Summary of the product characteristics

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1. NAME OF THE MEDICINAL PRODUCT

Amoxicillin Tablets for Oral Suspension USP 250 mg

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each dispersible tablet contains:

Amoxicillin USP (as Trihydrate)

Eq. to Anhydrous Amoxicillin 250mg

For the full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Dispersible Tablets

Orange to light orange coloured, round, flat uncoated. dispersible tablets with beveled edges h

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

Infections caused by Amoxicillin-sensitive organisms such as actinomycosis, biliary-tract infections, bronchitis, endocarditis, gastroenteritis, gonorrhoea, Lyme disease, mouth infections, otitis media, pneumonia, spleen disorders (pneumococcal infection prophylaxis), typhoid and paratyphoid fever, and urinary-tract infections.

4.2 Posology and Method of administration

The dose of Amoxicillin that is selected to treat an individual infection should take into account:

• The expected pathogens and their likely susceptibility to antibacterial agents (see section 4.4)

• The severity and the site of infection

• The age, weight and renal function of the patient; as shown below

The duration of therapy should be determined by the type of infection and the response of the patient, and should generally be as short as possible. Some infections require longer periods of treatment (see section 4.4 regarding prolonged therapy).

Adults and children ≥40 kg

Indication*	**Dose***
Acute bacterial sinusitis	250mg to 500mg every 8 hours or 750mg to 1g every 12 hours For severe infections 750mg to 1g every 8 hours Acute cystitis may be treated with 3g twice daily for one day
Asymptomatic bacteriuria in pregnancy	
Acute pyelonephritis	
Dental abscess with spreading cellulitis	
Acute cystitis	
Acute otitis media	500mg every 8 hours, 750mg to 1g every 12 hours
Acute streptococcal tonsillitis and pharyngitis	

Acute exacerbations of chronic bronchitis	For severe infections 750mg to 1g every 8 hours for 10 days
Community acquired pneumonia	500mg to 1g every 8 hours
Typhoid and paratyphoid fever	500mg to 2g every 8 hours
Prosthetic joint infections	500mg to 1g every 8 hours
Prophylaxis of endocarditis	2g orally, single dose 30 to 60 minutes before procedure
Helicobacter pylori eradication	750mg to 1g twice daily in combination with a proton pump inhibitor (e.g. omeprazole, lansoprazole) and another antibiotic (e.g. clarithromycin, metronidazole) for 7 days
Lyme disease (see section 4.4)	Early stage: 500mg to 1g every 8 hours up to a maximum of 4 g/day in divided doses for 14 days (10 to 21 days) Late stage (systemic involvement): 500mg to 2g every 8 hours up to a maximum of 6 g/day in divided doses for 10 to 30 days
*Consideration should be given to the official treatment guidelines for each indication	

Children <40 kg

Children may be treated with Amoxicillin capsules, dispersible tablets, suspensions or sachets.

Amoxicillin Paediatric Suspension is recommended for children under six months of age.

Children weighing 40kg or more should be prescribed the adult dosage.

Recommended doses:

Indication[+]	**Dose**[+]
Acute bacterial sinusitis	20 to 90 mg/kg/day in divided doses*
Acute otitis media	
Community acquired pneumonia	
Acute cystitis	
Acute pyelonephritis	
Dental abscess with spreading cellulitis	
Acute streptococcal tonsillitis and pharyngitis	40 to 90 mg/kg/day in divided doses*
Typhoid and paratyphoid fever	100 mg/kg/day in three divided doses
Prophylaxis of endocarditis	50 mg/kg orally, single dose 30 to 60 minutes before procedure
Lyme disease (see section 4.4)	Early stage: 25 to 50 mg/kg/day in three divided doses for 10 to 21 days Late stage (systemic involvement): 100 mg/kg/day in three divided doses for 10 to 30 days
+ Consideration should be given to the official treatment guidelines for each indication. *Twice daily dosing regimens should only be considered when the dose is in the upper range.	

Elderly

No dose adjustment is considered necessary.

