1.6. PRODUCT INFORMATION

1.6.1. PRESCRIBING INFORMATION
(SUMMARY OF PRODUCTS CHARACTERISTICS)

1 Product Name

Brand Name	**:**	SPAMOX CAPSULES 500
INN or Generic Name	**:**	Amoxicillin Capsules B.P. 500 mg
Dosage form	**:**	Hard Gelatin Capsules (Oral Solid Dosage Form)
Strength	**:**	Amoxicillin Trihydrate B.P. equivalent to Amoxicillin 500 mg

2. Qualitative and quantitative Composition

Sr. No.	Ingredients	Specification	Qty Per capsule (mg)	% of doses per capsule	Function
Content of Capsule					
1.	Amoxicillin Trihydrate BP Equivalent to Amoxicillin	B.P. 2018	580 ≈ 500 mg	98.31 %	Active Ingredient
2.	Purified Talc	B.P. 2018	4.000	0.68 %	Lubricant
3.	Colloidal Silicon Dioxide	B.P. 2018	1.000	0.17 %	Lubricant
4.	Magnesium Stearate	B.P. 2018	5.000	0.85 %	Lubricant
Subtotal 1		-	**590.00 mg**	**100.0%**	
Hard Gelatin Capsule					
5.	Empty Hard Gelatin Capsules Maroon/Yellow, Size "0" printed as SPARSH/AMOXY 500	I.H.S.	1.0 Capsule	---	In active
Subtotal 2		**---**	**96.00 mg**	**---**	**---**
Grand Total		**---**	**686.00 mg**	**---**	**---**

Where,

B.P. 2018 = British Pharmacopoeia 2018
I.H.S. = In-House Specifications

3. PHARMACEUTICAL FORM

Hard Gelatin Capsules (Oral Solid Dosage Form)

4. Clinical particulars

4.1 Therapeutic indications

Amoxicillin is a broad spectrum antibiotic indicated for the treatment of commonly occurring bacterial infections such as:

Respiratory tract infections caused by microorganisms such as non-penicillinase producing H. influenzae, staphylococci, and streptococci, including Streptococcus pneunoniae.

Gastrointestinal tract Infections caused by microorganisms such as Shigella, S. typhosa,

Salmonella, E.Coli, P. mirabilis and enterococci. Meningitis N. meningitides.

Genitourinary tract infections caused by microorganisms including Gonorrhea, E. Coli, P. mirabilis, enterococci, Shigella, S. typhosa, N. gonorrhea, Salmonella and other non penicillinase producing microorganisms.

Other bacterial infections such as:

Otitis media

Acute and chronic bronchitis

Chronic bronchial sepsis

Lobar and bronchopneumonia

Cystitis, urethritis, pyelonephritis

Bacteriuria in pregnancy

Gynaecological infections including puerperal sepsis and septic abortion

Gonorrhoea

Peritonitis

Intra-abdominal sepsis

Septicaemia

Bacterial endocarditis

Typhoid and paratyphoid fever

Skin and soft tissue infections

Dental abscess (as an adjunct to surgical management)

Helicobacter pylori eradication in peptic (duodenal and gastric) ulcer disease.

In children with urinary tract infection the need for investigation should be considered.

Prophylaxis of endocarditis: Amoxicillin may be used for the prevention of bacteraemia, associated with procedures such as dental extraction, in patients at risk of developing bacterial endocarditis.

4.2) POSOLOGY AND METHOD OF ADMINISTRATION:

Route of administration: oral use

Amoxicillin capsules, tablets & oral suspension may be given without regards to meals. The usual dosage regimen of amoxicillin is 250 to 500 mg three times a day. For children half of the adult dose may be used. Some infections may be treated with special dosage regimens given below:

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.

a) Respiratory tract infections - 3g twice a day

b) Acute urinary tract infections - 3g repeated once 12 hours later.

c) Gonorrhoea	-	3g single dose.
d) Dental Abcess	-	3g repeated once 8 hours later.
e) Prophylaxis of endocarditis	-	Single 3g dose one hour before dental procedure from which bacteraemia may arise. Repeated 6 hours later if necessary.

