

**Acyclovir**®  
(Acyclovir)  
200mg/5mL  
Oral Suspension U.S.P.  
400mg  
800mg  
Tablets U.S.P.  
**250mg, 500mg**  
For Injection U.S.P.  
For I.V. Infusion Only

ایکلوویر  
(ایسائیکلوویر)  
200mg/5mL  
اورال سسپنشن یو.س.پ.  
400mg  
800mg  
ٹیبلٹس یو.س.پ.  
250mg, 500mg  
ایکلوویر  
ایسائیکلوویر

موسمی بیماریوں کے لیے

#### QUALITATIVE AND QUANTITATIVE COMPOSITION

**Acyclovir Tablets U.S.P. 400mg**  
Each tablet contains: Acyclovir U.S.P. ....400mg

**Acyclovir Tablets U.S.P. 800mg**  
Each tablet contains: Acyclovir U.S.P. ....800mg

**Acyclovir Oral Suspension U.S.P. 200mg/5mL:**  
Each 5mL contains: Acyclovir U.S.P. ....200mg

**Acyclovir For Injection U.S.P. 250mg:**  
Each vial contains: Acyclovir Sodium eq. to Acyclovir.....250mg

**Acyclovir For Injection U.S.P. 500mg:**  
Each vial contains: Acyclovir Sodium eq. to Acyclovir.....500mg

#### DESCRIPTION

Acyclovir is a synthetic analogue of guanidine used in the treatment and prophylaxis of infections due to herpes simplex or varicella zoster viruses.

#### CLINICAL PHARMACOLOGY

**Mechanism of Action:** Acyclovir is a synthetic purine nucleoside analogue with in vitro and in vivo inhibitory activity against herpes simplex virus types 1 (HSV-1), 2 (HSV-2), and varicella-zoster virus (VZV). Acyclovir is a synthetic purine nucleoside analogue with in vitro and in vivo inhibitory activity against human herpes viruses, including Herpes simplex virus (HSV) types 1 and 2 and Varicella zoster virus (VZV), Epstein Barr virus (EBV) and Cytomegalovirus (CMV)

**Pharmacodynamics:** In cell culture acyclovir has the greatest antiviral activity against HSV-1, followed (in decreasing order of potency) by HSV-2, VZV, EBV, and CMV.

**Pharmacokinetics: Absorption:** Acyclovir is slowly and incompletely absorbed from the gastrointestinal tract. The peak plasma concentration occurs about 2 hours following ingestion. The pharmacokinetics of acyclovir after intravenous administration: after single doses ranging from 0.5 to 15 mg/kg and after multiple doses ranging from 2.5 to 15 mg/kg every 8 hours.

**Distribution:** Protein binding is reported to range from 9-33%. Acyclovir crosses the placenta and is excreted in breast milk in concentrations approximately 3 times higher than those in maternal serum.

**Metabolism and Elimination:** Renal excretion is the major route of elimination by both glomerular filtration and tubular secretion. The terminal or beta-phase half-life is reported to be about 2-3 hours for adults without renal impairment. In adults, the terminal plasma half-life of acyclovir after administration of acyclovir for infusion is about 2.9 hour. Most of the drug is excreted unchanged by the kidney.

#### INDICATIONS AND USAGE

**Acyclovir is indicated for:** the acute treatment of herpes zoster (shingles), initial episodes and the management of recurrent episodes of genital herpes, chickenpox (varicella), herpes Simplex Infections in immunocompromised patients, Herpes Simplex Encephalitis, Neonatal Herpes Simplex Virus Infection, Varicella-Zoster Infections in Immunocompromised Patients.

**CONTRAINDICATIONS:** Acyclovir is contraindicated for patients who develop hypersensitivity to acyclovir or valacyclovir.

**INTERACTIONS:** • Acyclovir is eliminated primarily unchanged in the urine via active renal tubular secretion. Any drugs administered concurrently that compete with this mechanism may increase Acyclovir plasma concentrations.

• **Cyclosporine:** There has been a small number of transplant patients with increased serum levels of cyclosporine and signs of nephrotoxicity when acyclovir is given concurrently. Renal function should be monitored closely in patients taking both drugs.

• **Cimetidine and probenecid:** Cimetidine and probenecid increase the AUC of Acyclovir by competing for active secretion by the renal tubules and reduce acyclovir renal clearance. Dosage adjustment is usually not necessary because of the wide therapeutic index of

Acyclovir.

• **Mycophenolate mofetil:** Coadministration of acyclovir and mycophenolate mofetil causes increase in plasma AUCs of acyclovir and of the inactive metabolite of mycophenolate mofetil.

• An experimental study indicates that concomitant therapy with acyclovir increases AUC of totally administered theophylline with approximately 50%.