Renal impairment

GFR (ml/min)	Adults and children ≥ 40kg	Children < 40 kg[#]
greater than 30	No adjustment necessary	No adjustment necessary
10 to 30	Maximum 500mg twice daily	15 mg/kg given twice daily (maximum 500mg twice daily)
less than 10	Maximum 500 mg/day	15 mg/kg given as a single dose (maximum 500 mg)
[#] In the majority of cases, parenteral therapy is preferred		

In patients receiving haemodialysis

Amoxicillin may be removed from the circulation by haemodialysis

	Haemodialysis
Adults and children over 40kg	500mg every 24h Prior to haemodialysis one additional dose of 500mg should be administered. In order to restore circulating blood levels, another dose of 500mg should be administered after haemodialysis
Children under 40kg	15 mg/kg/day given as a single daily dose (maximum 500mg). Prior to haemodialysis one additional dose of 15 mg/kg should be administered. In order to restore circulating blood levels, another dose of 15 mg/kg should be administered after haemodialysis

In patients receiving peritoneal dialysis

Amoxicillin maximum 500mg/day

Hepatic impairment

Dose with caution and monitor hepatic function at regular intervals

Upper respiratory tract infections Genito-urinary tract infections skin and soft tissue infections

Adults: 250 mg every 8 hours.

Children (under20 kg): 25 mg/kg/day in equally divided doses everyB hours.

In severe infections or those caused by less susceptible organisms

500 mg every 8 hours for adults and 50 mg/kg/day in equally divided doses every 8 hours for children

may be needed.

Lower respiratory tract infections

Adults: 500 mg every 8 hours.

Children (under 20 kg): 50 mg/kg/day in equally divided doses every 8 hours.

Prophylaxis of Endocarditis

Adults -3 g orally, 1 hour before procedure. A second dose may be given 6 hours later if considered

necessary.

Children under10- half the adult dose.

Children under 5- quarteradultdose.

Urethritis (due to Neisseria qonorrhoeae)

Adults: 3 gas single dose.

H. pylori Eradication to Reduce the Risk of Duodenal Ulcer Recurrence:

Triple Therapy: Amoxicillin/Clarithromycin/Lansoprazole The recommended adult oral dose is 1

gram Amoxicillin, 500 mg clarithromycin, and 30 mg lansoprazole, all given twice daily (q12h) for 14
days.

Route of administration: Oral

Direction for use: Disperse the tablet in a teaspoonful of boiled and cooled water before administration.

4.3 Contraindications

Amoxicillin is penicillin and should not be given to patients with a history of hypersensitivity to betalactam antibiotics (eg. penicillins, cephalosporins).

4.4 Special warnings and precautions for use

Serious and occasionally fatal hypersensitivity (anaphylactoid) reactions have been reported in patients
on penicillin therapy. These reactions are most likely in those with a history of hypersensitivity to betalactam antibiotics.

4.5 Interaction with other medicinal products and other forms of interact.

Probenecid

Concomitant use of probenecid is not recommended. Probenecid decreases the renal tubular secretion of amoxicillin. Concomitant use of probenecid may result in increased and prolonged blood levels of amoxicillin.

Allopurinol

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

Tetracyclines

Tetracyclines and other bacteriostatic drugs may interfere with the bactericidal effects of amoxicillin.

Oral anticoagulants

Oral anticoagulants and penicillin antibiotics have been widely used in practice without reports of
interaction. However, in the literature there are cases of increased international normalised ratio in
patients maintained on acenocoumarol or warfarin and prescribed a course of amoxicillin. If coadministration is necessary, the prothrombin time or international normalised ratio should be carefully monitored with the addition or withdrawal of amoxicillin. Moreover, adjustments in the dose of oral anticoagulants may be necessary

Methotrexate

Penicillins may reduce the excretion of methotrexate causing a potential increase in toxicity.

4.6 Fertility, Pregnancy and Lactation

Pregnancy

Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity.

Limited data on the use of amoxicillin during pregnancy in humans do not indicate an increased risk of congenital malformations. Amoxicillin may be used in pregnancy when the potential benefits outweigh the potential risks associated with treatment.

Breast-feeding

Amoxicillin is excreted into breast milk in small quantities with the possible risk of sensitisation. Consequently, diarrhoea and fungus infection of the mucous membranes are possible in the breast-fed infant, so that breast-feeding might have to be discontinued. Amoxicillin should only be used during breast-feeding after benefit/risk assessment by the physician in charge.