4.3) CONTRAINDICATION:

A history of allergic reaction to any of the penicillin is a contraindication. The use of this drug is contraindicated in individuals with a history of previous hypersensitivity reaction to any of the penicillins. Amoxicillin is also contraindicated in infections caused by penicillinase producing organisms.

4.4) SPECIAL WARNINGS AND PRECAUTIONS FOR USE:

Warnings

Serious and occasionally fatal hypersensitivity reactions have been reported in patients on parenteral penicillin therapy. These reactions may occur with oral penicillin particularly in individuals with a history of sensitivity to multiple allergens. There have been reports of individuals with a history of penicillin hypersensitivity who have experienced severe reactions when treated with cephalosporins. Before therapy with any penicillin careful inquiry should be made concerning previous hypersensitivity reactions to penicillins, cephalosporins or other allergens. If an allergic reaction occurs, appropriate therapy should be instituted and discontinuance of amoxicillin therapy considered. Serious anaphylactic reactions require immediate emergency treatment with Epinephrine, oxygen, intravenous steroids and air way management including intubations should also be administered as indicated.

Precautions

As with any potent drug periodic assessment of renal, hepatic and hemaropoietic function should be made during prolonged therapy. The possibility of super infections with mycotic or bacterial pathogens should be kept in mind during therapy.

Before initiating therapy with amoxicillin, careful inquiry should be made concerning previous hypersensitivity reactions to penicillins, cephalosporin’ s, or other allergens. If an allergic reaction occurs, amoxicillin should be discontinued and appropriate therapy instituted.

If super infections occur (usually involving Entero-bacter, pseudomonas or Candida), the drug should be discontinued and/or appropriate therapy instituted.

4.5) INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION:

Probenecid decreases the renal tubular secretion of Amoxicillin, concurrent use of Amoxicillin and Probenecid may result in increased and prolonged blood levels of amoxicillin.

Chloramphenicol, macrolides, sulfonamides and tetracyclines may interfere with the bactericidal effects of amoxicillin. This has been demonstrated invitro, however, the clinical significance of this interaction is not well documented.

Amoxicillin show possible antagonism effects with Demeclocycline, Doxycycline, Methacycline, Minocycline, Oxytetracycline, Rolitetracycline and Tetracycline.

This anti-infectious agent could decrease the effect of the oral contraceptive like Ethinyl Estradiol and Mestranol.

Amoxicillin increases the effect and toxicity of methotrexate.

Pseudomembranous colitis has been reported with nearly all-antibacterial agents, including amoxicillin, any may range in severity from mild to life threatening. Therefore, it is important to consider this diagnosis in patients who present with diarrhoea subsequent to the administration of antibacterial agents.

Treatment with antibacterial agents alters the normal flora of the colon and may permit overgrowth of clostridia. Studies indicate that a toxin produced by clostridium difficile is a primary cause of 'antibiotic-associated colitis'. After the diagnosis of pseudomembranous colitis has been established, appropriate therapeutic measure should be initiated. Mild cases of pseudomembranous colitis usually respond to drug discontinuation alone. In moderate to severe cases, consideration should be given to management with fluids and electrolytes, protein supplementation, and treatment and with antibacterial drug clinically effective against Clostridium difficile colitis.

4.6) PREGNANCY AND LACTATION:

PREGNANCY

Category B

Animal studies with Amoxicillin have shown no teratogenic effects. Although no controlled data in human pregnancy are available, literature reports of adverse fetal effects are lacking. Amoxicillin is only recommended during pregnancy when benefit outweighs risk.

LACTATION

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

4.7) EFFECTS ON ABILITY TO DRIVE AND USE MACHINES:

No effect on the above. No sedation / drowsiness has been reported.

4.8) UNDESIRABLE EFFECTS:

As with other penicillins, it may be expected that untoward reactions will be essentially limited to sensitivity phenomena. They are more likely to occur in individuals who have previously demonstrated hypersensitivity to penicillins and in those with a history of allergy, asthma, hay fever or uriticaria. The following adverse reactions have been reported as associated with the use of penicillin.

Gastrointestinal : Nausea, vomiting and diarrhoea.

Hypersensitivity: Erythematous maculopapular rashes and uriticaria have been reported.

