National Agency for Food & Drug Administration & Control (NAFDAC)

Registration & Regulatory Affairs (R & R) Directorate

1.0 NAME OF THE MEDICINAL PRODUCT :

1.1 Proprietary Name : Azuma®
1.2 International Non-Proprietary Name (INN) : Azithromycin Tablets

2.0 ANATOMIC THERAPEUTIC AND CHEMICAL (ATC) CLASSIFICATION AND DISTRIBUTION CATEGORY :

2.1 ATC Classification : J01F – Systemic Antibiotics, Macrolides.
2.2 Distribution Category : Prescription only medicine.

3.0 QUALITATIVE AND QUANTITATIVE COMPOSITION :

Tablets are available in two strengths.
Each film coated tablet contains –
Azithromycin Dihydrate PhEur equivalent to Anhydrous Azithromycin 500mg

4.0 PHARMACEUTICAL FORM :

4.1 Pharmaceutical dosage form : Tablets
4.2 Description :
White, capsule shaped, film coated tablets with "AZ500" engraving on one side and plain other side.

5.0 CLINICAL PARTICULARS :

5.1 Therapeutic indications : Azithromycin is an Azlalide antibiotic, part of Macrolide category. Azithromycin is indicated for the treatment of Respiratory, ENT and skin infections caused by susceptible pathogens. Azithromycin is used in adults for the treatment of mild to moderate upper and lower respiratory tract infections and uncomplicated skin and skin structure infections caused by susceptible organisms. It is also used for the treatment of urethritis or cervicitis caused by Chlamydia trachomatis or Neisseria gonorrhoeae, and for the treatment of chancroid caused by Haemophilus ducreyi. Azithromycin is used for the treatment of disseminated infections caused by Mycobacterium avium complex (MAC) in patients with human immunodeficiency virus (HIV) infection and for prevention of disseminated MAC infection (both primary and secondary prophylaxis) in HIV-infected individuals. It is used in children for the treatment of acute otitis media, community-acquired pneumonia, and pharyngitis or tonsillitis caused by susceptible organisms.

5.2 **Posology and method of administration :** As directed by the Physician OR
Pharyngitis and Tonsillitis - The usual oral dosage of Azithromycin in adults for the treatment of pharyngitis or tonsillitis (as second-line therapy) is 500 mg given as a single dose on the first day of therapy, followed by 250 mg once daily on days 2-5 (total cumulative dose: 1.5 g administered over 5 days). **Acute Sinusitis** - the usual adult oral dosage of Azithromycin tablets is 500 mg once daily for 3 days. **Acute Exacerbations of Chronic Bronchitis** - the usual adult dosage of Azithromycin is 500 mg once daily for 3 days or, alternatively, 500 mg given as a single dose on the first day of therapy followed by 250 mg once daily on days 2-5 (total cumulative dose: 1.5 g administered over 5 days). **Community-acquired Pneumonia** - the usual dosage of Azithromycin is 500 mg given as a single dose on the first day of therapy, followed by 250 mg once daily on days 2-5 (total cumulative dose: 1.5 g administered over 5 days).
For children : The usual dose for children is 10mg/kg body weight orally, once a day for 3 - 5 days. The required dose should be measured with the measure cup provided and administer orally.
Antacids interfere with the absorption of Azithromycin and must not be administered together.

5.3 **Contraindications :** Azithromycin is contraindicated in patients with known hypersensitivity to Azithromycin, erythromycin, or any macrolide or ketolide antibiotic.

5.4 **Special warnings and precautions for use :** Serious hypersensitivity reactions, including angioedema, anaphylaxis, and dermatologic reactions, have occurred rarely in patients receiving Azithromycin. Fatalities have been reported. Patients should be advised to discontinue Azithromycin therapy immediately and to contact their clinician if any signs of an allergic reaction occur. Severe acute hypersensitivity reactions should be treated with appropriate therapy (e.g., epinephrine, maintenance of an adequate airway, oxygen, IV fluids, maintenance of blood pressure as indicated). Keep the medicine out of reach of children.

5.5 **Interaction with other medicinal products and other forms of interaction :** It is contraindicated with the drugs affecting or metabolized by hepatic microsomal enzymes, Albendazole, Antacids, Antilipemic Agents, Antimalarial Agents, Antiretroviral Agents, Benzodiazepines, Carbamazepine, Cetirizine, Cimetidine, Co-trimoxazole, Cyclosporine, Digoxin, Ergot Alkaloids, Fluconazole, Ivermectin, Phenytoin, Pimozide, Rifabutin etc.

