SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF MEDICINAL PRODUCT
Amoxina 250mg/5ml powder for oral suspension

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
250 mg/5 ml powder for oral suspension – 60 ml and 100 ml bottles

After reconstitution, 5 ml of oral suspension contains Amoxicillin Trihydrate equivalent to 250 mg of Amoxicillin (50 mg per ml).

Excipient with known effects:
It contains sucrose

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM
Powder for oral suspension
White or almost white colour.

4. CLINICAL PARTICULARS
4.1. Therapeutic Indications
Amoxina 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
- Pharyngitis and acute streptococcal tonsillitis
- Exacerbations of chronic bronchitis
- Community-acquired pneumonia
- Acute cystitis
- Asymptomatic Bacteriuria in pregnancy
- Acute pyelonephritis
- Typhoid and paratyphoid fever
- Dental abscess with diffuse cellulitis
- Infections from articular prosthesis
- Eradication of *Helicobacter pylori*
- Lyme disease

Amoxina is also indicated for the prophylaxis of endocarditis.

Take into consideration the official guidelines on the appropriate use of antibacterial agents.

4.2. Posology and method of administration
Posology
When choosing the dose of Amoxina for the treatment of an infection, the following aspects must be considered:

- Presumed pathogens and their probable sensitivity to antibacterial agents (see section 4.4)
- Severity and seat of the infection
- The patient's age, weight and renal function, as illustrated below.

The duration of the therapy must be determined according to the type of infection and the patient's response; as a general rule, it must be as short as possible. Some infections require longer periods of treatment (see section 4.4 in relation to prolonged therapy).

Adults and children ≥40 kg

Indication*	**Dose***
Acute bacterial sinusitis	From 250 mg to 500 mg every 8 hours, or from 750 mg to 1 g

Asymptomatic Bacteriuria in pregnancy Acute pyelonephritis Dental abscess with diffuse cellulitis Acute cystitis	every 12 hours For severe infections, from 750 mg to 1 g every 8 hours Acute cystitis can be treated with 3 g twice a day, for one day
Acute otitis media Pharyngitis and acute streptococcal tonsillitis Exacerbations of chronic bronchitis	500 mg every 8 hours, or from 750 mg to 1 g every 12 hours For severe infections, from 750 mg to 1 g every 8 hours for 10 days
Community-acquired pneumonia	From 500 mg to 1 g every 8 hours
Typhoid and paratyphoid fever	From 500 mg to 2 g every 8 hours
Infections from articular prosthesis	From 500 mg to 1 g every 8 hours
Prophylaxis of endocarditis	2 g administered orally, in a single dose, 30-60 minutes before the procedure
Eradication of *Helicobacter pylori*	From 750 mg to 1 g twice a day combined 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: from 500 mg to 1 g every 8 hours up to a maximum of 4 g/day in separate doses for 14 days (from 10 to 21 days) Late stage (systemic level): from 500 mg to 2 g every 8 hours up to a maximum of 6 g/day in separate doses for 10-30 days)

* Take into consideration the official therapeutic guidelines for each indication

Children <40 kg
Children can be treated with Amoxina in powder for oral suspension or in dispersible tablets.
Amoxina powder for oral suspension is recommended for children under six months of age.
For children weighing 40 kg or more, the same posology that is used for adults must be prescribed.

Recommended doses:

Indication[+]	**Dose**[+]
Acute bacterial sinusitis Acute otitis media Community-acquired pneumonia Acute cystitis Acute pyelonephritis Dental abscess with diffuse cellulitis	From 20 to 90 mg/kg/days in separate doses*
Pharyngitis and acute streptococcal tonsillitis	From 40 to 90 mg/kg/days in separate doses*
Typhoid and paratyphoid fever	100 mg/kg/days in three separate doses
Prophylaxis of endocarditis	50 mg/kg administered orally, in a single dose, 30-60 minutes before the procedure
Lyme disease (see section 4.4)	Early stage: from 25 to 50 mg/kg/days in three separate doses for 10-21 days Late stage (systemic level): 100 mg/kg/days in three separate doses for 10-30 days
[+] Take into consideration the official therapeutic guidelines for each indication. * The double daily administration systems must be taken into consideration only when the dose falls within the upper range.	

Elderly
No dose adjustment is deemed necessary.