Note: Urticaria, other skin rashes and serum sickness-like reactions, may be controlled with antihistamines and, if necessary systemic coriticosteroids. Whenever such reactions occur Amoxicillin should be continued unless, in the opinion of the physician, the condition being treated is life-threatening and amenable only to Amoxicillin therapy.

Liver: A moderate use in serum glutamic oxaloacetic transaminases (SGOT) has been noted but the significance of this finding is unknown.

Central Nervous System: Reversible hypersensitivity, agitation, anxiety, insomnia, confusion, behavioral changes and/or dizziness have reported rarely.

Cytopenic purpura eosinophilia, leukopenia have been reported during therapy with the penicillins. These reactions are usually reversible on discontinuation of therapy and are believed to be hypersensitivity phenomena.

4.9) OVERDOSE:

In case of overdose, discontinue medication, treat symptomatically and institute supportive measures as required. In patients with renal function impairment, Amoxicillin class antibiotics can be removed by haemodialysis but not be peritoneal dialysis.

If the overdosage is very recent and there is no contraindication, an attempt at emesis or other means of removal of drug from the stomach may be performed.

Interstitial nephritis resulting in oliguric renal failure has been reported in a small number of patients after overdosage with amoxicillin. Renal impairment appears to be reversible with cessation of drug administration. High blood levels may occur more readily in patients with impaired renal function because of decreased renal clearance of amoxicillin.

Problems of overdose 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.

During administration of high doses of amoxicillin, adequate fluid intake and urinary output must be maintained to minimize the possibility of amoxicillin crystalluria. Amoxicillin can be removed from the circulation by haemodialysis.

5) PHARMACOLOGICAL PROPERTIES

5.1) PHARMACODYNAMIC PROPERTIES

Pharmacotherapeutic group: Antibiotics

ATC Code : J01CA04

ANATOMIC THERAPEUTIC CHEMICAL AND FORENSIC CLASSIFICATION:

J	**GENERAL ANTIINFECTIVES, SYSTEMIC**
J01	**SYSTEMIC ANTIBIOTICS**
C	**PENICILLINS WITH INCREASES EFFECT ON GRAM-NEGATIVE BACILLI**

MECHANISM OF ACTION

This drug acts by inhibiting the synthesis of bacterial cell walls wall by binding to one or more of the penicillin-binding proteins (PBPs). It inhibits cross-linkage between the linear peptidoglycan polymer chains that make up a major component of the cell walls of both Gram-positive and Gram-negative bacteria.

It has two ionizable groups in the physiological range (the amino group in alpha-position to the amide carbonyl group and the carboxyl group).

Amoxicillin inhibits the final transpeptidation step of peptidoglycan synthesis in bacterial cell wall

thus inhibiting cell wall biosynthesis resulting in bacterial lysis.

PHARMACODYNAMICS

Amoxicillin is a broad spectrum antibiotic.
It is rapidly bactericidal and possesses the safety profile of a penicillin.
The wide range of organisms sensitive to the bactericidal action of Amoxicillin.

It is usually the drug of choice within the class because it is better absorbed, following oral administration, than other beta-lactam antibiotics.

Amoxicillin exerts bactericidal action against susceptible organisms during the stage of active multiplication.

5.2) PHARMACOKINETIC PROPERTIES

Absorption

Amoxicillin is stable in the presence of gastric acid and may be given without regards to meals. It is rapidly absorbed after oral administration.

Distribution

Amoxicillin diffuses readily into most body tissues and fluids with the exception of the brain and spinal fluid, except when meninges are inflamed. The half life of amoxicillin is 61.2 minutes.

In blood serum, amoxicillin is approximately 20% protein bound as compared to 60% of penicillin G.Orally administered doses of 250mg and 500mg amoxicillin capsules result in average peak blood levels 1 to 2 hours after administration in the range of 3.5mcg/ml to 5.0 mcg/ml and 5.5 mcg/ml to 7.5mcg/ml respectively.

Detectable serum levels are observed upto 8 hours after and oral administered dose of Amoxicillin. Following a 1g dose and utilizing a special skin winsow technique to determine levels of antibiotic, it was noted that therapeutic levels were found in the intestinal fluids.

Metabolism

Hepatic metabolism accounts for less than 30% of the biotransformation of most penicillins

Converted to a limited extent to penicilloic acid.

