SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT
DEVAMOX 1 g tablet

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
Active substance: Each tablet contains amoxicillin trihydrate (derived from bovine, sheep or goat milk) equivalent to 1 g amoxicillin base.
Excipient(s):
For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM
Tablet
White, almost white, slightly convex, oblong tablets with “DMS-1000” debossed on one side, and the other side is scored in the middle.

4. CLINICAL PARTICULARS
4.1 Therapeutic indications
DEVAMOX 1 g tablet is indicated for the treatment of the following infections in adults and children:

- Acute bacterial sinusitis
- Acute otitis media
- Acute streptococcal tonsillitis and pharyngitis
- Acute exacerbation 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 in peptic ulcer
- Lyme disease
- Prophylaxis of endocarditis

Official guidelines on the appropriate use of antibacterial agents should be followed.

4.2 Posology and method of administration
Posology:
The dose of DEVAMOX that is selected to treat an individual infection should take into account:
- The expected pathogens and their likely susceptibility to antibacterial agents
- The severity and location of the infection
- The age, weight and renal function of the patient (as shown below)

The duration of treatment should be determined by the type of infection and the response of the patient, and should generally be as short as possible. Some infections may require

prolonged treatment.

Adults and children ≥40 kg:

Indication*	**Dosage***
Acute bacterial sinusitis	250 mg to 500 mg every 8 hours or 750 mg to 1000 mg every 12 hours For severe infections 750 mg to 1000 mg every 8 hours
Asymptomatic bacteriuria in pregnancy	
Acute pyelonephritis	
Dental abscess with spreading cellulitis	
Acute cystitis	Acute cystitis may be treated with 3000 mg twice daily for one day.
Acute otitis media Acute streptococcal tonsillitis and pharyngitis Acute exacerbation of chronic bronchitis	500 mg every 8 hours, 750 mg to 1000 mg every 12 hours For severe infections 750 mg to 1000 mg every 8 hours for 10 days
Community acquired pneumonia	500 mg to 1000 mg every 8 hours
Typhoid and paratyphoid fever	500 mg to 2000 mg every 8 hours
Prosthetic joint infections	500 mg to 1000 mg every 8 hours
Prophylaxis of endocarditis	2000 mg orally, as a single dose 30 to 60 minutes before the procedure
Helicobacter pylori eradication	750 mg to 1000 mg twice daily for 7 days in combination with a proton pump inhibitor (e.g. omeprazole, lansoprazole) and another antibiotic (e.g. clarithromycin, metronidazole).
Lyme disease	Early stage: 500 mg to 1000 mg every 8 hours in divided doses for 14 days, up to a maximum of 4000 mg/day (10 to 21 days) Late stage (systemic involvement): 500 mg to 2000 mg every 8 hours up to a maximum of 6000 mg/day in divided doses for 10 to 30 days.
*Consideration should be given to the official treatment guidelines for each indication.	

Children weighing <40 kg

Children may be treated with DEVAMOX tablets or suspension. DEVAMOX suspension is recommended for children under six months. Children weighing 40 kg or more should be prescribed the adult dosage.

Recommended doses

Indication +	**Dose** +
Acute bacterial sinusitis	In divided doses, 20 to 90 mg/kg/day*
Acute otitis media	
Community acquired pneumonia	

Acute cystitis	
Acute pyelonephritis	
Dental abscess with spreading cellulitis	
Acute streptococcal tonsillitis and pharyngitis	In divided doses, 40 to 90 mg/kg/day*
Typhoid and paratyphoid fever	100 mg/kg/day in three divided doses
Prophylaxis of endocarditis	50 mg/kg orally, as a single dose 30 to 60 minutes prior to the procedure
Lyme disease	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.	

In elderly
No dose adjustment is considered necessary.

Method of administration:
DEVAMOX is for oral use.
Absorption of DEVAMOX is not affected by food.
DEVAMOX 1 g tablet is used orally by swallowing with a glass of water.

Additional information on special populations:
Renal/Hepatic impairment:
Renal impairment:

GFR (mL/min)	**Adults and children ≥40 kg**	**Children <40 kg** #
greater than 30	No adjustment required.	No adjustment required.
10 to 30	Maximum 500 mg twice daily	15 mg/kg given twice daily (maximum 500 mg twice daily).
less than 10	Maximum 500 mg/day.	15 mg/kg given as a single daily dose (maximum 500 mg).
# In most cases, parenteral treatment is preferred.		

Patients undergoing hemodialysis
Amoxicillin may be removed from the circulation by hemodialysis.

