Summary of the Product Characteristics

1. NAME OF THE MEDICINAL PRODUCT

Remox 250 mg Capsules

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Amoxicillin 250 mg Capsules contain 250mg of amoxicillin as the trihydrate equivalent to 250mg amoxicillin

Excipients with known effect
For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Capsules.

Amoxicillin 250 mg Capsules are presented as hard gelatin capsules with a maroon cap and yellow body.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Treatment of Infection: Amoxicillin is a broad spectrum antibiotic indicated for the treatment of following infections in adult and children (see sections 4.2, 4.4 and 5.1)

- Acute bacterial sinusitis
- Acute otitis media
- Acute streptococcal tonsillitis and pharyngitis
- Acute exacerbations of chronic bronchitis
- Community acquired pneumonia
- Acute cystitis
- Asymptomatic bacteriuria in pregnancy
- Acute pyelonephritis
- Typhoid and paratyphoid fever
- Dental abscess with spreading cellulitis
- Prosthetic joint infections
- *Helicobacter pylori* eradication
- Lyme disease

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 on the appropriate use of antibacterial agents. Susceptibility of the causative organism 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

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 the 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	250 mg to 500 mg every 8 hours or 750 mg to 1 g every 12 hours For severe infections 750 mg to 1 g every 8 hours Acute cystitis may be treated with 3 g twice daily for one day
Asymptomatic bacteriuria in pregnancy	
Acute pyelonephritis	
Dental abscess with spreading cellulitis	
Acute cystitis	
Acute otitis media	500 mg every 8 hours, 750 mg to 1 g every 12 hours For severe infections 750 mg to 1 g every 8 hours for 10 days
Acute streptococcal tonsillitis and pharyngitis	
Acute exacerbations of chronic bronchitis	
Community acquired pneumonia	500 mg to 1 g every 8 hours
Typhoid and paratyphoid fever	500 mg to 2 g every 8 hours
Prosthetic joint infections	500 mg to 1 g every 8 hours
Prophylaxis of endocarditis	2 g orally, single dose 30 to 60 minutes before procedure
Helicobacter pylori eradication	750 mg to 1 g 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: 500 mg to 1 g 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): 500 mg to 2 g

	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 40 kg 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 ≥ 40 kg	Children < 40 kg#
greater than 30	no adjustment necessary	No adjustment necessary

10 – 30	maximum 500 mg twice daily	15 mg/kg given twice daily (maximum 500 mg twice daily)
Less than 10	maximum 500 mg/day	15 mg/kg given as a single daily 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 ≥ 40 kg	500 mg every 24 h Prior to haemodialysis one additional dose of 500 mg should be administered. In order to restore circulating drug levels, another dose of 500 mg should be administered after haemodialysis.
Children under 40 kg	15 mg/kg/day given as a single daily dose. Prior to haemodialysis one additional dose of 15 mg/kg should be administered. In order to restore circulating drug levels, another dose of 15 mg/kg should be administered after haemodialysis.

In patients receiving peritoneal dialysis

Amoxicillin maximum 500 mg/day.

Hepatic impairment

Dose with caution and monitor hepatic function at regular intervals (see sections 4.4 and 4.8).

Method of administration

Amoxicillin is for oral use.

Absorption of amoxicillin is unimpaired by food.

Therapy can be started parenterally according to the dosing recommendations of the intravenous formulation and continued with an oral preparation.

Swallow with water without opening capsule.

4.3 Contraindications

Amoxicillin is a penicillin. Hypersensitivity to the active substance, to any of the penicillins or to any of the excipients listed in section 6.1.Attention should be paid to possible cross-sensitivity with other beta-lactam antibiotics e.g. cephalosporins, carbapenem or monobactam.

4.4 Special warnings and precautions for use

Hypersensitivity reactions

Before initiating therapy with amoxicillin, careful enquiry should be made

concerning previous hypersensitivity reactions to penicillins and cephalosporins or other beta-lactam agents (see sections 4.3 and 4.8).

