105mm

105mm

170mm

Aciclovir

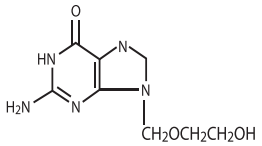
Hapivir

400 mg per 5 mL Suspension
Antiviral

PRODUCT DESCRIPTION:
This product contains aciclovir in a blue violet-colored, sweet grape-flavored suspension.

FORMULATION:
Each 5 mL (1 teaspoonful) contains:
Aciclovir, USP ..... 400 mg

PHARMACODYNAMICS AND PHARMACOKINETICS:
Aciclovir is a white, crystalline powder with the molecular formula $C_8H_{11}N_5O_3$ and a molecular weight of 225.2. The maximum solubility in water at 37°C is 2.5mg/mL. The pKa's of aciclovir are 2.27 and 9.25. The chemical name of aciclovir is 2-amino-1, 9-dihydro-9-[(2-hydroxyethoxy) methyl] 6H-purin-6-one; it has the following structure:



Aciclovir is a synthetic purine nucleoside analogue with in vitro and in vivo inhibitory activity against Herpes Simplex Viruses (HSV I & II) and Varicella Zoster Virus (VZV). The inhibitory activity of aciclovir is selective. The enzyme thymidine kinase (TK) converts aciclovir into ACV monophosphate, a nucleoside analogue, which is further converted to ACV diphosphate and finally to ACV triphosphate by cellular kinase. ACV triphosphate interferes with viral multiplication by blocking DNA polymerase, which leads to premature termination of DNA elongation, resulting to abnormal RNA production. The final result would be defective viral proteins, leading to reduced viral production.
Aciclovir is only partially absorbed in the gut. ACV is poorly water soluble and has poor oral bioavailability (15-30%); hence intravenous administration is necessary if high concentrations are required. ACV reaches its peak plasma concentration in 1-2 hrs. Only 9%-33% of ACV is protein bound in plasma, it is distributed with highest concentration in the kidney (10x of plasma concentration). The renal elimination of ACV is through glomerular filtration and tubular secretion.

INDICATIONS:
Hapivir suspension is indicated in the treatment of Herpes Simplex virus types 1 and 2 (cold sores and genital herpes) and Varicella Zoster virus (chickenpox and shingles) infections.

DOSAGE AND ADMINISTRATION:
Reference: The Sanford Guide to Antimicrobial Therapy, 39th edition, 2009
Recommended Dosage:
ADULT *For Genital Herpes:* 1 teaspoonful every 4 hours, 5 times daily for 10 days. If the herpes is recurrent, the usual adult dose is 400 mg (1 teaspoonful) 2 times daily for up to 12 months.
If genital herpes is intermittent, the usual adult dose is 200 mg or ½ teaspoon of suspension every 4 hours, 5 times a day for 5 days.
Therapy should be started at the earliest signs and symptoms.
For Herpes Zoster (Shingles): The usual adult dose is 800 mg or 2 teaspoonfuls every 4 hours, 5 times daily for 7 to 10 days.
For Chickenpox: The usual adult dose is 800 mg or 2 teaspoonfuls 4 times a day for 5 days.
If you have a kidney disorder, the dose will need to be adjusted by your doctor.
CHILDREN *For Chickenpox:* Recommended dosage of 20 mg/kg body weight for 4x (every 6 hrs) for 5 days, for children between 2-12 years of age.
Patient with Acute or Chronic Renal Impairment
In patients with renal impairment, the dose of Aciclovir (Hapivir 400 mg / 5 mL) Suspension should be modified as shown in Table 1.

Table 1. Dosage Modification for Renal Impairment

Normal Dose Regimen	Creatinine Clearance $\frac{mL}{min.1.73\ m^2}$	Adjusted Dosage Regimen	
		Dose (mg)	Dosing Interval
200 mg every 4 hours	>10	200	Every 4 hours 5x daily
	0-10	200	Every 12 hours
400 mg every 12 hours	>10	400	Every 12 hours
	0-10	200	Every 12 hours
800 mg every 4 hours	>25	800	Every 4 hours 5x daily
	10-25	800	Every 8 hours
	0-10	800	Every 12 hours

References: *Official (US) FDA Information on Aciclovir Dosage: http://www.drugs.com/dosage/acyclovir.html#Renal_Dose_Adjustment*
Hemodialysis:
For patients who require hemodialysis, the mean plasma half-life of aciclovir during hemodialysis is approximately 5 hours. This results in a 60% decrease in plasma concentration following a 6-hour dialysis. Therefore, the patient's dosing schedule should be adjusted so that an additional dose is administered after each dialysis.

