five times daily for 5 days has been recommended, preferably begun during the prodromal period.
For *prophylaxis* of herpes simplex in *immunocompromised* patients, the dose is 200 to 400 mg four times daily.
The usual oral dose of Acyclovir for treatment of **chickenpox** is 800 mg four or five times daily for 5 to 7 days; for herpes zoster 800 mg five times daily may be given for 7 to 10 days.
In **herpes simplex infections of the skin**, including genital herpes and herpes labialis, ***topical treatment*** with an ointment or cream containing Acyclovir 5% may be applied 5 or 6 times daily for periods of 5 to 10 days, preferably beginning in the prodromal period as soon as signs or symptoms occur. In herpes simplex
For details of doses in children, see Administration in Children, below.

ADMINISTRATION IN CHILDREN.

Acyclovir is licensed for use in infants and children for the treatment of herpes simplex and varicella- zoster infections, and for the prophylaxis of herpes simplex infections in the immunocompromised. It may be given by slow intravenous infusion over 1 hour, or orally.
Recommended ***intravenous doses*** vary according to country and age of the patient. In the *UK* the 8-hourly dose for children aged 3 months to 12 years is calculated by body-surface. The usual course of treatment is 5 to 10 days: herpes simplex and varicella-zoster infections in immunocompetent patients: 250 mg/m2
.varicella-zoster infection in immunocompromised children or those with herpes simplex encephalitis: 500 mg/m2 In the *USA*, the 8-hourly intravenous dose for children aged 3 months to 12 years is calculated by body-weight:
.Herpes simplex infections: 10 mg/kg for 7 days
.Varicella-zoster infections in immunocompromised children: 20 mg/kg for 7 days
.Herpes simplex encephalitis: 20 mg/kg for 10 days
In the *UK* and the *USA* the intravenous dose for neonates and infants up to 3 months of age is calculated by body-weight; an 8-hourly intravenous dose of 10 mg/kg may be given for the treatment of herpes simplex infections. Treatment for neonatal herpes simplex usually continues for 7 or 10 days. Higher intravenous doses of up to 20 mg/kg for at least 7 days have been recommended by the *BNFC* in neonates with varicella-zoster infections A similar dose given for 14 days (21 days if CNS involvement) is also recommended in the treatment of disseminated herpes simplex in neonates and infants up to 3 months of age.

ADMINISTRATION IN RENAL IMPAIRMENT.

Doses of acyclovir should be reduced in renal impairment according to creatinine clearance (CC) and licensed product information gives the following guidance: *intravenous* dosage:
.CC between 25 and 50 mL/minute: the interval between infusions may be increased to 12 hours
.CC 10 to 25 mL/minute: the interval between infusions may be increased to 24 hours
.CC less than 10 mL/minute: patients on *peritoneal dialysis* should receive half the usual appropriate dose given once every 24 hours; patients on *haemodialysis* should receive half the usual dose every 24 hours plus an extra half-dose after haemodialysis *oral* dosage:
.CC less than 10 mL/minute: *herpes simplex infections*:
200 mg every 12 hours; *varicella-zoster infections*: 800 mg every 12 hours
.CC between 10 and 25 mL/minute: *varicella-zoster infections*: 800 mg three times daily every 8 hours

PRECAUTIONS

Systemic Acyclovir should be used with caution and in reduced doses in patients with renal impairment. The elderly and patients with existing renal impairment should be closely monitored for neurological adverse effects. Adequate hydration should be maintained in patients given parenteral or high oral doses of Acyclovir. 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. Intravenous Acyclovir should also be used with caution in patients with underlying neurological abnormalities, with significant hypoxia, or with serious hepatic or electrolyte abnormalities.