Fertility

There are no data on the effects of amoxicillin on fertility in humans. Reproductive studies in animals

Infections and infestations

Very Rare: Muco-cutaneous candidiasis

Blood and lymphatic system disorders

Very rare: Reversible leucopenia (including severe neutropenia or agranulocytosis), reversible thrombocytopenia and haemolytic anaemia. Prolonged prothrombin and bleeding times (see section 4.4 - Special Warnings and Precautions for Use)

Immune system disorders

Very rare: As with other antibiotics, severe allergic reactions, including angioneurotic oedema, anaphylaxis (see Section 4.4 - Special Warnings and Precautions for Use), serum sickness and hypersensitivity vasculitis

Not known: Jarisch-Herxheimer reaction (see section 4.4)

If any 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 pseudomembraneous colitis and haemorrhagic colitis see section 4.4).
Black hairy tongue

Hepato-biliary disorders

Very rare: Hepatitis and cholestatic jaundice. A moderate rise in AST and/or ALT. The significance of a rise in AST and/or ALT is unclear.

Skin and subcutaneous tissue disorders

Clinical Trial Data

***Common:** Skin rash

***Uncommon:** Urticaria and pruritus

Post-marketing Data

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

section 4.4) and drug reaction with eosinophilia and systemic symptoms (DRESS).

(See also Immune system disorders).

Renal and urinary tract disorders

Very rare: Interstitial nephritis.

Very rare: Crystalluria (see Sections 4.4 and 4.9 Overdose).

*The incidence of these AEs was derived from clinical studies involving a total of approximately 6,000 adult and paediatric patients taking amoxicillin.

4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed. However, undesirable effects may occur (e.g. allergic reactions, dizziness, convulsions), which may influence the ability to drive and use machines.

4.8 Undesirable effects

The ADRs derived from clinical studies and post-marketing surveillance with amoxicillin, presented by MedDRA System Organ Class are listed below.

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

Very common (≥1/10),

Common (≥1/100 to <1/10),

Uncommon (≥1/1000 to <1/100),

Rare (≥1/10,000 to <1/1000),

Very rare (<1/10,000),

Not known (cannot be estimated from the available data)

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

The most commonly reported adverse drug reactions (ADRs) are diarrhoea, nausea and skin rash.

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

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via EFDA yellow Card Scheme, online at https://primaryreporting.who-umc.org/ET or toll free call 8482 to Ethiopian food and drug authority (EFDA).

4.9 Overdose

Symptoms and signs of overdose

Problems of overdosage with amoxicillin are unlikely to occur. Gastrointestinal symptoms (such as nausea, vomiting and diarrhoea) and disturbances of the fluid and electrolyte balances may be evident.

Amoxicillin crystalluria, in some cases leading to renal failure, has been observed. Convulsions may occur in patients with impaired renal function or in those receiving high doses.

Treatment of intoxication

Gastrointestinal symptoms may be treated symptomatically, with attention to the water/electrolyte balance.

Amoxicillin can be removed from the circulation by haemodialysis.

5.0 Pharmacological Properties

5.1 Pharmacodynamic Properties

Pharmacotherapeutic group: penicillins with extended spectrum; ATC code: J01CA04

Mechanism of action

Amoxicillin is a semisynthetic penicillin (beta-lactam antibiotic) that inhibits one or more enzymes (often referred to as penicillin-binding proteins, PBPs) in the biosynthetic pathway of bactericidal peptidoglycan, which is an integral structural component of the bacterial cell wall. Inhibition of peptidoglycan synthesis leads to weakening of the cell wall, which is usually followed by cell lysis and death.

Amoxicillin is susceptible to degradation by beta-lactamases produced by resistant bacteria and therefore the spectrum of activity of amoxicillin alone does not include organisms which produce these enzymes.

Pharmacokinetic/ pharmacodynamic relationship

The time above the minimum inhibitory concentration (T>MIC) is considered to be the major determinant of efficacy for amoxicillin.

Mechanisms of resistance

The main mechanisms of resistance to amoxicillin are:

• Inactivation by bacterial beta-lactamases

• Alteration of PBPs, which reduce the affinity of the antibacterial agent for the target.

Impermeability of bacteria or efflux pump mechanisms may cause or contribute to bacterial resistance, particularly in Gram-negative bacteria.

