Summary of Product Characteristics

1. Name of the medicinal product

ADCOCIN Capsules (Amoxicillin capsule 250mg)

2. Qualitative and quantitative composition

Each capsule contains 250mg amoxicillin as amoxicillin trihydrate
For full excipients, please see section 6.1 for details.

3. Pharmaceutical form:

Capsule, Hard, White to yellowish white powder and granules in hard gelatin capsule, size 1 capsule shell,red cap and yellow body

4. Clinical particulars

4.1.Therapeutic indications

Amoxicillin Capsules is indicated for the treatment of the following infections in adults and children (see sections 4.2, 4.4 and 5.1):

- Acute bacterial sinusitis
- Acute otitis media
- Acute streptococcal tonsillitis and pharyngitis
- Acute exacerbations of chronic bronchitis
- Community acquired pneumonia
- Acute cystitis
- Asymptomatic bacteriuria in pregnancy
- Acute pyelonephritis
- Typhoid and paratyphoid fever
- Dental abscess with spreading cellulitis
- Prosthetic joint infections
- *Helicobacter pylori* eradication
- Lyme disease

Amoxicillin Capsules is also indicated for the prophylaxis of endocarditis.

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

4.2.Posology and method of administration

The dose of Amoxicillin Capsules that is selected to treat an individual infection should take into account:

- The expected pathogens and their likely susceptibility to antibacterial agents (see section 4.4)
- The severity and the site of the infection
- The age, weight and renal function of the patient; as shown below

The duration of therapy should be determined by the type of infection and the response of the patient, and should generally be as short as possible. Some infections require longer periods oftreatment (see section 4.4 regarding prolonged therapy).

Adults and children ≥40 kg

Indication*	Dose*
Acute bacterial sinusitis	250 mg to 500 mg every 8 hours or 750 mg to 1 g every 12 hours For severe infections 750 mg to 1 g every 8 hours Acute cystitis may be treated with 3 g twice daily for one day
Asymptomatic bacteriuria in pregnancy	
Acute pyelonephritis	
Dental abscess with spreading cellulitis	
Acute cystitis	
Acute otitis media	500 mg every 8 hours, 750 mg to 1 g every 12 hours For severe infections 750 mg to 1 g every 8 hours for 10 days
Acute streptococcal tonsillitis and pharyngitis	
Acute exacerbations of chronic bronchitis	
Community acquired pneumonia	500 mg to 1 g every 8 hours
Typhoid and paratyphoid fever	500 mg to 2 g every 8 hours
Prosthetic joint infections	500 mg to 1 g every 8 hours
Prophylaxis of endocarditis	2 g orally, single dose 30 to 60 minutes before procedure
Helicobacter pylori eradication	750 mg to 1 g twice daily in combination with a proton pump inhibitor (e.g. omeprazole, lansoprazole) and another antibiotic (e.g. clarithromycin, metronidazole) for 7 days
Lyme disease (see section 4.4)	Early stage: 500 mg to 1 g every 8 hours up to a maximum of 4 g/day in divided doses for 14 days (10 to 21 days) Late stage (systemic involvement): 500 mg to 2 g every 8 hours up to a maximum of 6 g/day in divided doses for 10 to 30 days
* Consideration should be given to the official treatment guidelines for each indication	

Children <40 kg

Children may be treated with Amoxicillin capsules, dispersible tablets suspensions or sachets. Amoxicillin Capsules Paediatric Suspension is recommended for children under six months ofage.
Children weighing 40 kg or more should be prescribed the adult dosage.

Recommended doses:

Indication[+]	Dose[+]
Acute bacterial sinusitis	20 to 90 mg/kg/day in divided doses*
Acute otitis media	
Community acquired pneumonia	
Acute cystitis	
Acute pyelonephritis	
Dental abscess with spreading cellulitis	
Acute streptococcal tonsillitis and pharyngitis	40 to 90 mg/kg/day in divided doses*
Typhoid and paratyphoid fever	100 mg/kg/day in three divided doses
Prophylaxis of endocarditis	50 mg/kg orally, single dose 30 to 60 minutes before procedure
Lyme disease (see section 4.4)	Early stage: 25 to 50 mg/kg/day in three divided doses for 10 to 21 days Late stage (systemic involvement): 100 mg/kg/day in three divided doses for 10 to 30 days
+ Consideration should be given to the official treatment guidelines for each indication. *Twice daily dosing regimens should only be considered when the dose is in the upper range.	

Elderly

No dose adjustment is considered necessary.

