1. NAME OF THE MEDICINAL PRODUCT

Amoxicillin 500 mg/ 5 ml Powder for oral suspension

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5 ml dose of reconstituted oral suspension contains 500 mg of amoxicillin (100 mg per ml) in the form of amoxicillin trihydrate.

Excipient (s) with known effect:
Contains 15 mg of aspartame per 5 ml (3mg per ml)
Contains 3.750 mg of sodium benzoate per 5 ml (0.75 mg per ml)
Contains 3.5 mg of sodium per 5 ml (0.7 mg per ml)
Contains maltodextrin (glucose).
Contains benzyl alcohol.
For the full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Powder for oral suspension.

Off-White to pale yellow colour free flowing powder

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Amoxicillin is indicated for the treatment of the following infections in adults 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

Amoxicillin is also indicated for the prophylaxis of endocarditis.

Consideration should be given to the official guidance on the appropriate use of antibacterial agents.

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 to 30	Maximum 500 mg twice daily	15 mg/kg twice daily (maximum 500 mg twice daily)
Less than 10	Maximum 500 mg/day.	15 mg/kg given as a single daily
# In 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 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 (maximum 500 mg). 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.
For instructions on reconstitution of the medicinal product before administration, see section 6.6

4.3 Contraindications

Hypersensitivity to the active substance, to any of the penicillins or to any of the excipients listed in section 6.1.

History of a severe immediate hypersensitivity reaction (e.g. anaphylaxis) to another beta-lactam agent (e.g. cephalosporin, 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, cephalosporins or other beta-lactam agents (see sections 4.3 and 4.8).

Serious and occasionally fatal hypersensitivity reactions (including anaphylactoid and severe cutaneous adverse 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 (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 (AGEP 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 micro-organisms

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 contraindicated in this situation.

Prolonged therapy

Periodic assessment of organ system functions; including renal, hepatic and hematopoietic 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 the urine during amoxicillin treatment, enzymatic glucose oxidase methods should be used.
The presence of amoxicillin may distort assay results for oestriol in pregnant women.

Important information about excipients

- This medicine contains 15.000 mg aspartame in each 5 ml. Aspartame is a source of phenylalanine. It may be harmful if you have phenylketonuria (PKU), a rare genetic disorder in which phenylalanine builds up because the body cannot remove it properly.

- The medicine contains maltodextrin (glucose). Patients with rare glucose-galactose malabsorption should not take this medicine.

- This medicine contains 3.750 mg sodium benzoate in each 5 ml. Sodium benzoate may increase jaundice (yellowing of the skin and eyes) in new born babies (up to 4 weeks old)

- This medicine contains less than 1 mmol sodium (23 mg) per ml that is to say essentially 'sodium-free'.

- This medicine contains 0.32 mg benzyl alcohol in 5 ml. Benzyl alcohol may cause allergic reactions. Benzyl alcohol has been linked with the risk of severe side effects including breathing problems (called "gasping syndrome") in young children. Do not give to your newborn baby (up to 4 weeks old), unless recommended by your doctor.

- This medicine contains 3.750 mg benzoate salt in each 5 ml.

This medicine contains of sodium. This should be considered in patients controlling their dietary sodium intake.

4.5 Interaction with other medicinal products and other forms of interaction

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

Tetracycline 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).

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 sensitization. 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 have shown no effects on fertility.

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 (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.
The following terminologies have been used in order to classify the occurrence of undesirable effects.
Very common (≥1/10)
Common (≥1/100 to <1/10)
Uncommon (≥1/1000 to <1/100)
Rare (≥1/10,000 to <1/1,000)
Very rare (<1/10,000)
Not known (cannot be estimated from the available data)

Infections and infestations	
Very rare	Mucocutaneous candidiasis
Blood and lymphatic system disorders	
Very rare	Reversible leucopenia (including agranulocytosis or severe neutropenia), reversible thrombocytopenia and haemolytic anemia.