	Haemodialysis
Adults and children over 40 kg	500 mg every 24 hours An additional 500 mg dose should be given before haemodialysis. 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.

Patients receiving peritoneal dialysis
Maximum 500 mg/day of amoxicillin.

Hepatic impairment:
No specific warnings have been reported for these patients.

Pediatric population:
The dosage recommendations given above chart apply to children weighing less than 40 kg. Adult dosages should be applied to children with a body weight of 40 kg and above.

In neonates and young babies, due to immature renal function, elimination of amoxicillin may be delayed. For babies under 3 months of age, amoxicillin dose must be carefully adjusted. The maximum recommended dose of DEVAMOX for this age group is 30 mg/kg/day, divided into two equal doses administered every 12 hours.

Geriatric population:
There was no difference in response between young and elderly patients. However, it should be noted that elderly patients may have decreased renal function, so they need to be more sensitive in this regard. Dose selection should be made carefully and renal function should be monitored.

4.3 Contraindications
DEVAMOX is contraindicated in patients with hypersensitivity to amoxicillin, any of the excipients it contains, or penicillin.

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 treatment 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 sometimes fatal hypersensitivity reactions (including anaphylactoid and severe cutaneous adverse reactions) have been reported in patients receiving penicillin treatment. Hypersensitivity reactions may also progress to Kounis syndrome, a serious allergic reaction that may result in myocardial infarction (see Section 4.8). These reactions are more likely in individuals with a history of hypersensitivity to penicillin and in atopic individuals. If an allergic reaction occurs, treatment with amoxicillin should be discontinued and appropriate alternative therapy instituted.

Drug-induced enterocolitis syndrome (DIES)
Cases of drug-induced enterocolitis syndrome (DIES) have been reported, primarily in children receiving amoxicillin (see Section 4.8). DIES is an allergic reaction characterized by prolonged vomiting (1–4 hours after drug intake), in the absence of cutaneous or respiratory allergic symptoms. Other symptoms include abdominal pain, diarrhea, hypotension, or neutrophilic leukocytosis. Severe cases progressing to shock have been observed.

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 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, dosage adjustment should be based on the degree of impairment (see Section 4.2).

Skin reactions
At the beginning of treatment, feverish generalized erythema associated with pustules may be a symptom of acute generalized exanthematous pustulosis (AGEP, see Section 4.8). This reaction requires discontinuation of amoxicillin and is a contraindication for further use.

Amoxicillin should not be used when 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 observed following amoxicillin treatment of Lyme disease (see Section 4.8). It results directly from the bactericidal activity of amoxicillin on the causative bacteria of Lyme disease, the spirochaete *Borrelia burgdorferi*. Patients should be reassured that this is a common and usually self-limiting consequence of antibiotic treatment of Lyme disease.

Overgrowth of non-susceptible microorganisms
Prolonged use may occasionally result in the overgrowth of non-susceptible microorganisms.

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 develop diarrhea during or after antibiotic use. If antibiotic-associated colitis occurs, amoxicillin should be discontinued immediately, a physician should be consulted, and appropriate treatment initiated.

Anti-peristaltic drugs are contraindicated in this situation.

Prolonged treatment
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 rarely reported in patients receiving amoxicillin. Appropriate monitoring should be performed when anticoagulants are co-prescribed. Dose adjustment 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.

Enzymatic glucose oxidase methods should be used for urine glucose testing during amoxicillin treatment.

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

4.5 Interaction with other medicinal products and other forms of interaction
Methotrexate
Penicillins may reduce the excretion of methotrexate causing a potential increase in toxicity.

Probenecid
Co-administration with probenecid is not recommended. Probenecid may reduce the renal tubular secretion of amoxicillin. Concomitant use of probenecid may result in increased and prolonged blood levels of amoxicillin.

Allopurinol
Concomitant use of allopurinol during amoxicillin treatment can increase the likelihood of allergic skin reactions.

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

Oral anticoagulants
Oral anticoagulants and penicillin antibiotics have been widely used in clinical practice without reports of interactions. 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).

Additional information on special populations
Pediatric population: No data available.

4.6 Pregnancy and lactation
General recommendation
Pregnancy category: B

Women of childbearing potential / Birth control (Contraception)
Since the effectiveness of oral contraceptives containing estrogen/progesterone may be reduced, it may be advisable to use other effective birth control methods during treatment.

Pregnancy
Animal studies do not indicate direct or indirect harmful effects on pregnancy/embryonal/fetal development/birth or postnatal development.

