SmPC

1.5.1 Prescribing Information (Summary Of Product Characteristics)

1. Name of the medicinal product

AMYN DT 125 (Amoxicillin Tablets for Oral Suspension USP 125mg)

Strength : 125 mg

Pharmaceutical form : Tablets for Oral Suspension

2. Qualitative and quantitative composition

2.1 Qualitative declaration

Label Claim:

Each dispersible tablet contains:

Amoxicillin Trihydrate USP Equivalent to Amoxicillin …….125mg

2.2 Quantitative declaration

Composition of unit dose is given below:

Sr. No.	Ingredients	Qty /tab (In mg)	Function	Reference
(i) Active ingredients				
1.	Amoxicillin Trihydrate	143.50	Active Component	USP
(ii) Inactive ingredients (Compression)				
2.	Microcrystalline Cellulose PH-102	86.25	Diluent	BP
3.	Aspartame	6.00	Sweetening Agent	EP/BP
4.	Crospovidone	3.00	Disintegrant	BP
5.	Ess. Fl.DC.Trusil Lemon	1.50	Flavoring Agent	IH
6.	Flavour peppermint DC 117 Quest	1.50	Flavoring Agent	IH
7.	Magnesium Stearate	3.75	Lubricant	BP
8.	Purified Talc	3.00	Lubricant	BP
9.	Colloidal Anhydrous Silica	1.50	Glidant	BP
Total		**250.00**		

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

Dispersible Tablets:

AMYN DT 125 are White to off white round shaped, flat face beveled edge tablets plain on both sides without any visible defects.

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. bacterial pneumonia in children less than 5 years of age, acute exacerbations of chronic bronchitis, lobar and bronchopneumonia, uncomplicated community acquired pneumonia, H.inf uenzae 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.

4.2 Posology and method of administration

Paediatric population

Standard children's dosage (up to 10 years of age): 125 mg every 8 hours doubled in severe infections.

The dosage of Amoxicillin Dispersible Tablets in children with pneumonia.

Category of pneumonia	Age/ Weight of Child	Dosage of Amoxicillin Dispersible Tablets (250mg)
Fast breathing pneumonia	2 month up to 12 months (4-<10 kg)	1 Tablet twice a day X 5 days (10 tablets)
	12 months up to 5 years (10-19 kg)	2 Tablet twice a day X 5 days (20 tablets)
Fast breathing and chest in drawing pneumonia	2 month up to 12 months (4-<10 kg)	1 Tablet twice a day X 5 days (10 tablets)
	12 months up to 3 years (10-14 kg)	2 Tablet twice a day X 5 days (20 tablets)
	3 years up to 5 years (14-19 kg)	3 Tablet twice a day X 5 days (30 tablets)

Special populations

Patients with renal impairment: In renal impairment, the excretion of the antibiotic 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:

Children under 40Kg:

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

Moderate impairment (creatinine clearance 10.3ml/min) -5mg/kg b.i.d. maximum

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

4.3 Contraindications

Amoxicillin is penicillin and should not be given to penicillin hypersensitive patients. Attention should be paid to possible cross-sensitivity with other β-lactam antibiotics e.g. cephalosporins.

4.4 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 (anaphylactoid) reactions have been reported in patients on penicillin therapy. These reactions are more likely to occur in individuals with a history of hypersensitivity to β-lactam antibiotics (see contra-indications). Erythematous (morbilliform) rashes have been associated with glandular fever in patients receiving Amoxicillin. Prolonged use may also occasionally result in overgrowth of non-susceptible organisms. Dosage should be adjusted in patients with renal impairment (see posology and method of administration). This medicinal product contains aspartame, a source of phenylalanine, may be harmful for people with phenylketonuria.

4.5 Interaction with other medicaments and other form of medicaments:

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, false positive readings are common with chemical methods. Probenecid decreases the renal tubular secretion of Amoxicillin. Concurrent use with Amoxicillin may result in increased and prolonged blood levels of Amoxicillin.

4.6 Fertility, pregnancy and lactation

Use In Specific Populations

Pregnancy

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

Lactation/ Nursing Mothers:

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.

4.7 Effects on ability to drive and use machines

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

4.8 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 rash, pruritis and uticaria have been reported occasionally. Rarely, skin reaction 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 angioneuroticoedema, anaphylaxis, serum sickness and hypersensitivity vasculitis have been reported rarely.

Gastrointestinal reactions: Effects include nausea, vomiting and diarrhea. Intestinal candidiasis and antibiotic associated colitis (including pseudo-membranous colitis and hemorrhagic 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 β-lactam antibiotics, hepatitis and cholestatic jaundice have been reported rarely.

Hematological effects: As with other β-lactam antibiotics, reversible leucopenia (including severe neutropenia or agranulocytosis), reversible thrombocytopenia and hemolytic anemia have been reported rarely.

Prolongation of bleeding time and prothrombin time has also been reported rarely.

CNS effects: CNS effects have been reported rarely. They include hyperkinesias, 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 dispersible tablets. It can usually be removed by brushing.

4.9 Overdose

Problems of over dosage with amoxicillin 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 hemodialysis.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Amoxicillin is a semi-synthetic aminopenicillin of the β-lactam group of antibiotics. It 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 possesses the safety profile of penicillin.

