PRODUCT: OMACILLIN 500

(Amoxycillin capsules 500 mg)

MODULE 1 REGIONAL ADMINISTRATIVE INFORMATION

SECTION 1.3 – PRODUCT INFORMATION

SUB SECTION 1.3.1 SUMMARY OF PRODUCT CHARACTERISTICS

1.3.1 Summary of Product Characteristics (SPC)

1. NAME OF THE MEDICINAL PRODUCT

Omacillin 500

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each capsule contains Amoxicillin trihydrate equivalent to Amoxicillin 500 mg

Sr. No	Ingredients	Quantity mg/tablet	Function of Ingredients
1	Amoxycillin trihydrate equivalent to Amoxycillin	500.00	Active
2	Sodium Starch Glycollate	15.00	Disintegrant
3	Sodium lauryl sulfate	5.00	Surfactant
4	Magnesium stearate	2.00	Lubricant
5	Talc	1.00	Glidant
6	Empty hard gelatin capsule size '0' Elongated (Red – yellow)	1.0 No.	Capsule shell

3. PHARMACEUTICAL FORM

Hard gelatin capsules with yellow body having 'Omacillin 500 mg' printed in black colour and red cap with 'NPI' logo printed in white colour contains off-white to yellow powder.

4. CLINICAL PARTICULARS

4.1THERAPEUTIC INDICATIONS

4.1 Therapeutic Indication

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

Upper respiratory tract infection

Otitis media

Acute and chronic bronchitis

Lobar and bronchopneumonia

Cystitis, urethritis, pyelonephritis

Bacteriuria in pregnancy

Gynaecological infections including puerperal sepsis and septic abortion

Gonorrhoea

Peritonitis

Intra-abdominal sepsis

Septicaemia

Peritonitis

Intra-abdominal sepsis

Septicaemia

Bacterial endocarditis

Typhoid and paratyphoid fever

Skin and soft tissue infections

Dental abscess (as an adjunct to surgical management)

Helicobacter pylori eradication in peptic (duodenal and gastric) ulcer disease

In children with urinary tract infection the need for investigation should be considered.

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 Bacterial Endocarditis.

Consideration should be given to official local guidance (e.g. national requirements) on the appropriate use of antibacterial agents. Susceptibility of the causative organisms to the treatment should be tested (if possible), although the therapy may be initiated before the results are available.

4.2 POSOLOGY AND METHOD OF ADMINISTRATION

Posology

TREATMENT OF INFECTION:

Adult dosage (Including elderly patients)

Standard adult dosage: 250mg three times daily, increasing to 500mg three times daily for more severe infections.

High dosage therapy: (Maximum recommended oral dosage 6g daily in divided doses): A dosage of 3g twice daily is recommended in appropriate cases for the treatment of severe or recurrent purulent infection of the respiratory tract.

Short course therapy: Simple acute urinary tract infection: two 3g doses with 10 - 12 hours between the doses. Dental abscess: two 3g doses with 8 hours between the doses.

Gonorrhoea: Single 3g dose.

Dosage in impaired renal function:

The dose should be reduced in patients with severe renal function impairment. In patients with a creatinine clearance of less than 30 ml/min an increase in the dosage interval and a reduction in the total daily dose is recommended (see section 4.4).

Glomerular filtration rate >30ml/min: No adjustment necessary

Glomerular filtration rate 10-30ml/min: Amoxicillin max. 500mg BID

Glomerular filtration rate <10ml/min: Amoxicillin max. 500mg/day

Helicobacter eradication in peptic (duodenal and gastric) ulcer disease:

Amoxicillin is recommended twice daily in association with a proton pump inhibitor and antimicrobial agents as detailed below:

[Omeprazole 40mg daily, Amoxicillin 1g BID, Clarithromycin 500mg BID] x 7 days

Or

[Omeprazole 40mg daily, Amoxicillin 750mg–1g BID, Metronidazole 400mg TID] x 7 days

Children's dosage

Children weighing more than 40 kg should be given the usual adult dosage.

Children weighing < 40 kg

The capsule formulation of Amoxicillin Capsules BP 250mg may not be suitable for children. In such cases a suspension formulation should be used.

The daily dosage for children is 40 - 90 mg/kg/day in two to three divided doses* (not exceeding 3 g/day) depending on the indication, severity of the disease and the susceptibility of the pathogen (see special dosage recommendations below and sections 4.4, 5.1 and 5.2).

Route of Administration: Oral

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4.3 CONTRAINDICATIONS

Use in patients with hypersensitivity to penicillins, including ampicillin or cephalosporins, or to any of the excipients

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Prolonged use of anti-infective agent may result in superinfection by organisms resistant to that anti-infective.