Renal damage

GFR (ml/min)	**Adults and children ≥40 kg**	**Children <40 kg**[#]

over 30	no adjustment necessary	no adjustment necessary
from 10 to 30	maximum 500 mg twice a day	15 mg/kg administered twice a day (maximum 500 mg twice a day)
below 10	maximum 500 mg/days	15 mg/kg administered in single daily dose (maximum 500 mg)
[#] In most cases, parenteral therapy is preferable.		

In patients subjected to dialysis
Amoxicillin can be removed from circulation by means of haemodialysis.

	Haemodialysis
Adults and children ≥40 kg	15 mg/kg/days administered in one single daily dose. Before the haemodialysis, an additional dose of 15 mg/kg must be administered. To restore the drug levels in circulation, another dose of 15 mg/kg must be administered after the haemodialysis.

In patients subjected to peritoneal dialysis
Amoxicillin maximum 500 mg/days.
Hepatic impairment
Administer with caution and monitor hepatic function at regular intervals (see sections 4.4 and 4.8).

Method of administration
Amoxina is for oral use.

Food has no effect on the absorption of Amoxina.

Therapy can be started through the parenteral route according to the posology recommendations foreseen for the intravenous formulation, and continued with an oral preparation.

For information on the instructions for the reconstitution of the medicinal product before the administration, see section 6.6.

4.3. Contraindications
Hypersensitivity to the active ingredient, to any of the penicillins or to any of the excipients listed in section 6.1.
History of severe immediate hypersensitivity reaction (e.g. anaphylaxis) to another beta-lactam (e.g. cephalosporin, carbapenems or monobactams).

4.4. Special warnings and precautions for use
Hypersensitivity reactions
Before starting the therapy with amoxicillin, accurate information about any previous episodes of hypersensitivity reactions to penicillins, to cephalosporins or to other beta-lactam antibiotics must be gathered (see sections 4.3 and 4.8). Severe and occasionally fatal hypersensitivity reactions (including anaphylactoid reactions and severe adverse skin reactions) have been documented in patients treated with penicillins. Hypersensitivity reactions can also evolve into Kounis syndrome, a severe allergic reaction that can cause myocardial infarction (see section 4.8). The onset of such reactions is more likely in those patients with a history of hypersensitivity to penicillins and in atopic patients. If an allergic reaction occurs, amoxicillin therapy must be interrupted and an appropriate alternative therapy must be established.

Drug-induced enterocolitic syndrome (DIES) has been reported mainly in children taking amoxicillin (see section 4.8). DIES is an allergic reaction with the main symptom of prolonged vomiting (1-4 hours after use) in the absence of allergic skin or respiratory symptoms. Additional symptoms might include abdominal pain, diarrhea, hypotension, or leukocytosis with neutrophilia. Severe cases have occurred, including progression to shock.

Non-susceptible micro-organisms
Amoxicillin is not suitable for the treatment of some types of infections unless the sensitivity of the pathogen has already been documented and is known, or unless there is a very high likelihood that the pathogen will respond to the treatment with amoxicillin (see section 5.1). This is particularly applicable when assessing the treatment of patients with infections in the urinary tract and severe otorhinolaryngological infections.

Convulsions
In those patients with reduced renal function or under treatment with high doses, or in those patients with predisposing factors (e.g. history of epileptic fits, treated epilepsy or meningeal pathology), convulsions may occur (see section 4.8).

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

Skin reactions
At the beginning of the treatment, the onset of a generalised erythema with fever associated to pustule can by a symptom of acute generalised exanthematous pustulosis (AGEP, see section 4.8). Such reaction requires the interruption of the treatment with amoxicillin, and constitutes a contraindication for the subsequent re-administration. The use of amoxicillin must be avoided whenever infectious mononucleosis is suspected because the appearance of a morbilliform exanthem has been associated with such condition as a consequence of the use of amoxicillin.

Jarisch-Herxheimer reaction
After treating Lyme disease with amoxicillin, the Jarisch-Herxheimer reaction has appeared (see section 4.8). This is a direct consequence of the bactericidal action exerted by amoxicillin on the bacterium responsible for Lyme disease, the *Borrelia burgdorferi* spirochaete. Patients must be reassured that this is a common and usually self-limiting consequence of the antibiotic treatment of Lyme disease.

