1.6.1 PRESCRIBING INFORMATION (SUMMARY OF PRODUCTS CHARACTERISTICS)

1. NAME OF THE FINISHED PHARMACEUTICAL PRODUCT

AMYN-250 (Amoxicllin Capsules BP 250mg)

1.1 Strength

Amoxicillin 250mg

1.2 Pharmaceutical Form

Capsules

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

2.1 Qualitative declaration:

Each Capsule contains:

Amoxicllin Trihydrate BP

Equivalent to Amoxicillin…250 mg

2.2 Quantitative declaration:

For the full list of excipients, see section 6.1.

2.3 Salts and hydrates

Amoxicillin Trihydrate.

2.4 Esters and pro-drugs

Not applicable

2.5 Oral Powders for solution or suspension

Not applicable

2.6 Parenterals excluding powders for reconstitution

Not applicable

2.7 Powders for reconstitution prior to parenteral administration

Not applicable

2.8 Concentrates

Not applicable

2.9 Transdermal patches

Not applicable

2.10 Multidose solid or semi-solid products

Not applicable

2.11 Biological medicinal products

Not applicable

3. PHARMACEUTICAL FORM

Capsule

Maroon/Beige coloured filled hard gelatin capsules Size '2' printed 'AMOXY 250' on both the shells containing white to off white granular powder.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Amoxicillin is a broad-spectrum antibiotic indicated for the treatment of commonly occurring bacterial infections such as:

Upper respiratory tract infections: e.g. sinusitis, acute pharyngitis.

Lower respiratory tract infections: e.g. acute exacerbations of chronic bronchitis, lobar and bronchopneumonia, uncomplicated community acquired pneumonia, *H. influenza* infections.

Gastrointestinal tract infections: e.g. acute gastritis, peptic ulcer disease and invasive salmonellosis.

Skin and soft tissue infections: e.g. Cellulitis, erysipelas, osteomyelitis

Genito-urinary tract infections: e.g. cystitis, urethritis, pyelonephritis, bacteriuria in pregnancy, septic abortion, puerperal sepsis.

ENT Infections: Cervical adenitis, otitis media.

Dental infections: Dental abscess (as an adjunct to surgical management), suppurative odontogenic infections. Listerial meningitis.

Prophylaxis of endocarditis Amoxicillin may be used for the prevention of bacteraemia associated with procedures such as dental extraction, in patients at risk of developing of Endocarditis

4.2 Posology and Method of Administration

Posology:

Standard adult dosage:

250 mg three times daily increases to 500 mg three times daily for more severe infections.

High dose therapy: Maximum recommended oral dosage 6 gm in divided doses;

Short course therapy:

Simple acute urinary tract infections: Two 3g doses with 10-12 hours between the doses.

Dental abscess: Two 3g doses with 8 hours between the doses.

Urinary tract infections: 3 g repeated after 10-12 hrs.

Standard children dosage (upto 10 years of age) : For AMYN syrup

Child upto 10 years: 125 mg every 8 hours doubled in severe infections.

Patients with renal impairment: In renal impairment the excretion of the antibiotics will be delayed and depending on the degree of impairment, it may be necessary to reduce the total daily dosage according to the following scheme:

Adult and children over 40 Kg

Mild impairment (creatinine clearance > 30ml/min) – No change in dosage

Moderate impairment (creatinine clearance 10-30 ml/min) – 500 mg b.i.d. maximum

Severe impairment (creatinine clearance < 10 ml/min) – 500 mg/day maximum

Children under 40 Kg

Mild impairment (creatinine clearance > 30ml/min) – No change in dosage

Moderate impairment (creatinine clearance 10-30 ml/min) – 5 mg/ kg b.i.d. maximum

Severe impairment (creatinine clearance < 10 ml/min) – 15 mg/Kg o.d.

Route of administration: Oral

4.3 Method of Administration

Oral: Swallow a capsule with a glass of water as per dosage.

4.4 Contraindications

Amoxicillin is a penicillin and should not be given to penicillin hypersensitive patients. Attention should be paid to possible cross sensitivity with other beta lactam antibiotics .

4.5 Special warnings and precautions for use

Before initiating therapy with Amoxicillin, careful enquiry should be made concerning previous hypersensitivity reactions to penicillins, cephalosporins. Serious and occasionally fatal hypersensitivity reactions have been reported in patients on penicillin therapy. These reactions are more likely to occur in individuals with a history of hypersensitivity to betalactum antibiotics. Erythematous rashes have been associated with glandular fever in patients receiving Amoxicillin. Prolonged use may also occasionally result in overgrowth of nonsusceptible organisms.