Serious and occasionally fatal hypersensitivity (anaphylactoid) reactions have been reported in patients on penicillin therapy. Although anaphylaxis is more frequent following parenteral therapy, it has occurred in patients on oral penicillins. These reactions are more likely to occur in persons with a history of penicillin hypersensitivity and/ or a history of sensitivity to multiple allergens. There have been reports of individuals with a history of severe reactions when treated with cephalosporin. Before initiating therapy with any penicillin, careful inquiry should be made concerning previous hypersensitivity reactions to penicillins, cephalosporins, or other allergens.

If allergic reaction occurs, amoxicillin should be discontinued and appropriate therapy should be instituted and discontinuance of amoxicillin therapy considered.

Serious anaphylactoid reactions require immediate emergency treatment with epinephrine, oxygen, intravenous steroids, and airway management, including intubation, should be administered as indicated.

Erythematous (morbilliform) rashes have been associated with glandular fever in patients receiving amoxicillin.

In patients with renal impairment, the rate of excretion of amoxicillin will be reduced depending on the degree of impairment and it may be necessary to reduce the total daily unit amoxicillin dosage accordingly (see section 4.2).

In patients with reduced urine output crystalluria has been observed very rarely predominantly with parenteral therapy. During the administration of high doses of amoxicillin, it is advisable to maintain adequate fluid intake and urinary output in order to reduce the possibility of amoxicillin crystalluria (see section 4.9 Overdose).

Precaution should be taken in premature children and during the neonatal period: renal, hepatic and haematological functions should be monitored.

4.5 INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION

When administered concurrently, the following drugs may interact with amoxicillin:

Oral Contraceptives:

In common with other broad spectrum antibiotics, amoxicillin may reduce the efficacy of oral contraceptives and patients should be warned accordingly.

Bacteriostatic antibiotics:

Chloramphenicol, erythromycins, sulfonamides or tetracyclines may interfere with the bactericidal effects of penicillins. This has been demonstrated in vitro; however, the clinical significance of this interaction is not well documented. Probenecid may decrease renal tubular secretion of amoxicillin resulting in increased blood levels and/or amoxicillin toxicity.

*Drug/Laboratory **Test** Interactions:*

After treatment with amoxicillin, a false-positive reaction for glucose in the urine may occur with copper sulphate tests (Benedict's solution, fehling's solution, or Clinitest tablets) but not with enzyme based tests.

Allopurinol

Concurrent administration of allopurinol during treatment with amoxicillin can increase the likelihood of allergic skin reactions.

Methotrexate

Excretion of methotrexate is reduced by penicillins; increased risk of toxicity.

Oral typhoid vaccine

The oral typhoid vaccine is inactivated by antibacterials

Sulfinpyrazone

Excretion of penicillins is reduced by sulfinpyrazone.

Anticoagulants

Prolongation of prothrombin time has been reported rarely in patients receiving amoxicillin. Appropriate monitoring should be undertaken when anticoagulants are prescribed concurrently.

Muscle relaxants: Piperacillin (and possibly other penicillins) enhance the effects of non-depolarising muscle relaxants and suxamethonium.

Antibacterials: Absorption of phenoxymethylpenicillin (and possibly other penicillins) reduced by neomycin.

4.6 FERTILITY, PREGNANCY AND LACTATION

Animal studies with amoxicillin have shown no teratogenic effects. Amoxicillin has been in extensive clinical use and its suitability in human pregnancy has been well documented in clinical studies. The product should only be used during pregnancy where potential benefits outweigh the potential risks associated with treatment.

Amoxicillin may be administered during the period of lactation. With the exception of the risk of sensitisation 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

None

4.8 UNDESIRABLE EFFECTS

The following convention has been utilised for the classification of undesirable effects:-

Very common (>1/10), common (>1/100, <1/10), uncommon (>1/1000,<1/100), rare (>1/10,000, <1/1000), very rare (<1/10,000)

The majority of side effects listed below are not unique to amoxicillin and may occur when using other pencillins.

Unless otherwise stated, the frequency of adverse events has been derived from more than 30 years of post-marketing reports. **Infections and Infestations**

Very rare: Mucocutaneous candidiasis

Blood and lymphatic system disorders:

Very rare:

As with other beta-lactam antibiotics, reversible leucopenia (including severe neutropenia and

agranulocytosis), reversible thrombocytopenia and haemolytic anaemia have been reported.
Prolongation of bleeding time and prothrombin time have also been reported (see section 4.5 Interaction with other medicinal products and other forms of interaction).

Immune System disorders

Hypersensitivity reactions:

As with other antibiotics, severe allergic reactions including angioneurotic oedema, and anaphylaxis (see section 4.4 Special Warnings and Precautions for Use) serum sickness and hypersensitivity vasculitis have been reported rarely.

