UNIVIR

For use by a Registered Medical Practitioner or Hospital or a Laboratory

ACYCLOVIR (UNIVIR)

COMPOSITION:
TABLETS: Each tablet contains either 200mg or 400mg or 800mg Acyclovir U.S.P
SUSPENSION: Each 5 ml contains: Acyclovir U.S.P 200mg.
CREAM: Each 1g contains Acyclovir U.S.P 50 mg.

DESCRIPTION:
Acyclovir is 9-{[2-hydroxyethoxy] methyl}-9H-guanine. It is a synthetic purine nucleoside analogue with antiviral spectrum which is mainly limited to herpes viruses.

CLINICAL PHARMACOLOGY:
Acyclovir has inhibitory activity both in vitro and in vivo against human herpes viruses including herpes simplex types 1(HSV-1) AND 2(HSV-2), varicella zoster virus (VZV), Epstein-Barr virus (EBV) and cytomegalovirus (CMV). The inhibitory activity of acyclovir for HSV-1, HSV-2, VZV and EBV is highly selective.The enzyme thymidine kinase of normal uninfected cells does not effectively use acyclovir as a substrate. However, thymidine kinase encoded by HSV, VZV & EBV 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. Acyclovir triphosphate competes for endogenous deoxyguanosine triphosphate (dGTP) and thereby competitively inhibit viral DNA polymerase and to a much smaller extent, cellular DNA polymerase. It is incorporated into viral DNA, where it acts as a chain terminator because of the lack of 3'-hydroxyl group. The terminated DNA template containing acyclovir binds the enzyme and leads to irreversible inactivation of DNA polymerase. Acyclovir is preferentially taken up and selectively converted to the active triphosphate form by herpes virus-infected cells.

PHARMACOKINETICS:
The oral bioavailability of acyclovir ranges from 10 to 30% and decreases with increasing dose. Peak plasma concentrations average 0.4 to 0.8 g/ml after 200 mg and 1.6 g/ml after 800 mg doses.
The drug distributes widely in body fluids including versicular fluid, aqueous humour, and cerebrospinal fluid. Compared to plasma, salivary concentrations are low, and vaginal secretion concentrations range widely. Acyclovir is concentrated in breast milk, amniotic fluid, and placenta. Newborn plasma levels are similar to maternal ones. Percutaneus absorption of Acyclovir after topical administration is low.
The mean plasma half-life (t½) of elimination of Acyclovir is about 2.5 hours, with a range of 1.5 to 6 hours in adults with normal renal function. The plasma t½ of elimination of acyclovir is about 4 hours in neonates and increases to 20 hours in anuric patients. Renal excretion of unmetabolised acyclovir by glomerular filtration and tubular secretion is the principal route of elimination. Less than 15% is excreted as 9-carboxymethoxymethyl guanine or minor metabolite.

INDICATION:
Acyclovir is indicated for the treatment of initial and recurrent mucosal and Cutaneous Herpes Simplex (HSV-1) and, Varicella zoster (Shingles) in uncompromised patients. It is also indicated for herpes simplex encephalitis in patients over 6 months of age and for severe initial episodes of herpes genitalis in patients who are not immunocompromised.
Acyclovir has been employed effectively in the treatment of Chicken Pox (varicella), herpes zoster (Shingles) and cytomegalovirus.
It is indicated for the treatment of initial episodes and the management of recurrent episodes of genital herpes in certain patients.
Acyclovir is also approved for the topical treatment of non-fulminating HSV-1 and HSV-2 infection (except in the eye), however, it is moderately effective, especially against genital herpes in women. Hence Acyclovir cream 5% is indicated in the management of initial herpes genitalis and in limited non-life threatening mucocutaneous Herpes Simplex virus infections in immunocompromised patients.

CONTRAINDICATIONS:
Contraindicated in patients who are hypersensitive to Acyclovir or components of the formulation.

PRECAUTIONS:
The recommended dosage should not be exceeded.
The possibility of the appearance of less sensitive viruses in humans must be borne in mind when treating patients.
Caution should be exercised when administering Acyclovir to patients receiving potentially nephrotoxic agents since this may increase the risk of renal dysfunction.
Caution should be exercised when acyclovir is administered to a nursing woman. Acyclovir should not be used during pregnancy unless the potential benefit justifies the potential risk to the foetus.

DRUG INTERACTIONS:
Co-administration of probenecid with acyclovir has been shown to increase the mean half-life and the area under the concentration time-curve. Urinary excretion and renal clearance were correspondingly reduced. Acyclovir may decrease the renal clearance of other drugs eliminated by active renal secretion, such as methotrexate.
Co-administration of Acyclovir with other nephrotoxic drugs e.g. cyclosporine enhance the risk of nephrotoxicity.
Severe somnolence and lethargy may occur with combination of zidovudine and acyclovir.

SIZE 180MM X120MM

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ADVERSE REACTIONS:
Oral Acyclovir has been associated infrequently with nausea and vomiting, headache, diarrhoea, dizziness, skin rash, sore throat, anorexia, edema, lymphadenopathy (especially inguinal), and leg pain; and very rarely with renal insufficiency or neurotoxicity. In the long-term therapy, the above may be experienced including arthralgia, depression, acne, alopecia, fever, palpitations, muscle cramps and sensitivity to sunlight or artificical light.(e.g.sunbeds). The drug is mutagenic and should be avoided in pregnancy, if possible. Topically, adverse effects occur in about 30% of recipients and consist of local stinging, burning or pain, itching vulvitis and rash.

DOSAGE AND ADMINISTRATION :

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

2. 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 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.
Intermittent Therapy: 200 mg every 4 hours, 5 times daily for 5 days. Therapy should be initiated at the earliest sign or symptom of recurrence.

3. Herpes Simplex:
Usual Adult Dose for Herpes Simplex - Initial episode or intermittent therapy: 400 mg orally every 4 hours (5 times a day) for 7 - 10 days.
Recurrent episodes: 200 mg orally every 4 hours (5 times a day) for 5 days. Alternatively, 400 mg orally 3 times a day for 5 days, 800 mg orally twice a day for 5 days, or 800 mg orally 3 times a day for 2 days.
Usual Pediatric Dose for Herpes Simplex:
3 months to 11 years:
Initial episode: 10 to 20 mg /kg orally 4 times a day or 8 to 16 mg/kg orally 5 times a day for 7 to 10 days.
Maximum dose: 1 g per day.
12 years or older, over 40 kg:
Initial episode, severe initial episode, and recurrent episodes: Adult dose.

4. **Chicken Pox:**
Adult Dose: 800mg orally four times a day for 5 days.
Paediatric Dose:
Treatment for 5 days.
6 years and over : 800mg four times a day.
2 - 5 years : 400mg 4 times a day.
Under 2 years: 200mg 4 times a day.

Therapy should be initiated at the earliest sign of chickenpox, no later than 24 hours after onset of rash.

5. **Topical Application:**
Univir cream should be applied five times per day for four days. Therapy should be initiated as early as possible following the onset of signs or symptoms of herpes labialis i.e during the prodrome or when lesions appear.
For adolescents 12 years of age and older, the dosage is the same as adults.

Patients who experience difficulty in swallowing may disperse the tablets in a minimum of 50 ml water which should be stirred before taking.

PRESENTATION:
Tablets: Blister pack of 10's, 30's and 100's in unit boxes.
Cream : 10 gm aluminium collapsible tubes in unit boxes.
Suspension: 60 ml amber bottles in unit boxes.

STORAGE:
Do not store above 30° C. Store in a dry place. Protect from direct sunlight. Keep all medicines out of reach of children.

Manufactured by:

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