SCHEDULING STATUS S4

PROPRIETARY NAME AND DOSAGE FORM
AZROTRIN 500 Tablets

COMPOSITION
Each film coated tablet contains 500 mg Azithromycin.

PHARMACOLOGICAL CLASSIFICATION
A20.1.1-Medium and broad spectrum antibiotics.

PHARMACOLOGICAL ACTION
Azithromycin is a macrolide (azalide) antibiotic. It exerts its antibacterial action by binding reversibly to the 50S ribosomal subunit of the 70S ribosome of sensitive microorganisms, thereby inhibiting bacterial RNA-dependent protein synthesis. The *in vitro* antibacterial spectrum of pathogens sensitive to azithromycin includes: (*in vitro* sensitivity does not necessarily imply *in vivo* efficacy)
Staphylococcus aureus
Streptococcus spp., including *Streptococcus pyogenes (*Group A) and
Streptococcus pneumoniae
Haemophilus influenzae, Haemophilus ducreyi
Moraxella catarrhalis
Legionella pneumophila
Bordatella Pertussis
Borrelia burgdofreri
Mycoplasma pneumoniae
Chlamydia trachomatis
Treponema pallidum

Pharmacokinetics:
Azithromycin is absorbed rapidly from the gastrointestinal tract, with an oral bioavailability of approximately 37 %. No significant decrease in bioavailability occurs when azithromycin is administered with a meal. Peak concentration occurs approximately 2 to 3 hours after oral administration. Protein binding of azithromycin is low (51 %) and appears to be concentration dependent, decreasing with increasing concentrations. Azithromycin is widely distributed throughout the body and concentrates intracellulalry. Azithromycin (35 % of the dose) 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, while 6,5 % of the dose is eliminated in the urine, unchanged. The elimination half-life of azithromycin closely reflects the tissue depletion half-life of 2 to 4 days.

INDICATIONS
AZROTRIN 500 is indicated for the treatment of the following conditions in adult and children one year and older.
- Lower respiratory tract infections such as bronchitis and pneumonia caused by sensitive *Haemophilus influenza, Moraxella catarrhalis, Staphylococcus aureus or Streptococcus pneumoniae.*
- Upper respiratory tract infections such as sinusitis or pharyngitis caused by sensitive *Haemophilus influenza Staphylococcus aureus or Streptococcus pneumoniae.*
- Uncomplicated skin and soft tissue infections caused by sensitive *Staphylococcus aureus.*
- Uncomplicated genital tract infections caused by sensitive *Chlamydia trachomatis.*

For children 1 year and older, AZROTRIN 500 is indicated for the treatment of pharyngitis/tonsillitis and otitis media caused by susceptible organisms.

CONTRAINDICATIONS
Hypersensitivity to macrolide antibiotics or to any component of the formulation.
Co-administration with ergot alkaloids.
Liver function impairment – since biliary excretion is the major route of elimination.
Safety and efficacy in pregnancy and lactation have not been established.
Safety and efficacy in children under 1 year of age have not been established.

WARNINGS
AZROTRIN 500 should be used with caution in renal function impairment as there is no data regarding the use of AZROTRIN 500 in patients with impaired renal function.
Less frequently, serious allergic reactions, such as anaphylaxis, angioedema, fever, eosinophilia and skin eruptions have been reported in patients taking AZROTRIN 500. Despite discontinuation of AZROTRIN 500 and successful symptomatic treatment of the allergic reactions, allergic symptoms have recurred in some patients when the symptomatic therapy was discontinued.
These patients require prolonged periods of observation and symptomatic treatment.
Pseudomembranous colitis has been reported ranting from mild to life threatening.
Therefore it is important to consider this diagnosis in patients with diarrhoea subsequent to administration of AZROTRIN 500.

