Agycin –250

(Azithromycin Tablets USP 250 mg)

1. NAME OF THE FINISHED PHARMACEUTICAL PRODUCT

AGYCIN - 250

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Composition

Each film coated tablet contains:

Azithromycin USP (as dihydrate)

Equivalent to Azithromycin Anhydrous… 250 mg

Excipients ….. q.s.

Colour: Titanium dioxide

For full list of excipients refer section 6.1

3. PHARMACEUTICAL FORM

Tablets

4. DESCRIPTION

Azithromycin is a macrolide antibiotic belonging to the azalide group. The chemical name of azithromycin is 9-deoxy-9a-aza-9a-methyl-9a-homoerythromycin A. The molecular weight is 749.0.

5. CLINICAL PHARMACOLOGY

5.1 Mechanism of action

Azithromycin is an azalide, a sub-class of the macrolide antibiotics. By binding to the 50Sribosomal sub-unit, azithromycin avoids the translocation of peptide chains from one side of the ribosome to the other. As a consequence of this, RNA-dependent protein synthesis in sensitive organisms is prevented.

5.2 Mechanism of resistance:

Resistance to azithromycin may be inherent or acquired. There are three main mechanisms of resistance in bacteria: target site alteration, alteration in antibiotic transport and modification of the antibiotic.

Complete cross resistance exists among *Streptococcus pneumoniae*, betahaemolytic streptococcus of group A, *Enterococcus faecalis* and *Staphylococcus aureus*, including methicillin resistant *S. aureus* (MRSA) to erythromycin, azithromycin, other macrolides and lincosamides.

5.3 Pharmacokinetics

The reported bioavailability of azithromycin after oral administration is approximately 37%. Peak plasma concentrations were reported to be attained after 2-3 hours. The mean maximum concentration reported (Cmax) after a single dose of 500 mg was approximately 0.4 μg/ml.

Three days after administration of 500 mg as a single dose or in partial doses concentrations of 1.3-4.8 μg/g, 0.6-2.3 μg/g, 2.0-2.8 μg/g and 0-0.3 μg/ml have been measured in resp. lung, prostate, tonsil and serum. Binding of azithromycin to serum proteins varies from 52% at 0.05 mg/l to 18% at 0.5 mg/l, depending on the serum concentration. The reported terminal plasma elimination half-life closely reflects the elimination half-life from tissues of 2-4 days.

5.4 Indications

Azithromycin is indicated for the following bacterial infections induced by micro-organisms susceptible to azithromycin:

- Acute bacterial sinusitis (adequately diagnosed)
- Acute bacterial otitis media (adequately diagnosed)
- Pharyngitis, tonsillitis
- Acute exacerbation of chronic bronchitis (adequately diagnosed)
- Mild to moderately severe community acquired pneumonia
- Infections of the skin and soft tissues of mild to moderate severity e.g. folliculitis, cellulitis, erysipelas
- Uncomplicated Chlamydia trachomatis urethritis and cervicitis

Consideration should be given to official guidance on the appropriate use of antibacterial agents

5.5 Dosage and administration

Azithromycin should be given as a single daily dose. The tablets can be taken with or without food.

- **Children and adolescents with a body weight above 45 kg, adults and the elderly:**
    - The total dose is 1500 mg, administered as 500 mg once daily for 3 days. Alternatively, the same total dose (1500 mg) can be administered in a period of 5 days, 500 mg on the first day and 250 mg on day 2 to 5.
    - In the case of uncomplicated *Chlamydia trachomatis* urethritis and cervicitis, the dosage is 1000 mg as a single oral dose.
- **Children and adolescents with a body weight below 45 kg:**
  Other dosage forms should be considered for this group of patients.

5.6 Contraindications

In patients with hypersensitivity to azithromycin, erythromycin, any macrolide or ketolide antibiotic, or to any other component of this formulation

5.7 Warnings and precautions

- Rare serious allergic reactions including angioneurotic oedema and anaphylaxis (rarely fatal), have been reported. Some of these reactions with azithromycin have resulted in recurrent symptoms and required a longer period of observation and treatment.
- The use of azithromycin should be undertaken with caution in patients with significant hepatic disease.
- In case of signs and symptoms of liver dysfunction, such as rapid developing asthenia associated with jaundice, dark urine, bleeding tendency or hepatic encephalopathy, liver function tests/ investigations should be performed immediately. Azithromycin administration should be stopped if liver dysfunction has emerged.
- Prolonged cardiac repolarisation and QT interval, imparting a risk of developing cardiac arrhythmia and torsades de pointes, have been seen in treatment with other macrolides, including azithromycin

- Exacerbations of the symptoms of myasthenia gravis and new onset of myasthenia syndrome have been reported in patients receiving azithromycin therapy
- Azithromycin is not suitable for treatment of severe infections where a high concentration of the antibiotic in the blood is rapidly needed.