#### USE IN SPECIFIC POPULATION

**Pregnancy:** Category B: Acyclovir should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus

**Nursing mothers:** Acyclovir should be administered to a nursing mother with caution and only when indicated.

**Pediatric Use:** Safety and effectiveness of oral formulations of acyclovir in pediatric patients younger than 2 years of age have not been established.

#### WARNINGS AND PRECAUTIONS

**-Renal Patients:** The risk of renal impairment is increased by use with other nephrotoxic drugs. Acyclovir is eliminated by renal clearance; therefore, the dose must be reduced in patients with renal impairment.

**-Elderly patients:** are likely to have reduced renal function and therefore the need for dose reduction 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.

**-Immunocompromised individuals:** Prolonged or repeated courses of acyclovir in severely immunocompromised individuals may result in the selection of virus strains with reduced sensitivity, which may not respond to con-tinued acyclovir treatment.

**-Hydration status:** Care should be taken to maintain adequate hydration in patients receiving higher dose oral regimens or i.e., e.g. for the treatment of herpes zoster infection (4g daily), in order to avoid the risk of possible renal toxicity.

**-Acyclovir for infusion:** contains no antimicrobial preservative. Reconstitution and dilution should therefore be carried out under full aseptic conditions immediately before use and any unused solution discarded. This vial contains approximately 26mg of sodium in total. The sodium content should be taken into consideration when prescribing to patients requiring sodium restriction. -Approximately 1% of patients receiving intravenous acyclovir have manifested ncephalopathic changes characterized by either lethargy, obtundation, tremors, confusion, hallucinations, agitation, seizures, or coma. Acyclovir should be used with caution in those patients who have underlying neurologic abnormalities and those with serious renal, hepatic, or electrolyte abnormalities, or significant hypoxia

#### ADVERSE REACTIONS

**General:** Anaphylaxis, alopecia, angioedema, fatigue, fever, headache, pain, peripheral edema.

**Nervous:** Aggressive behavior, agitation, ataxia, coma, confusion, decreased consciousness, delirium, drowsiness, dizziness, dysarthria, encephalopathy, hallucinations, paresthesia, psychosis, seizure, somnolence, tremors. These symptoms may be marked, particularly in older adults or in patients with renal impairment.

**Digestive:** Diarrhea, gastrointestinal distress, nausea. Hematologic and Lymphatic: Anemia, leukocytoclastic vasculitis, leukopenia, lymphadenopathy, thrombocytopenia. Hepatobiliary Tract and Pancreas: Elevated liver function tests, hepatitis, hyperbilirubinemia, jaundice. Musculoskeletal: Myalgia. Skin: Erythema multiform, photosensitive rash, pruritus, rash, Stevens-Johnson syndrome, toxic epidermal necrolysis, urticaria. **Special Senses:** Visual abnormalities.

**Urogenital:** Renal failure, renal pain, elevated blood urea nitrogen, elevated creatinine, hematuria & crystalluria

#### DOSAGE AND ADMINISTRATION

##### Acyclovir (Acyclovir) Tablets & Suspension:

**Acute Treatment of Herpes Zoster:** 800 mg every 4 hours orally, 5 times daily for 7 to 10 days. **Genital Herpes:** Treatment of 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 Acyclovir.

**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. Treatment of Chickenpox: Children (2 years of age and older): 20 mg/kg per dose orally 4 times daily (80 mg/kg/day) for 5 days. Children over 40 kg should receive the adult dose for chickenpox.

**Adults and Children over 40 kg:** 800 mg 4 times daily for 5 days. Intravenous Acyclovir is indicated for the treatment of varicella-zoster infections in immunocompromised patients. When therapy is indicated, it should be initiated at the earliest sign or symptom of chickenpox. There is no information about the efficacy of therapy initiated more than 24 hours after onset of signs and symptoms.

Patients with Acute or Chronic Renal Impairment: In patients with renal impairment, the dose of Acyclovir Capsules, Tablets, or Suspension should be modified as shown in Table:

Table. Dosage Modification for Renal Impairment

Normal Dosage Regimen	Creatinine clearance (ml/min/1.73m <sup>2</sup> )	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

In patients with renal impairment, the dose of Acyclovir Capsules, Tablets, or Suspension should be modified as shown in Table:

**Aclovir (Acyclovir) For Injection: Caution:** Rapid or bolus intravenous injection and intramuscular or subcutaneous injection must be avoided. Therapy should be initiated as early as possible following onset of signs and symptoms of herpes infections. A maximum dose equivalent to 20 mg/kg every 8 hours should not be exceeded for any patient.