	Prolongation of bleeding time and prothrombin time (see section 4.4).
Immune system disorders	
Very rare	Severe allergic reactions, including angioneurotic oedema, anaphylaxis, serum sickness and hypersensitivity vasculitis (see section 4.4).
Not known	Jarisch-Herxheimer reaction (see section 4.4)
Nervous system disorders	
Very rare	Hyperkinesia, dizziness and convulsions (see section 4.4).
Not known	Aseptic meningitis
Cardiac disorders	
Not known	Kounis syndrome
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, see section 4.4). Black hairy tongue Superficial tooth discolouration[#]
Not known	Drug-induced enterocolitis syndrome
Hepatobiliary disorders	
Very rare	Hepatitis and cholestatic jaundice. A moderate rise in AST and/or ALT.
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).
Not known	Linear IgA disease
Renal and urinary tract disorders	
Very rare	Interstitial nephritis
Not known	Crystalluria (including acute renal injury)
*The incidence of these AEs was derived from clinical studies involving a total of approximately 6,000 adult and paediatric patients taking amoxicillin. # Superficial tooth discolouration has been reported in children. Good oral hygiene may help to prevent tooth discolouration as it can usually be removed by brushing.	

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 Yellow Card Scheme (www.mhra.gov.uk/yellowcard).

4.9 Overdose

Signs and symptoms of overdose

Gastrointestinal symptoms (such as nausea, vomiting and diarrhoea) and disturbance of the fluid and electrolyte balance 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 (see section 4.4 and 4.8)

Amoxicillin crystalluria, in some cases leading to renal failure, has been observed (see section 4.4).

Treatment of intoxication

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

Amoxicillin can be removed from the circulation by haemodialysis.

5. 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 bacterial 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 9.0.

Organism	**MIC breakpoint (mg/L)**	
	Susceptible ≤	**Resistant >**
Enterobacterales	8[1]	8
Pseudomonas spp.	-	-
Acinetobacter spp.	-	-
Staphylococcus spp.	Note[2]	Note[2]
Enterococcus spp.[3]	4	8
Streptococcus groups A, B, C and G	Note[4]	Note[4]
Streptococcus pneumoniae	0.5[5]	1[5]
Viridans group streptococci	0.5	2
Haemophilus influenzae,[6, HE]	2	2
Moraxella catarrhalis	-[7]	-[7]
Neisseria gonorrhoeae[8]	Note[8]	Note[8]
Neisseria meningitidis	0.125	1
Gram-positive anaerobes except *Clostridioides difficile*[9]	4	8
Gram-negative anaerobes[9]	0.5	2
Helicobacter pylori	0.125[10]	0.125[10]
Pasteurella multocida	1	1
Aerococcus sanguinicola and *urinae*	Note[11]	Note[11]
Kingella kingae	0.125[12]	0.125[12]
PK-PD (Non-species related) breakpoints	2	8

[1]Wild type Enterobacterales are categorised as susceptible to aminopenicillins. Some countries prefer to categorise wild-type isolates of *E. coli* and *P. mirabilis* as "Susceptible, increased exposure". When this is the case, use the MIC breakpoint S ≤ 0.5 mg/L and the corresponding zone diameter breakpoint S ≥ 50 mm.

[2]Most staphylococci are penicillinase producers, which make them resistant to benzylpenicillin, phenoxymethylpenicillin, ampicillin, amoxicillin, piperacillin and ticarcillin. When staphylococci test as susceptible to benzylpenicillin and cefoxitin they can be reported as susceptible to the above agents. However, the efficacy of oral formulations, particularly phenoxymethylpenicillin, is uncertain. Isolates that test as resistant to benzylpenicillin but susceptible to cefoxitin are susceptible to beta-lactamase inhibitor combinations, the isoxazolylpenicillins (oxacillin, cloxacillin, dicloxacillin and flucloxacillin), nafcillin and many cephalosporins. With the exception of ceftaroline and ceftobiprole, cefoxitin-resistant isolates are resistant to all beta-lactam agents. Ampicillin susceptible *S. saprophyticus* are *mecA*-negative and susceptible to ampicillin, amoxicillin and piperacillin (without or with a beta-lactamase inhibitor).