Excessive proliferation of non-susceptible micro-organisms
Prolonged use may occasionally lead to an excessive proliferation of non-susceptible organisms.
Episodes of antibiotic colitis have been documented with almost all antibacterial agents, with seriousness ranging from mild to potentially fatal (see section 4.8). Therefore, it is important to consider this diagnosis in those patients who suffer from diarrhoea during or after the administration of antibiotics. If antibiotic colitis appears, the treatment with amoxicillin must be immediately interrupted, a doctor must be consulted and an appropriate therapy must be started. Antiperistaltic medicinal products are contraindicated in such situation.

Prolonged therapy
During a prolonged therapy, it is recommended to periodically assess the systemic-organic function, including renal, hepatic and haematopoietic functions. Cases of increase of hepatic enzymes and cases of alteration in blood counts have been reported (see section 4.8).

Anticoagulants
The extension of prothrombin time has been rarely documented in the patients treated with amoxicillin. In case of concurrent prescription of anticoagulants, patients must be suitably monitored. In order to keep the desired level of anticoagulation, some dose adjustments of oral anticoagulants may be necessary (see sections 4.5 and 4.8).

Crystalluria
In those patients with reduced diuresis, crystalluria (including acute kidney damage) has been observed very rarely, mostly with parenteral therapy. When high doses of amoxicillin are administered, it is advisable to maintain adequate fluid intake and appropriate diuresis in order to reduce the likelihood of amoxicillin crystalluria. In patients with bladder catheters, patency should be regularly checked (see sections 4.8 and 4.9).

Interference with diagnostic tests
High serum and urinary levels of amoxicillin may influence certain laboratory tests. Due to the high urinary concentrations of amoxicillin, it is often possible to obtain false positive results with chemical methods.
When glycosuria is measured in patients under treatment with amoxicillin, it is recommended to use the enzymatic method with glucose-oxidase.
In pregnant women, the presence of amoxicillin may distort test results due to estriol.

Important information about excipients
This medicinal product contains sucrose. Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrose isomaltase deficiency should not take this medicinal product.

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

Probenecid

The concurrent use of probenecid is not recommended. Probenecid reduces renal tubular secretion of amoxicillin. Concomitant use of probenecid may cause increased and prolonged a blood levels of amoxicillin.

Allopurinol
Co-administration of allopurinol during treatment with amoxicillin may 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-based antibiotics have been widely used in clinical practice without any interactions documented. However, in literature, cases of increase in the INR (*International Normalised Ratio*) have been reported in patients to whom an amoxicillin cycle has been prescribed during the concomitant treatment with acenocoumarol or warfarin. If co-administration is necessary, carefully monitor the prothrombin time or the INR when starting or interrupting the treatment with amoxicillin. It may also be necessary to adjust the dose of oral anticoagulants (see sections 4.4 and 4.8).

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

4.6. Fertility, pregnancy and lactation

Pregnancy
Animal studies do not indicate direct or indirect harmful effects in terms of reproduction toxicity. The limited data regarding the use of amoxicillin during pregnancy in human beings do not indicate an increase in the risk of congenital deformities. Amoxicillin may be used during pregnancy when its potential benefits outweigh the risks associated with the treatment.

Lactation
Amoxicillin is excreted in human breast milk in small amounts, with a potential risk of sensitisation. There is a consequent possibility of the onset of diarrhoea and fungal infections of mucous membranes in breast-fed babies, with a possible need to interrupt lactation. Amoxicillin must be used during lactation only after the doctor assesses the benefit-risk ratio.

Fertility
There are no data available about the effects of amoxicillin on human fertility. In animal reproduction studies, no effects on fertility have been reported.

4.7. Effects on ability to drive and use machines

No studies have been conducted in relation to the ability to drive and use machines. However, there may be undesirable effects (e.g. allergic reactions, dizziness, convulsions) that could affect the ability to drive and use machines (see section 4.8).

4.8. Undesirable effects

The most commonly reported adverse reactions to the drug are diarrhoea, nausea and skin rash.
The list below includes the adverse reactions to the drug arising from clinical studies and from the post-marketing surveillance activity in relation to amoxicillin, which have been organised based on the systemic-organic classification according to MedDRA.