Peritoneal Dialysis:
No supplemental dose appears to be necessary after adjustment of the dosing interval.

CONTRAINDICATIONS:
Hapivir suspension is contraindicated in patients who develop hypersensitivity to the components of the formulation.

WARNINGS:
Hapivir suspension is intended *for oral use only*.

PRECAUTIONS:
General: The recommended dosage, frequency of applications, and length of treatment should not be exceeded (see DOSAGE AND ADMINISTRATION). There are no data to support the use of aciclovir to prevent transmission of infection to other person or prevent recurrent infections when administered in the absence of signs and symptoms. Clinically significant viral resistance associated with the use of aciclovir has not been observed, this possibility exists.
Carcinogenesis, Mutagenesis, Impairment of Fertility: Since aciclovir can also be incorporated into cellular DNA, it is a chromosome mutagen, therefore, its use should be avoided during pregnancy. However it has not been shown to cause any teratogenic or carcinogenic effects and is frequently prescribed for pregnant women.
Pregnancy: Teratogenic Effects: Pregnancy Category B. Aciclovir was not teratogenic in mouse, rabbit, or rat at exposures greatly in excess of human levels. There are no adequate and well-controlled studies of systemic aciclovir use in pregnant women.
Nursing Mothers: After oral administration, 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 per day. Nursing mothers, who have active herpetic lesions near or on the breast should avoid nursing.
Geriatric Use: Clinical studies of aciclovir did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger.
Pediatric Use: Safety and effectiveness in pediatric patients younger than 2 years of age have not been established.
Patients with renal impairment often exhibit elimination half-lives for the drug that are 5-6 times longer than in those with normal renal function, leading to accumulation of aciclovir in the plasma and the likelihood of development of toxic reactions such as lethargy, confusion and myoclonus.

DRUG INTERACTIONS: Probenecid reduces the renal clearance of aciclovir. Concurrent use with other nephrotoxic drugs may increase the risk of adverse renal effects.

ADVERSE REACTIONS:
Common adverse drug reactions (≥1% of patients) associated with systemic aciclovir therapy (oral or IV) include: nausea, vomiting, diarrhea and/or headache. In high doses, hallucinations have been reported. In frequent adverse effects (0.1–1% of patients) include: agitation, vertigo, confusion, dizziness, oedema, arthralgia, sore throat, constipation, abdominal pain, rash and/or weakness. Rare adverse effects (<0.1% of patients) include: coma, seizures, neutropenia, leukopenia, crystalluria, anorexia, fatigue, hepatitis, Stevens-Johnson syndrome, toxic epidermal necrolysis and/or anaphylaxis. In the controlled clinical trials, mild pain (including transient burning and stinging) was reported by about 30% of patients in both the active and placebo arms; treatment was discontinued in 2 of these patients. Local pruritus occurred in 4% of these patients. In all studies, there was no significant difference between the drug and placebo group in the rate or type of reported adverse reactions nor were there any differences in abnormal clinical laboratory findings.

OVERDOSE AND TREATMENT:
Overdose of aciclovir is unlikely to happen. The acute toxicity (LD50) of aciclovir may occur when given orally for more than 1000mg/kg. In rare cases, some patients may show overdose symptoms such as convulsions, hallucinations and decreased urination.
When the symptoms stated above occur, contact your health care provider or your local poison control center immediately.

STORAGE CONDITIONS:
Store at temperatures not exceeding 30°C.

AVAILABILITY:
Box of 1's; 60 mL amber glass bottle (Type III) with LDPE Flip-off Cap

CAUTION:
Foods, Drugs, Devices, and Cosmetics Act prohibits dispensing without prescription.

ADR REPORTING STATEMENT:
"For suspected adverse drug reaction, report to the FDA: www.fda.gov.ph". Seek medical attention immediately at the first sign of any adverse drug reaction.

You may also call (+632) 817 6695 to 96 or email us at feedback@folaresphama.com

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