SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Amoxicillin Capsules USP 250 mg

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each hard gelatin capsule contains:
Amoxicillin Trihydrate USP
eq. to Amoxicillin.....250 mg
Excipients .....q.s.
Approved colour used in capsule shells

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Oral Solid Dosage form, hard gelatin capsules

Each hard gelatin capsule shell having maroon color cap and yellow color body, size“2” filled with off white powder.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

The treatment of bacterial infections caused by amoxicillin-susceptible organisms.

It is principally indicated for respiratory, middle ear and urinary tract infections.

- Respiratory tract - pneumonia, acute and chronic bronchitis, upper respiratorytract infections
- Chronic bronchial sepsis
- Lobar and bronchopneumonia
- ENT - otitis media
- Urinary tract - cystitis, urethritis, pyelonephritis
- Biliary and intra-abdominal infections
- Bacteriuria in pregnancy
- Gynaecological infections including puerperal sepsis and septic abortion
- Gonorrhoea
- Peritonitis
- Intra-abdominal sepsis
- Septicaemia
- Bacterial endocarditis

- Skin and soft tissue infections
- Osteomyelitis
- Meningitis
- Enteric fevers (typhoid and paratyphoid fevers)
- Dental abscess (as an adjunct to surgical management)
- In children with urinary tract infection the need for investigation should beconsidered.

Prophylaxis of endocarditis: The prevention of bacteraemia, associated with procedures (e.g. dental), in patients at risk of developing bacterial endocarditis.

4.2. Posology and method of administration

Treatment of Infection:

Adult dosage (including elderly patients):

Standard adult dosage: 250mg every 8 hours, increasing to 500mg every 8 hours in severe infections.

High dosage therapy (maximum recommended oral dosage 6 g daily in divided doses): A dosage of 3 g twice daily is recommended in appropriate cases for the treatment of severe or recurrent purulent infection of the respiratory tract.

Short course therapy: Simple acute urinary tract infection: two 3 g doses with 10-12 hours between the doses. Dental abscess: two 3 g doses with 8 hours between the doses. Gonorrhoea: single 3 g dose.

Dosage in impaired renal function:

The dose should be reduced in patients with severe renal function impairment. In patients with a creatinine clearance of less than 30 ml/min an increase in the dosage interval and a reduction in the total daily dose is recommended: Glomerular filtration rate>30ml/min No adjustment necessary.

Glomerular filtration rate 10-30ml/min: Amoxicillin. max.500mg b.d

Glomerular filtration rate<10ml/min: Amoxicillin. Max. 500mg/day

Helicobacter eradication in peptic (duodenal and gastric) ulcer disease:

Amoxicillin is recommended at a dose of twice daily in association with a proton pump inhibitor and antimicrobial agents as detailed below:

Omeprazole 40 mg daily, Amoxicillin 1G BID, Clarithromycin 500mgBID

x 7days

or

Omeprazole 40mg daily, Amoxicillin750mg-1G BID, Metronidazole 400mgTID

x 7 days

Children's

Children weighing < 40 kg

The daily dosage for children is 40 - 90 mg/kg/day in two to three divided doses* (not exceeding 3 g/day) depending on the indication, severity of the disease and the susceptibility of the pathogen.

*PK/PD data indicate that dosing three times daily is associated with enhanced efficacy, thus twice daily dosing is only recommended when the dose is in the upper range.

Children weighing more than 40 kg should be given the usual adultdosage. Renal impairment in children under 40 kg:

Creatinine clearance ml/min	**Dose**	**Interval between administration**
> 30	Usual dose	No adjustment necessary
10 – 30	Usual dose	12 h (corresponding to 2/3 of the dose)
< 10	Usual dose	24 h (corresponding to 1/3 of the dose)

Special dosage recommendation

Tonsillitis: 50 mg/kg/day in two divided doses.

Acute otitis media

In areas with high prevalence of pneumococci with reduced susceptibility to penicillins, dosage regimens should be guided by national/local recommendations. In severe or recurrent acute otitis media, especially where compliance may be a problem, 750 mg twice a day for two days may be used as an alternative course of treatment in children aged 3 to 10 years.