INTERACTIONS
Concomitant use of AZROTRIN 500 with:-
- Antacids – decreases the peak serum concentration of AZROTRIN 500.
  Take AZROTRIN 500 one hour before or two hours after taking an antacid.
- Ergot alkaloids – has been associated with acute ergot toxicity characterised by severe peripheral vasospasm and dysethesia. Co-administration of AZROTRIN 500 and ergot alkaloids is not recommended. (See **CONTRAINDICATIONS**).
- Anticoagulants such as warfarin - Prothrombin time should be monitored.
- Digoxin – may increase serum digoxin concentrations. Monitoring of digoxin serum concentrations is recommended.
- Medicines metabolised by the cytochrome P450 enzyme system (e.g. alprazolam, cyclosporine, disopyramide, midazolam, omeprazole, quinidine, sildenafil, simvastatin, tacrolimus, triazolam, vinblastine, phenytoin and valproate) – AZROTRIN 500 may increase serum levels of these medicines. Serum concentrations of these medicines may require monitoring.
- Terfenadine – may increase serum concentration of terfenadine. Monitor serum levels of terfenadine.
- Theophylline – The area under the plasma concentration – time curve may be increased. Monitoring of theophylline serum concentrations is recommended.

No interactions have been reported with cimetidine, carbamazepine, methylprednisolone and zidovudine.

PREGNANCY AND LACTATION
Safety and efficacy in pregnancy and lactation has not been established.
DOSAGE AND DIRECTIONS FOR USE
The safety and efficacy of AZROTRIN 500 in children under 1 year of age has not been established.
The tablet formulation is not suitable for children under 45kg in weight.
Swallow tablets or capsules whole with some water. AZROTRIN 500 may be taken with or without meals.
Susceptible bacterial infections except sexually transmitted diseases Oral.
Adults and children over 45 kg in weight: 500 mg once daily for three days.
Over five days dosage regimen
Day 1, 500 mg, and then 250 mg daily on days 2 - 5
Sexually transmitted disease caused by *Chlamydia trachomatis*
Adults: 1 g given as a single dose.
A normal adult dose is recommended for use in the elderly patient.

SIDE EFFECTS AND SPECIAL PRECAUTIONS
Side effects:
Haemotological:
- Neutropaenia

Cardiovascular system:
- Palpitations, arrhythmias including ventricular tachycardia, chest pain

Central nervous system:
- Headache, dizziness, tinnitus, hearing loss, convulsions, somnolence, vertigo, fatigue, asthenia, paraesthesias

Gastrointestinal:
- Nausea, anorexia, vomiting, abdominal discomfort, flatulence, diarrhoea, loose stools, constipation, dyspepsia, malaena, taste changes
- *Less frequent:* Pseudomembranous colitis (abdominal cramps or pain, tenderness, severe, watery diarrheoa which may also be bloody, fever)

Kidney/Genitourinary:
- Interstitial nephritis acute renal failure, vaginitis

Liver:
- *Less frequent:* Transient elevations in liver enzymes, hepatitis, cholestatic jaundice

Skin:
- *Less frequent:* Erythema multiforme, Steven's-Johnson syndrome, toxic epidermal necrolysis

Other:
- Allergic reactions (difficulty in breathing, swelling of face, mouth, neck, hands and feet, arthralgia, urticarial, photosensitivity, skin rash, anaphylaxis)

Special precautions:
Use of AZROTRIN 500 may cause an overgrowth of non-susceptible organisms. Appropriate measures should be taken to prevent or treat such superinfection.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT
(See **SIDE EFFECTS AND SPECIAL PRECAUTIONS**)
Symptoms of overdose:
There is no data on overdosage of AZROTRIN 500. Typical symptoms are expected to be those associated with macrolide antibiotics and include severe gastrointestinal symptoms (nausea, vomiting and diarrhea) and hearing loss.
Treatment of overdose:
Treatment is symptomatic and supportive. Gastric lavage may be indicated.

IDENTIFICATION
AZROTRIN 500 tablets are oval, white scored film-coated tablets.

PRESENTATION
White PVC, light resistant opaque, foil, heat sealed to aluminium foil, containing 3 tablets per pack, in an outer cardboard carton.

STORAGE
Store below 25°C.
Protect from light.
Keep out of reach of children.

REGISTRATION NUMBER
37/20.1.1/0690

NAME AND BUSINESS ADDRESS OF APPLICANT
STRIDES PHARMA (SA) (Pty) LTD
106 16th Road
Building 2
Midrand
South Africa

DATE OF PUBLICATION OF PACKAGE INSERT
02 October 2017

Strides

Tel: 010 594 5610. Email: PV@kahmagroup.co.za