SCHEDULING STATUS

S4

1. NAME OF THE MEDICINE

ACYCLOVIR BIOTECH 200 Tablets

ACYCLOVIR BIOTECH 800 Tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

ACYCLOVIR BIOTECH 200: Each tablet contains 200 mg acyclovir.

ACYCLOVIR BIOTECH 800: Each tablet contains 800 mg acyclovir.

ACYCLOVIR BIOTECH 200 contains sugar (lactose hydrous, 190 mg).

For full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablets

ACYCLOVIR BIOTECH 200: Round, blue, flat-faced, bevelled-edged tablets, engraved "APO" over "200" on one side, other side plain.

ACYCLOVIR BIOTECH 800: Oval, blue, biconvex tablets, scored and engraved "APO 800" on one side, other side plain.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Herpes simplex infections of the skin and mucous membranes including genital herpes (initial and recurrent) if given as soon as possible after symptoms appear.

Suppression of recurrent herpes simplex infections in patients with an incompetent immune system.

Indicated for shingles if the lesion in not older than 72 hours.

If used within 24 hours after appearance of typical chickenpox rash, ACYCLOVIR BIOTECH is indicated for treatment of the varicella zoster or chickenpox virus.

In HIV positive patients, who are severely immunocompromised, ACYCLOVIR BIOTECH is indicated to reduce the risk of developing herpes infections. ACYCLOVIR BIOTECH could be used in combination with zidovudine in patients with advanced HIV disease.

4.2 Posology and method of administration

Posology

Initial and recurrent herpes simplex infections of skin and mucous membranes:

200 mg 5 times daily at 4 hourly intervals for 5 days.

In severe initial infection, extend treatment. In immunocompromised patients, dosage could be increased to 400 mg.

The first dose should be administered as early as possible after start of infection.

Suppression of recurrent genital herpes simplex infections in immunocompromised patients:

200 mg aciclovir 4 times daily at 6 hourly intervals, or 400 mg 12 hourly.

Some patients may have breakthrough infections on 800 mg daily. Interrupt therapy every 6 – 12 months to observe history of disease.

Prophylaxis of herpes simplex infections in immunocompromised patients:

200 mg 4 times daily at 6 hourly intervals.

In severely immunocompromised patients, or impaired absorption from the gut, dosage could be doubled to 400 mg.

Treatment of varicella zoster in adolescents (12-18 years):

800 mg 4 times a day for 5 days.

Treatment of varicella zoster and herpes zoster infections in adults:

800 mg 5 times daily at 4 hourly intervals for 7 days.

Start treatment as early as possible. In severely immunocompromised patients, or patients with impaired gut absorption, IV dosing should be considered.

Management of severely immunocompromised patients:

800 mg 4 times daily at 6 hourly intervals.

Special populations

Elderly:

Adequate hydration in patients taking high doses must be maintained. Aciclovir clearance in body declines parallel with creatinine clearance.

Renal impairment:

Treatment or prophylaxis of herpes simplex infections in patients with renal impairment:

200 mg every 12 hours if creatinine clearance > 10 mL/minute.

Treatment of varicella zoster, herpes zoster and immunocompromised patients with renal impairment:

800 mg twice daily at 12 hourly intervals (creatinine clearance > 10 mL/minute)

800 mg 3 times daily with 8 hourly intervals (creatinine clearance 10 - 25 mL/minute).

Paediatric population

Herpes simplex and prophylaxis of herpes simplex infections in immunocompromised patients 2 years and older:

Adult dose.

Orally administered aciclovir in children less than 2 years of age has not yet been fully studied.

Method of administration

For oral administration.

4.3 Contraindications

- Hypersensitivity to acyclovir or valaciclovir or to any of the excipients listed in section 6.1.
- Pregnancy and lactation: Safety has not been established.

4.4 Special warnings and precautions for use

ACYCLOVIR BIOTECH is eliminated by renal clearance; therefore, ACYCLOVIR BIOTECH should be administered with caution to patients with renal impairment and doses should be adjusted according to creatinine clearance (see 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.

Elderly patients, as well as patients with renal impairment, have an increased risk of developing neurological side effects. These groups of patients should be monitored for signs of neurological side effects. The side effects are generally reversible upon discontinuation of treatment (see section 4.8).

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

Prolonged use or repeated courses of ACYCLOVIR BIOTECH in patients with a compromised immune system, may lead to the selection of virus strains with reduced sensitivity to acyclovir treatment.

Adequate hydration levels should be maintained in patients receiving high doses of ACYCLOVIR BIOTECH.

Severe cutaneous adverse reaction (SCAR)

Drug reaction with eosinophilia and systemic symptoms (DRESS) and Acute Generalised Exanthematous Pustulosis (AGEP)

Severe cutaneous adverse reactions (SCARs) including DRESS and AGEP, which can be life-threatening or fatal, has been reported with unknown frequency in association with acyclovir treatment (i.e., ACYCLOVIR BIOTECH). At the time of prescription patients should be advised of the signs and symptoms and monitored closely for skin reactions.

DRESS and AGEP are considered serious cutaneous adverse reactions (SCARs) which are unpredictable and present an important risk to patients.

