SCHEDULING STATUS
S4

1. NAME OF THE MEDICINE
ADCO ACYCLOVIR 200 mg tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
Each ADCO ACYCLOVIR 200 mg tablet contains 200 mg acyclovir.
Contains sugar: Lactose 170 mg

For full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM
Tablets
White, hexagonal shaped tablets, scored on one side.

4. CLINICAL PARTICULARS
4.1 Therapeutic indications
1. Treatment of initial and recurrent *Herpes simplex* infections of the skin and mucous membranes including initial and recurrent genital *Herpes simplex* virus infections.
2. Suppression of recurrent genital *Herpes simplex* infections in immunocompetent patients
3. Prophylaxis of *Herpes simplex* infections in immunocompromised patients.
4. Treatment of *Herpes zoster* infections if the lesions are not older than 72 hours.
5. Treatment of *Varicella zoster* (chickenpox) within 24 hours after appearance of the typical chickenpox rash.

4.2 Posology and method of administration
Posology

(A) Dosage in adults
For treatment of initial and recurrent Herpes simplex infections of the skin and mucous membranes:
200 mg Acyclovir (one ADCO Acyclovir 200 mg tablet) should be taken five times per day at approximately four hourly intervals, omitting the night time dose. Treatment should continue for five days, but in 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 (two ADCO ACYCLOVIR 200 mg tablets) 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 acyclovir (one ADCO ACYCLOVIR 200 mg tablet) should be taken four times daily at approximately six-hourly intervals. Many patients may be conveniently managed on a regimen of 400 mg (two ADCO ACYCLOVIR 200 mg tablets) 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 (four ADCO ACYCLOVIR 200 mg tablets). 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 (two ADCO ACYCLOVIR 200 mg tablets), 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 (four ADCO ACYCLOVIR 200 mg tablets) should be taken daily for five days.

For treatment of Varicella zoster and Herpes zoster infections in adults:
A dose of 800 mg oral acyclovir (four ADCO ACYCLOVIR 200 mg tablets) should be taken five times daily at approximately four-hourly intervals, omitting the night time dose. Treatment should continue for seven 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.

Special populations
(B) 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.

(C) Dosage in renal impairment:
Dosage should be reduced in renal failure. The following is recommended:

Normal dosage regimen	Creatinine clearance (ml/min)	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	800	every 4 hours 5 times daily
	10 to 25	800	every 8 hours
	0 to 10	800	every 12 hours

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

Paediatric population:
Orally administered acyclovir in children less than 2 years of age has not yet been fully studied.

Method of administration:
Oral.

4.3 Contraindications

- Hypersensitivity to acyclovir, valacyclovir or any of the excipients listed in section 6.1.
- Safety in pregnancy and lactation has not been established.

4.4 Special warnings and precautions for use
Use in patients with renal impairment and in elderly patients:
Acyclovir as contained in ADCO ACYCLOVIR 200 mg, is eliminated by renal clearance, therefore the dose must be adjusted in patients with renal impairment (section 4.2).

Elderly patients are likely to have reduced renal function and therefore the need for dose adjustment must be considered in this group of patients. Both elderly patients and patients with renal impairment are at increased risk of developing neurological side effects and should be closely monitored for evidence of these effects. In the reported cases, these reactions may be reversible on discontinuation of treatment (see section 4.8).

Hydration status:
Care should be taken to maintain adequate hydration in patients receiving high oral doses of acyclovir as contained in ADCO ACYCLOVIR 200 mg.

Severe cutaneous adverse reactions (SCARs):

Drug reaction with eosinophilia and systemic symptoms (DRESS)
DRESS, which can be life-threatening or fatal, has been reported in associate with ADCO ACYCLOVIR 200 mg treatment. At the time of prescription patients should be advised of the signs and symptoms and monitored closely for skin reactions. If signs and symptoms suggestive of DRESS appear, ADCO ACYCLOVIR 200 mg should be withdrawn immediately, and an alternative treatment considered (as appropriate). If the patient has developed DRESS with the use of ADCO ACYCLOVIR 200 mg, treatment with ADCO ACYCLOVIR 200 mg must not be restarted in this patient at any time.
Excipients:
ADCO ACYCLOVIR 200 mg contains lactose. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

ADCO ACYCLOVIR 200 mg contains less than 1 mmol sodium (23 mg) per tablet, that is to say, it is essentially 'sodium-free'.