ADVERSE REACTIONS:

Acyclovir is generally well tolerated. When given intravenously as Acyclovir sodium it may cause local reactions at the injection site with inflammation and phlebitis; these reactions may be associated with extravasation that can lead to tissue necrosis. Renal impairment may be associated with systemic use of Acyclovir in some patients; it is usually reversible and is reported to respond to hydration and/or dosage reduction or withdrawal, but may progress to acute renal failure. The risk of renal toxicity is increased by conditions favouring deposition of Acyclovir crystals in the tubules such as when the patient is poorly hydrated, has existing renal impairment, or when the drug is given at a high dosage or by rapid or bolus injection. Some patients taking systemic Acyclovir may have transient increases in blood concentrations of urea and creatinine although this is more acute with intravenous dosage. Occasional adverse effects after systemic use include increased serum bilirubin and liver enzymes, haematological changes, skin rashes (including erythema multiforme, Stevens-Johnson syndrome, and toxic epidermal necrolysis), fever, headache, dizziness, and gastrointestinal effects such as nausea, vomiting, and diarrhoea. Anaphylaxis has been reported. Hepatitis and jaundice have been reported rarely. Reversible neurological effects including lethargy, somnolence, confusion, hallucinations, agitation, tremors, psychosis, convulsions, and coma have been reported in a small number of patients, particularly in those given intravenous Acyclovir and with predisposing factors such as renal impairment; these effects may be more marked in older patients. Thrombotic thrombocytopenic purpura and haemolytic uraemic syndrome, sometimes resulting in death, have occurred in immunocompromised patients given high parenteral doses of Acyclovir. Accelerated diffuse hair loss has also been reported.
Topical application of Acyclovir may produce transient stinging, burning, itching, or erythema. Eye ointments may occasionally produce transient stinging, superficial punctate keratopathy, blepharitis, or conjunctivitis.

Effects on the blood.

There has been no evidence of bonemarrow toxicity in patients given aciclovir after bone marrow transplantation.1,2 However, megaloblastic haematopoiesis was seen in the bone marrow of 3 patients given aciclovir for suspected or proven herpes simplex encephalitis.3 There has also been a report of inhibition of human peripheral blood lymphocytes in samples taken from healthy subjects given Acyclovir.

Storage: - Store at temperature not exceeding 30° C. Protect from light & moisture.
Improper Storage may deteriorate the product
Medicine: - Keep out of reach of children.
Presentation: - Each pack contain
250 mg /500 mg of Aciclovir Intravenous Infusion IP in a vial. And Sterile Water for Injection IP

Manufactured by:
AMERICAN REMEDIES©
Care & Cure with Research
American Remedies Healthcare Pvt. Ltd.
(An ISO 9001-2015 Certified Company)
Gala No. 105 to 111, 1st Flr., Bldg. No. E-15/A, Harihar Complex, Bhiwandi, Mumbai - 421302
At: Vill. Surajpur Nahan Road Paonta Sahib, Distt. Sirmour, Himachal Pradesh-173001
E-mail: info@americanremedies.in
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℞ Acyclovir Intravenous Infusion I.P.

CLOCIVIR

For Slow Intravenous Infusion After Dilution

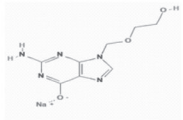
Composition:-

Each Vial Contains:-

Acyclovir Sodium (Sterile) (Lyophilized)		
Eq. to Acyclovir	I.P.	250 mg/500 mg

DESCRIPTION

Acyclovir sodium for Intravenous Infusion IP is a sterile lyophilized powder for intravenous administration only. Acyclovir sodium is white, crystalline powder with the molecular formula $C_8H_{10}N_5NaO_3$ and a molecular weight of 247.19. The chemical name of acyclovir sodium is 2-amino-1, 9-dihydro-9-[(2-hydroxyethoxy) methyl]-6*H*-purin-6-one monosodium salt; it has the following structural formula:



PHARMACOLOGY

PHARMACOKINETICS

Acyclovir is poorly absorbed from the gastrointestinal tract after oral doses. Bioavailability of oral Acyclovir is about 10 to 20%; orally active prodrugs such as Acyclovir have been developed to overcome this poor absorption. After intravenous dosage as Acyclovir sodium it is widely distributed to body tissues and fluids including the CSF where concentrations achieved are about 50% of those achieved in plasma. Protein binding is reported to range from 9 to 33%.
Acyclovir is excreted largely unchanged in the urine, by glomerular filtration and some active tubular secretion, with up to 14% appearing in the urine as the inactive metabolite 9-carboxymethoxymethylguanine. In patients with normal renal function, the half-life is about 2 to 3 hours. In patients with chronic renal failure, this value is increased and may be up to 19.5 hours in anuric patients. During haemodialysis the half-life has been reported to be reduced to 5.7 hours, with 60% of a dose of Acyclovir being removed. Faecal excretion may account for about 2% of a dose. Probenecid increases the half-life and the area under the plasma concentration-time curve of Acyclovir. Acyclovir crosses the placenta and is distributed into breast milk in concentrations about 3 times higher than those in maternal serum. Absorption of Acyclovir is usually slight after topical application to intact skin, although it may be increased by changes in formulation. Acyclovir is absorbed after application of a 3% ointment to the eye giving a relatively high concentration in the aqueous humour but negligible amounts in the blood.