Early Lyme disease (isolated erythema migrans)

50 mg/kg/day in three divided doses, over 14-21days.

Prophylaxis for endocarditis: See following tableAdministration: Oral:

Treatment should be continued for 2 to 3 days following the disappearance of symptoms. It is recommended that at least 10 days treatment be given for any infection caused by beta-haemolytic streptococci in order to achieve eradication of theorganism.

Prophylaxis of Endocarditis

CONDITION		**ADULTS' DOSAGE (INCLUDING ELDERLY)**	**CHILDREN'S DOSAGE (< 40 kg)**	**NOTES**
Dental procedures: prophylaxis for patients undergoing extraction, scaling or surgery involving gingival tissues and who have not received a penicillin in the previous month. (N.B. Patients with prosthetic heart valves should be referred to hospital - see below).	Patient not having general anaesthetic.	3 g 'Amoxicillin' orally, 1 hour before procedure. A second dose may be given 6 hours later, if considered necessary.	50 mg amoxicillin/kg body weight given as a single dose one hour preceding the surgical procedure	Note 1. If prophylaxiswith 'Amoxicillin' is given twice within one month, emergence of resistant streptococci is unlikely to be a problem. Alternative antibiotics are recommended if more frequent prophylaxis is required, or if the
	Patient having general anaesthetic: if oralantibiotics considered to be appropriate.	Initially 3 g 'Amoxicillin' orally 4 hours prior to anaesthesia, followed by 3 g orally (or 1 g IV or IM if oral dosenot tolerated) as soon as possible after the operation.		

				patient has received a course of treatment with a penicillin during the previousmonth. Note 2 To minimise pain on injection, 'Amoxicillin' may be given as two injections of 500 mg dissolved in sterile 1%
	Patient having general anaesthetic: if oralantibiotics not appropriate.	1 g 'Amoxicillin'IV or IM immediately before induction;with 500 mg orally, 6 hourslater.		

				lidocaine solution.
Dental procedures: patients for whom referral to hospital is recommended: a) Patients to be given a general anaesthetic who have been given a penicillin in the previous month. b) Patients to be given a general anaesthetic who have a prosthetic heart valve. c) Patients who have had one or more attacks of endocarditis.		Initially: 1 g 'Amoxicillin' IV or IM with 120 mg gentamicin IV or IM immediately priorto anaesthesia (if given) or 15minutes prior todental procedure. Followed by (6 hours later): 500 m g 'Amoxicillin' orally.	50 mg amoxicillin/kg body weight givenas a single doseone hour preceding thesurgical procedure	See Note 2. Note 3. 'Amoxicillin' andgentamicin shouldnot be mixed inthe same syringe. Note 4. Pleaseconsult the appropriate datasheet for full prescribing information ongentamicin.
Genitourinary Surgery or Instrumentation: prophylaxis for patients who have no urinary tract infection and who are to have genito-urinary surgery or instrumentation under general anaesthesia. In the case of Obstetric and Gynaecological Procedures and Gastrointestinal Procedures– routine prophylaxis isrecommended only for patients with prosthetic heart valves.		Initially: 1 g 'Amoxicillin' IV or IM with 120 mg gentamicin IV or IM, immediately before induction. Followed by (6 hours later): 500 m g 'Amoxicillin' orally or IV or IM according to clinical condition.		See Notes 2, 3 and 4 above.

Surgery or Instrumentation of the Upper Respiratory Tract	Patients other than those with prosthetic heart valves.	1 g 'Amoxicillin' IV or IM immediately before induction; m g 'Amoxicillin' IV or IM 6 hours later.	50 mg amoxicillin/kg body weight given as a single dose one hour preceding the surgical procedure	See Note 2 above. Note 5. The second dose of 'Amoxicillin' may be administered orally as 'Amoxicillin' Syrup SF/DF.
	Patients with prosthetic heart valves.	Initially: 1 g 'Amoxicillin' IV or IM with 120 mg gentamicin IV or IM, immediately	50 mg amoxicillin/kg body weight given as a single dose one hour preceding the	See Notes 2, 3, 4 and 5 above.

		before induction; followed by (6 hours later) 500 m g 'Amoxicillin' IV or IM.	surgical procedure	

Method of administration
THEOMOX 250 is administered orally.

