IV Injection

Hypovir

Lyophilized Powder for Solution for Infusion

ہائپوور آئی وی انجکشن

(Acyclovir for Injection USP)

(ایسائیکلوویر USP) لائیوفلائیزڈ پاؤڈر برائے سلوشن برائے انفیوژن

COMPOSITION: Each vial contains:
Acyclovir USP … 250mg
(As the Sodium Salt) [USP Specs.]

Each vial contains:
Acyclovir USP … 500mg
(As the Sodium Salt) [USP Specs.]

PHARMACODYNAMICS: Mechanism of Antiviral Action: Acyclovir Sodium 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). The inhibitory activity of Acyclovir is highly selective due to its affinity for the enzyme Thymidine Kinase (TK) encoded by HSV and VZV. This viral enzyme converts Acyclovir into Acyclovir 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, Acyclovir triphosphate stops replication of herpes viral DNA. This is accomplished in 3 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.

PHARMACOKINETICS: Average steady-state peak and trough concentrations from 1-hour infusions administered every 8 hours are given in Table.

Dosage Regimen	C^{SS} max	C^{SS} trough
5mg/kg q 8 hr (n = 8)	9.8mcg/ml range: 5.5 to 13.8	0.7mcg/ml range: 0.2 to 1.0
10mg/kg q 8 hr (n = 7)	22.9 mcg/ml range: 14.1 to 44.1	1.9mcg/ml range: 0.5 to 2.9

Plasma protein binding is relatively low (9% to 33%) and drug interactions involving binding site displacement are not anticipated. Renal excretion of unchanged drug is the major route of Acyclovir elimination accounting for 62% to 91% of the dose. The only major urinary metabolite detected is 9-carboxymethoxymethylguanine accounting for up to 14.1% of the dose in patients with normal renal function.

INDICATIONS: It is indicated for the treatment of Herpes simplex infections in immunocompromised patients and severe initial genital herpes in the non-immunocompromised, the prophylaxis of Herpes simplex infections in immunocompromised patients, treatment of shingles (Varicella zoster virus) in immunocompetent patients in whom a serious course of the illness can be anticipated, treatment of initial and recurrent Varicella zoster infections in immunocompromised patients, the treatment of Herpes encephalitis, the treatment of Herpes simplex infections in the neonate and infant up to 3 months of age.

DOSAGE AND ADMINISTRATION:
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): 5mg/kg infused at a constant rate over 1 hour, every 8 hours for 7 days.
Pediatrics (Under 12 years of age): 10mg/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): 5mg/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): 10mg/kg infused at a constant rate over 1 hour, every 8 hours for 10 days.
Pediatrics (3 months to 12 years of age): 20mg/kg infused at a constant rate over 1 hour, every 8 hours for 10 days.
Neonatal Herpes Simplex Virus Infections (Birth to 3 months): 10mg/kg infused at a constant rate over 1 hour, every 8 hours for 10 days. In neonatal herpes simplex infections, doses of 15mg/kg or 20mg/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): 10mg/kg infused at a constant rate over 1 hour, every 8 hours for 7 days.
Pediatrics (Under 12 years of age): 20mg/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.

Creatinine Clearance (ml/min/1.73m²)	Percent of Recommended Dose	Dosing Interval (hours)
> 50	100%	8
25-50	100%	12
10-25	100%	24
0-10	50%	24

Hemodialysis: For patients who require dialysis, the mean plasma half-life of Acyclovir during hemodialysis is approximately 5 hours. This results in a 60% decrease in plasma concentrations following a 6-hour dialysis period. Therefore, the patient's dosing schedule should be adjusted so that an additional dose is administered after each dialysis.

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

Method of Preparation: Each 10ml vial contains Acyclovir USP 250mg or 500mg (As the Sodium Salt). The contents of the vial should be dissolved in Sterile Water for Injection as follows:

Contents of Vial	Amount of Diluent
250mg	10ml
500mg	10ml

The resulting solution in each case contains 50mg Acyclovir per ml (pH approximately 11). Shake the vial well to assure complete dissolution before measuring and transferring each individual dose. The reconstituted solution should be used within 12 hours. Refrigeration of reconstituted solution may result in the formation of a precipitate which will redissolve at room temperature. DO NOT USE BACTERIOSTATIC WATER FOR INJECTION CONTAINING BENZYL ALCOHOL OR PARABENS.

