PROFESSIONAL INFORMATION

SCHEDULING STATUS: S4

PROPRIETARY NAMES AND DOSAGE FORM:

Aciclovir Sandoz® 200 (tablets)

Aciclovir Sandoz® 400 (tablets)

COMPOSITION:

ACICLOVIR SANDOZ 200:

Each ACICLOVIR SANDOZ 200 tablet contains aciclovir 200 mg.

Excipients:

Cellulose microcrystalline, copolyvidone, lactose monohydrate, magnesium stearate, silica (colloidal anhydrous) and sodium starch glycollate (Type A).

Contains sugar (lactose monohydrate 213,6 mg per tablet).

ACICLOVIR SANDOZ 400:

Each ACICLOVIR SANDOZ 400 tablet contains aciclovir 400 mg.

Excipients:

Cellulose microcrystalline, copolyvidone, magnesium stearate, silica colloidal anhydrous and sodium starch glycollate (Type A).

Sugar free.

PHARMACOLOGICAL CLASSIFICATION:

A 20.2.8 Antiviral agents

PHARMACOLOGICAL ACTION:

Aciclovir is active *in vitro* against *Herpes simplex* type I and type II and *Varicella zoster* virus.

Once inside the herpes infected cells, aciclovir is phosphorylated to the active compound aciclovir triphosphate. Aciclovir triphosphate acts as an inhibitor of and substrate for the herpes specified DNA polymerase, preventing further viral DNA synthesis, without affecting normal cellular processes.

INDICATIONS:

- Treatment of initial and recurrent *Herpes simplex* infections of the skin and mucous membranes, including initial and recurrent genital *Herpes simplex* virus infections.
- Prophylaxis of *Herpes simplex* infections in immunocompromised patients.
- Treatment of Herpes zoster (shingles) infections if the lesions are not older than 72 hours.
- Treatment of *Varicella zoster* (chickenpox), within 24 hours of the appearance of the typical chickenpox rash.
- Reduction of mortality and risk of developing *Herpes virus* infections in certain severely immunocompromised patients, i.e. those with advanced HIV disease (CD4+ counts < 200/ m^3 including patients with AIDS and ARC) or following bone marrow transplantation. In advanced HIV disease, oral aciclovir has been used in conjunction with oral zidovudine.
- In patients following bone marrow transplantation, oral aciclovir must be preceded by one month’s intravenous treatment with aciclovir.

CONTRAINDICATIONS:

Hypersensitivity to aciclovir or any of the other ingredients of ACICLOVIR SANDOZ (see “COMPOSITION”).

Safety in pregnancy and lactation has not been established.

WARNINGS AND SPECIAL PRECAUTIONS:

Aciclovir should be administered with caution to patients with renal impairment and doses should be adjusted according to creatinine clearance (see “DOSAGE AND DIRECTIONS FOR USE”).

Precautions relating to excipients:

ACICLOVIR SANDOZ contains lactose monohydrate. Patients with the rare hereditary conditions of galactose intolerance e.g. galactosaemia, Lapp lactase deficiency, glucose-galactose malabsorption or fructose intolerance should not take ACICLOVIR SANDOZ.

ACICLOVIR SANDOZ contains lactose monohydrate, which may have an effect on the glycaemic control of patients with diabetes mellitus.

INTERACTIONS:

Probenecid - concomitant administration leads to an increase in the plasma half-life of aciclovir.
The risk of renal impairment is increased by the concomitant use of other nephrotoxic agents.

DOSAGE AND DIRECTIONS FOR USE:

Adults:

Treatment of recurrent Herpes simplex infection of skin and mucous membranes:

200 mg five times per day every 4 hours, omitting the night time dose. Treatment should continue for 5 days but in case of severe initial infection, this period may have to be extended.
In patients that are severely immunocompromised or in patients with decreased gut absorption the dose may be doubled to 400 mg or alternatively, intravenous aciclovir should be considered.
Dosing should be started as early as possible, following the start of infection and for recurrent episodes this should be in the prodromal stages or when lesions first appear.

Suppression of recurrent genital Herpes simplex infections in immuno-competent adults:

200 mg four times per day at 6 hourly intervals. Patients may be conveniently managed at a dose of 400 mg twice daily at 12 hourly intervals. This dose may be titrated down to 200 mg aciclovir 8 to 12 hourly.

Therapy should be interrupted, every 6 to 12 months, to observe possible changes in the natural history of the disease.

Prophylaxis of Herpes simplex infections in immunocompromised adults:

200 mg four times daily at 6 hourly intervals.

In patients that are severely immunocompromised or in patients with decreased gut absorption the dose may be doubled to 400 mg or alternatively intravenous aciclovir should be considered.

The duration of prophylactic administration is determined by the duration of the period at risk.

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

800 mg four times daily for 5 days.

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

800 mg five times daily at 4 hourly intervals, omitting the nighttime dose for a minimum period of 7 days. Dosing should be initiated as early as possible after the start of an infection.

Dosage for management of severely immunocompromised patient:

800 mg four times daily, every 6 hours.