5.8 Superinfections:

- As with any antibiotic preparation, it is recommended to pay attention to signs of superinfection with non-susceptible micro-organisms like fungi. A superinfection may require an interruption of the azithromycin treatment and initiation of adequate measures.
- In patients with severe renal impairment (GFR < 10 ml/min) a 33% increase in systemic exposure to azithromycin was observed
- In areas with a high incidence of erythromycin A resistance, it is especially important to take into consideration the evolution of the pattern of susceptibility to azithromycin and other antibiotics.
- In bacterial pharyngitis the use of azithromycin is recommended only in cases where first line therapy with beta-lactams is not possible.
- Susceptibility testing is considered a precondition for treatment of soft tissue infections with azithromycin.
- Azithromycin should be used with caution in patients with neurological or psychiatric disorders.
- Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose- galactose malabsorption should not take this medicine.

5.9 Drug-drug Interactions

- Azithromycin and P-gp substrates such as digoxin are administered concomitantly, the possibility of elevated serum concentrations of the substrate should be considered.
- Concurrent use of azithromycin with ergot derivatives is not recommended
- Caution is advised in the co-administration of Astemizole, alfentanil with Azithromycin because of the known enhancing effect of these medicines when used concurrently with the macrolid antibiotic erythromycin.

- Concomitant administration of cisapride may cause the increase of QT interval prolongation, ventricular arrhythmias and torsades de pointes.
- Caution should be exercised before considering concurrent administration of azithromycin and cyclosporin

5.10 Adverse effects

The commonly reported adverse effects are diarrhoea, abdominal pain, nausea, flatulence, abdominal discomfort, loose stools, anorexia, dizziness, headache, paraesthesia, dysgeusia, visual impairment, deafness, rash, pruritus, arthralgia, fatigue.

5.11 Over dosage

Symptoms

The typical symptoms of an overdose with macrolide antibiotics include reversible loss of hearing, severe nausea, vomiting and diarrhoea.

Treatment

In the event of overdose, general symptomatic and supportive measures are indicated as required

5.12 Usage in Special populations

Pregnancy:

Azithromycin should only be used during pregnancy if the benefit outweighs the risk

Lactation:

It is recommended to discard the milk during treatment and up until 2 days after discontinuation of treatment. Nursing may be resumed thereafter.

Renal Insufficiency:

Dose adjustment is not required in patients with mild to moderate renal impairment (GFR 10-80 ml/min). In patients with severe renal impairment (GFR < 10 ml/min) a 33% increase in systemic exposure to azithromycin was observed

Hepatic insufficiency:

Dose adjustment is not required for patients with mild to moderate hepatic dysfunction. Administered with caution in patients with significant hepatic disease

Elderly:

Dose adjustment is not recommended

Infants, toddlers, children and adolescents:

Pharmacokinetics has been studied in children aged 4 months – 15 years taking capsules, granules or suspension. At 10 mg/kg on day 1 followed by 5 mg/kg on days 2-5, the C_{max} achieved is slightly lower than in adults, with 224 µg/l in children aged 0.6-5 years and after 3 days dosing, and 383 µg/l in those aged 6-15 years. The half-life of 36 h in the older children was within the expected range for adults

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

- Microcrystalline Cellulose
- Maize Starch
- Sodium Starch Glycolate
- Sodium Benzoate
- Purified talc
- Magnesium Stearate
- Wincoat-WT-1001 White
- Isopropyl Alcohol
- Dichloromethane

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 Months

6.4 Special precautions for storage

Store in cool and dry place below 30^0C. Protect from light.

6.5 Nature and contents of container

6 tablets in a blister of Aluminium/PVC foil in monocarton along with insert.

6.6 Instructions for use and handling and disposal

Not Applicable

7. MARKETING AUTHORISATION HOLDER

BLISS GVS PHARMA LIMITED,

102, Hyde Park, Saki-Vihar road, Andheri (East) Mumbai 400 072, INDIA