5.2 Pharmacokinetic properties

Amoxicillin is well absorbed. Oral administration, usually at convenient t.d.s. dosage, produces high serum levels, independent of the time at which food is taken. 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 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 Preclinical safety data

An oral dose of 4000mg amoxicillin/kg was essentially without effect on the barbiturate sleep, electroshock convulsion and pain response to tail pinch in mice, and on the body temperature, blood pressure, heart rate, electrocardiogram pattern and urine volume in unanesthesized rats. Similarly, an oral dose of 1000mg amoxicillin/kg produced no effect on the blood pressure, heart rate and intestinal motility in unanesthesized dogs.

At concentration of 0.5mg/ml, amoxicillin had no effect on the spontaneous motilities of isolated rat uterus and rabbit ileum, and on the contraction of guinea pig ileum induced by acetylcholine, histamine and barium chloride, and of rat stomach contraction from serotonin.

Amoxicillin had no local irritating and anesthetic effect on the rabbit eyes at concentration of 4%.

QT-interval-prolonging potential of Amoxicillin was studied in a conscious dog model. Three doses of test compounds or vehicle were administered orally to male beagle dogs (n=4), and telemetry signals were recorded for 24 h after administration.

Administration of Amoxicillin did not produce any significant change in the QTc interval. Amoxicillin at a dose level of 70, 200, and 500mg/kg had no significant effect on any parameters measured at any dose. The maximum group-mean-difference in QTcF interval from the time-matched vehicle values at 70, 200, and 500mg/kg was 0%, 2%, and 4%, respectively.

The effects of enteral administration of doxycycline, **amoxicillin**, cephalexin, and enrofloxacin at therapeutic dosages for a typical duration were determined on hemostatic variables in healthy Beagle dogs.

Doxycycline (10 mg/kg, PO, q 12 h), **amoxicillin (30 mg/kg, PO, q 12 h)**, cephalexin (30 mg/kg, PO, q 12 h), and enrofloxacin (20 mg/kg, PO, q 24 h) were administered in random order to 10 healthy dogs at standard therapeutic dosages for 7 days, with a 7-day washout period between subsequent antimicrobials. In addition, 4 Beagles served as control dogs. Variables were evaluated before and after antimicrobial administration; they included platelet count, Hct, 1-stage prothrombin time (PT), activated partial thromboplastin time (PTT), fibrinogen concentration, and platelet function. Platelet function was assessed *via*buccal mucosal bleeding time, aggregation, and a platelet-function analyzer.

Administration of all antimicrobials caused a slight prolongation of 1-stage PT and activated PTT and slight decrease in fibrinogen concentration. Cephalexin caused a significant increase in 1-stage PT and activated PTT, **amoxicillin caused a significant increase in activated PTT**, and enrofloxacin caused a significant decrease in fibrinogen concentration. Platelet count or function did not differ significantly after administration of any antimicrobial.

It was concluded that oral administration of commonly used antimicrobials in healthy dogs resulted in minor secondary hemostatic abnormalities, with no change in platelet count or function.

Drug-related immunologic destruction of granulocytes usually develops after the second week of amoxicillin therapy but may be delayed and occur weeks or months into a course of therapy. It is characterized by a sudden fall in the peripheral neutrophil count; fever may be present. Absolute neutropenia can be severe and may place the patient at increased risk of infection. Drug-induced neutropenia may be due to antibodies to the neutrophil. The neutropenia seen with prolonged high-dose

therapy with penicillins and cephalosporins is of uncertain etiology, but it may not have an immunologic basis as rechallenge is not associated with an accelerated recurrence of the neutropenia and the neutrophil count may fall more slowly.

An antibody-induced immune thrombocytopenia has been described with the penicillins and cephalosporins. These are reversed quickly when the particular drug is discontinued.

Although oral administration of amoxicillin to rabbits and guinea pigs for 30 days did not form antibodies, parenteral administration caused the formation of antibodies and hemagglutinins and passive cutaneous anaphylaxis. The cross reactivity of amoxicillin was observed in erythrocyte coagulation and passive cutaneous anaphylaxis reactions.

6. Pharmaceutical particulars

6.1 List of excipients

Microcrystalline Cellulose PH 102, Aspartame, Crospovidone, Ess. Fl. DC. Trusil Lemon, Flavour peppermint DC 117 quest, Magnesium Stearate, Purified Talc, Colloidal anhydrous silica.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years (36 Months)

6.4 Special precautions for storage

Store below 30ºC in a dry place.

6.5 Nature and contents of container

Strip of 10's, 20's, 30's and 100's Tablets.

6.6 Special precautions for disposal and other handling

No special requirements.

7. Marketing Authorization Holder And Manufacturing Site Addresses

Marketing authorization holder

Kopran Limited,

1076, Parijat House, Dr. E. Moses Road,

Worli, Mumbai - 400 018, India,

Manufacturing Site Addresses

Kopran Limited,

Pen Plant, Village Savroli

Taluka Khalapur, District Raigad – 410202, India

8. Marketing authorization number(s)

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9. Date of first authorization/renewal of the authorization

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10. Date of revision of the text

Oct. 2019