4.3. Contraindications

Amoxicillin is contra-indicated in patients with hypersensitivity to penicillins.

Attention should also be paid to possible cross-reactivity with other beta-lactam antibiotics e.g. cephalosporins.

It should not be given to patients with infectious mononucleosis (glandular fever) since they are especially susceptible to amoxicillin-induced skin rashes.

4.4. Special warnings and precautions for use

Before initiating therapy with amoxicillin, careful enquiry should be made concerningprevious hypersensitivity reactions to penicillin and cephalosporins.

Serious and occasionally fatal hypersensitivity (anaphylactoid) reactions have been reported in patients on penicillin therapy. These reactions are most likely in those witha history of hypersensitivity to beta-lactam antibiotics.

Amoxicillin should be used with caution in those with impaired renal function and dose reduction may be necessary in severe impairment.

Patients with infectious mononucleosis (glandular fever), lymphatic leukaemia and possibly with HIV infection are particularly prone to developing erythematous rashes with amoxicillin. Amoxicillin should be discontinued if a skin rash occurs.

Prolonged use of an anti-infective may result in the overgrowth of non-susceptible organisms (superinfection).

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.

Abnormal prolongation of prothrombin time (increased INR) has been reported rarely in patients receiving amoxicillin and oral anticoagulants. 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. Precaution should be taken in premature children and during the neonatal period: renal, hepatic and haematological functions should be monitored.

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

In the literature there are rare 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.

Excretion of penicillins is reduced by probenecid. Concurrent use with amoxicillin may result in increased and prolonged blood levels of amoxicillin

Concurrent administration of allopurinol during treatment with amoxicillin can increase the likelihood of allergic skin reactions.

It is recommended that when testing for the presence of glucose in urine during amoxicillin treatment, enzymatic glucose oxidase methods should be used. Due to the high urinary concentrations of amoxicillin, false positive readings are common with chemical methods.

4.6. Fertility pregnancy and lactation general principlesPregnancy:

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

Breast feedings:

Amoxicillin may be given during lactation. With the exception of the risk of sensitisation associated with the excretion of trace quantities of amoxicillin in breast milk, there are no known detrimental effects for the breast-fed infant.

4.7. Effects on ability to drive and use machines

There are no effects on ability to drive or to operate machinery.

4.8. Undesirable effects

The following convention has been utilised for the classification of undesirable effects:

Very common (≥1/10), common (≥1/100, <1/10), uncommon (≥1/1000, <1/100), rare (≥1/10,000, <1/1000), very rare (<1/10,000)
The majority of side effects listed below are not unique to amoxicillin and may occur when using other penicillins.
Unless otherwise stated, the frequency of adverse events has been derived from more than 30 years of post-marketing reports.

Infections and infestations

Very Rare: Muco-cutaneous candidiasis

Blood and lymphatic system disorders

Very rare: Reversible leucopenia (including severe neutropenia or agranulocytosis), reversible thrombocytopenia and haemolytic anaemia.
Prolonged prothrombin and bleeding times

Immune system disorders

Very rare: As with other antibiotics, severe allergic reactions, including angioneurotic oedema, anaphylaxis, serum sickness and vasculitis

If any hypersensitivity reaction occurs the treatment should be discontinued

Nervous system disorders

Very rare: Hyperkinesia, dizziness and convulsions. Convulsions may occur in patients with impaired renal function or inthose receiving high doses.

Unknown: Paraesthesia

Gastrointestinal disorders

Clinical Trial Data

***Common**: Diarrhoea and nausea.

***Uncommon**: Vomiting.

Post-marketing Data

Very rare: Antibiotic associated colitis (includingpseudomembraneous colitis and haemorrhagic colitis). Black hairy tongue
Superficial tooth discolouration has been reported in children. Good oral hygiene may help to prevent tooth discolouration as it can usually be removed by brushing.

Hepato-biliary disorders

Very rare: Hepatitis and cholestatic jaundice. A moderate rise inAST and/or ALT.

The significance of a rise in AST and/or ALT is unclear.