If hypersensitivity reaction occurs, the treatment should be discontinued. (See also skin and subcutaneous tissue disorders)

Nervous system disorders:

Very rare: Hyperkinesia, dizziness and convulsions. Convulsions may occur in patients with impaired renal function or in those receiving high doses.

Gastrointestinal disorders:

Clinical Trial Data

*Common: Diarrhoea and nausea

*Uncommon: Vomiting

Post-marketing data

Very rare: Antibiotic associated colitis including pseudomembranous colitis and haemorrhagic colitis have been reported

Black hairy tongue.

Superficial tooth discolouration has been reported in children. This may respond to brushing.

Hepato-biliary disorders:

Very rare:	Hepatitis and cholestatic jaundice. A moderate rise in AST and/or ALT, but the significance of this is unclear.

Skin and subcutaneous tissue disorders

Clinical Trial Data

*Common:	Skin rash,
*Uncommon:	Pruritus and urticaria.

Post Marketing Data

Very rare:	Skin reactions such as erythema multiforme and Stevens-Johnson syndrome, toxic epidermal necrolysis, bullous and exfoliative dermatitis and acute generalised exanthematous pustulosis (AGEP).(See also Immune System Disorders)

Renal and Urinary Tract disorders:

Very rare:	Interstitial nephritis
Very rare:	Crystalluria (See section 4.9 Overdose) can occur

4.9OVERDOSE

Gastrointestinal effects such as nausea, vomiting and diarrhoea may be evident and should be treated symptomatically with attention to the water/electrolyte balance. Amoxicillin crystalluria, in some cases leading to renal failure has been observed (see section 4.4 Special warnings and precautions for use).

Amoxicillin may be removed from the circulation by haemodialysis.

5. PHARMACOLOGICAL PROPERTIES

5. 1 Pharmacodynamic Properties

Absorption

Fexofenadine hydrochloride is rapidly absorbed into the body following oral administration, with T_{max} occurring at approximately 1-3 hours post dose. The mean C_{max} value was approximately 427 ng/ml following the administration of a 120 mg dose once daily.

Distribution

Fexofenadine is 60-70% plasma protein bound.

Biotransformation and elimination

Fexofenadine undergoes negligible metabolism (hepatic or non-hepatic), as it was the only major compound identified in urine and faeces of animals and man. The plasma concentration profiles of fexofenadine follow a bi-exponential decline with a terminal elimination half-life ranging from 11 to 15 hours after multiple dosing. The single and multiple dose pharmacokinetics of fexofenadine are linear for oral doses up to 120 mg BID. A dose of 240 mg BID produced slightly greater than proportional increase (8.8%) in steady state area under the curve, indicating that fexofenadine pharmacokinetics are practically linear at these doses between 40 mg and 240 mg taken daily. The major route of elimination is believed to be via biliary excretion while up to 10% of ingested dose is excreted unchanged through the urine.

Anaerobes:

Clostridium species

5.2 Pharmacokinetic properties

Amoxicillin Trihydrate is rapidly absorbed when given by mouth. It is widely distributed and is reported to produce peak antibiotic plasma concentrations that are up to twice as high as those from the same dose of ampicillin. Peak plasma-amoxicillin concentrations of about 5ug per ml have been observed 2 hours after a dose of 250mg. The presence of food in the stomach does not appear to diminish absorption significantly.

Amoxicillin is mainly excreted in the urine, about 60% being excreted in 6 hours.

In preterm infants with gestational age 26-33 weeks, the total body clearance after intravenous dosing of amoxicillin, day 3 of life, ranged between 0.75-2ml/min, very similar to the inulin clearance (GFR) in this population. Following oral administration, the absorption pattern and the bioavailability of amoxicillin in small children may be different to that of adults. Consequently, due to the deceased CL, the exposure is expected to be elevated in this group of patients, although this increase in exposure may in part be diminished be decreased bioavailability when given orally.v

5.3 Preclinical safety data

Not applicable

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MODULE 1 REGIONAL ADMINISTRATIVE INFORMATION

6.1 List of excipient (s)

Sodium starch glycollate

Sodium lauryl sulfate

Magnesium stearate

Talc

Empty hard gelatin capsule size '0' Elongated (Red – yellow)

6. 2 Incompatibilities

Not applicable

6.3 Shelf life

3 years

6. 4 Special precautions for storage

Store below 30°C. Protect from light & moisture.

6.5 NATURE AND CONTENTS OF CONTAINER

Omacillin 500 is packed in PVC/PE/PVDC backed up with printed aluminium foil.

7. MARKETING AUTHORISATION HOLDER

National Pharmaceutical Industries Co. (SAOG)
Road No. 15,
P.O Box 120
Postal Code 124
Rusayl, Sultanate of Oman