

# OSPAMOX®

**500 mg film-coated tablets**

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## 1. NAME OF THE MEDICINAL PRODUCT

Ospamox 500 mg Film-Coated Tablet

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film-coated tablet contains Amoxicillin 500 mg.

White to off-white, oblong, biconvex, scored on both sides. Approx. 7mm x 18mm.

## 3. PHARMACEUTICAL FORM

Film-coated tablet.

## 4. CLINICAL PARTICULARS

### 4.1 Therapeutic Indications

Ospamox is useful in the treatment of infections caused by amoxicillin-susceptible organisms:

#### *Respiratory tract infections*

- Upper airways and ENT infections
- Lower airways infections, e.g. acute and chronic bronchitis, pneumonia, lung abscesses, pertussis (incubation period and early stages)

#### *Urogenital Infections*

- Acute and chronic pyelonephritis, pyelitis, prostatitis, epididymitis
- Cystitis, urethritis, asymptomatic bacteriuria during pregnancy
- Gonorrhea

*Gynecologic infections* (septic abortion, adnexitis, endometritis, etc.)

#### *Gastro-intestinal infections*

- Typhoid fever, paratyphoid, particularly if complicated by septicemia (in combination with an aminoglycoside antibiotic); control of Salmonella carriers
- Shigellosis
- Infections of the biliary system (cholangitis, cholecystitis)

#### *Skin and soft tissue infections*

#### *Leptospirosis*

#### *Acute and latent listeriosis*

Unless parenteral treatment (e.g. with ampicillin) is required, Ospamox is also active in the conditions below:

- Short-term (24 to 48 hours) prophylactic treatment of patients undergoing surgery (e.g. in the oral cavity).
- Endocarditis, e.g. enterococcal endocarditis (alone or in combination with an aminoglycoside antibiotic).
- Bacterial meningitis (pending the outcome of susceptibility tests; particularly in children).
- Septicemias caused by amoxicillin-susceptible pathogens.

Infections caused by pathogens with established with penicillin G susceptibility should preferentially be treated with penicillin G.

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

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### 4.2 Posology and method of administration

#### Posology

The dose depends on the susceptibility of the offending organism and on the site of the infection. In general, the total daily dose should be divided into 2 (3 to 4) fractions.

Doses for children, which were calculated relative to kg body weight, should not exceed maximal adult doses.

#### Average dose levels for

|                         |                               |
|-------------------------|-------------------------------|
| Children:               | 30 - 60 mg/kg body weight/day |
| Adolescents and adults: | 1,500 - 2,000 mg/day          |

#### Specific dosing recommendations:

|                         |                 |          |
|-------------------------|-----------------|----------|
| Children 10 - 14 years: | 1 tablet b.i.d. | 500 mg   |
| Adolescents:            | 1 tablet b.i.d. | 750 mg   |
| Adults:                 | 1 tablet b.i.d. | 1,000 mg |

As Ospamox is highly effective and excellently absorbed, even severe infections will respond to oral drug treatment. In severe disease daily doses should, however, be increased:

|           |                             |
|-----------|-----------------------------|
| Children: | 100 mg/kg body weight daily |
| Adults:   | up to 6,000 mg daily        |

Doses of 200 mg/kg body weight and 8,000 mg daily have been tolerated by children and adults, respectively, without any complications.

For acute febrile infections of the gastro-intestinal tract (typhoid fever, paratyphoid) and the biliary system or for gynecologic infections adults should be given 1,500 to 2,000 mg t.i.d. or 1,000 to 1,500 mg q.i.d.

#### *Leptospirosis:*

Adults: 500 to 750 mg q.i.d. for 6 to 12 days

#### *Chronic Salmonella carriers:*

Adults: 1,500 to 2,000 mg t.i.d. for 2 to 4 weeks

#### *Prevention of endocarditis secondary to dental extractions:*

Adults should receive 3,000 to 4,000 mg 1 hour prior to extractions followed, if necessary, by another dose 8 to 9 hours later. Children are given half this dose.