Excretion

Most of the amoxicillin is excreted unchanged in urine; excretion can be delayed by concurrent administration of probenecid.

Approximately 60% of an orally administered dose of amoxicillin is excreted in the urine within six to eight hours by glomerular filtration and tubular secretion.

Excreted via the faeces. May be removed by haemodialysis.

MICROBIOLOGY:

Amoxicillin is similar to Ampicillin in its bactericidal action against susceptible organisms during the stage of active multiplication. It acts through the inhibition of cell wall mucopolypeptides. Amoxicillin has been shown to be active against most strains of the following microorganisms, both in-vitro and in clinical infections as described in INDICATION.

Aerobic Gram-positive Microorganisms:

Enterococcus faecalis.

Staphylococcus spp. (lactamase-negative strains only)

Streptococcus pneumoniae.

Streptococcus spp (and haemolytic strains only)

Streptococcus pyogenes

Streptococcus viridans

Staphylococcus aureus (penicillin-sensitive strains only)

Corynebacterium species

Bacillus anthracis

Listeria monocytogenes

Staphylococci, which are susceptible to Amoxicillin but resistant to methicillin/oxacillin, should be considered as resistant to amoxicillin.

Aerobic Gram-negative Microorganisms:

Escherichia coli (lactamase- negative strains only)

Haemophilus Influenzae (lactamase- negative strains only)

Neisseria gonorrhoeae (lactamase- negative strains only)

Proteus mirabilis (lactamase- negative strains only)

Helicobacter pylori.

Salmonella species

Shigella species

Bordetella pertussis

Brucella species

Neisseria meningitidis

Vibrio cholerae

Pasteurella septica

Anaerobic Microorganisms:

Clostridium species

5.3) PRECLINICAL SAFETY DATA

Preclinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity and toxicity to reproduction.

6 Pharmaceutical particulars

6.1 List of excipients

1) Purified Talc
2) Colloidal Silicon Dioxide
3) Magnesium Stearate
4) Empty Hard Gelatin Capsules Maroon/Yellow, Size "0" printed as SPARSH/AMOXY 500

6.2 Incompatibilities:

It is observed that Amoxicillin Trihydrate is a stable molecule and exhibits good amount of compatibility with the above listed excipients tested for three month at 40°C / 75% RH. Hence these excipients are not expected to cause any stability problems in the formulation.

6.3 Shelf life

2 Years

6.4 Special precautions for storage:

Store in a cool, dry place, Protect from light. Do not store above 25°C.

Keep all medicines out of sight & reach of Children.

6.5 Nature and contents of container:

The capsules are available in the following packing and pack size:

1. Blister Pack:

A blister of 10 capsules and such 10 blisters are placed in carton along with a product leaflet.

Primary Packing : Alu-PVC Blister pack of 10 Capsules

Unit pack:

One blister contains 10 capsules.

Secondary Packing:

10 blisters are packed in printed outer cartons along with a product leaflet. Such 100 cartons are packed in a corrugated box.

2. JAR PACK:

500 capsules packed in a polythene bag. This polythene bag is placed in a 850ml HDPE Plastic Rib Jar. Two packs of silica gel and one product leaflet is placed in the jar. The HDPE Plastic Rib Jar is sealed with an aluminum tragger, capped and labeled.

Primary Packing : 500 Capsules packed in P.P. bag.

Unit pack:

500 Capsules packed in a P.P. bag

Secondary Packing:

500 Capsules P.P. bag are packed in HDPE plastic Rib Jar. Two packs of silica gel and one product leaflet is placed in the jar Such 30 HDPE Plastic Rib Jars are packed in a corrugated box.

6.6 Special precautions for disposal

No special requirements

7. Marketing authorization holder and manufacturing site addresses.

SPARSH BIO-TECH PVT. LTD.

Plot No. 1, Survey No. 242/243/244, Village lakhabavad, Jamnagar – 361006, India.

8. Marketing authorization Number

Product license Number G/1174

9. Date of first authorization/renewal of the authorization

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10. Date of revision of the text

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11. Dosimetry : Not Applicable

12 Instructions for Preparation of Radio pharmaceuticals : Not Applicable