Breakpoints

MIC breakpoints for amoxicillin are those of the European Committee on Antimicrobial Susceptibility Testing (EUCAST) version 5.0.

Organism	**MIC breakpoint (mg/L)**	
	Susceptible ≤	**Resistant >**
Enterobacteriaceae	8[1]	8
Staphylococcus spp.	Note[2]	Note[2]
Enterococcus spp.[3]	4	8
Streptococcus groups A, B, C and G	Note[4]	Note[4]
Streptococcus pneumoniae	Note[5]	Note[5]
Viridans group steprococci	0.5	2
Haemophilus influenzae	2[6]	2[6]
Moraxella catarrhalis	Note[7]	Note[7]
Neisseria meningitidis	0.125	1
Gram positive anaerobes except *Clostridium difficile*[8]	4	8
Gram negative anaerobes[8]	0.5	2
Helicobacter pylori	0.125[9]	0.125[9]
Pasteurella multocida	1	1
Non-species related breakpoints[10]	2	8

[1]Wild type Enterobacteriaceae are categorised as susceptible to aminopenicillins. Some countries prefer to categorise wild type isolates of *E. coli* and *P. mirabilis* as intermediate. When this is the case, use the MIC breakpoint S≤ 0.5 mg/L
[2]Most staphylococci are penicillinase producers, which are resistant to amoxicillin. Methicillin resistant isolates are, with few exceptions, resistant to all beta-lactam agents.
[3]Susceptibility to amoxicillin can be inferred from ampicillin
[4]The susceptibility of streptococcus groups A, B, C and G to penicillins is inferred from the benzylpenicillin susceptibility
[5]Breakpoints relate only to non-meningitis isolates. For isolates categorised as intermediate to ampicillin avoid oral treatment with amoxicillin. Susceptibility inferred from the MIC of ampicillin
[6]Breakpoints are based on intravenous administration. Beta-lactamase positive isolates should be reported resistant
[7]Beta lactamase producers should be reported resistant
[8]Susceptibility to amoxicillin can be inferred from benzylpenicillin.

[9]The breakpoints are based on epidemiological cut-off values (ECOFFs), which distinguish wild-type isolates from those with reduced susceptibility.
[10]The non-species related breakpoints are based on doses of at least 0.5g x 3 or 4 doses daily (1.5 to 2 g/day).

The prevalence of resistance may vary geographically and with time for selected species, and local information on resistance is desirable, particularly when treating severe infections. As necessary, expert advice should be sought when the local prevalence of resistance is such that the utility of the agent in at least some types of infections is questionable.

***In vitro* susceptibility of micro-organisms to Amoxicillin**
Commonly Susceptible Species
Gram-positive aerobes: *Enterococcus faecalis* Beta-hemolytic streptococci (Groups A, B, C and G) *Listeria monocytogenes*
Species for which acquired resistance may be a problem

Gram-negative aerobes: *Escherichia coli* *Haemophilus influenzae* *Helicobacter pylori* *Proteus mirabilis* *Salmonella* typhi *Salmonella* paratyphi *Pasteurella multocida*
Gram-positive aerobes: Coagulase negative staphylococcus *Staphylococcus aureus*[£] *Streptococcus pneumoniae* Viridans group streptococcus
Gram-positive anaerobes: *Clostridium* spp.
Gram-negative anaerobes: *Fusobacterium* spp.
Other: *Borrelia burgdorferi*
Inherently resistant organisms[†]
Gram-positive aerobes: *Enterococcus faecium*†
Gram-negative aerobes: *Acinetobacter* spp. *Enterobacter* spp. *Klebsiella* spp. *Pseudomonas* spp.
Gram-negative anaerobes: *Bacteroides* spp. (many strains of *Bacteroides fragilis* are resistant)
Others: *Chlamydia* spp. *Mycoplasma* spp. *Legionella* spp.
[†] Natural intermediate susceptibility in the absence of acquired mechanism of resistance. [£] Almost all *S.aureus* are resistant to amoxicillin due to production of penicillinase. In addition, all methicillin-resistant strains are resistant to amoxicillin.

