Hypovir

Tablets / Oral Suspension

ہائپوور گولیاں/اورل سسپنشن

(ایسائیکلوور یو ایس پی)

(Acyclovir Tablets / Oral Suspension USP)

COMPOSITION:

Tablets:
Each tablet contains:
Acyclovir USP… 400mg & 800mg.
[USP Specs.]

Oral Suspension
Each 5ml contains:
Acyclovir USP … 200mg
[USP Specs.]

INDICATIONS:

HYPOVIR Tablets and Oral Suspension is indicated for the acute treatment of herpes zoster (shingles), suppression (prevention of recurrence) of recurrent infections and prophylaxis of herpes simplex virus infection in immunocompromised patients, initial episodes and the management of recurrent episodes of genital herpes and for the treatment of chickenpox (varicella).

PHARMACODYNAMICS:

Mechanism of Action: 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 I and II and varicella zoster virus (VZV). The inhibitory activity of Acyclovir for HSV I, HSV II and VZV is highly selective. Acyclovir triphosphate interferes with the viral DNA polymerase and inhibits viral DNA replication with resultant chain termination following its incorporation into the viral DNA.

PHARMACOKINETICS: The pharmacokinetics of Acyclovir after oral administration have been evaluated in healthy volunteers and in immunocompromised patients with herpes simplex or varicella-zoster virus infection. Acyclovir pharmacokinetic parameters are: Plasma protein binding 9% to 33%, plasma elimination half-life 2.5 to 3.3 hr. Average oral bioavailability 10% to 20% *(*Bioavailability decreases with increasing dose). In one multiple-dose, it was shown that increases in plasma acyclovir concentrations were less than dose proportional with increasing dose. The only known urinary metabolite is 9-[(carboxymethoxy) methyl] guanine.

Special Populations: Adults with Impaired Renal Function: The half-life and total body clearance of Acyclovir are dependent on renal function. A dosage adjustment is recommended for patients with reduced renal function.

Geriatrics: Acyclovir plasma concentrations are higher in geriatric patients compared to younger adults, in part due to age-related changes in renal function. Dosage reduction may be required in geriatric patients with underlying renal impairment.

Pediatrics: In general, the pharmacokinetics of Acyclovir in pediatric patients is similar to that of adults. Mean half-life after oral doses of 300mg/m^2 and 600mg/m^2 in pediatric patients aged 7 months to 7 years was 2.6 hours (range 1.59 to 3.74 hours).

DOSAGE AND ADMINISTRATION:

There was no effect of food on the absorption of Acyclovir, therefore. **HYPOVIR Tablets and Oral Suspension** may be administered with or without food.

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

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

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

Intermittent Therapy: 200mg 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): 20mg/kg per dose orally 4 times daily (80mg/kg/day) for 5 days. Children over 40kg should receive the adult dose for chickenpox.

Adults and Children over 40Kg: 800mg 4 times daily for 5 days.

Patients with Acute or Chronic Renal Impairment: In patients with renal impairment, the dose of **HYPOVIR Tablets or Suspension** should be modified as shown in Table 1:

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

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 (2.5mg/ml) is exceeded in the intratubular fluid.

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Overdosage has been reported following inappropriately high doses and in patients whose fluid and electrolyte balance were not properly monitored. This has resulted in elevated 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.

CONTRAINDICATIONS:
HYPOVIR Tablets and Oral Suspension is contraindicated for patients who develop hypersensitivity to Acyclovir or any of the excipients.

WARNING & PRECAUTION:
Use in patients with renal impairment and in elderly patients: Acyclovir 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 Acyclovir in severely immune-compromised individuals may result in the section of virus strains with reduced sensitivity, which may not respond to continued acyclovir treatment.
Hydration status: Care should be taken to maintain adequate hydration in patients receiving high oral doses of Acyclovir. The risk of renal impairment is increased by use with other nephrotoxic drugs.

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. Probenecid and Cimetidine increase the AUC of Acyclovir by this mechanism, and reduce Acyclovir renal clearance. Similarly 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. However, no dosage adjustment is necessary because of the wide therapeutic index of Acyclovir. It is recommended to measure plasma concentrations during concomitant therapy with Acyclovir.

FERTILITY, PREGNANCY AND LACTATION:
Pregnancy: The occurrence rate of birth defects approximates that found in the general population. However, the small size of the registry is insufficient to evaluate the risk for less common defects or to permit reliable or definitive conclusions regarding the safety of Acyclovir in pregnant women and their developing fetuses. **HYPOVIR Tablets and Oral Suspension** should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.
Breast-feeding: HYPOVIR Tablets and Oral Suspension should be administered to a nursing mother with caution and only when indicated.
Fertility: There is no evidence that **HYPOVIR Tablets and Oral Suspension** has any effect on female human fertility.

EFFECTS ON ABILITY TO DRIVE AND USE OF MACHINES:
There have been no studies to investigate the effect of Acyclovir on driving performance or the ability to operate machinery. Further, a detrimental effect on such activities cannot be predicted from the pharmacology of the active substance.

SIDE EFFECTS:
General: Anaphylaxis, angioedema, fever, headache, pain and peripheral edema.
Nervous: Aggressive behavior, agitation, ataxia, coma, confusion, decreased consciousness, delirium, dizziness, dysarthria, encephalopathy, hallucinations, paresthesia, psychosis, seizure, somnolence and 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 and thrombocytopenia.
Hepatobiliary Tract and Pancreas: Elevated liver function tests, hepatitis and hyperbilirubinemia and jaundice.
Musculoskeletal: Myalgia.
Skin: Alopecia, erythema multiforme, photosensitive rash, pruritus, rash, Stevens-Johnson syndrome, toxic epidermal necrolysis and urticaria.
Special Senses: Visual abnormalities.
Urogenital: Renal failure, elevated blood urea nitrogen, elevated creatinine and hematuria.

INSTRUCTIONS: Store below 30°C. Protect from heat, light and moisture. Keep out of the reach of children. Keep the bottle tightly closed. Do not freeze.

PRESENTATION:
Hypovir Tablets 400mg & 800mg are available in the pack size of 35's and 20's respectively.
Hypovir Oral Suspension 200mg/5ml is available in pack size of 60ml.

ہدایات: ۳۰ ڈگری سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔ گرمی، روشنی اور نمی سے بچائیں۔ بچوں کی پہنچ سے دور رکھیں۔ استعمال کے بعد ڈھکن کو اچھی طرح بند کردیں۔ منجمد ہونے سے بچائیں۔

Manufactured by:
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