# PACKAGE INSERT FOR AZERO

## SCHEDULING STATUS

S4

## PROPRIETARY NAME AND DOSAGE FORM

**AZERO** film coated tablets

## COMPOSITION

*Active ingredient:*

**AZERO** contains azithromycin dihydrate equivalent to 500 mg azithromycin base.

*Inactive ingredients:*

Pregelatinised starch, anhydrous dibasic calcium phosphate, croscarmellose sodium, magnesium stearate, Opadry clear (containing hypromellose and macrogol).

Sugar free.

## PHARMACOLOGICAL CLASSIFICATION

A 20.1.1 Broad and medium spectrum antibiotics

## PHARMACOLOGICAL ACTION

### Pharmacodynamic properties

Azithromycin is a macrolide antibiotic which acts by inhibiting protein synthesis by binding reversibly to 50 S ribosomal subunits of sensitive microorganisms.

### Pharmacokinetic properties

Azithromycin is absorbed rapidly and has a bioavailability of approximately 37 %. Peak plasma concentrations are achieved 2 to 3 hours after a dose. Protein binding of azithromycin is low (51 %) and appears to be concentration-dependent, decreasing with increasing concentrations.

Azithromycin is metabolised by the liver to inactive metabolites and excreted in the bile. More than 50 % of the dose is eliminated unchanged via the bile and only 12 % of an oral dose is excreted unchanged in the urine. The plasma terminal half-life closely reflects the tissue depletion half-life of 2 to 4 days.

Following oral administration, azithromycin is widely distributed throughout the body (except to cerebrospinal fluid) and concentrates mainly intracellular (phagocytes and fibroblasts).

## INDICATIONS

**AZERO** is indicated in the treatment of mild to moderate infections caused by susceptible organisms in lower respiratory tract infections including bronchitis (due to *Haemophilus influenzae*, *Moraxella catarrhalis*, *Streptococcus pneumoniae* or *Staphylococcus aureus*) and pneumonia (due to *Streptococcus pneumoniae* or *Haemophilus influenzae*).

**AZERO** is also indicated in the treatment of uncomplicated skin and soft tissue infections, sinusitis (due to *Haemophilus influenzae*, *Streptococcus pneumoniae* or *Staphylococcus aureus*) and as an alternative to first line therapy of pharyngitis/tonsillitis.

**AZERO** is indicated in the treatment of uncomplicated genital tract infections due to *Chlamydia trachomatis* in sexually transmitted diseases.

## CONTRAINDICATIONS

Hypersensitivity to azithromycin, erythromycin, any of the macrolide antibiotics or to any of the other excipients in **AZERO** (see **COMPOSITION**).

- **AZERO** should not be co-administered with ergot derivatives due to the risk of ergotism.
- **AZERO** is contraindicated in patients with liver disease.

## WARNINGS AND SPECIAL PRECAUTIONS

Serious allergic reactions, such as anaphylaxis and angioedema, have been reported in patients taking azithromycin. Despite discontinuation of azithromycin and successful symptomatic treatment of the allergic reactions, allergic symptoms soon recurred in some patients when the symptomatic therapy was discontinued. These patients require prolonged periods of observation and symptomatic treatment.

Mild to life-threatening pseudomembranous colitis has been reported. It is therefore important to consider the diagnosis of diarrhoea in patients who had been treated with **AZERO**.

The safety of **AZERO** in children under the age of 1 year has not been established.

Prolonged cardiac repolarisation and QT interval, imparting a risk of developing cardiac dysrhythmia and torsades de pointes, have been seen in treatment with other macrolides. A similar effect with **AZERO** cannot be completely ruled out in patients at increased risk for prolonged cardiac repolarisation (see **SIDE EFFECTS**). Therefore, caution is required when treating patients:

- With congenital or documented acquired QT prolongation.
- Currently receiving treatment with other active substances known to prolong QT interval such as antidysrhythmics of classes IA and III, cisapride and terfenadine.
- With electrolyte disturbance, particularly in cases of hypokalaemia and hypomagnesaemia.
- With clinically relevant bradycardia, cardiac dysrhythmia or severe cardiac insufficiency.

Caution should be taken when prescribing **AZERO** to patients with renal impairment.

Patients treated with **AZERO** should be closely monitored for signs or symptoms of superinfections (including fungi).

**Effects on ability to drive and use machines**

Patients should be advised to use caution when driving a car or operating hazardous machinery until they are reasonably certain that their performance is not affected by **AZERO**.

