VIRAX

Suspension

Composition
Each 5 ml contains Acyclovir 200 mg

Action
Acyclovir is an antiviral agent with activity against Herpes simplex virus types 1 and 2, (HSV-1 and HSV-2) and varicella zoster virus (VZV). Acyclovir is phosphorylated after entry into herpes infected cells to the active compound acyclovir triphosphate. The first step in this process is dependent on the presence of the HSV coded thymidine kinase. Thymidine kinase converts acyclovir into acyclovir monophosphate. The monophosphate is converted to diphosphate by cellular guanylate kinase and to triphosphate, which is the active form of the medicine. Acyclovir triphosphate interferes with HSV and VZV DNA polymerase and inhibits viral DNA replication.

Clinical uses of Acyclovir
Virax indicated in the treatment of the following infections due to the following organisms:
- *Herpes Simplex* virus (types 1 and 2).
- *Varicella Zoster* virus (Herpes Zoster and Chickenpox).
- Herpes Simplex infections including *Herpes Keratitis, Herpes Labialis* and Genital Herpes respond to Acyclovir given by intravenous, oral or topical routes as soon as possible after symptoms appear.
- Both initial and recurrent infections can be successfully treated.

Prolonged treatment can reduce the incidence of recurrence that is important in immunocompromised patients. However, when prolonged treatment is withdrawn infections may recur. Virax also improves for healing of Herpes Zoster lesions when given intravenously or by oral route, although studies indicate that it has little effect on pain.

Pharmacokinetics
Acyclovir is only partially absorbed from the gut. Mean steady state peak plasma concentrations (C^{SS}max) following doses of 200mg aciclovir administered four-hourly were 3.1 microMol (0.7 microgram/ml) and the equivalent trough plasma levels (C^{SS}min) were 1.8 microMol (0.4 microgram/ml). Corresponding steady-state plasma concentrations following doses of 400mg and 800mg aciclovir administered four-hourly were 5.3 microMol (1.2 microgram/ml) and 8 microMol (1.8 microgram/ml) respectively, and equivalent trough plasma levels were 2.7 microMol (0.6 microgram/ml) and 4 microMol (0.9 microgram/ml).

In adults the terminal plasma half-life after administration of intravenous acyclovir is about 2.9 hours. Most of the drug is excreted unchanged by the kidney. Renal clearance of acyclovir is substantially greater than creatinine clearance, indicating that tubular secretion, in addition to glomerular filtration, contributes to the renal elimination of the drug.

9-carboxymethoxymethylguanine is the only significant metabolite of acyclovir, and accounts for 10-15% of the dose excreted in the urine. When acyclovir is given one hour after 1 gram of probenecid the terminal half-life and the area under the plasma concentration time curve is extended by 18% and 40% respectively.

In adults, mean steady state peak plasma concentrations (C^{SS}max) following a one hour infusion of 2.5mg/kg, 5mg/kg and 10mg/kg were 22.7 microMol (5.1 microgram/ml), 43.6 microMol (9.8 microgram/ml) and 92 microMol (20.7 microgram/ml), respectively. The corresponding trough levels (C^{SS}min) 7 hours later were 2.2 microMol (0.5 microgram/ml), 3.1 microMol (0.7 microgram/ml) and 10.2 microMol (2.3 microgram/ml), respectively.

In children over 1 year of age similar mean peak (C^{SS}max) and trough (C^{SS}min) levels were observed when a dose of 250mg/m^2 was substituted for 5mg/kg and a dose of 500mg/m^2 was substituted for 10mg/kg. In neonates (0 to 3 months of age) treated with doses of 10mg/kg administered by infusion

over a one-hour period every 8 hours the C^{SS}max was found to be 61.2 microMol (13.8 microgram/ml) and C^{SS}min to be 10.1 microMol (2.3 microgram/ml). The terminal plasma half-life in these patients was 3.8 hours. A separate group of neonates treated with 15 mg/kg every 8 hours showed approximate dose proportional increases, with a Cmax of 83.5 micromolar (18.8 microgram/ml) and Cmin of 14.1 micromolar (3.2 microgram/ml).

In the elderly total body clearance falls with increasing age associated with decreases in creatinine clearance although there is little change in the terminal plasma half-life.

In patients with chronic renal failure the mean terminal half-life was found to be 19.5 hours. The mean acyclovir half-life during haemodialysis was 5.7 hours. Plasma acyclovir levels dropped approximately 60% during dialysis.