To classify the frequency with which undesirable effects occur, the terms indicated below are used.
Very common (≥1/10)
Common (≥1/100, <1/10)
Uncommon (≥1/1,000, <1/100)
Rare (≥1/10,000, <1/1,000)
Very rare (<1/10,000)
Unknown (the frequency cannot be defined on the basis of available data)

Infections and infestations	
Very rare	Mucocutaneous candidiasis

Blood and lymphatic system disorders	
Very rare	Reversible leukopenia (including severe neutropenia or agranulocytosis), reversible thrombocytopenia and haemolytic anaemia. Increase of the bleeding time and of the 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
Gastrointestinal disorders	
Not known	Drug-induced enterocolitic syndrome
Data deriving from Clinical Studies	
*Common	Diarrhoea and nausea
*Uncommon	Vomiting
Post-Marketing Data	
Very rare	Antibiotic colitis (including pseudomembranous colitis and haemorrhagic colitis, see section 4.4). Black hairy tongue Superficial alteration of the colour of teeth[#]
Heart disease	
Not known	Kounis syndrome (see section 4.4)
Hepatobiliary disorders	
Very rare	Hepatitis and cholestatic jaundice. Slight increase in the AST and/or ALT values.
Skin and subcutaneous tissue disorders	
Not known	Linear IgA diseas
Data deriving from Clinical Studies	
*Common	Skin rash
*Uncommon	Urticaria and pruritus
Post-Marketing Data	
Very rare	Skin reactions such as erythema multiforme, Stevens-Johnson's syndrome, toxic epidermal necrolysis, bullous dermatosis or exfoliative dermatitis, acute generalised exanthematous pustulosis (AGEP) (see section 4.4) and drug reactions with eosinophilia and systemic symptoms (DRESS).
Renal and urinary disorders	
Very rare	Interstitial nephritis Crystalluria (including acute kidney damage, see sections 4.4 and 4.9 overdose)
* The incidence of these adverse events has been calculated on the basis of clinical studies that have involved a total number of around 6,000 paediatric and adult patients treated with amoxicillin. [#]In children, the superficial alteration of the colour of teeth has been reported. Good oral hygiene may help prevent the alteration of the colour of teeth, which can generally be eliminated with brushing.	

Reporting suspected adverse reactions

Reporting suspected adverse reactions seen after the authorisation of the medicinal product is important. It allows continued monitoring of benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any

suspected adverse reaction via the Italian national reporting system to this address: http://www.aifa.gov.it/content/segnalazioni-reazioni-avverse.

4.9. Overdose

Symptoms and signs of overdose

Gastrointestinal symptoms (e.g., nausea, vomiting, and diarrhea) and altered hydroelectrolyte balances may occur. Amoxicillin crystalluria has been observed, leading to renal failure in some cases (see section 4.4). Convulsions may occur in patients with impaired renal function or those treated with high doses (see sections 4.4 and 4.8).

Treatment in case of intoxication

Gastrointestinal symptoms can be managed with symptomatic treatment, paying attention to the hydroelectric balance. Amoxicillin can be removed from circulation by means of haemodialysis.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Pharmacotherapeutic Group: broad-spectrum penicillins; ATC Code: J01CA04

Mechanism of action

Amoxicillin is a semi-synthetic penicillin (beta-lactam antibiotic) that inhibits one or more enzymes (which are often indicated with the name of penicillin-binding proteins or PBPs) by means of the biosynthesis of the bacterial peptidoglycan, a structural component that is part of the bacterial cell wall. When the peptidoglycan synthesis is inhibited, the cell wall gets weaker, and that generally leads to the cell lysis and to its death.
Amoxicillin is vulnerable to the degradation caused by the beta-lactamases produced by resistant bacteria; therefore, the spectrum of action of amoxicillin alone does not include the organisms that produce such enzymes.

Pharmacokinetics/pharmacodynamics report

The time above the minimum inhibitory concentration (T>MIC) is considered to be the main parameter that determines the effectiveness of amoxicillin.

Mechanisms of resistance

The main mechanisms of resistance to amoxicillin are:

- The inactivation caused by bacterial beta-lactamases.
- The alteration of PBPs, with the consequent reduction of the affinity of the antibacterial agent with its own target.

Bacterial impermeability or the mechanisms of efflux pumps may cause bacterial resistance or contribute to it, particularly in Gram-negative bacteria.