**INTERACTIONS**

Macrolides, including azithromycin, have the potential to interact with a large number of medicines through their action on hepatic cytochrome P450 isoenzymes. Macrolides inhibit medicine metabolism by microsomal cytochromes by competitive inhibition and by the formation of inactive complexes. Macrolide-induced inhibition of metabolism can result in severe adverse effects, including ventricular dysrhythmias with astemizole and cisapride.

An increase in the serum concentrations of ciclosporin, digoxin, hexobarbital and phenytoin has been reported with the concurrent use of azithromycin.

Concurrent use with aluminium and magnesium containing antacids has increased the peak serum concentration by approximately 24 %. **AZERO** should be given at least 1 hour before or 2 hours after the antacid.

Co-administration of **AZERO** with ergotamine or dihydro-ergotamine has been associated with acute ergot toxicity (see **CONTRAINDICATIONS**).

Concurrent use of warfarin and azithromycin has been associated with increased anticoagulant effects. The prothrombin time/INR of these patients should be monitored.

Azithromycin has been reported to decrease oral contraceptive efficacy. It is recommended that additional contraceptive precautions should be used while taking and for 7 days after stopping **AZERO**.

**AZERO** may cause a reduction in the gastrointestinal absorption of methotrexate.

## PREGNANCY AND LACTATION

Safety in pregnancy and lactation has not been established.

## DOSAGE AND DIRECTIONS FOR USE

**AZERO** tablets should be taken whole.

These tablets can be taken with or without food and in a single daily dose.

### Adults

For all indications other than sexually transmitted diseases, the dose is 500 mg daily for 3 days.

For sexually transmitted diseases caused by *Chlamydia trachomatis* the dose is 1 g given as a single dose.

### Use in elderly

No dosage adjustments are necessary for elderly patients.

### Use in children

For children over 45 kg body weight, the dose is as for adults. Note that this formulation is not suitable for children with a body weight under 45 kg. Safety and efficacy of **AZERO** in children under 1 year of age have not been established.

## SIDE EFFECTS

### Blood and the lymphatic system disorders

*Less frequent:* neutropenia

**Immune system disorders**

*Less frequent:* allergic reactions including angioedema, anaphylaxis, skin rash

**Nervous system disorders**

*Less frequent:* dizziness, headache, fatigue, paraesthesia, somnolence, convulsions

**Ear and labyrinth disorders**

*Less frequent:* vertigo, tinnitus, hearing loss

**Cardiac disorders**

*Less frequent:* palpitations, dysrhythmias including ventricular tachycardia, chest pain

**Gastrointestinal disorders**

*Less frequent:* abdominal pain, diarrhoea, nausea, vomiting, anorexia, flatulence, constipation, loose stools, dyspepsia, melaena

*Frequency unknown:* pseudomembranous colitis, taste disturbances

**Hepatobiliary disorders**

*Less frequent:* transient elevations in liver enzymes, hepatitis, cholestatic jaundice

**Skin and subcutaneous tissue disorders**

*Less frequent:* erythema multiforme, toxic epidermal necrolysis, urticaria, Stevens-Johnson syndrome, photosensitivity

**Musculoskeletal, connective tissue and bone disorders**

*Less frequent:* arthralgia

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**Renal and urinary disorders**

*Less frequent:* interstitial nephritis, acute renal failure

**Reproductive system and breast disorders**

*Less frequent:* vaginitis.

## KNOWN SYMPTOMS OF OVERDOSE AND PARTICULARS OF ITS TREATMENT

There are no known symptoms of overdosage. Typical symptoms of overdosage with macrolide antibiotics include hearing loss, severe nausea, vomiting and diarrhoea. Gastric lavage is indicated and further treatment is symptomatic and supportive.

## IDENTIFICATION

White to off-white capsule shaped, biconvex film coated tablets with a break line on one side.

## PRESENTATION

Aluminium/PVC/PVdC blisters strips containing 3 or 10 tablets per blister strip. 1 blister strip is placed in an outer carton.

## STORAGE INSTRUCTIONS

Store at or below 25 °C.

Keep the blister strips in the outer carton until required for use.

KEEP OUT OF REACH OF CHILDREN.

## REGISTRATION NUMBER

44/20.1.1/0492

## NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION

Zydus Healthcare SA (Pty) Ltd.

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## DATE OF PUBLICATION OF THE PACKAGE INSERT

1 March 2013

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