Approved Package Insert

SCHEDULING STATUS

S4

PROPRIETARY NAME AND DOSAGE FORM

AMOXYCILLIN 250 mg AUSTELL CAPSULES

AMOXYCILLIN 500 mg AUSTELL CAPSULES

COMPOSITION

AMOXYCILLIN 250 mg AUSTELL: Each capsule contains Amoxicillin Trihydrate equivalent to Amoxicillin 250 mg.

AMOXYCILLIN 500 mg AUSTELL: Each capsule contains Amoxicillin Trihydrate equivalent to Amoxicillin 500 mg

PHARMACOLOGICAL CLASSIFICATION

A 20.1.2 Penicillins

PHARMACOLOGICAL ACTION:

Amoxicillin is a semisynthetic beta-lactamase-susceptible penicillin, which has *in vitro* bactericidal activity against broad spectrum of non beta-lactamase-producing Gram positive and Gram negative organisms. The spectrum of activity does not include those organisms that produce beta lactamases, namely resistant staphylococci, and all strains of *Pseudomonas, Klebsiella and Enterobacter.*

The following organisms are generally sensitive to the bactericidal action of Amoxicillin *in vitro*. *In vitro* sensitivity does not mean *in vivo* efficacy [(*) denotes sensitivity tests must be performed].

Gram positive bacteria

Staphylococcus aureus (Penicillin-sensitive)*

Streptococcus pyogenes

*Streptococcus viridans**

*Streptococcus faecalis**

*Streptococcus Pneumoniae**

*Corynebacterium species**

*Clostridium species**

*Bacillus anthracis**

Listeria monocytogenes

Gram negative bacteria

*Neisseria meningitidis *(except the carrier state)*

*Neisseria gonorrhoeae**

*Haemophilus influenza**

Bordetella pertussis

*Escherichia coli**

*Salmonella species**

*Shigella species**

*Proteus mirabilis**

*Pasteurella multocida**

*Fusabacterium species**

Helicobacter pylori

Leptospira species

Pharmacokinetic properties:

Absorption:

Amoxicillin is stable in the presence of acidic gastric secretions. Peak blood levels are achieved 1-2 hrs after administration. There is a linear dose response in peak serum levels.
Food does not interfere with the absorption of Amoxicillin.

Distribution:

Approximately 18 % of the total plasma Amoxicillin content is protein bound. Amoxicillin diffuses readily into most body tissues with the exception of the brain and spinal fluid. Inflammation generally increases the permeability of the meninges to penicillins and this may apply to Amoxicillin%.

Metabolism:

There is no evidence that alendronate is metabolised in animals or humans.

Excretion

The elimination half-life is approximately 1 hour. Amoxicillin is primarily excreted via the kidneys. Small amounts of the drug are also excreted in the faeces and bile. Amoxicillin crosses the placenta and is distributed into breast milk.

INDICATIONS:

AMOXYCILLIN AUSTELL formulations are indicated for the treatment of mild to moderately severe infections caused by susceptible organisms:

- Upper respiratory tract infections such as sinusitis, otitis media, tonsillitis.
- Lower respiratory tract infections such as bronchitis, lobar and bronchopneumonia.
- Gastro-intestinal infections such as typhoid fever.
- Other infections including Borreliosis (Lyme disease).
- In the following infections, Amoxicillin therapy should be initiated only if there is microbiological evidence that the causative organism is sensitive to Amoxicillin:

  Skin and soft tissue infections.

Urinary tract infections: cystitis, urethritis, pyelonephritis, bacteriuria in pregnancy.

- "As part of combination therapy in established Helicobacter pylori infection, associated with duodenal ulceration."
- Prophylaxis of endocarditis.

CONTRAINDICATIONS

Hypersensitivity to penicillins or to cephalosporins. Cross-sensitivity between penicillins and cephalosporins is well documented.

WARNINGS AND SPECIAL PRECAUTIONS:

Serious and occasionally fatal hypersensitivity (anaphylactic) reactions have been reported in patients on penicillin therapy. Before initiating therapy with AMOXYCILLIN AUSTELL careful enquiry should be made concerning previous hypersensitivity reactions to penicillins, cephalosporins or other allergens. Although anaphylaxis is more frequent following parenteral therapy, it has occurred in patients on oral penicillins. These reactions are more likely to occur in individuals with a history of penicillin hypersensitivity and/or 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.

