4000003727

Acylex

(Aciclovir) Tablets, Suspension, Cream and Ointment

Product Specifications: B.P.
Acylex Tablets 200 mg
Each film coated tablet contains: Aciclovir B.P. ..... 200 mg
Product contains Lactose
Acylex Tablets 400 mg
Each film coated tablet contains: Aciclovir B.P. ..... 400 mg
Product contains Lactose
Acylex Tablets 800 mg
Each film coated tablet contains: Aciclovir B.P. ..... 800 mg
Acylex Suspension 200 mg / 5 mL
Each 5 mL of suspension contains: Aciclovir B.P. ..... 200 mg
Acylex Cream 5% w/w
Each gram contains: Aciclovir B.P. ..... 50 mg
Product Specifications: U.S.P.
Acylex Ointment 5% w/w
Each gram contains: Acyclovir U.S.P. ..... 50 mg

DESCRIPTION

Aciclovir is a synthetic purine nucleoside analogue with in vitro and in vivo inhibitory activity against human herpes viruses, including herpes simplex virus (HSV) types I and II and varicella zoster virus (VZV).

CLINICAL PARTICULARS

Therapeutic indications

Tablets and Suspension

- Acylex (aciclovir) Tablets and Suspension are indicated for the treatment of herpes simplex virus infections of the skin and mucous membranes including initial and recurrent genital herpes (excluding neonatal HSV and severe HSV infections in immunocompromised children).
- Acylex (aciclovir) Tablets and Suspension are indicated for the suppression (prevention of recurrences) of recurrent herpes simplex infections in immunocompetent patients.
- Acylex (aciclovir) Tablets and Suspension are indicated for the prophylaxis of herpes simplex infections in immunocompromised patients.
- Acylex (aciclovir) Tablets and Suspension are indicated for the treatment of varicella (chickenpox) and herpes zoster (shingles) infections [Acylex tablets 800 mg are indicated for the treatment of varicella (chickenpox) and herpes zoster (shingles) infections (excluding neonatal HSV and severe HSV infections in immunocompromised children)].
- Acylex (aciclovir) 800mg tablets is recommended in children over the age of 6.

Ointment Acylex (aciclovir) Ointment is indicated in the management of initial genital herpes and in limited non-life-threatening mucocutaneous Herpes simplex virus infections in immunocompromised patients.

Cream Acylex (aciclovir) cream is indicated for the treatment of Herpes Simplex virus infections of the skin including initial and recurrent genital herpes and herpes labialis.

Posology and method of administration

Tablets and Suspension

Dosage in adults

Treatment of herpes simplex infections: 200 mg Acylex (aciclovir) should be taken five times daily at approximately four hourly intervals omitting the night time dose. Treatment should continue for 5 days, but in severe initial infections this may have to be extended.

In severely immunocompromised patients (e.g. after marrow transplant) or in patients with impaired absorption from the gut the dose can be doubled to 400 mg Acylex (aciclovir) or alternatively intravenous dosing could be considered.

Dosing should begin as early as possible after the start of an infection; for recurrent episodes this should preferably be during the prodromal period or when lesions first appear.

Treatment of Genital Herpes:

Initial Genital Herpes: 200 mg every 4 hours, 5 times daily for 10 days.

Chronic Suppressive Therapy for Recurrent Disease: 400 mg 2 times daily for up to 12 months, followed by re-evaluation. Alternative regimens have included doses ranging from 200 mg 3 times daily to 200 mg 5 times daily.

The frequency and severity of episodes of untreated genital herpes may change over time. After 1 year of therapy, the frequency and severity of the patient's genital herpes infection should be re-evaluated to assess the need for continuation of therapy with Acylex (aciclovir).

Intermittent Therapy: 200 mg every 4 hours, 5 times daily for 5 days. Therapy should be initiated at the earliest sign or symptom (prodrome) of recurrence.

Suppression of herpes simplex infections in immunocompetent patients: 200 mg Acylex (aciclovir) should be taken four times daily at approximately six-hourly intervals.

Many patients may be conveniently managed on a regimen of 400 mg Acylex (aciclovir) twice daily at approximately twelve-hourly intervals.

Dosage titration down to 200 mg Acylex (aciclovir) taken thrice daily at approximately eight-hourly intervals or even twice daily at approximately twelve-hourly intervals may prove effective.

Some patients may experience break-through infection on total daily doses of 800 mg Acylex (aciclovir).

Therapy should be interrupted periodically at intervals of six to twelve months, in order to observe possible changes in the natural history of the the disease.

