SOUTH AFRICAN PROFESSIONAL INFORMATION FOR MEDICINES FOR HUMAN USE

SCHEDULING STATUS

S4

PROPRIETARY NAME AND DOSAGE FORM

CYCLIVEX 400 mg TABLETS

COMPOSITION

Each tablet of CYCLIVEX 400 mg TABLETS contains 400 mg of acyclovir.

Excipients:

Dye Lennon blue (C.I. 42090), Dye Lennon lake blue (C.I. 73015), magnesium stearate, microcrystalline cellulose, modified cellulose gum, polyvinylpyrrolidone, purified talc

Sugar free

CATEGORY AND CLASS

A 20.2.8 Antiviral agents

PHARMACOLOGICAL ACTION

Pharmacodynamic properties

Acyclovir is active *in vitro* against Herpes simplex virus (HSV) types I and II and Varicella-zoster virus.

This is activity due to intracellular conversion of acyclovir to acyclovir triphosphate by viral thymidine kinase.

Acyclovir triphosphate inhibits viral DNA synthesis and replication.

INDICATIONS

- Treatment of initial and recurrent Herpes simplex infections of the skin and mucous membranes including initial and recurrent genital Herpes simplex infections.
- Suppression of recurrent genital Herpes simplex infections in immunocompetent patients.
- Prophylaxis of Herpes simplex infections in immuno-compromised patients.
- Treatment of Herpes zoster infections if the lesions are not older than 72 hours.
- Treatment of Varicella zoster (chickenpox) within 24 hours after appearance of the typical chickenpox rash.

CONTRAINDICATIONS

CYCLIVEX 400 mg TABLETS are contraindicated in patients known to be hypersensitive to acyclovir.

The safety of CYCLIVEX 400 mg TABLETS in pregnancy has not been established, therefore CYCLIVEX 400 mg TABLETS should not be administered to pregnant women.

CYCLIVEX 400 mg TABLETS should not be administered to nursing women as acyclovir does pass into breast milk.

WARNINGS AND SPECIAL PRECAUTIONS

Use with caution in patients with renal impairment.

Resistance has also been reported with Varicella-zoster virus.

In the elderly, total acyclovir body clearance declines, thus adequate hydration should be maintained. Special attention should be given to dosage reduction in elderly patients with impaired renal function.

INTERACTIONS

The risk of renal impairment is increased by the concomitant use of nephrotoxic medicine.

Probenecid blocks the renal clearance of acyclovir.

HUMAN REPRODUCTION

The safety of CYCLIVEX 400 mg TABLETS in pregnancy has not been established, therefore CYCLIVEX 400 mg TABLETS should not be administered to pregnant women.

CYCLIVEX 400 mg TABLETS should not be administered to nursing women as acyclovir does pass into breast milk.

DOSAGE AND DIRECTIONS FOR USE

Dosage in adults

For treatment of initial and recurrent Herpes simplex infections of the skin and mucous membranes:

200 mg Acyclovir should be taken 5 times per day at approximately four hourly intervals omitting the night time dose. Treatment should continue for 5 days, but in a case of severe initial infection the treatment period may have to be extended.

In severely immunocompromised patients e.g. after marrow transplant or in patients with impaired absorption from the gut the dose can be doubled to 400 mg or, alternatively, intravenous dosing could be considered.

The first dose should be administered as early as possible after the start of an infection and for recurrent episodes this should preferably be during the prodromal period or when lesions first appear.

For suppression of recurrent genital Herpes simplex infections in immunocompetent adults:

A dose of 200 mg of acyclovir should be taken four times daily at approximately six-hourly intervals.

Many patients may be conveniently managed on a regimen of 400 mg of oral acyclovir taken twice daily at approximately twelve-hourly intervals. Dosage titration down to 200 mg oral acyclovir taken at approximately eight-hourly intervals, or even twice daily at approximately twelve-hourly intervals may prove effective. Some patients may experience break-through infections on total doses of 800 mg acyclovir.

Therapy should be interrupted periodically at intervals of six to twelve months, in order to observe possible changes in the natural history of the disease.

For prophylaxis of Herpes simplex infections in immunocompromised adults:

200 mg Acyclovir should be taken four times daily at approximately six hourly intervals.

In severely immunocompromised patients (e.g. after marrow transplants) or in patients with impaired absorption from the gut the dose can be doubled to 400 mg, or alternatively intravenous dosing could be considered. The duration of prophylactic administration is determined by the duration of the period at risk.

For treatment of Varicella zoster infections in adolescents (12 to 18 years):

A dose of 800 mg oral acyclovir should be taken four times daily for five days.

For treatment of Varicella zoster and Herpes zoster infections in adults:

A dose of 800 mg oral acyclovir should be taken five times daily at approximately four-hourly intervals, omitting the night-time dose. Treatment should continue for 7 days.

In severely immunocompromised patients (e.g. after marrow transplant) or in patients with impaired absorption from the gut, consideration should be given to intravenous dosing. Dosing should begin as easily as possible after the start of an infection: treatment yields better results if initiated as soon as possible after rash onset.

Dosage in the elderly

In the elderly, total acyclovir body clearance declines, thus adequate hydration should be maintained. Special attention should be given to dosage reduction in elderly patients with impaired renal function.

Dosage in renal impairment

Dosage should be reduced in renal failure.

The following is recommended:

Normal dose regimen	Creatinine Clearance ($ml/min/1,73m^2$)	Adjusted Dosage Regimen	
		Dose (mg)	Dosing interval
200 mg every four hours for Herpes simplex infections	0 to 10	200	Every 12 hours
800 mg every four hours for Varicella zoster infections	> 25 10 to 25 0 to 10	800 800 800	Every 4 hours 5 times daily Every 8 hours Every 12 hours

Patients on haemodialysis should receive their usual appropriate daily dosage after each dialysis.

SIDE EFFECTS

There have been reports of skin rashes, headaches and gastro-intestinal effects such as nausea, vomiting and diarrhoea.

Patients with a suppressed immune response may be particularly prone to acyclovir-resistant mucocutaneous Herpes simplex infections.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENTS

Symptoms

See SIDE EFFECTS and WARNINGS AND SPECIAL PRECAUTIONS.

Treatment

Treatment is symptomatic and supportive.

IDENTIFICATION

An oblong, light blue, biconvex tablet, engraved with a mortar and pestle.

PRESENTATION

60 or 70 tablets are packed in a white polypropylene container with a white low density polyethylene snap-on cap, with a tamper-proof seal, with a white foam insert and a leaflet.

The tablets are packed in a clear polyvinylchloride blister strip sealed with an aluminium foil backing. The blister strips are packed into an outer cardboard carton together with a leaflet.

Not all packs and pack sizes are necessarily marketed.

STORAGE INSTRUCTIONS

Store at or below 25 °C in airtight containers.

Keep in original packaging until required for use.

KEEP OUT OF REACH OF CHILDREN.

REGISTRATION NUMBER

31/20.2.8/0298

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION

PHARMACARE LIMITED

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DATE OF PUBLICATION OF THE PROFESSIONAL INFORMATION FOR MEDICINES FOR HUMAN USE

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