Breakpoints

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

Micro-organism	**MIC Breakpoint (mg/L)**	
	Sensitive ≤	**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]
Streptococci of the *viridans* group	0.5	2
Haemophilus influenzae	2[6]	2[6]
Moraxella catarrhalis	Note[7]	Note[7]
Neisseria meningitidis	0.125	1
Gram-positive Anaerobic bacteria except for *Clostridium difficile*[8]	4	8
Gram-negative Anaerobic bacteria[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 classified as sensitive to aminopenicillins. Some countries prefer classifying wild-type isolates of *E. coli* and *P. mirabilis* as intermediate. In such case, use the MIC breakpoint S ≤0.5 mg/L.
[2]Most staphylococci produce penicillinase and are resistant to amoxicillin. Except for a few exceptions, methicillin-resistant isolates are resistant to any beta-lactam.
[3]Sensitivity to amoxicillin can be inferred on the basis of sensitivity to ampicillin.
[4]Sensitivity to the penicillins of streptococci groups A, B, C and G can be inferred on the basis of sensitivity to benzylpenicillin.
[5]Breakpoints only refer to non-meningitis isolates. For those isolates classified as intermediate for ampicillin, avoid the oral treatment with amoxicillin. Sensitivity inferred on the basis of the MIC of ampicillin.
[6]Breakpoints based on intravenous administration. Positive isolates for beta-lactamases must be classified as resistant.
[7]Those micro-organisms that produce beta-lactamases must be classified as resistant.
[8]Sensitivity to amoxicillin can be inferred on the basis of sensitivity to benzylpenicillin. [9]Breakpoints based on epidemiological cut-off values (ECOFF), which distinguish wild-type isolates from those with reduced sensitivity.
[10]Non-species related breakpoints are based on doses of at least 0.5 g x 3 or 4 doses per day (from 1.5 to 2 g/day).

The prevalence of resistance may vary depending on the geographical area and on the time for selected species, and it is desirable to have local information about resistance, especially when treating serious infections. If necessary, ask for advice to a specialist whenever the local prevalence of resistance is such that the usefulness of the agent for treating at least some types of infection is questionable.

***In vitro* susceptibility of micro-organisms to amoxicillin**
Commonly Sensitive Species
Gram-positive Aerobic Bacteria: *Enterococcus faecalis* Beta-haemolytic streptococci (groups A, B, C and G) *Listeria monocytogenes*
Species for which acquired resistance may constitute a problem
Gram-negative Aerobic Bacteria: *Escherichia coli* *Haemophilus influenzae* *Helicobacter pylori* *Proteus mirabilis* *Salmonella typhi* *Salmonella paratyphi* *Pasteurella multocida*
Gram-positive Aerobic Bacteria: Coagulase-negative staphylococcus *Staphylococcus aureus*[£] *Streptococcus pneumoniae* Streptococcus of the *viridans* group
Gram-positive Anaerobic Bacteria: *Clostridium* spp.
Gram-negative Anaerobic bacteria: *Fusobacterium* spp.
Other: *Borrelia burgdorferi*
Micro-organisms with intrinsic resistance[†]
Gram-positive Aerobic Bacteria: *Enterococcus faecium*[†]
Gram-negative Aerobic Bacteria: *Acinetobacter* spp. *Enterobacter* spp. *Klebsiella* spp. *Pseudomonas* spp.

Gram-negative Anaerobic bacteria: *Bacteroides* spp. (numerous strains of *Bacteroides fragilis* are resistant).
Other activities: *Chlamydia* spp. *Mycoplasma* spp. *Legionella* spp.
† Natural intermediate sensitivity in absence of a mechanism of acquired resistance. £ Almost all *S. aureus* bacteria are resistant to amoxicillin because they produce penicillinase. In addition, all methicillin-resistant strains are resistant to amoxicillin.

5.2. Pharmacokinetic properties

Absorption

Amoxicillin is completely dissociated in water solution with physiological pH. It is rapidly and well absorbed with oral administration. After oral administration, it has a bioavailability of around 70%. The time at the plasma maximum concentration (T_{max}) is around 1 hour.

The table below shows the pharmacokinetic results obtained in a study that included the administration of amoxicillin at the dose of 250 mg three times a day on an empty stomach in groups of healthy volunteers.

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 250 to 3000 mg range, bioavailability is linear in proportion to the dose (measured in terms of C_{max} and AUC).
Absorption is not influenced by the simultaneous consumption of food.
To eliminate amoxicillin, haemodialysis can be used.