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 and acute generalised exanthematous pustulosis (AGEP)

Renal and urinary tract disorders

Very rare:	Interstitial nephritis.
Very rare:	Crystalluria

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

4.9. Overdose

Problems of overdosage with amoxicillin are unlikely to occur. If encountered, gastrointestinal effects such as nausea, vomiting and diarrhoea may be evident and should be treated symptomatically with attention to the water/electrolyte balance. Amoxicillin crystalluria, in some cases leading to renal failure, has been observed. Amoxicillin may be removed from the circulation by haemodialysis.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Pharmacotherapeutic group: ATC code: J01CA04

Amoxicillin is bactericidal. Like all penicillins it acts by interfering with the synthesis of the cell wall of the bacterium.

Amoxicillin is inactivated by penicillinase. Penicillinase-producing strains of Staphylococcus aureus and Gram negative organisms (e.g. Escherichia coli, Proteus, Klebsiella) are resistant.

Complete cross-resistance occurs with ampicillin and amoxicillin.

The wide range of organisms sensitive to the bactericidal action of Amoxicillin include:

Aerobes:	
Gram-positive	**Gram-negative**
Streptococcus faecalis	*Haemophilus influenzae*

Streptococcus pneumoniae	*Escherichia coli*

Streptococcus pyogenes	*Proteus mirabilis*
Streptococcus viridans	*Salmonella* species
Staphylococcus aureus	*Shigella* species
(penicillin-sensitive strains only)	*Bordetella pertussis*
	Brucella species
Corynebacterium species	*Neisseria gonorrhoeae*
Bacillus anthracis	*Neisseria meningitidis*
Listeria monocytogenes	*Vibrio cholerae*
	Pasteurella septica
Anaerobes:	
Clostridium species	

5.2. Pharmacokinetic properties:

Amoxicillin is stable in the acid gastric secretion and is rapidly absorbed from the gastrointestinal tract after oral administration. The presence of food does not interfere with this process. Peak plasma concentrations are obtained in about two hours, producing around 2.5 times the peak concentration resulting from comparable dosesof ampicillin.

Protein binding is similar to that of ampicillin: up to 25%.

Effective levels in the cerebrospinal fluid are obtained only in the presence of inflammation and then irregularly. About 60% of an orally administered dose is excreted unchanged in the urine. It penetrates well in to purulent and mucoid sputum.

In preterm infants with gestational age 26-33 weeks, the total body clearance after intravenous dosing of amoxicillin, day 3 of life, ranged between 0.75 – 2 ml/min, very similar to the inuline clearance (GFR) in this population. Following oral administration, the absorption pattern and the bioavailability of amoxicillin in small children may be different to that of adults. Consequently, due to the decreased CL, the exposure is expected to be elevated in this group of patients, although this increase in exposure may in part be diminished by decreased bioavailability when given orally.

5.3. Preclinical safety data

Not Applicable

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

- Microcrystalline Cellulose (102)

- Purified Talc
- Magnesium Stearate
- Colloidal anhydrous silica
- Empty hard gelatin capsule size “2” Maroon/Yellow

Qualitative Composition of empty capsule Shell

Maroon Cap Shell Composition	**Yellow Body Shell Composition**
Gelatin	Gelatin
Purified Water	Purified Water
Sodium Lauryl Sulphate	Sodium Lauryl Sulphate
Sodium Methylparaben	Sodium Methylparaben
Sodium Propylparaben	Sodium Propylparaben

6.2. Incompatibilities

Not applicable

6.3. Shelf life

36 months

6.4. Special precautions for storage

Do not store above 30^{o}C.

Protected from light and moisture.

6.5. Nature and contents of container

An Alu-PVC blister of 10 capsules & 10 such Alu-PVC blisters packed in a cartonalong with package insert.

“Prescription Only Medicine”

6.6. Special precautions for disposal

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

7. MARKETING AUTHORISATION HOLDER

Theon Pharmaceuticals Limited
Plot No. 400 Industrial Area Phase
-1Panchkula -134113
Haryan
aIndia

8. MARKETING AUTHORISATION NUMBER(S)

TAN 21 HM 0297

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THEAUTHORISATION

20th August, 2021

10. DATE OF REVISION OF THE TEXT

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