Prophylaxis of herpes simplex infections in immunocompromised patients: 200 mg Acylex (aciclovir) should be taken four times daily at approximately six-hourly intervals.

In severely immunocompromised patients (e.g. after marrow transplant) or in patients with impaired absorption from the gut, the dose can be doubled to 400 mg Acylex (aciclovir), or alternatively, intravenous dosing could be considered.

The duration of prophylactic administration is determined by the duration of the period at risk.

Treatment of varicella and herpes zoster infections: 800 mg Acylex (aciclovir) should be taken five times daily at approximately four-hourly intervals, omitting the night time dose. Treatment should continue for seven days.

In severely immunocompromised patients (e.g. after marrow transplant) or in patients with impaired absorption from the gut, consideration should be given to intravenous dosing.

Dosing should begin as early as possible after the start of an infection: Treatment of herpes zoster yields better results if initiated as soon as possible after the onset of the rash. Treatment of chickenpox in immunocompetent patients should begin within 24 hours after onset of the rash.

Dosage in children

Treatment of herpes simplex infections, and prophylaxis of herpes simplex infections in the immunocompromised: Children aged two years and over should be given adult dosages and children below the age of two years should be given half the adult dose.

For treatment on neonatal herpes virus infections, intravenous aciclovir is recommended.

Treatment of varicella infection

6 years and over: 800 mg Acylex (aciclovir) four times daily.
2 - 5 years: 400mg Acylex (aciclovir) four times daily.
Under 2 years: 200mg Acylex (aciclovir) four times daily.
Treatment should continue for five days.

Dosing may be more accurately calculated as 20 mg/kg bodyweight (not to exceed 800 mg) Acylex (aciclovir) four times daily.

Children over 40 kg should receive the adult dose for chickenpox (varicella).

No specific data are available on the suppression of herpes simplex infections or the treatment of herpes zoster infections in immunocompetent children.

Dosage in the elderly

The possibility of renal impairment in the elderly must be considered and the dosage should be adjusted accordingly (see Dosage in renal impairment below).

Adequate hydration of elderly patients taking high oral doses of aciclovir should be maintained.

Dosage in renal impairment

Caution is advised when administering aciclovir to patients with impaired renal function. Adequate hydration should be maintained.

Dosage Modification for Renal Impairment:

Normal Dosage Regimen	Creatinine Clearance (mL/min/1.73 m^2)	Adjusted Dosage Regimen	
		Dose (mg)	Dosing Interval
200 mg every 4 hours	>10 0-10	200 200	every 4 hours, 5x daily every 12 hours
400 mg every 12 hours	>10 0-10	400 200	every 12 hours every 12 hours
800 mg every 4 hours	>25 10-25 0-10	800 800 800	every 4 hours, 5x daily every 8 hours every 12 hours

Ointment and cream

Adults and Children: Acylex (aciclovir) ointment or cream should be applied five times daily at approximately four hourly intervals, omitting the night time application. Acylex (aciclovir) ointment or cream should be applied to the lesions or impending lesions as soon as possible, preferably during the early stages (prodrome or erythema). Treatment can also be started during the later (papule or blister) stages.

Treatment should be continued for at least 4 days for herpes labialis and for 5 days for genital herpes. If healing has not occurred then treatment may be continued for up to an additional 5 days.

Method of administration

Acylex (aciclovir) tablets and suspension is for oral administration. Acylex (aciclovir) tablets should be swallowed whole with a little water. Ensure that patients on high doses of aciclovir are adequately hydrated. Acylex (aciclovir) ointment and cream are for topical administration; do not use in eyes.

CONTRAINDICATION

Hypersensitivity to aciclovir or valaciclovir, or to any of the excipients.

WARNINGS AND PRECAUTIONS

Tablets and suspension

Use in patients with renal impairment and in elderly patients

Aciclovir is eliminated by renal clearance; therefore the dose must be adjusted in patients with renal impairment. Elderly patients are likely to have reduced renal function and therefore the need for dose adjustment must be considered in this group of patients. Both elderly patients and patients with renal impairment are at increased risk of developing neurological side effects and should be closely monitored for evidence of these effects. Prolonged or repeated courses of aciclovir in severely immune-compromised individuals may result in the selection of virus strains with reduced sensitivity, which may not respond to continued aciclovir treatment.

Thrombotic thrombocytopenic purpura/hemolytic uremic syndrome (TTP/HUS), which has resulted in death, has occurred in immunocompromised patients receiving aciclovir therapy.