Caution should be exercised when administering to pregnant women.

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.

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

Reproductive ability/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 are diarrhoea, nausea and skin rash. Undesirable effects observed in clinical trials and post-marketing surveillance are listed below according to the following frequency categories:

Very common (≥ 1/10); common (≥ 1/100 to < 1/10); uncommon (≥ 1/1,000 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 leukopenia (including severe neutropenia or agranulocytosis), reversible thrombocytopenia, 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, Jarisch-Herxheimer reaction (see Section 4.4).

Nervous system disorders:
Very rare: Hyperkinesia, dizziness, convulsions, aseptic meningitis (see Section 4.4).
Not known: Aseptic meningitis

Cardiac disorders:
Not known: Kounis syndrome

Gastrointestinal disorders:
Clinical trial data
*Common: Nausea, diarrhoea
*Uncommon: Vomiting

Post-marketing Data
Very rare: Antibiotic-associated colitis (including pseudomembranous colitis and haemorrhagic colitis, see Section 4.4), black hairy tongue
Not known: Drug-induced enterocolitis syndrome (DIES)

Hepatobiliary disorders:
Very rare: Hepatitis and cholestatic jaundice, moderate increases 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 pustulos (AGEP) (see Section 4.4) and drug reaction with eosinophilia and systemic symptoms (DRESS).
Not known: Linear IgA disease

Renal and urinary disorders:
Very rare: Interstitial nephritis, crystalluria (see Sections 4.4 and 4.9)

Not known: Crystalluria (including acute renal injury)

*The incidence of these adverse reactions is based on data from clinical trials involving approximately 6,000 adult and pediatric patients treated with amoxicillin.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorization of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system.

4.9 Overdose and treatment
Signs and symptoms of overdose
Gastrointestinal symptoms (such as nausea, vomiting and diarrhea) and disturbances of fluid and electrolyte balance may occur. Amoxicillin crystalluria has been observed, in some cases leading to renal failure (see Section 4.4). Convulsions may occur in patients with impaired renal function or those receiving high doses (see Sections 4.4 and 4.8).

Management of intoxication
Gastrointestinal symptoms can be treated symptomatically with attention to the water/electrolyte balance.

Amoxicillin can be removed from the circulation by hemodialysis.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties
Pharmacotherapeutic group: Beta-lactam antibacterials, penicillins, extended spectrum penicillins
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
Time above the minimum inhibitory concentration (MIC) (T>MIC) is considered the major determinant of the efficacy of amoxicillin.

Mechanisms of Resistance
The main mechanisms of resistance to amoxicillin are:
- Inactivation by bacterial beta-lactamases.
- Alterations in PBPs that reduce affinity of the antibacterial agent to its 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 based on European Committee on Antimicrobial Susceptibility Testing (EUCAST) version 5.0 are listed below.

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

[1] Wild-type Enterobacteriaceae are categorized as susceptible to aminopenicillins. Some countries prefer to categorize wild-type *E. coli* and *P. mirabilis* isolates as intermediate. Use S ≤ 0.5 mg/L as MIC limit.

[2] Most staphylococci produce penicillinase, which confers resistance to amoxicillin. Methicillin-resistant isolates are, with few exceptions, resistant to all beta-lactam agents.

[3] Amoxicillin susceptibility may be inferred from ampicillin data.

[4] Susceptibility of streptococcal groups A, B, C, and G to penicillins may be inferred from the benzylpenicillin susceptibility.

[5] Breakpoints are valid only for isolates not associated with meningitis. Oral amoxicillin treatment should be avoided for isolates categorized as intermediately susceptible to ampicillin. Susceptibility is inferred from ampicillin MIC values.

[6] Breakpoints are based on intravenous administration. Beta-lactamase positive isolates should be reported as resistant.

[7] Beta-lactamase-producing organisms should be reported as resistant.

[8] Amoxicillin susceptibility may be inferred from benzylpenicillin data.

[9] Breakpoints are based on epidemiological cut-off values (ECOFFs) that distinguish wild-type isolates from low-susceptibility types.

[10] Species-independent breakpoints are based on doses of at least 0.5 g x 3 or 4 doses/day (1.5 to 2 g/day).