Therefore, if a patient develops reactions classified as SCARs during ACYCLOVIR BIOTECH use, treatment should be withdrawn immediately, and an alternative treatment considered (as appropriate), and treatment with ACYCLOVIR BIOTECH must not be restarted for the patient at any time.

ACYCLOVIR BIOTECH 200 contains lactose hydrous. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or of glucose-galactose malabsorption should not take ACYCLOVIR BIOTECH 200.

This medicine contains less than 1 mmol sodium (23 mg) per dosage unit, that is to say essentially 'sodium-free'.

4.5 Interaction with other medicines and other forms of interaction

Probenecid blocks the renal clearance of ACYCLOVIR BIOTECH and thus increases the mean half-life.

ACYCLOVIR BIOTECH 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 ACYCLOVIR BIOTECH.

Probenecid and cimetidine increase the AUC of ACYCLOVIR BIOTECH by means of this mechanism and reduces the renal clearance of ACYCLOVIR BIOTECH.

The plasma AUCs of ACYCLOVIR BIOTECH and of the inactive metabolite of mycophenolate mofetil, may be increased when the medicines are co-administered.

No dosage adjustment may be necessary because of the wide therapeutic index of ACYCLOVIR BIOTECH.

Available data indicates that ACYCLOVIR BIOTECH 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 ACYCLOVIR BIOTECH.

4.6 Fertility, pregnancy and lactation

Pregnancy

Safety has not been established during pregnancy.

Breastfeeding

Safety has not been established during lactation.

Fertility

There is no information on the effect of acyclovir on human female fertility.

4.7 Effects on ability to drive and use machines

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

However, ACYCLOVIR BIOTECH may cause dizziness which may influence the ability to drive and use machines (see section 4.8).

4.8 Undesirable effects

Tabulated list of adverse reactions

MedDRA System Organ Class	**Frequency**	**Adverse effect**
Blood and lymphatic system disorders:	*Less frequent*	Anaemia, leukopenia, thrombocytopenia.
Immune system disorders:	*Less frequent*	Anaphylaxis.
Psychiatric disorders*:	*Frequent*	Headache, dizziness.

	Less frequent	Agitation, confusion, hallucinations, psychotic symptoms.
Nervous system disorders*:	*Less frequent*	Convulsions, tremor, ataxia, dysarthria, encephalopathy, coma, somnolence.
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 which disappear after withdrawal of medication, photosensitivity.
	Less frequent	Urticaria, accelerated diffuse hair loss, angioedema.
	Unknown frequency	Acute generalised exanthematous pustulosis (AGEP), Drug reaction with eosinophilia and systemic symptoms (DRESS).
Renal and urinary disorders:	*Less frequent*	Elevations 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).

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.

4.9 Overdose

ACYCLOVIR BIOTECH is removed by haemodialysis. Treatment is symptomatic and supportive. Overdoses of ACYCLOVIR BIOTECH may cause gastrointestinal effects (such as nausea and vomiting) and neurological effects (headache and confusion).

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties:

Category and class: A 20.2.8 Antiviral Agents.

Pharmacotherapeutic group: Direct acting antivirals, Nucleosides and nucleotides excl. reverse transcriptase inhibitors

ATC code: J05AB01.

Acyclovir is phosphorylated after entering the herpes infected cells to the active acyclovir triphosphate compound. It is active *in vitro* against type 1 and 2 herpes simplex (HSV) and varicella zoster viruses.

The HSV coded thymidine kinase must be present before phosphorylation can take place. The Acyclovir triphosphate prevents DNA synthesis by inhibiting herpes specified DNA polymerase. This process takes place without affecting the normal cellular processes.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

ACYCLOVIR BIOTECH 200:

Colloidal silicone dioxide

Croscarmellose sodium

Indigotine lake (CI 73015)

Lactose, hydrous

Magnesium stearate

Microcrystalline cellulose

ACYCLOVIR BIOTECH 800:

Brilliant blue FCF lake (CI 42090)

Colloidal silicone dioxide

Croscarmellose sodium

Indigotine lake (CI 73015)

Magnesium stearate

Microcrystalline cellulose

6.2 Incompatibilities

Not applicable

6.3 Shelf life

24 months

6.4 Special precautions for storage

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

6.5 Nature and contents of container

ACYCLOVIR BIOTECH 200 tablets are available in white plastic bottles of 100, 250, 500 and 1 000 tablets.

ACYCLOVIR BIOTECH 800 tablets are available in white plastic bottles of 100, 250, 500 tablets, and in blister packages of 100 tablets.

Not all strengths may be marketed.

6.6 Special precautions for disposal and other handling

No special requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Biotech Laboratories (Pty) Ltd

Ground Floor, Block K West, Central Park,

400 16th Road, Randjespark,

Midrand, 1685.

8. REGISTRATION NUMBERS

ACYCLOVIR BIOTECH 200: 31/20.2.8/0430

ACYCLOVIR BIOTECH 800: 31/20.2.8/0431

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of registration: 29 May 2001

10. DATE OF REVISION OF THE TEXT

23 June 2023