[3]Susceptibility to ampicillin, amoxicillin and piperacillin with and without beta-lactamase inhibitor can be inferred from ampicillin.

[4]The susceptibility of streptococcus groups A, B, C and G to penicillins is inferred from the benzylpenicillin susceptibility with the exception of phenoxymethylpenicillin and isoxazolylpenicillins for streptococcus group B.

[5]The oxacillin 1unit disk screen test shall be used to exclude beta-lactam resistance mechanisms. When the screen is negative (inhibition zone ≥20 mm) all beta-lactam agents for which clinical breakpoints are available can be reported susceptible without further testing. When the screen is positive (inhibition zone <20 mm) consider susceptible for oxacillin zone ≥8 mm, if oxacillin zone <8 mm see breakpoint recommendations (for oral amoxicillin without and with inhibitor).

[6]Beta-lactamase positive isolates can be reported resistant to ampicillin, amoxicillin and piperacillin without inhibitors. Tests based on a chromogenic cephalosporin can be used to detect the beta-lactamase.

[7]Most *M. catarrhalis* produce beta-lactamase, although beta-lactamase production is slow and

may give weak results with *in vitro* tests. Beta-lactamase producers should be reported resistant to penicillins and aminopenicillins without inhibitors.
[8]Always test for beta-lactamase. If positive, report resistant to benzylpenicillin, ampicillin and amoxicillin. Tests based on a chromogenic cephalosporin can be used to detect the beta-lactamase. The susceptibility of beta-lactamase negative isolates to ampicillin can be inferred from benzylpenicillin.
[9]Susceptibility to ampicillin, amoxicillin, piperacillin and ticarcillin can be inferred from susceptibility to benzylpenicillin.
[10]The breakpoints are based on epidemiological cut-off values (ECOFFs), which distinguish wild-type isolates from those with reduced susceptibility.
[11]Infer susceptibility form ampicillin susceptibility.
[12]Susceptibility can be inferred from benzylpenicillin susceptibility.
[HE]High exposure for agent

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-haemolytic streptococci (Group 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.
Others:
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. It is rapidly and well absorbed by the oral route of 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 $_{(0-24h)}$	$T_{1/2}$
(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 mg, 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 0.4 l/kg.

Following intravenous administration, amoxicillin has been found in gall bladder, abdominal tissue, skin, fat, muscle tissues, 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 amoxicillin is excreted unchanged in urine during the first 6 hours after administration of a single 250 mg or 500 mg dose of amoxicillin. Various studies have found the urinary excretion to be 50 to 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 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

Silicon dioxide
Aspartame (E 951)
Xanthan gum
Sodium benzoate (E211)
Tri sodium citrate dehydrate
Colloidal silicon dioxide
Strawberry Flavor 052311 AP0551
Benzyl alcohol

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

Dry powder: 3 years
Reconstituted suspension: 14 days
Reconstituted suspension: Store up to 14 days at 2°C – 8°C in a refrigerator.

6.4 Special precautions for storage

Dry powder: Do not store above 25°C

Store upto 14 days at 2°C - 8°C in a refrigerator.

For storage conditions after reconstitution of the medicinal product, see section 6.3

6.5 Nature and contents of container

Amoxicillin 5 mg/ 5 ml powder for oral suspension filled into a 150 ml HDPE bottle containing 100 ml of product. and a 115 ml HDPE bottle containing 60 ml of product closed with polypropylene child resistant caps containing polymers liners These primary packs are placed in a carton with or without a dosing syringe of 5 ml.

Dosing syringe graduation: 0.5 ml to 5 ml

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

No special requirements.

Check cap seal is intact before use.
Invert and shake bottle to loosen powder.
Fill the bottle with water to just below the mark on the bottle.
Invert and shake well, then top up with water to the mark. Invert and shake again.
Shake well before taking each dose.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Brown & Burk UK Limited
5, Marryat Close,
Hounslow West,
Middlesex TW4 5DQ
United Kingdom

8. MARKETING AUTHORISATION NUMBER(S)

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9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

09/01/2020

10. DATE OF REVISION OF THE TEXT

21/02/2023