Renal impairment

GFR (ml/min)	Adults and children ≥ 40 kg	Children < 40 kg#
greater than 30	no adjustment necessary	no adjustment necessary
10 to 30	maximum 500 mg twice daily	15 mg/kg 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 the majority of cases, parenteral therapy is preferred.

In patients receiving haemodialysis

Amoxicillin may be removed from the circulation by haemodialysis.

Haemodialysis Adults and children500 mg every 24 h

	red after haemodialysis. 15 mg/kg/day given as a single daily dose (maximum 500 mg).
over 40 kg	Prior to haemodialysis one additional dose of 15 mg/kg should be administered.
Children under 40 kg	In order to restore circulating drug levels, another dose of 15 mg/kg should be administered after haemodialysis.

In patients receiving peritoneal dialysis

Amoxicillin maximum 500 mg/day.

Hepatic impairment

Dose with caution and monitor hepatic function at regular intervals (see sections 4.4 and 4.8).Method of administration
Amoxicillin Capsules is for oral use.

Absorption of Amoxicillin Capsules is unimpaired by food.

Therapy can be started parenterally according to the dosing recommendations of the intravenousformulation and continued with an oral preparation.
Swallow with water without opening capsule.

4.3.Contraindications

Hypersensitivity to the active substance, to any of the penicillins or to any of the excipients listedin section 6.1.
History of a severe immediate hypersensitivity reaction (e.g. anaphylaxis) to another beta-lactamagent (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

Serious and occasionally fatal hypersensitivity reactions (including anaphylactoid and severe cutaneous adverse reactions) have been reported in patients on penicillin therapy. These reactionsare more likely to occur in individuals with a history of penicillin hypersensitivity and in atopic individuals. If an allergic reaction occurs, amoxicillin therapy must be discontinued and appropriate alternative therapy instituted.

Non-susceptible microorganisms

Amoxicillin is not suitable for the treatment of some types of infection unless the pathogen isalready 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 dosesor 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 ofimpairment (see section 4.2).

Skin reactions

The occurrence at the treatment initiation of a feverish generalised erythema associated with pustula may be a symptom of acute generalised exanthemous pustulosis (AGEP, see section 4.8).This reaction requires amoxicillin discontinuation and contra-indicates any subsequent administration.

Amoxicillin should be avoided if infectious mononucleosis is suspected since the occurrence of amorbilliform rash has been associated with this condition following the use of amoxicillin.

Jarisch-Herxheimer reaction

The Jarisch-Herxheimer reaction has been seen following amoxicillin treatment of Lyme disease(see section 4.8). It results directly from the bactericidal activity of amoxicillin on the causative

bacteria of Lyme disease, the spirochaete *Borrelia burgdorferi*. Patients should be reassured that this is a common and usually self-limiting consequence of antibiotic treatment of Lyme disease.Overgrowth of non-susceptible 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 rangein 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 administrationof 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 contra-indicated 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 bloodcounts 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 amoxicillintreatment, 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 prolongedblood 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 drugs may interfere with the bactericidal effects ofamoxicillin.
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 inpatients maintained on acenocoumarol or warfarin and prescribed a course of amoxicillin. If co-administration is necessary, the prothrombin time or international normalised ratio should be carefully monitored with the addition or withdrawal of amoxicillin. Moreover, adjustments in the dose of oral anticoagulants may be necessary (see sections 4.4 and 4.8).
Methotrexate

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

4.6.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 breast-feeding might have to be discontinued. Amoxicillin should only be used during breast-feeding after benefit/risk assessment by the physician in charge.
Fertility

There are no data on the effects of amoxicillin on fertility in humans. Reproductive studies inanimals have shown no effects on fertility.

4.7.Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed. However, undesirable effects may occur (e.g. allergic reactions, dizziness, convulsions), which may influence the ability to drive and use machines (see section 4.8).

4.8.Undesirable effects

The most commonly reported adverse drug reactions (ADRs) are diarrhoea, nausea and skin rash.The ADRs derived from clinical studies and post-marketing surveillance with amoxicillin, presented by MedDRA System Organ Class are listed below.
The following terminologies have been used in order to classify the occurrence of undesirableeffects.
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 leucopenia (including severe neutropenia

	or agranulocytosis), reversible thrombocytopeniaand haemolytic anaemia. Prolongation of bleeding time and prothrombin time (see section 4.4).
Immune system disorders	
Very rare	Severe allergic reactions, including angioneuroticoedema, 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 section4.4).
Gastrointestinal disorders	
Clinical Trial Data	
*Common	Diarrhoea and nausea
*Uncommon	Vomiting
Post-marketing Data	
Very rare	Antibiotic associated colitis (including pseudomembraneous colitis and haemorrhagic colitissee section 4.4). Black hairy tongue
Hepatobiliary disorders	Hepatitis and cholestatic jaundice. A moderate risein AST and/or ALT.
Very rare	
Skin and subcutaneous tissue disorders	
Clinical Trial Data	