Distribution

Around 18% of the total plasma amoxicillin concentration is associated to proteins, and the apparent volume of distribution is approximately 0.3-0.4 l/kg.
After intravenous administration, amoxicillin has been found in the gall bladder, in the abdominal tissue, in the skin, in the adipose tissue, in muscles, in the synovial and peritoneal fluids, in the bile and in pus. Amoxicillin is not suitably distributed in the cerebrospinal fluid.
Animal studies have not given any evidence of significant retention at tissue level of material deriving from the drug.
Amoxicillin, like most penicillins, can be found in human breast milk (see section 4.6).
It has been proven that amoxicillin passes the placental barrier (see section 4.6).

Biotransformation

Amoxicillin is partially excreted in the urine as inactive penicilloic acid in an amount equivalent to 10-25% of the initial dose.

Elimination

The principal route of elimination of amoxicillin is in the urine.
Amoxicillin has an average elimination half-life of around one hour and an average total clearance of around 25 l/h in healthy patients. Around 60-70% of amoxicillin is excreted unchanged in urine during the 6 hours immediately after the administration of a single 250 mg or 500 mg dose of amoxicillin. Several studies have shown a urinary excretion of amoxicillin of 50-85% in 24 hours.
The concomitant use of probenecid delays the excretion of amoxicillin (see section 4.5).

Age

The elimination half-time of amoxicillin is similar in children who are approximately from 3 months to 2 years old, in older children and in adults. In very young babies (including premature infants), the administration frequency during the first week of life should not exceed the twice-a-day administration because the renal route of elimination is still

immature. Given the fact that elderly patients are more likely to have reduced renal function, the selection of the dose requires caution, and it may be useful to monitor the renal function.

Gender
After the oral administration of amoxicillin to healthy males and females, gender does not have a significant impact on the pharmacokinetics of amoxicillin.

Renal damage
The total serum clearance of amoxicillin decreases proportionally to the reduction of the renal function (see sections 4.2 and 4.4).

Hepatic impairment
In those patients with hepatic impairment, the administration of amoxicillin requires caution, and the hepatic function must be monitored at regular intervals.

5.3. Preclinical safety data
Preclinical data do not evidence particular risks for human beings on the basis of *safety pharmacology* studies, toxicity with repeated doses, genotoxicity and reproductive and developmental toxicity.

No carcinogenicity studies with amoxicillin have been conducted.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

60 ml bottle
Carboxymethyl cellulose
Sucrose
Ammonium glycyrrhizate
Lyophilised banana
Lyophilised pineapple
Cream flavour

100 ml bottle
Carboxymethyl cellulose
Sucrose
Ammonium glycyrrhizate
Banana flavour
Apricot flavour

6.2. Incompatibilities
Not applicable

6.3. Shelf life
Unopened package: 2 years.
Reconstituted suspension: 7 days
Reconstituted suspension: store at temperatures between +2 and +8°C (in the fridge). Do not freeze.

6.4. Special precautions for storage
Keep inside the original package
For information on the storage conditions after reconstitution, see section 6.3.

6.5. Nature and contents of container
Amoxina 250 mg/5 ml powder for oral suspension is packaged in yellow glass bottles with a nominal volume of 60 ml or 100 ml, closed with aluminium caps with polymeric coating. This primary packaging is put inside a box with a dosing glass.

Maybe not all packages are marketed.

6.6. Special precautions for disposal and other handling
Make sure that the cap seal is intact before use.

Add a tiny amount of water in the bottle, shake well, and let rest for a few minutes. Then add more water, until reaching the level indicated on the bottle, and shake again.
After reconstitution, every ml of suspension contains 50 mg of amoxicillin.

The product must be administered by using the special dosing glass with the level marks for 2.5 ml, 5 ml and 10 ml of suspension, which are equivalent to 125 mg, 250 mg and 500 mg of amoxicillin, respectively.

The bottle must be shaken vigorously before each administration.

Medicines no longer used or medical waste should be disposed of in compliance with the local regulations in force.

7. MARKETING AUTHORISATION HOLDER
AESCULAPIUS FARMACEUTICI S.r.l. - Via Cefalonia, 70 - 25124 BRESCIA.

8. MARKETING AUTHORISATION NUMBERS

250mg/5ml Powder for oral suspension - 60 ml Bottle	MA No. 023966082
250mg/5ml Powder for oral suspension - 100 ml Bottle	MA No. 023966106

9. DATE OF FIRST AUTHORISATION/ RENEWAL OF THE AUTHORISATION
Date of renewal: June 2010

10. DATE OF REVISION OF THE TEXT
May 2023