Hydration status: Care should be taken to maintain adequate hydration in patients receiving high doses of aciclovir.

The risk of renal impairment is increased by use with other nephrotoxic drugs.

The data currently available from clinical studies is not sufficient to conclude that treatment with aciclovir reduces the incidence of chickenpox-associated complications in immunocompetent patients.

Ointment and Cream: Aciclovir ointment and cream are not recommended for application to mucous membranes such as in the mouth, eye or vagina, as it may be irritant. Particular care should be taken to avoid accidental introduction into the eye. In severely immunocompromised patients (e.g. AIDS patients or bone marrow transplant recipients) oral Aciclovir dosing should be considered. Such patients should be encouraged to consult a physician concerning the treatment of any infection. Aciclovir ointment and cream contains a specially formulated base and should not be diluted or used as a base for the incorporation of other medicaments. Aciclovir cream has

a potential for irritation and contact sensitization. The effect of Aciclovir cream has not been established in immunocompromised patients.

Excipients: Aciclovir ointment and cream contains propylene glycol; propylene glycol may cause skin irritation. Do not use aciclovir cream or ointment in neonates with open wounds or large areas of broken or damaged skin (such as burns). Aciclovir cream contains 7.5 mg of sodium lauril sulfate per gram of product. Sodium lauril sulfate may cause local skin reactions (such as stinging or burning sensation) or increase skin reactions caused by other products when applied on the same area.

USE IN SPECIFIC POPULATIONS

Pregnancy The use of aciclovir should be considered only when the potential benefits outweigh the possibility of unknown risks.

Ointment and cream: The use of Aciclovir should be considered only when the potential benefits outweigh the possibility of unknown risks however the systemic exposure to aciclovir from topical application of Aciclovir ointment or cream is very low.

Teratogenicity: Effects in non-clinical studies were observed only at exposures considered sufficiently in excess of the maximum human exposure to indicate little relevance to clinical use.

Nursing Mothers Following oral administration of 200 mg Aciclovir five times a day, aciclovir has been detected in breast milk at concentrations ranging from 0.6 to 4.1 times the corresponding plasma levels. These levels would potentially expose nursing infants to aciclovir dosages of up to 0.3 mg/kg/day. Caution is therefore advised if aciclovir is to be administered to a nursing woman.

Ointment and cream: 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 Aciclovir ointment or cream would be insignificant.

Females and Males of Reproductive Potential 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.

Drug Interactions

Aciclovir is eliminated primarily unchanged in the urine via active renal tubular secretion. Any drugs administered concurrently that compete with this mechanism may increase aciclovir plasma concentrations. Probenecid and cimetidine increase the AUC of aciclovir by this mechanism, and reduce aciclovir renal clearance. Similarly increases in plasma AUCs of aciclovir and of the inactive metabolite of mycophenolate mofetil, an immunosuppresant agent used in transplant patients have been shown when the drugs are co-administered. However no dosage adjustment is necessary because of the wide therapeutic index of aciclovir.

An experimental study on five male subjects indicates that concomitant therapy with aciclovir increases AUC of totally administered theophylline with approximately 50%. It is recommended to measure plasma concentrations during concomitant therapy with aciclovir.

Ointment and cream: No clinically significant interactions have been identified when applied topically.

Adverse Reactions

The following convention has been used for the classification of undesirable effects in terms of frequency:- 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.

Tablets and Suspension

Common: Headache, dizziness, Nausea, vomiting, diarrhoea, abdominal pains, Pruritus, rashes (including photosensitivity), Fatigue, fever. Uncommon: Urticaria. Accelerated diffuse hair loss.

Rare: Dyspnoea, Anaphylaxis, Reversible rises in bilirubin and liver related enzymes, Angioedema, Increases in blood urea and creatinine. Very rare: Agitation, confusion, tremor, ataxia, dysarthria, hallucinations, psychotic symptoms, convulsions, somnolence, encephalopathy, coma, Anaemia, leukopenia, thrombocytopenia, Hepatitis, jaundice, Acute renal failure, renal pain.

Ointment and cream

Uncommon: Transient burning or stinging following application of Aciclovir ointment and cream, mild drying or flaking of the skin, itching.

Rare: Erythema, Contact dermatitis following application. Very rare: Immediate hypersensitivity reactions including angioedema and urticaria.

Post marketing experience (Aciclovir cream): Angioedema, anaphylaxis, Contact dermatitis, eczema.

EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

There have been no studies to investigate the effect of aciclovir on driving performance or the ability to operate machinery. A detrimental effect on such activities cannot be predicted from the pharmacology of the active substance, but the adverse event profile should be borne in mind.

OVERDOSAGE

Tablets and Suspension

Symptoms and signs: Aciclovir is only partly absorbed in the gastrointestinal tract. Patients have ingested overdoses of up to 20g aciclovir on a single occasion, usually without toxic effects. Accidental, repeated overdoses of oral aciclovir over several days have been associated with gastrointestinal effects (such as nausea and vomiting) and neurological effects (headache and confusion).

Management: Patients should be observed closely for signs of toxicity. Haemodialysis significantly enhances the removal of aciclovir from the blood and may, therefore, be considered a management option in the event of symptomatic overdose.

Ointment and cream

No untoward effects would be expected if the entire contents of a 10 gram tube of Aciclovir ointment or 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.

CLINICAL PHARMACOLOGY

Pharmacodynamics

The inhibitory activity of aciclovir for HSV I, HSV II and VZV is highly selective. The enzyme thymidine kinase (TK) of normal, uninfected cells does not use aciclovir effectively as a substrate, hence toxicity of mammalian host cells is low; however, TK encoded by HSV and VZV converts aciclovir to aciclovir monophosphate, a nucleoside analogue which is further converted to the diphosphate and finally to the triphosphate by cellular enzymes. Aciclovir triphosphate interferes with the viral DNA polymerase and inhibits viral DNA replication with resultant chain termination following its incorporation into the viral DNA.

Pharmacokinetics

Absorption: Aciclovir is only partially absorbed from the gut. Mean peak plasma concentrations (C_{ssmax}) increase to 0.7 microgram/ml (3.1 micromoles) at steady state following doses of 200 mg administered every four-hours. A less than proportional increase is observed for C_{ssmax} concentration following doses of 400 mg and 800 mg administered four-hourly, with values reaching 1.2 and 1.8 microgram/ml (5.3 and 8 micromoles), respectively.

Distribution: The mean volume of distribution of 26 L indicates that aciclovir is distributed within total body water. Apparent values after oral administration (Vd/F) ranged from 2.3 to 17.8 L/kg. Cerebrospinal fluid levels are approximately 50% of corresponding plasma concentration at steady-state. As plasma protein binding is relatively low (9 to 33%), drug interactions involving binding site displacement are not anticipated.

Biotransformation: Aciclovir is predominantly excreted unchanged by the kidney. 9-carboxymethoxymethyl-guanine is the only significant urinary metabolite of acyclovir and accounts for 10-15% of the dose excreted in the urine.

Elimination: In adults mean systemic exposure (AUC0-∞) to aciclovir ranges between 1.9 and 2.2 microgram*h/mL after a 200 mg dose. At this dose, the mean terminal plasma half-life after oral administration has been shown to vary between 2.8 and 4.1 hours. The half-life and total clearance of aciclovir are dependent on renal function. Therefore, dosage adjustment is recommended for renally impaired patients. There are no pharmacokinetic data for the oral formulation in neonates

Cream: Pharmacology studies have shown only minimal systemic absorption of aciclovir following repeated topical administration of Aciclovir cream.

Reporting of side effects

If you get any side effects, talk to your doctor, or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via our website: https://ferozsons-labs.com/safety-reporting-form/

By reporting side effects, you can help provide more information on the safety of this medicine.

HOW SUPPLIED

Acylex Tablets 200 mg: Pack of 25 Tablets
Acylex Tablets 400 mg: Pack of 20 Tablets
Acylex Tablets 800 mg: Pack of 10 Tablets
Acylex Suspension 200 mg / 5 mL: Pack of 60 ml
Acylex Cream 5% w/w: Pack of 10 gram
Acylex Ointment 5% w/w: Pack of 5 gram

STORAGE

Tablets: Do not store above 30°C.
Suspension: Store at or below 25°C in a dry place.
Cream: Do not store above 30°C.
Ointment: Store below 25°C.

The expiration date refers to the product correctly stored at the required condition.

INSTRUCTIONS

Keep away from heat, light and moisture.
Keep all medicines out of the reach of children.
To be sold on the prescription of a registered medical practitioner only.

Cream and Ointment are for external use only

Please read the contents cautiously before use.
This package insert is regularly and timely updated.

Manufactured by:
FEROZSONS LABORATORIES LIMITED
P. O. Ferozsons, Nowshera-Pakistan
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