Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Aciclovir Agepha 30 mg/g eye ointment

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

1 g ointment contains 30 mg aciclovir.

For the full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Eye ointment

White to whitish grey, homogeneous eye ointment.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Aciclovir "Agepha" 30 mg/g eye ointment is indicated for the treatment of herpes simplex keratitis.

4.2 Posology and method of administration

Adults:
Unless otherwise prescribed, a 1cm ribbon of ointment should be placed inside the lower conjunctival sac five times a day (at approximately 4 hourly intervals). The treatment should continue for at least 3 days after the healing is complete.

Paediatric population:
As for adults

Use in elderly people (≥ 65 years):
No adjustment in dosage is required.

Use in people with impaired renal and liver function:
No adjustment in dosage is required.

Method of administration:
Ocular use.

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1
- Hypersensitivity to Valaciclovir.

4.4 Special warnings and precautions for use

For ocular use only. Not for injection or oral intake.
There is insufficient clinical data on the use of Xorox eye ointment for deep corneal defects and the combined use of Xorox eye ointment with topical corticosteroids.

In case of a bacterial coinfection, an additional antibiotic therapy must be carried out.

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

Patients should avoid wearing contact lenses when using Aciclovir "Agepha" eye ointment.

4.5 Interaction with other medicinal products and other forms of interactions

No clinically significant interactions have been identified when applied topically.

4.6 Fertility, pregnancy and lactation

Fertility
No studies have been performed to investigate the effect of topically ophthalmic use of aciclovir on 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.With the recommended use of Aciclovir "Agepha" , the systemic exposure of aciclovir is expected to be negligible and no risk is anticipated.

Pregnancy
A post-marketing aciclovir pregnancy registry has documented pregnancy outcomes in women exposed to 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.

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

With the recommended use of Aciclovir "Agepha" no effects during pregnancy are anticipated since systemic exposure of aciclovir is expected to be negligible. When necessary, Aciclovir "Agepha" eye ointment can be used during pregnancy.

Breast Feeding
Limited 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 Aciclovir "Agepha" eye ointment would be insignificant. The use of Aciclovir "Agepha" eye ointment can be considered during breast feeding.

4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed.
Aciclovir "Agepha" eye ointment can affect visual ability and therefore caution is advised when driving or using machines.

4.8 Undesirable effects

Immediately after the application of the ophthalmic ointment, a temporary slight pricking or burning may occur but this may not interfere with the treatment.
Serious side effects after the use of systemically applied aciclovir are rare and most of the symptoms are reversible.

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)
Not known: frequency cannot be estimated from the available data.

Due to the nature of the side effects, it is not possible to clearly determine whether these reactions were caused by the disease or the administration of the drug. Post-marketing spontaneous reports served as the basis for assigning frequencies of side effects.

Immune system disorders:

Very rare: Immediate hypersensitivity reactions, including angioedema (Quincke's oedema, pale swelling of the skin especially in the face) and urticaria (hives)

Eye disorders:
Very common: Superficial punctate keratopathy. This did not necessitate an early termination of therapy and healed without sequelae.

Common: Transient mild stinging or burning 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 via HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; E-mail: medsafety@hpra.ie.

4.9 Overdose

No case of overdose has been reported. Even if the entire content of a 4.5 g tube of Aciclovir "Agepha" eye ointment, containing 135 mg aciclovir, is swallowed, no undesirable effects would be expected.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group:
Ophthalmologicals, antiinfectives, antivirals, Aciclovir

ATC-Code
S01AD03

Mechanism of action: Aciclovir is a purine nucleoside analogue and shows *in vitro* high activity against herpes simplex virus type 1 and 2, as well as against the Varicella-Zoster virus.

In the Herpes infected cells, aciclovir is phosphorylated to monophosphate by viral thymidine kinase in a first step. In further steps, it is converted to di- and triphosphate with participation of the cell's own enzyme. On the one hand, Acyclovir triphosphate inhibits the viral DNA polymerase and on the other hand it gets integrated into the viral DNA instead of deoxyguanosine triphosphate which results in a disruption of the viral DNA synthesis.
Due to the fact that aciclovir is preferentially taken up by Herpes infected cells and the selective conversionto the active triphosphate form, there is low toxicity to human cells that are not affected by the virus.

5.2 Pharmacokinetic properties

Absorption
Aciclovir is rapidly absorbed by the corneal epithelium and the superficial ocular tissues, penetrates into the aqueous humor and reaches there a therapeutic level of about 7.5 mmol/l.

Distribution
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.

Biotransformation
Aciclovir is metabolized by the enzyme aldehyde dehydrogenase to 9- Carboxymethoxymethylguanin.

Elimination
Aciclovir is excreted via the kidneys, both by glomerular filtration and tubular secretion.

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 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 rabbits, rats or mice.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

White soft paraffin.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

5 years.
Chemical and physical in-use stability has been demonstrated for 30 days at 25 °C.
From a microbiological point of view, once opened, the product may be stored for a maximum of 28 days at 25°C. Other in-use storage times and conditions are the responsibility of the user.

6.4 Special precautions for storage

Store below 25°C.

6.5 Nature and contents of container

White aluminium tube with internal epoxy phenol lacquer and white, HDPE cannula and cap containing 4.5 g ointment.

6.6 Special precautions for disposal

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

AGEPHA Pharma s.r.o.
Dialnicná cesta 5
Senec 90301
Slovakia

8 MARKETING AUTHORISATION NUMBER

PA22584/001/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 19th August 2019

10 DATE OF REVISION OF THE TEXT

April 2021