5.6 **Pregnancy and lactation :** Preliminary data indicate that Azithromycin may be safe and effective in the treatment of chlamydial infections in pregnant women; however, there are insufficient data to recommend routine use of the drug during pregnancy. Azithromycin has been detected in human milk. The drug should be used with caution in nursing women.

5.7 **Effects on ability to drive and use machines :** No need of caution when operating machinery or driving a motor vehicle unless effects of drug on individual are known.

5.8 **Undesirable effects :** Generally Azithromycin is well tolerated in adults and children. Most side effects are mild and rarely needs discontinuation of therapy. The most common adverse effects are diarrhea/loose stools, nausea, abdominal pain, serious allergic (i.e., angioedema, anaphylaxis, bronchospasm) and dermatologic (i.e., erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis) reactions, sometimes resulting in death, have been reported rarely in patients receiving Azithromycin. Abnormal liver function, including cholestatic jaundice and hepatitis, and pancreatitis has been reported infrequently in clinical trials or during postmarketing studies with Azithromycin. Hepatic necrosis and hepatic failure, sometimes resulting in death, have occurred rarely. Palpitations, chest pain, edema, hypotension or syncope has been reported in 1% or less of patients receiving oral Azithromycin.

5.9 **Overdose :** Limited information is available on the acute toxicity of Azithromycin. The acute lethal dose of the drug in humans is not known. The oral LD50 of Azithromycin in mice or rats is 3000-4000 mg/kg. In the events of an acute over dosage the stomach should be emptied. The patient with overdose should be observed and symptomatic and supportive treatment shall be given.

6.0 PHARMACOLOGICAL PROPERTIES :

6.1 **Pharmacodynamic properties :** This drug is primarily bacteriostatic, but can be bactericidal depending on the concentration given. It is effective against aerobic Gram-positive microorganisms, and some Gram-negative organisms. However, azithromycin does not appear to have any inherent direct activity against Pseudomonas aeruginosa (a Gram-negative, rod-shaped, opportunistic pathogen).

6.2 **Pharmacokinetic properties : Absorption -** Following oral administration, azithromycin is rapidly absorbed and widely distributed throughout the body. Rapid distribution of azithromycin into tissues and high concentration within cells result in significantly higher azithromycin concentrations in tissues than in plasma or serum. The drug is metabolized in the liver and excreted mainly in the urine. **Elimination -** Plasma concentrations of azithromycin following single 500 mg oral and i.v. doses declined in a polyphasic pattern with a mean apparent plasma clearance of 630 mL/min and terminal elimination half-life of 68 hours. The prolonged terminal half-life is thought to be due to extensive uptake and subsequent release of drug from tissues. Biliary excretion of azithromycin, predominantly as unchanged drug, is a major route of elimination. Over the course of a week, approximately 6% of the administered dose appears as unchanged drug in urine.

6.3 **Preclinical safety data :** Phospholipidosis (intracellular phospholipid accumulation) has been observed in some tissues of mice, rats, and dogs given multiple doses of azithromycin. It has been demonstrated in numerous organ systems (e.g., eye, dorsal root ganglia, liver, gallbladder, kidney, spleen, and pancreas) in dogs treated with azithromycin at doses which, expressed on the basis of mg/m^2, are approximately equal to the recommended adult human dose, and in rats treated at doses approximately one-sixth of the recommended adult human dose. This effect has been shown to be reversible after cessation of azithromycin treatment. Phospholipidosis has been observed to a similar extent in the tissues of neonatal rats and dogs given daily doses of azithromycin ranging from 10 days to 30 days.

7.0 PHARMACEUTICAL PARTICULARS :

7.1 **List of Excipients :** Calcium Hydrogen Phosphate, Magnesium Stearate, Pregelatinized Starch, Croscarmellose Sodium, Colloidal Anhydrous Silica, Titanium Dioxide, Polyethylene Glycol, Sodium Lauryl Sulphate, Hydroxy Propyl Methyl Cellulose.

7.2 **Incompatibilities :** No Incompatibilities.

7.3 **Shelf life :** 2 years when stored under recommended conditions.

7.4 **Special precautions for storage :** Store in a dry place below 25˚C. Protect from light.

7.5 **Nature and contents of container :**
Blister pack of 3 Tablets. Each blister pack in an inner box along with a leaflet. 30 such inner boxes in an outer box.

7.6 **Special precautions for disposal :** No special requirement.

8.0 **Registrant :**
SHELYS PHARMACEUTICALS LTD.,
Plot No. 696, New Bagamoyo Road, Mwenge,
P.O. Box 32781, Dar Es Salaam, Tanzania.

9.0 **Date of revision of the text :** 05th November, 2009