*Common	Skin rash
*Uncommon	Urticaria and pruritus
Post-marketing Data	
Very rare	Skin reactions such as erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis, bullous and exfoliative dermatitis, acute generalised exanthematous pustulosis (AGEP) (see section 4.4), and drug reaction with eosinophilia andsystemic symptoms (DRESS).
Renal and urinary tract disorders	**Interstitial nephritis** Crystalluria (see sections 4.4 and 4.9 Overdose)
Very rare:	

* 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

Symptoms and signs of overdose

Gastrointestinal symptoms (such as nausea, vomiting and diarrhoea) and disturbance of the fluidand 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 inthose receiving high doses (see sections 4.4 and 4.8).

Treatment of intoxication

Gastrointestinal symptoms may be treated symptomatically, with attention to the water/ electrolytebalance.
Amoxicillin can be removed from the circulation by haemodialysis.

5. Pharmacological properties

5.1.Pharmacodynamic properties

Pharmacotherapeutic group: penicillins with extended spectrum; ATC code: J01CA04.Mechanism of action

Amoxicillin is a semisynthetic penicillin (beta-lactam antibiotic) that inhibits one or more enzymes (often referred to as penicillin-binding proteins, PBPs) in the biosynthetic pathway ofbacterial 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 producethese enzymes.
Pharmacokinetic/pharmacodynamic relationship

The time above the minimum inhibitory concentration (T>MIC) is considered to be the major determinant of efficacy for amoxicillin.
Mechanisms of resistance

The main mechanisms of resistance to amoxicillin are:

• Inactivation by bacterial beta-lactamases.

• Alteration of PBPs, which reduce the affinity of the antibacterial agent for the target. Impermeability of bacteria or efflux pump mechanisms may cause or contribute to bacterialresistance, particularly in Gram-negative bacteria.
Breakpoints

MIC breakpoints for amoxicillin are those of the European Committee on Antimicrobial Susceptibility Testing (EUCAST) version 5.0.
Organism MIC breakpoint (mg/L)

	Susceptible ≤	**Resistant >**
Enterobacteriaceae	81	8
Staphylococcus spp.	Note2	Note 2
Enterococcus spp.3	4	8
Streptococcus groups A, B, C and G	Note 4	Note 4
Streptococcus pneumoniae	Note 5	Note 5
Viridans group steprococci	0.5	2
Haemophilus influenzae	26	26
Moraxella catarrhalis	Note 7	Note 7
Neisseria meningitidis	0.125	1
Gram positive anaerobes except *Clostridium difficile*8	4	8
Gram negative anaerobes8	0.5	2

Helicobacter pylori	0.1259	0.1259
Pasteurella multocida	1	1
Non- species related breakpoints10	2	8

1Wild type Enterobacteriaceae are categorised as susceptible to aminopenicillins. Some countries prefer tocategorise wild type isolates of *E. coli* and *P. mirabilis* as intermediate. When this is the case, use the MICbreakpoint S ≤ 0.5 mg/L
2Most staphylococci are penicillinase producers, which are resistant to amoxicillin. Methicillin resistant isolates are, with few exceptions, resistant to all beta-lactam agents.
3Susceptibility to amoxicillin can be inferred from ampicillin

4The susceptibility of streptococcus groups A, B, C and G to penicillins is inferred from the benzylpenicillin susceptibility.
5Breakpoints relate only to non-meningitis isolates. For isolates categorised as intermediate to ampicillinavoid oral treatment with amoxicillin. Susceptibility inferred from the MIC of ampicillin.
6Breakpoints are based on intravenous administration. Beta-lactamase positive isolates should be reportedresistant.
7Beta lactamase producers should be reported resistant
8Susceptibility to amoxicillin can be inferred from benzylpenicillin.
9The breakpoints are based on epidemiological cut-off values (ECOFFs), which distinguish wild-typeisolates from those with reduced susceptibility.
10The non-species related breakpoints are based on doses of at least 0.5 g x 3or 4 doses daily (1.5 to 2 g/day).

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 theutility of the agent in at least some types of infections is questionable.

