will adversely affect ability to drive and operate 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 ≥ 1/1000 and <1/100, rare ≥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.

4.9 Overdose

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

orally.

5 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 and varicella zoster viruses.

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 the herpes specified DNA polymerase preventing further viral DNA synthesis without affecting normal cellular processes.

5.2 Pharmacokinetic properties

Aciclovir is rapidly absorbed from the eye ointment through the corneal epithelium and superficial ocular tissues with the result that viraltoxic concentrations are achieved in the aqueous humor. It has not been possible to detect aciclovir in the blood by existing methods after topical application to the eye. However, trace quantities may be measured in the urine. These levels are not clinically significant.

5.3 Preclinical safety data

The results of a wide range of mutagenicity test *in vitro* and *in vivo* indicates that aciclovir is unlikely to 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.
There is no information on the effect of Zovirax Ophthalmic Ointment on human female fertility. In patients with normal sperm count, chronically administered oral aciclovir has been shown to have no clinically significant effect on sperm count, motility or morphology.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

White soft paraffin.

6.2 Incompatibilities

Not applicable.

6.3 Shelf Life

The shelf-life expiry date of this product shall be the date shown on the container and outer package of the product on the market in the country of origin.

6.4 Special precautions for storage

Do not store above 25°C.
Discard one month after opening.

6.5 Nature and contents of container

White to pale yellow sterile ointment contained in pure tin or lacquered aluminium tubes with a tamper evident screw cap.
Pack size: 4.5g tube.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

No special requirements.

7 Parallel Product Authorisation Holder

B&S Healthcare
Unit 4
Bradfield Road
Ruislip
Middlesex
HA4 0NU
United Kingdom

8 Parallel Product Authorisation Number

PPA 1328/67/1

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of First Authorisation 12th January 2007

10 DATE OF REVISION OF THE TEXT

February 2007