1.17 Summary Product Characteristics
1.17.1 Product Information for Health Professionals

1. Name of the medicinal product

Azithromycin for Oral Suspension USP 200 mg / 5 ml-SKAZI 200

2. Qualitative and quantitative composition

Each 5ml (after reconstitution) contains:
Azithromycin USP (As Dihydrate)
Equivalent to Azithromycin (Anhydrous)…….. 200 mg
Excipients …….. q.s.

3. Pharmaceutical form:

Liquid Oral Dosage Form- Powder for suspension

Dry powder: White coloured, free flowing powder with mint odour.

After reconstitution: White homogenous suspension with mint odour.

4. Clinical particulars

4.1 Therapeutic indications

Upper respiratory tract infections, malaria, skin infections.

Azithromycin is active against gram-negative pathogens such as Haemophilus influenzae and Moraxella catarrhalis (Branhamella catarrhalis), as well as some of the Enterobacteriaceae such as Escherichia coli and Salmonella and Shigella spp. Azithromycin is also active against Chlamydia trachomatis and some opportunistic mycobacteria, including Mycobacterium avium complex. It has activity against the protozoa Toxoplasma gondii and Plasmodium falciparum.

4.2 Posology and method of administration

Azithromycin suspension should be given as a single daily dose.

Azithromycin suspension can be taken with or without food.

Children over 45 Kg body weight and adults , including elderly patients:

The total dose of Azithromycin is 1500 mg which should be given over three days (500 mg once daily)

In children under 45 Kg body weight: Azithromycin Suspension should be used for children under 45 Kg. There is no information on children less than 6 months of age.

The dose in children is 10 mg/kg as a single daily dose for 3 days:

Children :15-25 kg (3-7 years): 5 ml (200 mg) given as 1x 5 ml spoonful ,once daily for 3 days.

26-35 kg (8-11 years): 7.5 ml (300 mg) given as 1x7.5 ml spoonful ,once daily for 3 days.

36-45 kg (12-14 years): 10 ml (400 mg) given as 1X10 ml spoonful, once daily for 3 days.

Or

As directed by physician. For oral administration.

4.3 Contraindications

Gastrointestinal disturbances are the most frequent adverse effect but are usually mild and less frequent than with erythromycin. Transient elevations of liver enzyme values have been reported and, rarely, cholestatic jaundice. Rashes, headache, and dizziness may occur. Severe hypersensitivity reactions occur rarely but may be prolonged. Transient alterations in neutrophil counts have been seen in patients receiving azithromycin. Pain and inflammation may occur at the site of intravenous infusions. The manufacturers suggest that azithromycin should not be used in patients with hepatic impairment.

4.4 Special warnings and precautions for use

Before taking azithromycin,

- Tell your doctor and pharmacist if you are allergic to azithromycin, clarithromycin dirithromycin, erythromycin, telithromycin, any other medications, or any of the ingredients in azithromycin suspension
- Tell your doctor and pharmacist what other prescription and nonprescription medications, vitamins, nutritional supplements, and herbal products you are taking or plan to take. Be sure to mention any of the following: anticoagulants ('blood thinners') such as warfarin;

cyclosporine; digoxin; dihydroergotamine; ergotamine; medications for irregular heartbeat such as amiodarone, dofetilide, procainamide, quinidine, and sotalol; nelfinavir; phenytoin; and terfenadine.

- If you are taking antacids containing aluminum hydroxide or magnesium hydroxide (Maalox, Mylanta, Tums, others), you will need to allow some time to pass between when you take a dose of these antacids and when you take a dose of azithromycin tablets or liquid. Ask your doctor or pharmacist how many hours before or after you take azithromycin you may take these medications.
- Tell your doctor if you have ever had jaundice (yellowing of the skin or eyes) or other liver problems while taking azithromycin. Your doctor will probably tell you not to take azithromycin.
- Tell your doctor if you or anyone in your family has or has ever had a prolonged QT interval (a rare heart problem that may cause irregular heartbeat, fainting, or sudden death) or a fast, slow, or irregular heartbeat, and if you have low levels of magnesium or potassium in your blood; if you have a blood infection; heart failure; cystic fibrosis; myasthenia gravis (a condition of muscles and the nerves that control them); or if you have kidney or liver disease.
- Tell your doctor if you are pregnant, plan to become pregnant, or are breastfeeding. If you become pregnant while taking azithromycin, call your doctor.

4.5 Interaction with other medicinal products and other forms of interaction

Concurrent administration of antacids containing aluminium or magnesium salts can reduce the rate, but not the extent, of absorption of azithromycin. Absorption reduced by food. Antacids reduce rate of absorption. Increases absorption of Digoxin and Cyclosportne Increased rifabutin toxicity has been reported in patients receiving azithromycin.

