ACIVIR Cream (Aciclovir)

Composition

ACIVIR Cream

Aciclovir, BP ..... 5% w/w

In a cream base.....q.s.

Dosage Form

Cream

Pharmacology

Pharmacodynamics

Aciclovir is a synthetic purine nucleoside analogue with *in vitro* and *in vivo* inhibitory activity against herpes simplex virus type 1 (HSV-1) and type 2 (HSV-2), and varicella-zoster virus (VZV).

The inhibitory activity of aciclovir is highly selective due to its affinity for the enzyme thymidine kinase (TK) encoded by HSV and VZV. This viral enzyme converts aciclovir into aciclovir monophosphate, a nucleotide analogue. The monophosphate is further converted into diphosphate by cellular guanylate kinase and into triphosphate by a number of cellular enzymes. *In vitro*, aciclovir triphosphate stops replication of the herpes viral DNA. This is accomplished in three ways: 1) competitive inhibition of viral DNA polymerase; 2) incorporation into and termination of the growing viral DNA chain; and 3) inactivation of the viral DNA polymerase. The greater antiviral activity of aciclovir against HSV compared with VZV is due to its more efficient phosphorylation by the viral TK.

Pharmacokinetics

Adults: A clinical pharmacology study was performed with aciclovir cream in adult volunteers to evaluate the percutaneous absorption of aciclovir. In this study, which included 6 male volunteers, the cream was applied to an area of 710 cm^2 on the backs of the volunteers 5 times daily at intervals of 2 hours for a total of 4 days. The weight of cream applied and urinary excretion of aciclovir were measured daily. Plasma concentration of aciclovir was assayed 1 hour after the final application. The average daily urinary excretion of aciclovir was approximately 0.04% of the daily applied dose. Plasma aciclovir concentrations were below the limit of detection (0.01 µM) in 5 subjects and barely detectable (0.014 µM) in 1 subject. Systemic absorption of aciclovir from aciclovir cream is minimal in adults.

Paediatric Patients: The systemic absorption of aciclovir following topical application of cream has not been evaluated in patients less than 18 years of age.

Indications

ACIVIR Cream is indicated for the treatment of recurrent herpes labialis (cold sores) in adults and adolescents (12 years of age and older).

Dosage and Administration

ACIVIR Cream should be applied 5 times per day for 4 days. Therapy should be initiated as early as possible following onset of signs and symptoms (i.e. during the prodrome or when lesions appear). For adolescents 12 years of age and older, the dosage is the same as in adults.

Contraindications

ACIVIR Cream is contraindicated in patients with a known hypersensitivity to aciclovir, valaciclovir, or any component of the formulation.

Warnings and Precautions

ACIVIR Cream is intended for cutaneous use only and should not be used in the eyes or inside the mouth, nose or vagina as it may cause irritation. **ACIVIR Cream** should only be used on herpes labialis on the affected external aspects of the lips and face. Aciclovir cream has a potential for irritation and contact sensitization. The effect of aciclovir cream has not been established in immunocompromised patients.

Drug Interactions

Clinical experience has identified no interactions resulting from topical or systemic administration of other drugs concomitantly with aciclovir cream.

Pregnancy

Pregnancy Category B

The birth defects described amongst subjects exposed to aciclovir have not shown any uniqueness or consistent pattern to suggest a common cause. The use of aciclovir cream should be considered only when the potential benefits outweigh the possibility of unknown risks.

Lactation

It is not known whether topically applied aciclovir is excreted in breast milk. Systemic exposure following topical administration is minimal.

After oral administration of aciclovir, aciclovir concentrations have been documented in breast milk in 2 women and ranged from 0.6 to 4.1 times the corresponding plasma levels. These concentrations would potentially expose the nursing infant to a dose of aciclovir up to 0.3 mg/kg/day.

Nursing mothers who have active herpetic lesions near or on the breast should avoid nursing.

Paediatric Use

Safety and effectiveness in paediatric patients less than 12 years of age have not been established.

Geriatric Use

Clinical studies of aciclovir cream did not include sufficient numbers of subjects aged 65 years and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. Systemic absorption of aciclovir after topical administration is minimal.

Undesirable Effects

In five double-blind, placebo-controlled trials, 1,124 patients were treated with aciclovir cream and 1,161 with placebo (vehicle) cream. Aciclovir cream was well tolerated; 5% of patients on aciclovir cream and 4% of patients on placebo reported local application site reactions.

The most common adverse reactions at the site of topical application were dry lips, desquamation, dryness of skin, cracked lips, burning skin, pruritus, flakiness of skin, and stinging sensation on the skin; each event occurred in less than 1% of patients receiving aciclovir cream and vehicle. Treatment was discontinued by 3 patients on aciclovir cream and 1 patient on placebo due to an adverse event. An additional study, enrolling 22 healthy adults, was conducted to evaluate the dermal tolerance of aciclovir cream compared with vehicle, using a single occluded and semi-occluded patch testing methodology. Both aciclovir cream and vehicle showed a high and cumulative irritation potential. Another study, enrolling 251 healthy adults, was conducted to evaluate the contact sensitization potential of aciclovir cream using repeat insult patch testing methodology. Of 202 evaluable subjects, possible cutaneous sensitization reactions were observed in the same 4 (2%) subjects with both aciclovir cream and vehicle, and these reactions to both aciclovir cream and vehicle were confirmed in 3 subjects upon re-challenge. The sensitizing ingredient(s) has not been identified.

The safety profile in patients aged 12 to 17 years was similar to that observed in adults.

Observed During Clinical Practice

In addition to adverse events reported from clinical trials, the following events have been identified during post-approval use of aciclovir cream. Because they are reported voluntarily from a population of unknown size, estimates of frequency cannot be made.

These events have been chosen for inclusion due to a combination of their seriousness, frequency of reporting, or potential causal connection to aciclovir cream.

General

Angio-oedema, anaphylaxis.

Skin

Contact dermatitis, eczema, application site reactions including signs and symptoms of inflammation.

Overdosage

No untoward effects would be expected if the entire contents of a 10 g tube of aciclovir cream containing 500 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.

Shelf-Life

3 years

Storage and Handling Instructions

Store in a cool dry place.

Packaging Information

ACIVIR Cream: Tube of 5 g

Last Updated: *Aug 2012*
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