Cerebrospinal fluid levels are approximately 50% of corresponding plasma levels. Plasma protein binding is relatively low (9 to 33%) and drug interactions involving binding site displacement are not anticipated.

Indications

- Herpes Zoster Infections: Virax indicated for the acute treatment of herpes zoster (shingles).
- Genital Herpes: Virax indicated for the treatment of initial episodes and the management of recurrent episodes of genital herpes.
- Chickenpox: Virax indicated for the treatment of chickenpox (varicella).

Contraindications

Acyclovir contraindicated for patients who develop hypersensitivity or intolerance to the components of the formulations.

Warnings

Acyclovir suspension intended for oral ingestion only.

Adverse Reactions

Skin rashes have been reported in a few patients receiving acyclovir tablets; the rashes have resolved on withdrawal of the drug.

Gastrointestinal effects, including nausea, vomiting, diarrhoea, and abdominal pains, have been reported in some patients receiving acyclovir tablets.

Other events reported rarely in patients receiving oral formulations of acyclovir include mild, transient rises in bilirubin and liver related enzymes, small increases in blood urea and creatinine, small decreases in haematological indices, headaches, mild reversible neurological reactions and fatigue.

Precautions

Dosage adjustment is recommended when administering Acyclovir to patients with renal impairment. Caution should also be exercised when administering acyclovir to patients receiving potentially nephrotoxic agents since this may increase the risk of renal dysfunction and/or the risk of reversible central nervous system symptoms such as those that have been reported in patients treated with intravenous acyclovir.

Information for Patients

Patients are instructed to consult with their physician if they experience severe or troublesome adverse reactions, they become pregnant or intend to become pregnant, they intend to breastfeed while taking orally administered Acyclovir, or they have any other questions.

Herpes Zoster: There are no data on treatment initiated more than 72 hours after onset of the zoster rash. Patients should be advised to initiate treatment as soon as possible after a diagnosis of herpes zoster.

Genital Herpes Infections: Patients should be informed that acyclovir is not a cure for genital herpes. There are no data evaluating whether Acyclovir will prevent transmission of infection to others. Because genital herpes is a sexually transmitted disease, patients should avoid contact with lesions or intercourse when lesions and/or symptoms are present to avoid infecting partners. Genital herpes can also be transmitted in the absence of symptoms through asymptomatic viral shedding. If medical management of a genital herpes recurrence is indicated, patients should be advised to initiate therapy at the first sign or symptom of an episode.

Chickenpox: Chickenpox in otherwise healthy children is usually a self-limited disease of mild to moderate severity. Adolescents and adults tend to have more severe disease. Treatment was initiated within 24 hours of the typical chickenpox rash in the controlled studies, and there is no information regarding the effects of treatment begun later in the disease course.

Pregnancy
Category C
Animal reproduction studies have shown an adverse effect on the fetus and there are no adequate and well-controlled studies in humans, but potential benefits may warrant use of the drug in pregnant women despite potential risks.

Nursing Mothers
Acyclovir concentration have been documented in breast milk in two women following oral administration of Acyclovir and ranged from 0.6 to 4.1 times corresponding plasma levels. These concentrations would potentially expose the nursing infant to a dose of acyclovir up to 0.3 mg/kg/day. Caution should be exercised when Acyclovir is administered to a nursing woman.

Paediatric Use
Safety and effectiveness in pediatric patients less than two years of age have not been adequately studied.

Geriatric Use
In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased renal function, and of concomitant disease or other drug therapy.

Drug Interactions
Co-administration of probenecid with intravenous acyclovir has been shown to increase acyclovir half-life and systemic exposure. Urinary excretion and renal clearance were correspondingly reduced.

Dosage and Administration
Children (Two Years of Age and Older)
20 mg/kg per dose orally four times daily (80 mg/kg/day) for five days. Children over 40 kg should receive the adult dose.

Over Dosage
Acyclovir is only partly absorbed in the gastrointestinal tract. Patients have ingested overdoses of up to 20 g acyclovir on a single occasion, usually without toxic effects. Accidental, repeated overdoses of oral acyclovir over several days have been associated with gastrointestinal effects (such as nausea and vomiting) and neurological effects (headache and confusion).

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 intravenous overdosage.

Management
Patients should be observed closely for signs of toxicity. Haemodialysis significantly enhances the removal of acyclovir from the blood and may be considered a management option in the event of symptomatic overdose.

Presentation
Bottle of 60 ml