# ACIVIR Eye Ointment (Acyclovir 3%)

*For the use of a Registered Medical Practitioner or a Hospital or a Laboratory only*

## Qualitative and Quantitative Composition

Aciclovir IP.....3.0% w/w

Benzalkonium chloride IP....0.01% w/w

## Dosage Form and Strength

Ophthalmic ointment of Aciclovir 3% w/w

## Clinical Particulars

### Therapeutic Indications

Treatment of herpes simplex keratitis.

### 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.

### Contraindications

Aciclovir ophthalmic ointment is contraindicated in patients with a known hypersensitivity to aciclovir or valaciclovir or any of the ingredients included in the formulation.

### Special Warnings and Precautions for Use

FOR OPHTHALMIC USE ONLY.

Patients should be informed that transient, mild stinging immediately following application may occur. Patients should avoid wearing contact lenses when using **ACIVIR** 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 immune-compromised 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.

## Drug interactions

No clinically significant interactions have been identified.

## Use in Special Population

## Pregnant Women

*Pregnancy Category B3*

A post-marketing aciclovir pregnancy registry has documented pregnancy outcomes in women exposed to any formulation of Aciclovir. The registry findings have not shown an increase in the number of birth defects described amongst Aciclovir exposed subjects compared with the general population, and any birth defects showed no uniqueness or consistent pattern to suggest a common cause.

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. **ACIVIR** eye ointment should not be used during pregnancy unless the benefits to the patient clearly outweigh the potential risks to the foetus.

## Lactating Women

Limited human data show that aciclovir does not pass into breast milk following systemic administration. However, the dosage received by the nursing infant following maternal use of aciclovir ophthalmic ointment would be insignificant. Aciclovir should only be administered to nursing mothers if the benefits to the mother outweigh the potential risks to the baby.

## Effects on Ability to Drive and Use Machines

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

## Undesirable 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 aciclovir ophthalmic 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.

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.

## Post-marketing

There have been very rare reports of immediate hypersensitivity reactions including

angiodema with topical aciclovir.

If you experience any side effects, talk to your doctor or pharmacist or write to drugsafety@cipla.com. You can also report side effects directly via the national pharmacovigilance program of India by calling on 1800 180 3024 or you can report to Cipla Ltd. on 18002677779. By reporting side effects, you can help provide more information on the safety of this product.

### Overdose

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

### Mechanism of Action

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. However, the relationship between *in vitro* sensitivity of herpes viruses to aciclovir and clinical response to therapy has yet to be established.

### Pharmacodynamic Properties

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, 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, achieving significant 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.

## Nonclinical Properties

### Animal Toxicology or Pharmacology

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 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.

# 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 Aciclovir Ophthalmic Ointment contains 30 mg of aciclovir in white soft paraffin base (aciclovir 3 per cent).

# Pharmaceutical Particulars

## Incompatibilities

None known.

## Shelf-Life

As on the pack

## Packaging Information

**ACIVIR** Eye Ointment: Tube of 5 gm

## Storage and Handling Instructions

Store below 25°C.

# Patient Counselling Information

Patients should avoid wearing contact lenses when using **ACIVIR** ophthalmic ointment.

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

# Details of Manufacturer

Mfd. By Cipla Ltd.

Registered Office:

Cipla House, Peninsula Business Park,

Ganpatrao Kadam Marg

Lower Parel

Mumbai – 400 013, India

# Details of Permission or Licence Number with Date

28A-KD/2149-A – 2017

## Date of Revision

18/12/2019