Administration: The calculated dose should then be removed and added to any appropriate intravenous solution at a volume selected for administration during each 1-hour infusion. Infusion concentrations of approximately 7mg/ml or lower are recommended. Higher concentrations (e.g., 10mg/ml) may produce phlebitis or inflammation at the injection site upon inadvertent extravasation. Standard, commercially available electrolyte and glucose solutions are suitable for intravenous administration; biologic or colloidal fluids (e.g., blood products, protein solutions, etc.) are not recommended. Once diluted for administration, each dose should be used within 24 hours.

CONTRA-INDICATIONS: Hypersensitivity to the active substance Acyclovir, or Valacyclovir, or to any of the excipients.

ADVERSE EFFECTS: The common side effects are: phlebitis, dyspnea, nausea, vomiting, reversible increases in liver-related enzymes, pruritus, urticaria, rashes (including photosensitivity), increases in blood urea and creatinine. Rapid increases in blood urea and creatinine levels are believed to be related to the peak plasma levels and the state of hydration of the patient. To avoid this effect the drug should not be given as an intravenous bolus injection but by slow infusion over a one-hour period.

OVERDOSAGE: Overdosage of intravenous Acyclovir has resulted in elevations of serum creatinine, blood urea nitrogen and subsequent renal failure. Neurological effects including confusion, hallucinations, agitation, seizures and coma have been described in association with overdosage.

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

WARNING & PRECAUTION: Adequate hydration should be maintained in patients. Intravenous doses should be given by infusion over one hour to avoid precipitation of Acyclovir in the kidney; rapid or bolus injection should be avoided. The risk of renal impairment is increased by use with other nephrotoxic drugs. Care is required if administering IV Acyclovir with other nephrotoxic drugs. Contact with the eyes and the unprotected skin must be avoided.

Use in patients with renal impairment and in elderly patients: Acyclovir is eliminated by renal clearance, therefore the dose must be reduced in patients with renal impairment.

Dosage in the elderly: In the elderly, total Acyclovir body clearance declines in parallel with creatinine clearance. Special attention should be given to dosage reduction in elderly patients with impaired creatinine clearance. 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. Reconstituted Acyclovir has a pH of approximately 11 and should not be administered by mouth.

INTERACTION: 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, e.g probenecid and cimetidine. However, no dosage adjustment is necessary because of the wide therapeutic index of Acyclovir. Increases in plasma AUCs of Acyclovir and of the inactive metabolite of mycophenolate mofetil, an immunosuppressant agent used in transplant patients have been shown when the drugs are coadministered. If lithium is administered concurrently with high dose Acyclovir IV, the lithium serum concentration should be closely monitored because of the risk of lithium toxicity. Care is also required (with monitoring for changes in renal function) if administering intravenous Acyclovir with drugs which affect other aspects of renal physiology (e.g. ciclosporin, tacrolimus).

FERTILITY, PREGNANCY AND LACTATION: The use of Acyclovir should be considered only when the potential benefits outweight the possibility of unknown risks.

Fertility: There is no information on the effect of Acyclovir on human female fertility.

EFFECTS ON ABILITY TO DRIVE AND USE MACHINES: Acyclovir IV for infusion is generally used in an in-patient hospital population and information on ability to drive and operate machinery is not usually relevant.

INSTRUCTIONS: Store below 25°C. Protect from heat, light and moisture. Keep out of the reach of children.

PRESENTATION: Hypovir 250mg & 500mg IV Injection (Lyophilized Powder for Solution for Infusion) is available in pack of 1's with 10ml Water for Injection.

ہدایات: ۲۵ ڈگری سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔ گرمی، روشنی اور نمی سے بچائیں۔ بچوں کی پہنچ سے دور رکھیں۔

Manufactured by:
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