Dosage should be adjusted in patients with renal impairment.

4.6 Interaction with other medicinal products and other forms of interaction

In common with other broad spectrum antibiotics, Amoxicillin may reduce the efficacy of oral contraceptives and patients should be warned accordingly. Concurrent administration of Allopurinol during treatment with Amoxicillin can increase the likelihood of allergic skin reactions. Prolongation of prothrombin time has been reported rarely in patients

receiving Amoxicillin. Appropriate monitoring should be undertaken when anticoagulants are prescribed concurrently.

It is recommended that when testing for the presence of glucose in urine during Amoxicillin treatment, enzymatic glucose oxidase methods should be used. Due to the high urinary concentrations of Amoxicillin, Concurrent use with Amoxicillin may result in increased and prolonged blood levels of Amoxicillin.

4.7 Additional information on special populations

None

4.8 Pregnancy and Lactation

Use in pregnancy:

Animal studies with Amoxicillin have shown no Teratogenic effects. However treatment with Amoxicillin may be considered appropriate when the potential benefits outweight the potential risks associated with treatment.

Use in lactation:

Amoxicillin may be given during lactation. With the exception of the risk of sensitization associated with the excretion of trace quantities of Amoxicillin in breast milk, there are no known detrimental effects for the breast-fed infant.

4.9 Effects on ability to drive and use machine

Adverse effects on the ability to drive or operate machinery have not been observed.

4.10 Undesirable effects

Side effects as with other penicillins, are uncommon and mainly of a mild and transitory nature.

Hypersensitivity reactions: if any hypersensitivity occurs, the treatment should be discontinued. Skin rashes, pruritus and urticarial have been reported occasionally. Rarely, skin reactions such as erythema multiforme and Steven-Johnson syndrome, toxic epidermal necrolysis and bullous and

exfoliative dermatitis have been reported. As with other antibiotics, severe allergic reactions including angioneurotic oedema, anaphylaxis, serum sickness and hypersensitivity vasculitis have been reported rarely.

Gastrointestinal reactions: Effects include nausea, vomiting and diarrhea. Intestinal candidiasis and antibiotic associated colitis have been reported rarely intestinal nephritis can occur rarely.

Hepatic effects: A moderate rise in AST and/or ALT has been occasionally noted but the significance of this is unclear. As with other beta lactam antibiotics, hepatitis and cholestatic jaundice have been reported rarely.

Hematological effects: As with other beta lactam antibiotics, reversible leucopenia, reversible thrombocytopenia and haemolytic anaemia have been reported rarely.

CNS effects: CNS effects have been reported rarely. They include hyperkinesiais, dizziness and convulsions. Convulsions may occur in patients with impaired renal function or in those receiving high doses.

Miscellaneous: Superficial tooth discoloration has been reported rarely and mostly with

the suspension and chewable tablets. It can usually be removed by brushing.

4.11 Overdose

Problems of overdosage with Amoxicllin are unlikely to occur. If encountered, gastrointestinal effects such as nausea, vomiting and diarrhea may be evident and should be treated symptomatically with attention to the water/electrolyte balance. During the administration of high doses of amoxicillin, adequate fluid intake and urinary output must be maintained. Amoxicillin can be removed from the circulation by haemodialysis.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: ATC code: J01CA04

Mechanism of Action: Amoxicillin has a broad spectrum of antibacterial activity against many Gram-positive and Gram-negative micro-organisms, acting through the inhibition of biosynthesis of cell wall mucopeptide. It is

rapidly bactericidal and possess the safety profile of penicillin. Amoxicillin binds to penicillin-binding protein 1A (PBP-1A) located inside the bacterial cell wall. Penicillins acylate the penicillin-sensitive transpeptidase C-terminal domain by opening the lactam ring. This inactivation of the enzyme prevents the formation of a crosslink of two linear peptidoglycan strands, inhibiting the third and last stage of bacterial cell wall synthesis. Cell lysis is then mediated by bacterial cell wall autolytic enzymes such as autolysins; it is possible that amoxicillin interferes with an autolysin inhibitor.

5.2 Pharmacokinetic properties

Amoxicillin is stable in the acid gastric secretion and is rapidly absorbed from the gastrointestinal tract after oral administration. The presence of food does not interfere with this process. Peak plasma concentrations are obtained in about two hours, producing around 2.5 times the peak concentration resulting from comparable doses of ampicillin. Amoxicillin is not highly protein bound; approximately 18% of total plasma drug content is bound to protein. Amoxicillin diffuses readily into most body tissues and fluids, with the exception of the brain and spinal fluid. Inflammation generally increases the permeability of the meninges to penicillins and this may apply to amoxicillin.