ANTIVIRAL ACTION

Acyclovir is active against herpes simplex virus type 1 and type 2 and against varicella-zoster virus. This activity requires intracellular conversion of Acyclovir by viral thymidine kinase to the monophosphate with subsequent conversion by cellular enzymes to the di-phosphate and the active triphosphate. This active form inhibits viral DNA synthesis and replication by inhibiting the herpesvirus DNA polymerase enzyme as well as being incorporated into viral DNA. This process is highly selective for infected cells. Studies in *animals* and *in vitro* have found various sensitivities but show that target viruses are inhibited by concentrations of Acyclovir that are readily achieved clinically. Herpes simplex virus type 1 appears to be the most susceptible, then type 2, followed by varicella-zoster virus. The Epstein-Barr virus and CMV are also susceptible to Acyclovir to a lesser extent. However, for CMV it does not appear to be activated by thymidine kinase and may act via a different mechanism. Epstein-Barr virus may have reduced thymidine kinase activity but its DNA polymerase is very sensitive to inhibition by Acyclovir triphosphate, which may account for the partial activity.
Acyclovir has no activity against latent viruses, but there is some evidence that it inhibits latent herpes simplex virus at an early stage of reactivation.

USES AND ADMINISTRATION

Acyclovir is a synthetic purine nucleoside analogue structurally related to guanine. It is used mainly for the treatment and prophylaxis of viral infections due to herpes simplex virus types 1 and 2 and varicella- zoster virus (herpes zoster and chickenpox). Herpes simplex infections, including herpes keratitis, herpes labialis, and genital herpes, respond to acyclovir by the intravenous, oral, or topical route, given as soon as possible after symptoms appear. Both initial and recurrent infections can be successfully treated. Prolonged treatment can reduce the incidence of recurrence which is particularly important in immunocompromised patients. However, when prolonged treatment is withdrawn, infections may recur. Acyclovir also improves the healing of herpes zoster lesions and reduces acute pain when given intravenously or by mouth; use to prevent postherpetic neuralgia is controversial. Beneficial effects may be more marked in immunocompromised patients.
Acyclovir is given by ***intravenous infusion*** as the sodium salt over 1 hour. Doses are expressed in terms of the base. Acyclovir sodium 1.1 g is equivalent to about 1 g of Acyclovir. Solutions for infusion are usually prepared to give a concentration of Acyclovir of 25 or 50 mg/mL; this must then be further diluted to a final concentration not greater than about 5 mg/mL (0.5%). Alternatively, a solution containing 25 mg/mL may be given by injection using a controlled-rate infusion pump, over 1 hour. In obese patients the dose should be calculated on the basis of ideal body-weight, to avoid over-dosage.
For **herpes simplex infections** in the *immunocompromised*, and for severe initial *genital herpes*, or for *prophylaxis* of herpes simplex infections in *immunocompromised* patients the dose by the intravenous route is 5 mg/kg given every 8 hours, and recommended periods of treatment range from 5 to 7 days. A higher dose of 10 mg/kg every 8 hours is given in the treatment of *herpes simplex encephalitis*, and treatment is usually continued for 10 days.
For **varicella-zoster infections** in immunocompetent patients, a dose of 5 mg/kg every 8 hours may also be given. In *immunocompromised* patients the higher dose of 10 mg/kg every 8 hours should be used.
for *suppression* of recurrent herpes simplex in *immunocompetent* patients, the oral dose is 800 mg daily in two to four divided doses; dosage reduction to 400 to 600 mg daily can be tried. Higher doses of 1 g daily have also been used. Therapy should be interrupted every 6 to 12 months for reassessment of the condition Chronic suppressive treatment is not suitable for mild or infrequent recurrences of herpes simplex. In such cases *episodic treatment* of recurrences may be preferred; a dose of 200 mg