1.6.1.1 Name of the medicinal Product

EMZOR ACYCLOVIR TABLETS USP 400 MG

1.6.1.1.1 strength

400 mg/tablet

1.6.1.1.2 Pharmaceutical Form

Oral tablet

1.6.1.2 Qualitative and Quantitative Composition

1.6.1.2.1 Qualitative declaration

Acyclovir USP

1.6.1.2.2 Quantitative declaration

Sr. No	Ingredients Chemical Name	Specification	Quantity/ tablet (mg)	Reason for Inclusion
MIXING				
01	Acyclovir (A)	USP	400.0	Antiviral agent
02	Calcium Hydrogen Phosphate	BP	45.00	Diluent
03	Maize Starch (C)	BP	94.50	Diluent
BINDING				
04	Maize Starch	BP	20.00	Binder
05	Purified Water #	BP	Q.S.	Vehicle
LUBRICATION				
06	Maize Starch	BP	24.50	Disintegrant
07	Purified Talc	BP	2.000	Glidant
08	Magnesium Stearate	BP	3.000	Lubricant
09	Sodium Lauryl Sulfate	BP	3.000	Wetting agent
10	Sodium Starch Glycolate (Type-A)	BP	5.000	Super Disintegrating agent

Note:

(A)=Quantity of active ingredient is to be calculated on the basis of 100% potency and on anhydrous basis.

(C)= Quantity of Maize Starch BP to be reduced against incremental increase in quantity of Acyclovir USP due to assay compensation

= Do not remain in the final product.

Latest version of pharmacopoeia is used.

1.6.1.3 Pharmaceutical Form

Oral, Uncoated Tablet

White coloured, round shaped, flat, uncoated tablets, plain on one side and break line on other side.

1.6.1.4 Clinical Particulars

1.6.1.4.1 Therapeutic Indications

Acyclovir Tablets USP is indicated for

- 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 immunocompromised 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.

1.6.1.4.2 Posology and Method of Administration

Oral Route

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 immune-compromised 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 4 times daily at 6-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 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 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 of800 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 fourhourly 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 early 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 Rena/Impairment: **Dosage should be reduced in renal failure as below:**

Normal Dose Regimen	Creatinine Clearance (mL/min/1.73 m1)	Adjusted Dosage Regimen	
		Dose (mg)	Dosing interval
400 mg every four hours for herpes simplex infections	0-10	400 mg	Every 12 hours
800 mg every four hours for Varicella zoster infections	>25 10-25 0-10	800 800 800	Every 4 hours Every 8 hours Every 12 hours

1.6.1.4.3 Contraindications

Acyclovir tablet is contraindicated in patients known to be hypersensitive to acyclovir. The safety of acyclovir in pregnancy has not been established. Acyclovir should not be administered to pregnant women or nursing women as acyclovir passes into breast milk.

1.6.1.4.4 Special Warnings and Special Precautions for Use

Acyclovir should be administered with caution to patients with renal impairment and doses should be adjusted according to creatinine clearance. The risk of renal impaim1ent is increased by the concomitant use of other nephrotoxic agents.

1.6.1.4.5 Interaction with other medicinal products and other forms of interaction

Probenecid blocks the renal clearance of acyclovir and thus increases the mean half life.

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

1.6.1.4.6 Fertility, Pregnancy and Lactation

Pregnancy: Acyclovir should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Lactation: Acyclovir should be administered to a nursing mother with caution and only when indicated

1.6.1.4.7 Effects on ability To Drive and use Machines

There have been no studies to investigate the effect of acyclovir on driving performance or the ability to operate machinery.

1.6.1.4.8 Undesirable Effects

Effects on skin: Skin rashes which disappear after withdrawal of medication.

Effects on gastro-intestinal tract: Nausea, vomiting, diarrhoea and vomiting.

Other reactions: Reversible neurological reactions, dizziness, hallucinations and somnolence especially in patients with renal impairment. Rises in bilirubin and liver related enzymes, elevations in blood and creatinine; minimal decreases in haematological indices, headaches and fatigue. Accelerated diffuse hair loss has also been reported.

Patients with a suppressed immune response may be particularly prone to acyclovir-resistant mucocutaneous herpes simplex infections. Resistance has also been reported with Varicella-zoster virus.

1.6.1.4.9 Overdose

Acyclovir is removed by haemodialysis. Treatment is symptomatic and supportive, although no data is available on the effects after ingest ion of high doses.

1.6.1.5 Pharmacological Properties

1.6.1.5.1 Pharmacodynamics Properties

Acyclovir is an antiviral drug which after intracellular uptake, converted to acyclovir monophosphate by virally-encoded thymidine kinase, which is then phosphorylated after entering into the herpes infected cells to the active acyclovir triphosphate compound. The acyclovir triphosphate inhibits viral DNA polymerase and thereby inhibits viral DNA synthesis and replication. This process takes place without affecting the normal cellular processes. Acyclovir triphosphate is active in vitro against type I and II herpes simplex and Varicella zoster viruses.

1.6.1.5.2 Pharmacokinetic Properties

Absorption: Acyclovir can be given orally. When it is given orally, only 20% of the dose is absorbed and peak plasma concentrations are reached in 1-2 hours.

Distribution: The drug is widely distributed, reaching concentrations in the CSF that are 50% of those in the plasma.

Excretion: It is excreted by kidneys, partly by glomerular filtration and partly by tubular secretion.

1.6.1.5.3 Preclinical Safety Data

Not Applicable.

1.6.1.6 Pharmaceutical Particulars

1.6.1.6.1 List of Excipients

Calcium Hydrogen Phosphate BP
Maize Starch BP
Purified Talc BP
Magnesium Stearate BP
Sodium Lauryl Sulfate BP
Sodium Starch Glycolate (Type - A) BP
Purified Water BP

1.6.1.6.2 Incompatibilities

Not applicable.

1.6.1.6.3 Shelf Life

36 months

1.6.1.6.4 Special Precautions for Storage

Store below 30°C. Protect from light.

1.6.1.6.5 Nature and Contents of Container

10 Tablets are packed in Alu-PVC Blister Pack. Such 10 Blisters are packed in printed Carton with Packing Insert.

1.6.1.6.6 Special precaution for disposal and other handling

Any unused product or waste material should be disposed of in accordance with local requirements.

1.6.1.7 Marketing Authorization Holder And Manufacturing Site Addresses

Emzor Pharmaceutical Industries Limited
Km 1 Flowergate Mixed Development Scheme,
Sagamu/Benin Expressway,Makun,Sagamu,Ogun-State

1.6.1.7.1 Name and Address of Marketing Authorization Holder

Emzor Pharmaceutical Industries Limited
Km 1 Flowergate Mixed Development Scheme,
Sagamu/Benin Expressway,Makun,Sagamu,Ogun-State

1.6.1.8 Marketing Authorization Number

To be included after obtaining first registration.

1.6.1.9 Date of First <Registration> / Renewal of The <Registration>

It will be applicable after registration of this product.

1.6.1.10 **Date of Revision of the Text**

1.6.1.11 Dosimetry (If Applicable)

Not Applicable

1.6.1.12 Instructions for preparation of radiopharmaceuticals (if Applicable)

Not Applicable