The excipients tartrazine (E102), sunset yellow (E110), carmosine (E122) and brilliant blue (E133) may cause hypersensitivity reactions.

Serious and occasionally fatal hypersensitivity (including anaphylactoid and severe cutaneous reactions) have been reported in patients on penicillin therapy. Hypersensitivity reactions can also progress to Kounis syndrome, a serious allergic reaction that can result in myocardial infarction (see section 4.8). These reactions are more likely to occur in individuals with a history of penicillin hypersensitivity and in atopic individuals. If an allergic reaction occurs, amoxicillin therapy must be discontinued and appropriate alternative therapy instituted.

Drug-induced enterocolitis syndrome (DIES) has been reported mainly in children receiving amoxicillin/clavulanate (see section 4.8). DIES is an allergic reaction with the leading symptom of protracted vomiting (1-4 hours after drug administration) in the absence of allergic skin or respiratory symptoms. Further symptoms could comprise abdominal pain, diarrhoea, hypotension or leucocytosis with neutrophilia. There have been severe cases including progression to shock.

Non-susceptible microorganisms

Amoxicillin is not suitable for the treatment of some types of infection unless the pathogen is already documented and known to be susceptible or there is a very high likelihood that the pathogen would be suitable for treatment with amoxicillin (see section 5.1). This particularly applies when considering the treatment of patients with urinary tract infections and severe infections of the ear, nose and throat.

Convulsions

Convulsions may occur in patients with impaired renal function or in those receiving high doses or in patients with predisposing factors (e.g. history of seizures, treated epilepsy or meningeal disorders (see section 4.8).

Renal impairment

In patients with renal impairment, the dose should be adjusted according to the degree of impairment (see section 4.2).

Skin reactions

The occurrence at the treatment initiation of a feverish generalised erythema associated with pustula may be a symptom of acute generalised exanthemous pustulosis (AEGP, see section 4.8). This reaction requires amoxicillin discontinuation and contra-indicates any subsequent administration.

Amoxicillin should be avoided if infectious mononucleosis is suspected since the occurrence of a morbilliform rash has been associated with this condition following the use of amoxicillin.

Jarisch-Herxheimer reaction

The Jarisch-Herxheimer reaction has been seen following amoxicillin treatment of Lyme disease (see section 4.8). It results directly from the bactericidal activity of amoxicillin on the causative bacteria of Lyme disease, the spirochaete *Borrelia burgdorferi*. Patients should be reassured that this is a common and usually self-limiting consequence of antibiotic treatment of Lyme disease.

Overgrowth of non-susceptible microorganisms

Prolonged use may occasionally result in overgrowth of non-susceptible organisms.

Antibiotic-associated colitis has been reported with nearly all antibacterial agents and may range in severity from mild to life threatening (see section 4.8). Therefore, it is important to consider this diagnosis in patients who present with diarrhoea during, or subsequent to, the administration of any antibiotics. Should antibiotic-associated colitis occur, amoxicillin should immediately be discontinued, a physician consulted and an appropriate therapy initiated. Anti-peristaltic medicinal products are contra-indicated in this situation.

Prolonged therapy

Periodic assessment of organ system functions; including renal, hepatic and haematopoietic function is advisable during prolonged therapy. Elevated liver enzymes and changes in blood counts have been reported (see section 4.8).

Anticoagulants

Prolongation of prothrombin time has been reported rarely in patients receiving amoxicillin. Appropriate monitoring should be undertaken when anticoagulants are prescribed concomitantly. Adjustments in the dose of oral anticoagulants may be necessary to maintain the desired level of anticoagulation (see sections 4.5 and 4.8).

Crystalluria

In patients with reduced urine output, crystalluria (including acute renal injury) 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. In patients with bladder catheters, a regular check of patency should be maintained (see sections 4.8 and 4.9).