4.6 Fertility, pregnancy and breast-feeding

There are no adequate data from the use of azithromycin in pregnant women. In reproduction toxicity studies in animals azithromycin was shown to pass the placenta, but no teratogenic effects were observed. The safety of azithromycin has not been confirmed with regard to the

use of the active substance during pregnancy. Therefore Azithromycin should only be used during pregnancy if definitely indicated.

Azithromycin passes into breast milk. Because it is not known whether azithromycin may have adverse effects on the breast-fed infant, nursing should be discontinued during treatment with Azithromycin. Among other things diarrhoea, fungus infection of the mucous membrane as well as sensitisation is possible in the nursed infant. It is recommended to discard the milk during treatment and up until 2 days after discontinuation of treatment. Nursing may be resumed thereafter.

4.7 Effects on ability to drive and use machines

There is no evidence to suggest that azithromycin may have an effect on a patient's ability to drive or operate machinery.

4.8 Undesirable effects

Nausea, vomiting, abdominal pain, diarrhoea, dyspepsia, flatulence, dizziness, headache and vertigo.

4.9 Overdose

Symptoms: hearing loss, severe nausea, vomiting and diarrhoea.

Treatment: gastric lavage, general supportive measures.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: antibacterials for systemic use; macrolides; azithromycin.

ATC code: J01FA10

Mechanism of action

Azithromycin is an azalide, a sub-class of the macrolide antibiotics. By binding to the 50S-ribosomal 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.

PK/PD relationship

For azithromycin the AUC/MIC is the major PK/PD parameter correlating best with the efficacy of azithromycin.

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.

Susceptibility

The prevalence of acquired resistance may vary geographically and with time for selected species and local information on resistance is desirable, particularly when treating severe infections.

5.2 Pharmacokinetic properties

Absorption

The biological availability of azithromycin after oral administration is approximately 37%. Peak plasma levels are achieved 2-3 hours after taking the medicinal product.

Distribution

After oral administration, azithromycin is distributed throughout the entire body. Pharmacokinetic studies have shown clearly higher azithromycin levels in the tissues than in the plasma (up to 50 times the maximum observed concentration in plasma). This indicates that the substance is bound in the tissues in considerable quantities.

Concentrations in the infected tissues, such as lungs, tonsil and prostate are higher than the MRC90 of the most frequently occurring pathogens after a single dose of 500 mg.

The protein binding of azithromycin in serum is variable and varies, depending on the serum concentration, from 52% at 0.05 mg/l to 12% at 0.5 mg/l. The steady state distribution volume is 31.1 l/kg.

Elimination

The terminal plasma-elimination half-life closely follows the tissue depletion half-life from 2 to 4 days.

Approximately 12% of an intravenously administered dose of azithromycin is, over a period of 3 days, excreted unchanged in the urine. High concentrations of unchanged azithromycin were found in human bile. In this, ten metabolites were also detected (formed by N- and O-desmethylation, by hydroxylation of the desosamin and aglycon rings and by splitting the cladinose conjugate). A comparison of fluid chromatography and microbiological assessment methods shows that the metabolites are microbiologically inactive.

In animal models high concentrations of azithromycin were found in phagocytes. Also it has been shown that during active phagocytosis higher concentrations of azithromycin are released than during inactive phagocytosis. In animal models this process was shown to contribute to the accumulation of azithromycin in infectious tissue.

5.3 Preclinical safety data

No relevant information.

6. Pharmaceutical particulars

6.1 List of excipients

Sucrose (Pharma grade), Xanthan gum, Carmellose Sodium, Trusil Peppermint Powder, Saccharin Sodium, Tribasic Sodium Phosphate Dodecahydrate (Dried).

6.2 Incompatibilities

None stated

6.3 Shelf life

36 months

6.4 Special precautions for storage

Store in dry place, below 30°C. Protect from light.

Shake well before use.

Keep the medicine out of reach of children.

6.5 Nature and contents of container

15 ml amber color glass Bottle.

6.6 Special precautions for disposal and other handling

Any unused product or waste material should be disposed of in accordance with local requirements

7. APPLICANT

Manufactured by:

S Kant HEALTHCARE Ltd.

1802-1805, G.I.D.C., Phase III,

Vapi - 396 195. Gujarat, INDIA.

8. WHO PREQUALIFICATION REFERENCE NUMBER

Not applicable

9. DATE OF PREQUALIFICATION / RENEWAL OF PREQUALIFICATION

Not applicable

10. DATE OF REVISION OF THE TEXT

Not applicable