Treatment should be continued for 2 to 5 days after symptoms have subsided. To prevent sequels, streptococcal infections should be treated for at least 10 days (WHO recommendation).

#### Dose in patients with reduced elimination:

In patients with reduced renal function or plasma creatinine levels above 4 mg (creatinine clearance below 30 mL/minute) as well as in premature or newborn infants dose levels and/ or dose intervals should be adjusted to match the reduced renal elimination. If creatinine clearances are between 15 and 40 mL/minute, amoxicillin should be dosed at approximately 12-hourly intervals. Anuric patients should not be given more than 2,000 mg within 24 hours. Urinary tract infections require normal dose levels.

#### Hepatic impairment

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

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### **Method of administration**

Amoxicillin is for oral use.

Absorption of amoxicillin is unimpaired by food.

### **Film-coated tablets**

The film-coated tablets should be swallowed whole with sufficient liquid (e.g., a glass of water).

### **4.3 Contraindications**

Hypersensitivity to the active substance, to any of the penicillins or to any of the excipients.

History of a severe immediate hypersensitivity reaction (e.g. anaphylaxis) to another beta-lactam agent (e.g. a 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 receiving therapy with beta-lactams. Before initiating therapy with Ospamox, careful inquiry should be made concerning previous hypersensitivity reactions to penicillins, cephalosporins, carbapenems or other beta-lactam agents. If an allergic reaction occurs, Ospamox must be discontinued and appropriate alternative therapy instituted.

#### **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 contraindicates 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.

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### 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 contraindicated 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 section 4.5 and 4.8).

### Crystalluria

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. In patients with bladder catheters, a regular check of patency should be maintained (see section 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**

### 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 medicinal products 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

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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 section 4.4 and 4.8).

### Methotrexate

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

## 4.6 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.

### Breastfeeding

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 breastfeeding might have to be discontinued. Amoxicillin should only be used during breastfeeding 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.

### **Infections and infestations**

*Very rare:* Mucocutaneous candidiasis

### **Blood and lymphatic system disorders**

*Very rare:* Reversible leucopenia (including severe neutropenia or agranulocytosis), reversible thrombocytopenia and haemolytic anaemia, 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

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### Gastrointestinal disorders

#### Post-marketing data

*Very rare:* Antibiotic associated colitis (including pseudomembranous colitis and haemorrhagic colitis), black hairy tongue

### Hepatobiliary disorders

*Very rare:* Hepatitis and cholestatic jaundice, moderate rise in AST and/or ALT

### Skin and subcutaneous tissue disorders

#### 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)

### Renal and urinary tract disorders

*Very rare:* Interstitial nephritis, crystalluria (see section 4.4 and 4.9)

## 4.9 Overdose

### Symptoms and signs of overdose

Gastrointestinal symptoms (such as nausea, vomiting and diarrhoea) and disturbance 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 (see section 4.4 and 4.8).

### 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. PHARMACOLOGICAL PROPERTIES

### 5.1 Pharmacodynamics properties

Pharmacotherapeutic group: Antibacterials for systemic use, beta-lactam antibacterials, penicillins, 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.

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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 7.1.