Interference with diagnostic tests

Elevated serum and urinary levels of amoxicillin are likely to affect certain laboratory tests. Due to the high urinary concentrations of amoxicillin, false positive readings are common with chemical methods.

It is recommended that when testing for the presence of glucose in urine

during amoxicillin treatment, enzymatic glucose oxidase methods should be used.

The presence of amoxicillin may distort assay results for oestriol in pregnant women

4.5 Interaction with other medicinal products and other forms of interaction

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

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 co-administration 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 (see sections 4.4 and 4.8).

4.6 Fertility, pregnancy and lactation

Pregnancy:
Animal studies with amoxicillin have shown no teratogenic effects. Amoxicillin has been in extensive clinical use since 1972 and its suitability in human pregnancy has been well documented in clinical studies. When antibiotic therapy is required during pregnancy amoxicillin may be considered appropriate when the potential benefits outweigh the potential risks associated with treatment.

Breast-feeding:
Amoxicillin may be given during 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.

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

4.7 Effects on ability to drive and use machines

Adverse effects on the ability to drive or operate machinery have not been observed. However, undesirable effects may occur (e.g. allergic reactions, dizziness, convulsions), which may influence the ability to drive and use machines (see section 4.8).

4.8 Undesirable effects

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

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

Undesirable effects have been classified using the following convention:
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).
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.
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

Skin and subcutaneous tissue disorders
Clinical Trial Data
***Common**: Skin rash,
***Uncommon**: Pruritis 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 section 4.4), and drug reaction with eosinophilia and systemic symptoms (DRESS).
Not known: Linear IgA disease.

Immune system disorders:
Very rare: As with other antibiotics severe allergic reactions, including angioneurotic oedema, anaphylaxis (see section 4.4), serum sickness and hypersensitivity vasculitis.

If a hypersensitivity reaction is reported, the treatment must be discontinued. (see also skin and subcutaneous tissue disorders)

Renal and urinary tract disorders:
Very rare: Interstitial nephritis.
Not known: Crystalluria (including acute renal injury) (see sections 4.4 and 4.9)

Gastrointestinal disorders:
Clinical Trial Data
***Common**: Nausea and diarrhoea.
***Uncommon**: Vomiting.
Post marketing Data
Very rare: Antibiotic associated colitis (including pseudomembraneous colitis and haemorrhagic).
Black hairy tongue
Superficial tooth discolouration has been reported in children, mostly with the suspension and chewable tablets. It can usually be removed by brushing.
Not known: Drug-induced enterocolitis syndrome

Hepato –biliary disorders *:*
Very rare: A moderate rise in AST and/or ALT. The significance of rise in AST and /or ALT is unclear.

Hepatitis and cholestatic jaundice.

Blood and lymphatic system disorders:
Very rare: As with other beta lactams, eversible leucopenia (including severe neutropenia or agranulocytosis), reversible thrombocytopenia and haemolytic anaemia.

Prolongation of bleeding time and prothrombin time (see section 4.4)

Nervous system disorders:
Very rare: Hyperkinesias, dizziness and convulsions. Convulsions may occur in patients with impaired renal function or in those receiving high doses.
Not known: Aseptic meningitis.

Cardiac disorders:
Not known: Kounis syndrome.

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

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 the Yellow Card Scheme
Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

Symptoms and signs of overdose

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). Convulsions may occur in patients with impaired renal function or in those receiving high doses (see sections 4.4 and 4.8).

Treatment of intoxication

Gastrointestinal symptoms may be treated symptomatically, with attention to the water/electrolyte balance. Amoxicillin may be removed from the circulation by haemodialysis (see sections 4.4 and 4.8).

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

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

General Properties:

Amoxicillin is a broad spectrum antibiotic and kills bacteria by interfering with the synthesis of the bacterial cell wall.

Amoxicillin possesses the safety profile of a penicillin.

Susceptibility:

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. This information gives only approximate guidance on the probability as to whether micro-organisms will be susceptible to amoxicillin or not.