4.5 Interaction with other medicines and other forms of interaction

- Acyclovir as contained in ADCO ACYCLOVIR 200 mg, is eliminated primarily unchanged in the urine via active renal tubular secretion. Any medicines administered concurrently that compete with this mechanism may increase the plasma concentrations of ADCO ACYCLOVIR 200 mg. Probenecid and cimetidine increases, the AUC of ADCO ACYCLOVIR 200 mg by this mechanism, and reduces ADCO ACYCLOVIR 200 mg renal clearance.
- Similarly, increases in plasma AUCs of acyclovir contained in ADCO ACYCLOVIR 200 mg and of the inactive metabolite of mycophenolate mofetil, an immunosuppressant medicine used in transplant patients have been shown when the medicines are co-administered.
- Available data indicates that acyclovir as contained in ADCO ACYCLOVIR 200 mg may increase the AUC of totally administered theophylline when administered concomitantly. It is thus recommended to measure plasma concentrations of theophylline during concomitant treatment with ADCO ACYCLOVIR 200 mg.

4.6 Fertility, pregnancy and lactation
Pregnancy
Safety in pregnancy has not been established.

Lactation
Acyclovir does pass into the breast milk
Safety in lactation has not been established.

Fertility
No data available

4.7 Effects on ability to drive and use machines

ADCO ACYCLOVIR 200 mg can cause dizziness. If affected, patients should not drive or operate machinery.

4.8 Undesirable effects

System Organ Class	Frequency	Side effects
Blood and the lymphatic system disorders:	*Less frequent*	Small decreases in haematological indices (anaemia, leukopenia, thrombocytopenia)
Immune system disorders:	*Less frequent*	Anaphylaxis, angioedema.
***Psychiatric and nervous system disorders:**	*Frequent*	Headache, dizziness.
	Less frequent	Agitation, confusion, tremor, ataxia, dysarthria, hallucinations, psychotic symptoms, convulsions, somnolence, encephalopathy, coma.
Respiratory, thoracic and mediastinal disorders:	*Less frequent*	Dyspnoea.
Gastrointestinal disorders:	*Frequent*	Nausea, vomiting, diarrhoea, abdominal pains.
Hepato-biliary disorders:	*Less frequent*	Reversible rises in bilirubin and liver related enzymes, hepatitis, jaundice.
Skin and subcutaneous tissue disorders:	*Frequent*	Pruritus, skin rashes photosensitivity urticaria, accelerated diffuse hair loss

Renal and urinary disorders:	*Less frequent*	Increases in blood urea and creatinine, acute renal failure, renal pain, Renal pain may be associated with renal failure and crystalluria.
General disorders and administration site conditions	*Frequent*	Fatigue, fever.

* The above symptoms are usually reversible and are generally reported in patients with renal impairment (see section 4.4).

Post-marketing experience:
The following adverse reaction has been identified during post approval use of ADCO ACYCLOVIR 200 mg.
Immune: Drug reaction with eosinophilia and systemic symptoms (DRESS) (see Section 4.4).

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare providers are asked to report any suspected adverse reactions to SAHPRA via the "**6.04 Adverse Drug Reactions Reporting Form**", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8.
You may also report to Adcock Ingram Limited using the following e-mail address: Adcock.AEReports@adcock.com.

4.9 Overdose
Ingestion of doses of acyclovir in excess of 5 g warrants close observation of the patient. Acyclovir is dialysable. Treatment is symptomatic and supportive.

Symptoms and signs: 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 IV 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, therefore, be considered a management option in the event of symptomatic overdose.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

A 20.2.8 Antiviral agents

Acyclovir has antiviral activity that is essentially confined to the herpes viruses. It is particularly active in vitro against Herpes simplex type 1 and Herpes simplex type 2. Acyclovir inhibits viral replication by inhibiting DNA synthesis. This inhibition is due to intracellular conversion of acyclovir by viral thymidine kinase to the monophosphate with subsequent conversion to the diphosphate and the active triphosphate. This active form inhibits the herpes virus DNA polymerase enzyme as well as being incorporated into viral DNA.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

- Microcrystalline Cellulose
- Sodium starch Glycolate
- Stearic Acid
- Magnesium Stearate
- Colloidal Silicon Dioxide
- Pregelatinized Maize Starch
- Sodium Lauryl Sulphate
- Lactose

6.2 Incompatibilities

No data available

6.3 Shelf life

24 months

6.4 Special precautions for storage

Store at or below 25 °C in a dry place.
Protect from light.

6.5 Nature and contents of container

Pack size of 25 tablets packed in a white polypropylene securitainer with a white LDPE closure.
Pack size of 25 tablets packed in blisters using PVC film and aluminium foil.

Not all pack sizes may be marketed

6.6 Special precautions for disposal and other handling

No special requirements

7. HOLDER OF CERTIFICATE OF REGISTRATION

Adcock Ingram Limited
1 New Road,
Erand Gardens,
Midrand,
1685
Customer Care: 0860 ADCOCK / 232625

8. REGISTRATION NUMBER

28/20.2.8/0552

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

18 April 1997

10. DATE OF REVISION OF THE TEXT

08 November 2024

Botswana (S2): BOT1803283 Namibia (NS2): 04/20.2.8/1554

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