| Organism                                                                  | MIC breakpoint (mg/l) |                     |
|---------------------------------------------------------------------------|-----------------------|---------------------|
|                                                                           | Susceptible ≤         | Resistant >         |
| Enterobacteriaceae                                                        | 8 <sup>1</sup>        | 8                   |
| <i>Staphylococcus</i> spp.                                                | Note <sup>2,3</sup>   | Note <sup>2,3</sup> |
| <i>Enterococcus</i> spp. <sup>4</sup>                                     | 4                     | 8                   |
| Streptococcus groups A, B, C and G                                        | Note <sup>5</sup>     | Note <sup>5</sup>   |
| <i>Streptococcus pneumoniae</i>                                           | Note <sup>6</sup>     | Note <sup>6</sup>   |
| Viridans group streptococci                                               | 0.5                   | 2                   |
| <i>Haemophilus influenzae</i>                                             | 2 <sup>7</sup>        | 2 <sup>7</sup>      |
| <i>Moraxella catarrhalis</i>                                              | Note <sup>8</sup>     | Note <sup>8</sup>   |
| <i>Neisseria gonorrhoeae</i> <sup>9</sup>                                 | Note <sup>9</sup>     | Note <sup>9</sup>   |
| <i>Neisseria meningitidis</i>                                             | 0.125                 | 1                   |
| Gram positive anaerobes except <i>Clostridium difficile</i> <sup>10</sup> | 4                     | 8                   |
| Gram negative anaerobes <sup>10</sup>                                     | 0.5                   | 2                   |
| <i>Helicobacter pylori</i>                                                | 0.125 <sup>11</sup>   | 0.125 <sup>11</sup> |
| <i>Pasteurella multocida</i>                                              | 1                     | 1                   |
| <i>Aerococcus sanguinicola</i> and <i>urinae</i>                          | Note <sup>12</sup>    | Note <sup>12</sup>  |
| <i>Kingella kingae</i>                                                    | 0.125 <sup>13</sup>   | 0.125 <sup>13</sup> |
| PK/PD (non-species related) breakpoints                                   | 2                     | 8                   |

- <sup>1</sup> 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  $S \leq 0.5$  mg/l and the corresponding zone diameter breakpoint  $S \geq 50$  mm.
- <sup>2</sup> Most staphylococci are penicillinase producers, which are resistant to benzylpenicillin, phenoxymethylpenicillin, ampicillin, amoxicillin, piperacillin and ticarcillin. Isolates negative for penicillinase and susceptible to methicillin can be reported susceptible to these agents. Isolates positive for penicillinase and methicillin susceptible are susceptible to beta-lactamase inhibitor combinations and isoxazolympenicillins (oxacillin, cloxacillin, dicloxacillin and flucloxacillin). Methicillin resistant isolates are, with few exceptions, resistant to all beta-lactam agents.
- <sup>3</sup> Ampicillin susceptible *S. saprophyticus* are mecA -negative and susceptible to ampicillin, amoxicillin and piperacillin (without or with a beta-lactamase inhibitor).
- <sup>4</sup> Susceptibility to ampicillin, amoxicillin and piperacillin with and without beta-lactamase inhibitor can be inferred from ampicillin.
- <sup>5</sup> The susceptibility of streptococcus groups A, B, C and G to penicillins is inferred from the benzylpenicillin susceptibility with the exception of phenoxymethylpenicillin and isoxazolympenicillins for streptococcus group B.
- <sup>6</sup> Breakpoints for penicillins other than benzylpenicillin relate only to non-meningitis isolates. Isolates fully susceptible to benzylpenicillin (MIC  $\leq 0.06$  mg/l and/or susceptible by oxacillin disk screen) can be reported susceptible to beta-lactam agents for which clinical breakpoints are listed (including those with "Note"). For isolates categorised as intermediate to ampicillin avoid oral treatment with amoxicillin, amoxicillin or amoxicillin-clavulanic acid. Susceptibility inferred from the MIC of ampicillin.

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|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--|
| <p><sup>7</sup> Breakpoints are based on intravenous administration. 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.</p> <p><sup>8</sup> Most <i>M. catarrhalis</i> produce beta-lactamase, although beta-lactamase production is slow and may give weak results with <i>in vitro</i> tests. Beta-lactamase producers should be reported resistant to penicillins and aminopenicillins without inhibitors.</p> <p><sup>9</sup> 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 and amoxicillin can be inferred from benzylpenicillin.</p> <p><sup>10</sup> Susceptibility to ampicillin, amoxicillin, piperacillin and ticarcillin can be inferred from susceptibility to benzylpenicillin.</p> <p><sup>11</sup> The breakpoints are based on epidemiological cut-off values (ECOFFs), which distinguish wild-type isolates from those with reduced susceptibility.</p> <p><sup>12</sup> Infer susceptibility from ampicillin susceptibility.</p> <p><sup>13</sup> Susceptibility can be inferred from benzylpenicillin susceptibility.</p> |  |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--|

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.