Susceptible:

Gram-positive	Gram-negative
Streptococcus faecalis	*Haemophilus influenze*
Streptococcus pneumoniae	*Escherichia coli*
Streptococcus pyogenes	*Proteus mirabilis*
Streptococcus viridans	*Salmonella* species
Staphylococcus aureus	*Shigella* species
(penicillin-sensitive strains only)	*Bordetella pertussis*
	Brucella species
Corynebacterium species	*Neisseria gonorrhoeae*
Bacillus anthracis	*Neisseria meningitides*
Listeria monocytogenes	*Vibrio cholerae*

Pasteurella septica

Helicobacter pylori

Anaerobes:

Clostridium species

Resistant:

Gram-negative

Klebsiella and Enterobacter spp

Indole-positive proteus spp

Pseudomonas aeruginosa

Resistance to Enterobacter spp. is reported to be due to poor penetration of amoxicillin into the organisms and its subsequent destruction by β-lactamase. Amoxicillin is therefore not active against penicillinase-producing organisms due to instability to this particular β-lactamase.

Organisms resistant to ampicillin are also resistant to amoxicillin as there is complete cross-resistance between the two compounds.

5.2 Pharmacokinetic properties

It is well absorbed by the oral and parenteral routes. Oral administration, usually at convenient dosage, produce high serum levels independent of the time at which food is taken. It gives good penetration into bronchial secretions and high urinary concentrations of unchanged antibiotic.

Absorption:
The absolute bioavailability of amoxicillin depends on the dose and ranges between 75 and 90%. In the dose range between 250mg and 3000mg the bioavailability (parameters: AUC and/or recovery in urine) is linearly proportional to the dose. At higher doses the extent of absorption decreases. Absorption is not affected by concomitant food intake. The time to peak plasma concentration (Tmax) 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.

Cmax	Tmax *	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)			

Haemodialysis can be used for elimination of amoxicillin.

Distribution:
Protein binding for amoxicillin is approximately 17%. Therapeutic drug levels are rapidly achieved in serum, lung tissue, bronchial secretions, middle ear fluid, bile and urine.
Amoxicillin can penetrate inflamed meninges and enter the cerebrospinal fluid. Amoxicillin crosses the placenta and a small percentage is excreted in breast milk.

Biotransformation and Elimination:
The main route of excretion of amoxicillin is the kidney. About 60 – 80% of an oral dose of amoxicillin is excreted in unchanged active form in the urine within 6 hours of admin-istration and a small fraction is excreted in the bile. Approximately 7-25%

of the administered dose is metabolised to inactive penicilloic acid. The serum half-life in patients with normal renal function is approximately 1-1.5 hours. In patients with end- stage renal failure the half-life ranges between 5 to 20 hours. The substance is haemodialysable.

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 sections 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 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Colloidal anhydrous silica
Magnesium stearate
Gelatin
Titanium dioxide (E 171)
Erythrosine (E 127)
Iron Oxide Black (E 172)
Iron Oxide Red (E 172)
Iron Oxide Yellow (E 172)

6.2 Incompatibilities

Not applicable.

6.3 Shelf-life

Blister, 36 months.

Container, 24 months

6.4 Special precautions for storage

Blister: Do not store above 25ºC. Store in original package.

Container: Do not store above 25°C, Store in Original Package, Keep container tightly closed

6.5 Nature and contents of container

PVC/Aluminium blister packs

6.6 Special precautions for disposal

No special requirements.

7. MARKETING AUTHORISATION HOLDER AND MANUFACTURING SITE ADDRESSES

Aspee Pharmaceuticals Limited - Plt 66 Blk F Asamang-Ejisu, Ashanti Region, Ghana

8 MARKETING AUTHORISATION NUMBER

FDA/SD.245-081510

9 DATE OF FIRST AUTHORISATION/RENEWAL

8/29/2024

10 DATE OF REVISION OF THE TEXT

09/2025