***In vitro* susceptibility of micro-organisms to AmoxicillinCommonly Susceptible Species**

Gram-positive aerobes:

Enterococcus faecalis

Beta-hemolytic streptococci (Groups A, B, C and G)

Listeria monocytogenes

Species for which acquired resistance may be a problem

Gram-negative aerobes:*Escherichia coli Haemophilus influenzaeHelicobacter pylori Proteus mirabilis* *Salmonella* typhi *Salmonella* paratyphi *Pasteurella multocida*

Gram-positive aerobes:

Coagulase negative staphylococcus*Staphylococcus aureus*£ *Streptococcus pneumoniae* Viridans group streptococcus

Gram-positive anaerobes:

Clostridium spp.

Gram-negative anaerobes:

Fusobacterium spp.Other:
Borrelia burgdorferi

Inherently resistant organisms†Gram-positive aerobes:
Enterococcus faecium†

Gram-negative aerobes:

Acinetobacter spp.*Enterobacter* spp. *Klebsiella* spp.
Pseudomonas spp.

Gram-negative anaerobes:

Bacteroides spp. (many strains of *Bacteroides fragilis* are resistant).Others:
Chlamydia spp.

Mycoplasma spp.

Legionella spp.

† Natural intermediate susceptibility in the absence of acquired mechanism of resistance.

£ Almost all *S.aureus* are resistant to amoxilcillin due to production of penicillinase. In addition, all methicillin-resistant strains are resistant to amoxicillin.

5.2.Pharmacokinetic properties

Absorption

Amoxicillin fully dissociates in aqueous solution at physiological pH. It is rapidly and well absorbed by the oral route of administration. Following oral administration, amoxicillin is approximately 70% bioavailable. The time to peak plasma concentration (Tmax) is approximatelyone hour.

The pharmacokinetic results for a study, in which an amoxicillin dose of 250 mg three times daily was administered in the fasting state to groups of healthy volunteers are presented below.

Cmax	Tmax *	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 range 250 to 3000 mg the bioavailability is linear in proportion to dose (measured asCmax and AUC). The absorption is not influenced by simultaneous food intake. Haemodialysis can be used for elimination of amoxicillin.
Distribution

About 18% of total plasma amoxicillin is bound to protein and the apparent volume of distribution is around 0.3 to 0.4 l/kg.
Following intravenous administration, amoxicillin has been found in gall bladder, abdominal tissue, skin, fat, muscle tissues, synovial and peritoneal fluids, bile and pus. Amoxicillin does notadequately distribute into the cerebrospinal fluid.
From animal studies there is no evidence for significant tissue retention of drug-derived material.Amoxicillin, like most penicillins, can be detected in breast milk (see section 4.6).
Amoxicillin has been shown to cross the placental barrier (see section 4.6).Biotransformation
Amoxicillin is partly excreted in the urine as the inactive penicilloic acid in quantities equivalent to up to 10 to 25% of the initial dose.
Elimination

The major route of elimination for amoxicillin is via the kidney.

Amoxicillin has a mean elimination half-life of approximately one hour and a mean total clearance of approximately 25 l/hour in healthy subjects. Approximately 60 to 70% of 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 havedecreased renal function, care should be taken in dose selection, and it may be useful to monitorrenal function.
Gender

Following oral administration of amoxicillin/ to healthy males and female subjects, gender has nosignificant 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 atregular intervals.

5.3.Preclinical safety data

Non-clinical data reveal no special hazard for humans based on studies of safety pharmacology,repeated dose toxicity, genotoxicity and toxicity to reproduction and development.
Carcinogenicity studies have not been conducted with amoxicillin.

6. Pharmaceutical particulars

6. 1 List of excipients

Magnesium stearate, Purified talc, **Gelatin Capsule shell** - **Cap:** Bright blue, Amaranth, Titaniumdioxide, dodecyl, **Body:** Titanium dioxide, Dodecyl

6. 2 Incompatibilities

Not applicable.

3. Shelf life

36 months.

4. Special precautions for storage

Do not store above
30°C.Protect from light.

5. Nature and contents of container Aluminum foil-PVC blister. 10capsules/blister,10blisters/ box,200boxes/carton

6. Special precautions for disposal and other handling

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

7. Marketing authorisation holder

Advanov Pharma Pvt. Ltd, A/202 Empire Business Hub, Science City Rd, Gujarat, India

Manufacturer: Reyoung Pharmaceutical Co., Ltd, No.1 Ruiyang Road, Yiyuan County, Shandong Province,China

8. Marketing authorization number(s)

TAN 22 HM 0239

9. Date of first authorization/renewal of the authorization

19th July, 2022

10. Date of revision of the test