5.2 Pharmacokinetic Properties

Absorption

Amoxicillin fully dissociates in aqueous solution at physiological pH. Amoxicillin is stable in the acid gastric secretion and is rapidly absorbed from the gastrointestinal tract after oral administration. Following oral administration, amoxicillin is approximately 70% bioavailable. The time to peak plasma concentration (T_{max}) is approximately one hour.

The pharmacokinetic results for a study, in which an amoxicillin dose of 250 mg three times daily was administered in the fasting state to groups of healthy volunteers are presented below.

C_{max}	T_{max}*	$AUC_{(0-24h)}$	T ½
(µg/ml)	(h)	(µg.h/ml)	(h)
3.3 ± 1.12	1.5 (1.0-2.0)	26.7 ± 4.56	1.36 ± 0.56
*Median (range)			

In the range 250 to 3000 the bioavailability is linear in proportion to dose (measured as C_{max} and AUC). The absorption is not influenced by simultaneous food intake.

Haemodialysis can be used for elimination of amoxicillin.

Distribution

About 18% of total plasma amoxicillin is bound to protein and the apparent volume of distribution is around 0.3 to 0.41/kg. Following intravenous administration, amoxicillin has been found in gall bladder, abdominal tissue, skin, fat, muscle tissue, synovial and peritoneal fluids, bile and pus. Amoxicillin does not adequately distribute into the cerebrospinal fluid.

From animal studies there is no evidence for significant tissue retention of drug-derived material. Amoxicillin, like most penicillins, can be detected in breast milk (see section 4.6)

Amoxicillin has been shown to cross the placental barrier (see section 4.6).

Biotransformation

Amoxicillin is partly excreted in the urine as the inactive penicilloic acid in quantities equivalent to up to 10 to 25% of the initial dose.

Elimination

The major route of elimination for amoxicillin is via the kidney.

Amoxicillin has a mean elimination half-life of approximately one hour and a mean total clearance of approximately 25 l/hour in healthy subjects. Approximately 60 to 70% of an orally administered dose is excreted unchanged in the urine during the first 6 hours after administration of a single 250mg or 500mg dose of amoxicillin. Various studies have found the urinary excretion to be 50-85% for amoxicillin over a 24 hour period.

Concomitant use of probenecid delays amoxicillin excretion (see section 4.5)

Age

The elimination half-life of amoxicillin is similar for children aged around 3 months to 2 years and older children and adults. For very young children (including preterm newborns) in the first week of life the interval of administration should not exceed twice daily administration due to immaturity of the renal pathway of elimination. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and it may be useful to monitor renal function.

Gender

Following oral administration of amoxicillin to healthy males and female subjects, gender has no significant impact on the pharmacokinetics of amoxicillin.

Renal impairment

The total serum clearance of amoxicillin decreases proportionately with decreasing renal function (see section 4.2 and 4.4).

Hepatic impairment

Hepatically impaired patients should be dosed with caution and hepatic function monitored at regular intervals.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on studies of safety pharmacology, repeated dose toxicity, genotoxicity and toxicity to reproduction and development.

Carcinogenicity studies have not been conducted with amoxicillin.

6.0 Pharmaceutical Particulars

6.1 List of Excipients

Croscarmellose Sodium, Microcrystalline Cellulose pH 102, Aspartame, Citric Acid Monohydrate, Flavour Orange dry, Colour Sunset Yellow lake, Colloidal Anhydrous Silica, Magnesium Searate

6.2 Incompatibilities

Not applicable

6.3 Shelf life

36 months from the date of manufacture.

6.4 Special precautions for storage

Store at a temperature not exceeding 30°C in a dry place. Protect from light. Keep out of reach of children.

6.5 Nature and contents of container

10 Tablets packed in Printed Blister Aluminium foil and Clear PVC film and such 10 blisters packed in a unit carton along with package insert.

6.6 Special precautions for disposal

No special requirements

7. MARKETING AUTHORISATION HOLDER

MEDICAMEN Biotech Limited
SP-1192 A&B, PHASE - IV,
Industrial Area,
Bhiwadi - 301 019
Distt. Alwar,
Rajasthan, India.

8. NUMBER(S) IN THE NATIONAL REGISTER OF FINISHED PHARMACEUTICAL PRODUCTS

Certificate No: 08214/08781/NMR/2021

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Dec 15, 2022

10. DATE OF REVISION OF THE TEXT

August 2023