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| <b><i>In vitro</i> susceptibility of microorganisms to amoxicillin</b>                                                                                                                                                                                                                        |
| <b>Commonly susceptible species</b>                                                                                                                                                                                                                                                           |
| Gram-positive aerobes:<br><i>Enterococcus faecalis</i><br>Beta-hemolytic streptococci (Groups A, B, C and G)<br><i>Listeria monocytogenes</i>                                                                                                                                                 |
| <b>Species for which acquired resistance may be a problem</b>                                                                                                                                                                                                                                 |
| Gram-negative aerobes:<br><i>Escherichia coli</i><br><i>Haemophilus influenzae</i><br><i>Helicobacter pylori</i><br><i>Proteus mirabilis</i><br><i>Salmonella typhi</i><br><i>Salmonella paratyphi</i><br><i>Pasteurella multocida</i>                                                        |
| Gram-positive aerobes:<br>Coagulase negative staphylococcus<br><i>Staphylococcus aureus</i> <sup>£</sup><br><i>Streptococcus pneumoniae</i><br>Viridans group streptococcus                                                                                                                   |
| Gram-positive anaerobes:<br><i>Clostridium</i> spp.                                                                                                                                                                                                                                           |
| Gram-negative anaerobes:<br><i>Fusobacterium</i> spp.                                                                                                                                                                                                                                         |
| Other:<br><i>Borrelia burgdorferi</i>                                                                                                                                                                                                                                                         |
| <b>Inherently resistant organisms<sup>†</sup></b>                                                                                                                                                                                                                                             |
| Gram-positive aerobes:<br><i>Enterococcus faecium</i> <sup>†</sup>                                                                                                                                                                                                                            |
| Gram-negative aerobes:<br><i>Acinetobacter</i> spp.<br><i>Enterobacter</i> spp.<br><i>Klebsiella</i> spp.<br><i>Pseudomonas</i> spp.                                                                                                                                                          |
| Gram-negative anaerobes:<br><i>Bacteroides</i> spp. (many strains of <i>Bacteroides fragilis</i> are resistant).                                                                                                                                                                              |
| Others:<br><i>Chlamydia</i> spp.<br><i>Mycoplasma</i> spp.<br><i>Legionella</i> spp.                                                                                                                                                                                                          |
| <sup>†</sup> Natural intermediate susceptibility in the absence of acquired mechanism of resistance.<br><sup>£</sup> Almost all <i>S.aureus</i> are resistant to amoxicillin due to production of penicillinase. In addition, all methicillin-resistant strains are resistant to amoxicillin. |

## 5.2 Pharmacokinetics

### 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.

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.

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### 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.

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. Approximately 60 to 70% of the 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 50-85% 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, 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.

## **6. PHARMACEUTICAL PARTICULARS**

### **6.1 Incompatibilities**

Not applicable.

### **6.2 Shelf-life**

If properly stored, Ospamox film-coated tablets retain their full potency to the date of expiration shown on the pack.

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## **6.3 Special precautions for storage**

Film-coated tablets

Store below 25°C, protect from light and moisture.

Do not use after the expiry date stated on the carton and the container.

## **6.4 Presentation**

Film-coated tablets

Single packs of 12 and 14 tablets, hospital packs of 80, 100, 500 & 1000 tablets.

*Not all pack sizes may be marketed.*

## **6.5 Special precautions for disposal and other handling**

Film-coated tablets

No special requirements.

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

## **7. PRODUCT REGISTRATION HOLDER**

Sandoz Products Malaysia Sdn. Bhd.  
3A-2 & 3A-3, Level 3A, Menara KEN TTDI,  
No. 37, Jalan Burhanuddin Helmi, Taman Tun Dr Ismail,  
60000 Kuala Lumpur, Malaysia

## **8. DATE OF REVISION OF THE TEXT**

Aug 2026