The effective levels in the cerebrospinal fluid are obtained only in the presence of inflammation and then irregularly. The elimination half-life is approximately 1 hour. The major route of elimination for amoxicillin is via the kidney. Approximately 60-70% of amoxicillin is excreted unchanged in urine during the first 6 hours after administration of a standard dose. Amoxicillin is partly excreted in the urine as the inactive penicilloic acid in quantities equivalent to 10- 25% of the initial dose.

5.3 Pre-clinical safety data

Toxicology of Amoxicillin trihydrate has been reported through a number of pharmacological, preclinical and clinical studies.

Kopran Limited has not conducted any toxicological trials or studies to establish toxicology profile of Amoxicillin trihydrate capsules. However,

selected references and ***e***xcerpts from the published literature are provided in the following pages:

Single dose toxicity

a) Acute toxicity:

Investigations of the acute toxicity (LD50) of amoxicillin in adult animals and neonates have confirmed the very low

toxicity potential. The following LD50 values have been reported in experimental animals:

LD50 > 15000 mg/Kg, oral, rat

> 25000 mg/Kg, oral, mouse

>12500 mg/Kg, oral, rabbit.

Administration of amoxicillin does not result in any unexpected or synergistic toxicity.

b) Chronic toxicity / subchronic toxicity:

Extensive studies of the chronic toxicity have been carried out based on international standards. Solely after high doses (corresponding to 20 to 50 fold the maximal human dose) were mild haematological and blood-chemical changes observed which regressed completely following discontinuation of the therapy.

Repeat dose toxicity:

Extensive studies of the chronic toxicity have been carried out based on international standards. Solely after high doses (corresponding to 20 – to 50 – fold the maximal human dose) of amoxicillin were mild haematological and blood-chemical changes observed which regressed completely following discontinuation of the therapy.

Carcinogenesis:

Skin: Prolonged or repeated skin contact with amoxicillin may cause allergic skin reaction and hyper sensitization.

Inhalation: Prolonged or repeated inhalation may rarely cause allergic reaction and hypersensitization. The symptoms might include running nose,

sneezing, itching, coughing, pulmonary obstruction, signs similar to asthma, wheezing, difficulty breathing.

Ingestion: The chronic exposure to amoxicillin may lead to possible allergic reaction. The symptoms may include swelling of face and difficulty breathing.

The other adverse reactions from either inhalation or ingestion may include swelling of the face, hives, itching, a sudden severe drop in blood pressure, headache, vaginal itching or discharge, fever, shortness of breath and joint pain. Amoxicillin Trihydrate is not reported to be carcinogenic to humans. IARC, NTP and OSHA do not list amoxicillin as a carcinogen for humans.

Mutagenesis:

Mutagenic effects are reported in bacteria and yeast. Repeated and prolonged exposure to amoxicillin Trihydrate may produce target organs damage.

Reproductive Toxicity:

Specific developmental abnormalities were not detected in pregnant rats after amoxicillin ingestion. The sexual abilities in these animals were not affected. There was no weight loss in test group animals as compared to control group. Serum pyridoxine and pyridoxal 5-phosphate were found to be unaffected in the maternal liver as compared to control group. Blood hemoglobin, serum transaminases, renal concentrations of FAD, FMN and other serum enzyme parameters were also found to be in normal range. There was no fetal liver hypertrophy observed in treated group of animals. Amoxicillin trihydrate was thus devoid of any reproductive effects under the experimental conditions tested.

Teratogenic Effect:

There have not been any reports in human of teratogenicity associated with amoxicillin. Amoxicillin may be used during pregnancy.

6. PHARMACEUTICAL PARTICULARS

6.1 List of Excipients-

Sodium Lauryl Sulphate, Purified Talc Magnesium stearate, Size "2" Empty hard gelatin Maroon/Beige capsules with circular printed 'AMOXY 250'

6.2 Incompatibilities

None

6.3 Shelf life

36 Months (3 years)

6.4 Special precautions for storage

Store below 30ºC in a dry place. Protect from light.

6.5 Nature and contents of container

Primary Packaging: Alu / PVC Blister and HDPE jar pack

Secondary Packaging: Paperboard carton

7. MARKETING AUTHORIZATION HOLDER AND MANUFACTURING SITE ADDRESSES

KOPRAN LIMITED
Village Savroli, Taluka Khalapur,
District-Raigad-410202
India

8. MARKETING AUTHORIZATION REGISTRATION NUMBER(S).

Not applicable

9. DATE OF FIRST AUTHORIZATION REGISTRATION/RENEWAL OF THE AUTHORIZATION

Not applicable