In the management of bone marrow recipients, this would be preceded by up to one month's therapy with intravenous aciclovir 500 mg/m^2 three times daily. The duration of treatment studied in bone marrow transplant patients was 6 months (from 1 to 7 months post-transplant). In patients with advanced HIV disease, study treatment was 12 months.

Dosage in children:

Treatment and prophylaxis of Herpes simplex infections in immunocompromised children:

2 years and older: Adult dosage.

Below 2 years: Half the adult dosage.

Oral administration of aciclovir in patients less than 2 years of age has not been fully studied.

Dosing for *Varicella* (chickenpox) may be calculated as 20 mg aciclovir per kg body mass (not exceeding 800 mg) four times daily.

Treatment should be initiated within 24 hours after appearance of typical chickenpox rash, and should be continued for 5 days.

Limited data suggests that for severely immunocompromised children over 2 years, the adult dosage can be administered.

Elderly:

Total aciclovir body clearance declines with creatinine clearance. Adequate hydration of elderly patients receiving high oral aciclovir should be maintained. Dosage reduction is recommended in elderly patients with renal impairment.

Dosage in renal impairment:

Treatment and prophylaxis of Herpes simplex infection in patients with impaired renal function:

The recommended oral dose will not lead to accumulation of aciclovir.

A dose of 200 mg every 12 hours is recommended in patients with severe renal impairment (creatinine clearance less than 10 mℓ/min).

Treatment of Varicella and Herpes zoster infections:

Severe renal impairment (creatinine clearance less than 10 mℓ/min): adjust dosage to 800 mg twice daily at 12 hourly intervals.

Moderate renal impairment (creatinine clearance ranging between 10 to 25 mℓ/min): adjust dose to 800 mg three times daily every 8 hours.

Normal dosage (5 times daily)	***Creatinine clearance (mℓ/min/1,73 m^2)***	***Adjusted dosage***	
		Dose (mg)	***Dosing interval (hours)***
200 mg every 4 hours	> 10	200	Every 4 hours 5 times daily
	0 to 10	200	Every 12 hours
800 mg every 4 hours	10 to 25	800	Every 8 hours
	0 to 10	800	Every 12 hours

SIDE EFFECTS:

Skin rashes have occurred however, these have resolved following withdrawal of the oral formulation. Gastro-intestinal effects, including nausea, vomiting, diarrhoea and abdominal cramps have been reported.

Reversible neurological reactions including dizziness, confusional states, hallucinations and somnolence have been reported, usually in patients with renal impairment or other predisposing factors.

Reports of accelerated diffuse hair loss have been received but the relationship between this phenomena and aciclovir therapy is unclear.

The following have also been reported:

Transient rises in bilirubin and liver related enzymes, increases in blood urea and creatinine, small decreases in blood indices, headaches, reversible neurological reactions, fatigue, fever, haematological changes, agitation, tremors, seizures, and coma have been reported, particularly in those who are immunocompromised.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:

(see “SIDE EFFECTS” and “WARNINGS AND SPECIAL PRECAUTIONS”).

No data are available on the effects of ingestion of high doses. Aciclovir is dialysable by haemodialysis. Treatment is supportive and symptomatic.

IDENTIFICATION:

ACICLOVIR SANDOZ 200: White, round, convex tablets with a breaking notch on the other side.

ACICLOVIR SANDOZ 400: White, round, biconvex tablets with a breaking notch on the other side.

PRESENTATIONS:

ACICLOVIR SANDOZ 200: Transparent or white opaque PVC/ Aluminium blister packs containing 25 tablets.

ACICLOVIR SANDOZ 400: Transparent or white opaque PVC/ Aluminium blister packs containing 70 tablets.

STORAGE INSTRUCTIONS:

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

KEEP OUT OF THE REACH OF CHILDREN.

REGISTRATION NUMBERS:

ACICLOVIR SANDOZ 200: 32/20.2.8/0378

ACICLOVIR SANDOZ 400: 32/20.2.8/0379

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATES OF REGISTRATION:

Sandoz SA (Pty) Ltd[1]

Magwa Crescent West

Waterfall City

Jukskei View

Midrand

2090

DATE OF PUBLICATION OF THE PACKAGE INSERT:

Date of registration:

ACICLOVIR SANDOZ 200: 10 October 2000

ACICLOVIR SANDOZ 400: 28 March 2001

Date of the most recent approval of the professional information: 22 August 2019

Additional countries registration details:

Country	***Product name***	***Scheduling status (or Category of distribution)***	***Registration number***
Botswana	ACICLOVIR SANDOZ 200	S2	BOT1202216
	ACICLOVIR SANDOZ 400	S2	BOT1202215
Namibia	ACICLOVIR SANDOZ 400	NS2	04/20.2.2/1361

ATC Code: J05AB01 – Nucleosides and nucleotides excl. reverse transcriptase inhibitors

Name and address of manufacturer:

Salutas Pharma GmbH

Otto-von-Guericke-Allee 1,

D-39179, Barleben,

Germany

[1] Company Reg.No.:1990/001979/07