ZORAX CREAM 5% W/W

Composition:
Acyclovir 5% w/w

Product Description:
White, smooth, water-miscible cream.

Pharmacodynamics:
Acyclovir is a synthetic acyclic purine nucleoside analogue with in vitro inhibitory activity against herpes simplex type 1 (HSV-1) and type 2 (HSV-2), varicella zoster, Epstein-Barr and cytomegalovirus. In cell cultures, the inhibitory activity of acyclovir for herpes simplex virus is highly selective. Cellular thymidine kinase does not effectively utilize acyclovir as a substrate. Herpes simplex virus-coded thymidine kinase, however, converts acyclovir into acyclovir monophosphate, a nucleotide. The monophosphate is further converted into diphosphate by cellular guanylate kinase and into triphosphate by a number of cellular enzymes. Acyclovir triphosphate interferes with herpes simplex virus α-DNA polymerase and inhibits viral DNA replication. Acyclovir triphosphate also inhibits cellular α-DNA polymerase but to a lesser degree. In vitro, acyclovir triphosphate can be incorporated into growing chains of DNA by viral DNA polymerase and to a much smaller extent by cellular α-DNA polymerase. When incorporation occurs, the DNA chain is terminated. Acyclovir is preferentially taken up and selectively converted to the active triphosphate form by herpes virus infected cells. Thus, acyclovir is much less toxic in vitro for normal uninfected cells because: 1) less is taken up 2) less is converted to the active form 3) cellular α-DNA polymerase is less sensitive to the effects of the active form.

Pharmacokinetics:
Absorption of acyclovir is usually slight following topical application to intact skin, although it may be increased by changes in formulation.

Indication:
It is indicated for the topical treatment of herpes simplex virus infections of the skin including initial and recurrent herpes genitalis and herpes labialis.

Recommended Dosage:
Apply sufficient quantity to adequately cover all lesions every 3 or 4 hours 5 or 6 times daily for periods of 5 to 10 days. A finger cot or rubber glove should be used when applying acyclovir to prevent autoinoculation of other body sites and transmission of infection to other persons. Therapy should be initiated as early as possible following onset of signs and symptoms. It is particularly important to start treatment of recurrent episodes during the prodromal period or when lesions first appear.

Route of Administration: Topical

Contraindications:
It is contraindicated in patients who develop hypersensitivity or chemical intolerance to acyclovir.

Warnings and Precautions:
All patients should be cautioned to ensure they avoid the potential of virus transmission, particularly when active lesions are present.
It is not recommended for application to buccal or vaginal mucous membranes. Particular care should be taken to avoid accidental introduction into the eye. Animal studies indicate that reversible irritation may result from introduction of the cream into the vagina.
In severely immune-compromised patients (e.g. AIDS patients or bone marrow transplant recipients) oral acyclovir dosing should be considered. Such patients should be encouraged to consult a physician concerning the treatment of any infection.
Carcinogenicity
Acyclovir was not found to be carcinogenic in long term studies in the rat and the mouse.
Mutagenicity
The results of a wide range of mutagenicity tests in vitro and in vivo indicate that acyclovir does not pose a genetic risk to man.
Effects on Fertility
Largely reversible adverse effects on spermatogenesis in association with overall toxicity in rats and dogs have been reported only at doses of systemic acyclovir greatly in excess of those employed therapeutically. Two-generation studies in mice did not reveal any effect of orally administered acyclovir on fertility. There is no experience on the effect of acyclovir on human female fertility. It has been shown to have no definitive effect upon sperm count, morphology or motility in man.

Interactions with Other Medicaments:
No known drug interaction since acyclovir cream applied topically is not absorbed.

Pregnancy and Lactation:
There are no adequate and well-controlled studies in pregnant women. Acyclovir should not be used during pregnancy unless the potential benefit justifies the potential risk to the fetus. It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when acyclovir is administered to a nursing woman.

Side Effects:
Topical application of acyclovir, especially to genital lesions, may sometimes produce transient stinging, burning, or erythema.
Mild drying or flaking of the skin has occurred in about 5% of patients. Erythema and itching have been reported in a small proportion of patients. Contact dermatitis has been reported rarely following application. When sensitivity tests have been conducted, the reactive substances have most often been shown to be components of the cream base rather than acyclovir.

Symptoms and Treatment of Overdose:
Overdosage by topical application of acyclovir cream 5% is unlikely because of limited transcutaneous absorption. No untoward effects would be expected if ingested orally. Doses of 800mg 5 times daily (4g/day), have been administered for 7 days without adverse effects. Treatment: Ingestion of doses of acyclovir in excess of 5g warrants close observation of the patients. Acyclovir is dialysable by haemodialysis.

Effects on Ability to Drive and Use Machine: Not applicable.

Storage Conditions:
Store at or below 30ºC. Protect from light.

Pack Size:
A jar of 10g.
A tube of 5g and 10g.

Pack Size (export only):
A jar of 12g and 400g.
A tube of 15g and 30g.

Shelf-Life: 2 years.

FURTHER INFORMATION CONCERNING THIS DRUG CAN BE OBTAINED FROM YOUR FAMILY PHYSICIAN / LOCAL GENERAL PRACTITIONER / PHARMACIST.

Manufacturer & Product Registration Holder:
Sunward Pharmaceutical Sdn. Bhd.
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