The prevalence of resistance may vary geographically and over time for selected species. Local resistance information is required, 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 microorganisms to amoxicillin**
Commonly susceptible species
Gram-positive aerobes: *Enterococcus faecalis* Beta-haemolytic streptococci (Groups A, B, C, and G) *Listeria monocytogenes*
Species for which acquired resistance may be a problem
Gram-negative aerobes: *Escherichia coli* *Haemophilus influenzae* *Helicobacter pylori* *Proteus mirabilis* *Salmonella typhi* *Salmonella paratyphi* *Pasteurella multocida*
Gram-positive aerobes: Coagulase-negative staphylococci *Staphylococcus aureus*£
Streptococcus pneumoniae Viridans group streptococci
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.
† Naturally intermediate susceptibility in the absence of acquired resistance mechanisms.
£ Almost all *S. aureus* strains are resistant to amoxicillin due to penicillinase production. In addition, all methicillin-resistant strains are resistant to amoxicillin.

5.2 Pharmacokinetic properties

General properties

Absorption:

Amoxicillin fully dissociates in aqueous solution at physiological pH. It is rapidly and well absorbed when administered orally. Following oral administration, the bioavailability of amoxicillin is approximately 70%. The time to peak plasma concentration (T_{max}) is approximately one hour.

The pharmacokinetic results from a study in which healthy volunteers were administered 250 mg of amoxicillin 3 times a day on an empty stomach are presented below.

C_{max}	Tmax*	Area Under the Curve AUC (0–24 h)	T½
(mcg/mL)	(hours)	(mcg.h/mL)	(hours)
3.3. ± 1.12	1.5 (1–2)	26.7 ± 4.56	1.36 ± 0.56
* Median (range)			

Within the dose range of 250 to 3000 mg, bioavailability is linear and dose-proportional (measured as C_{max} and AUC). Absorption is not affected by simultaneous food intake.

Hemodialysis can be used to remove amoxicillin.

Distribution:

Approximately 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 the gall bladder, abdominal tissue, skin, fat, muscle tissue, synovial and peritoneal fluids, bile, and pus. Amoxicillin does not distribute sufficiently into cerebrospinal fluid.

Animal studies have not provided evidence of significant tissue retention of drug-derived material. Like most penicillins, amoxicillin 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 partially excreted in the urine as the inactive penicilloic acid in amounts equivalent to 10-25% of the initial dose.

Elimination:

The major route of elimination of amoxicillin is via the kidneys.

In healthy subjects, the average elimination half-life of amoxicillin is approximately one hour, and the average clearance is about 25 L/h. Within the first six hours after a single dose of 250 mg or 500 mg dose of amoxicillin, approximately 60% to 70% of the dose is excreted unchanged in the urine. Various studies have found the urinary excretion to be 50-85% for amoxicillin over a 24 hour period.

Concurrent use of probenecid delays the excretion of amoxicillin (see Section 4.5).

Age:
The elimination half-life of amoxicillin is similar in children aged around 3 months to 2 years, older children, and adults. In very young children (including preterm neonates), the dosing interval should not exceed twice daily during the first week of life due to immature renal elimination pathways. Caution is advised when selecting doses for elderly patients as reduced renal function may be more likely. Monitoring of renal function may be useful.

Gender:
No significant effect of gender on the pharmacokinetics of amoxicillin was observed following oral administration to healthy male and female subjects.

Renal impairment:
Total serum clearance of amoxicillin decreases proportionally with decreasing renal function (see Sections 4.2 and 4.4).

Hepatic impairment:
Patients with hepatic impairment should be dosed with caution and liver function should be monitored regularly.

Linearity/Non-linearity:
Not available.

5.3 Preclinical safety data
Non-clinical data based on conventional studies of pharmacology, repeated dose toxicity, genotoxicity, and reproduction and developmental toxicity do not indicate any special hazard for humans.
No carcinogenicity studies have been conducted with amoxicillin.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients
Crospovidone
Mint flavour
Sodium cyclamate
Sodium saccharin
Magnesium stearate

6.2 Incompatibilities
Not applicable.

6.3 Shelf life
48 months

6.4 Special precautions for storage
Should be stored below 25°C and in a dry place.

6.5 Nature and contents of container
Blisters of 8 tablets, one side covered with transparent PVDC and the other side covered with printed aluminium foil.
Each carton box contains 16 tablets.

6.6 Special precautions for disposal and other handling

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

7. MARKETING AUTHORISATION HOLDER

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8. MARKETING AUTHORISATION NUMBER(S)

198/80

9. DATE OF FIRST AUTHORISATION / RENEWAL OF THE AUTHORISATION

Date of first authorisation: 28.12.2001
Date of renewal of the authorisation:

10. DATE OF REVISION OF THE TEXT