**Herpes Simplex Infections:** Mucosal and Cutaneous Herpes Simplex (HSV-1 and HSV-2) Infections in Immunocompromised Patients: Adults and Adolescents (12 years of age and older): 5 mg/kg infused at a constant rate over 1 hour, every 8 hours for 7 days.

**Pediatrics (Under 12 years of age):** 10 mg/kg infused at a constant rate over 1 hour, every 8 hours for 7 days. Severe Initial

**Clinical Episodes of Herpes Genitalis:** Adults and Adolescents (12 years of age and older): 5 mg/kg infused at a constant rate over 1 hour, every 8 hours for 5 days.

**Herpes Simplex Encephalitis:** Adults and Adolescents (12 years of age and older): 10 mg/kg infused at a constant rate over 1 hour, every 8 hours for 10 days.

**Pediatrics (3 months to 12 years of age):** 20 mg/kg infused at a constant rate over 1 hour, every 8 hours for 10 days. Neonatal Herpes Simplex Virus Infections (Birth to 3 months): 10 mg/kg infused at a constant rate over 1 hour, every 8 hours for 10 days. In neonatal herpes, simplex infections, doses of 15 mg/kg or 20 mg/kg (infused at a constant rate over 1 hour every 8 hours) have been used; the safety and efficacy of these doses are not known. Varicella Zoster Infections: Zoster in Immunocompromised Patients: Adults and Adolescents (12 years of age and older): 10 mg/kg infused at a constant rate over 1 hour, every 8 hours for 7 days.

**Pediatrics (Under 12 years of age):** 20 mg/kg infused at a constant rate over 1 hour, every 8 hours for 7 days.

**Obese Patients:** Obese patients should be dosed at the recommended adult dose using Ideal Body Weight.

Table 5. Dosage Adjustments for Patients with Renal Impairment

Creatinine Clearance (ml/min/1.73 m <sup>2</sup> )	Percent of Recommended Dose	Dosing Interval (hours)
>50	100%	8
25-50	100%	12
10-25	100%	24
0-10	50%	24

## OVERDOSAGE

Adverse events that have been reported in association with overdosage include agitation, coma, seizures, and lethargy. Precipitation of acyclovir in renal tubules may occur when the solubility (2.5 mg/mL) is exceeded in the intratubular fluid. Overdosage has been reported following bolus injections or inappropriately high doses and in patients whose fluid and electrolyte balance were not properly monitored. This has resulted in elevated Blood Urea Nitrogen (BUN) and serum creatinine and subsequent renal failure. In the event of acute renal failure and anuria, the patient may benefit from hemodialysis until renal function is restored.

## INSTRUCTIONS

Dosage as directed by the physician.

Store at 15°C - 25°C. Protect from light and moisture. Keep all medicines out of the reach of children.

## PRESENTATION

Aclovir (Acyclovir) Tablets U.S.P 400mg are available in Alu-Alu blister pack of 5 x 7's along with leaflet.

Aclovir (Acyclovir) Tablets U.S.P 800mg are available in Alu-Alu blister pack of 2 x 10's along with leaflet.

Aclovir (Acyclovir) Oral Suspension U.S.P 200mg/5mL is available in 60mL Amber PET bottle along with leaflet.

Aclovir (Acyclovir) for Injection U.S.P 250mg is available in pack of 1 Vial + 10mL Sterile Water for Injection with Leaflet.

Aclovir (Acyclovir) for Injection U.S.P 500mg is available in pack of 1 Vial + 10mL Sterile Water for Injection with Leaflet.

علامات اور طریقہ استعمال: اکلو ویر ہرپس زوسٹر، چیکن پاکس، ہرپس سیمپلکس

انسینفا لائیس وور سیلا زوسٹر کے علاج کیلئے تجویز کردہ ہے۔

مضمر اثرات: گھٹین، تمکھن، بخار، سردرد، متلی، دست، خارش، رگڑ، پروردنڈ۔

احتیاطی تدابیر: حاملہ خواتین اور دودھ پلانے والی ماں میں ضرورت پڑنے کے

پیش نظر صرف ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔ بچے بزرگ اور

جگر کے امراض میں مبتلا مریض صرف ڈاکٹر کے مشورے کے مطابق

استعمال کریں۔ سوڈیم کی موجودگی کے پیش نظر سوڈیم کنٹرولڈ ڈاٹ ایف کے

مریض ایلکو اور فیوژن کا استعمال صرف ڈاکٹر کی ہدایت کے مطابق کریں۔

ہدایات:

خوراک ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔

15 سے 25 ڈگری سینٹی گریڈ پر رکھیں۔

اور سل سپینش کوروشنی سے محفوظ رکھیں۔

روشنی اور نمی سے محفوظ رکھیں۔

تمام دوائیں بچوں کی پہنچ سے دور رکھیں۔

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