If an allergic reaction occurs, AMOXYCILLIN AUSTELL should be discontinued and the appropriate therapy instituted. Serious anaphylactic reactions may require immediate emergency treatment with adrenaline. Oxygen, intravenous steroids and airway management, including intubation may also be required.

AMOXYCILLIN AUSTELL should be avoided if infectious mononucleosis is suspected since the occurrence of a morbilliform rash has been associated with this condition following the use of Amoxicillin.

Prolonged use may result in overgrowth of non-susceptible organisms. Pseudomembranous enterocolitis has been reported.

Prolongation of prothrombin time has been reported rarely in patients receiving AMOXYCILLIN AUSTELL**.** Appropriate monitoring should be undertaken when anticoagulants are prescribed concurrently.

Periodic assessment of organ function, including renal, hepatic and haematopoietic functions, is advisable during prolonged therapy.

Transient hepatitis and cholestatic jaundice has been reported. AMOXYCILLIN AUSTELL should be used with caution in patients with evidence of hepatic dysfunction

Special precautions:

Caution is needed when administering Amoxicillin to patients with syphilis, as the Jarisch-Herxheimer reaction may occur in these patients.

When high doses are administered, adequate fluid intake and urinary output must be maintained.

The sodium content must be taken into account in patients on sodium-restricted diet if the administration of high doses is necessary.

The use of lignocaine or benzyl alcohol together with Amoxicillin must be used only when administering an intramuscular injection, and not given intravenously.

Periodic assessment of organ system functions, including renal, hepatic and haematopoietic function, is advisable during prolonged therapy. Since AMOXYCILLIN AUSTELL contains Amoxicillin, an aminopenicillin, it is not the treatment of choice in patients presenting with sore throat or pharyngitis because of the possibility that the underlying cause is infectious mononucleosis, in the presence of

which there is a high incidence of rash if Amoxicillin is used. AMOXYCILLIN AUSTELL should be given with caution to patients with lymphatic leukemia since they are especially susceptible to Amoxicillin induced skin rashes.

The possibility of superinfections with mycotic or bacterial pathogens should be kept in mind during therapy. If superinfections occur, the agent should be discontinued and/or appropriate therapy instituted.

Impaired hepatic function

Changes in liver function tests have been observed in some patients receiving AMOXYCILLIN AUSTELL It should be used with care in patients with evidence of severe hepatic dysfunction. In patients with moderate or severe renal impairment AMOXYCILLIN AUSTELL dosage should be adjusted. (See dosage and administration.)

Use in lactation:

Amoxicillin is excreted in the milk. Therefore, caution should be exercised when AMOXYCILLIN AUSTELL is administered to a nursing woman.

The use of AMOXYCILLIN AUSTELL may lead to the selection of resistant strains of organisms and sensitivity testing should, therefore, be carried out whenever possible, to demonstrate the appropriateness of therapy.

INTERACTIONS

Probenecid decreases the renal tubular secretion of AMOXYCILLIN AUSTELL. Concurrent use with AMOXYCILLIN AUSTELL may result in increased and prolonged blood concentrations of AMOXYCILLIN AUSTELL

AMOXYCILLIN AUSTELL may reduce the efficacy of oral contraceptives and patients should be warned accordingly.

The concomitant administration of allopurinol and ampicillin substantially increases the incidence of skin rashes in patients receiving both agents as compared to patients receiving ampicillin alone. It is not known whether this potentiation of ampicillin rashes is due to allopurinol or the hyperruricaemia present in these patients.

Tetracyclines and other bacteriostatic drugs may interfere with the bactericidal effects of AMOXYCILLIN AUSTELL

Interaction with Laboratory tests:

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

PREGNANCY AND LACTATION

Use in pregnancy:

The safety of AMOXYCILLIN AUSTELL in pregnancy has not been established.

Use in lactation:

AMOXYCILLIN AUSTELL is distributed into breast milk. Although significant problems in humans have not been documented, the use of AMOXYCILLIN AUSTELL by nursing mothers may lead to sensitization, diarrhoea, candidiasis and skin rash in the infant.

DOSAGE AND DIRECTIONS FOR USE

The total daily dose as below is administered in divided doses. The most common regimen is 8 hourly.

Oral administration

Treatment should be continued for 48 to 72 hours beyond the time that a clinical response has been obtained. It is recommended that at least 10 days treatment be given for any infection caused by beta-haemolytic streptococci to prevent the occurrence of acute rheumatic fever or glomerulonephritis.

The absorption of AMOXYCILLIN AUSTELL is not affected significantly when taken with food.

Adults and children over 40 kg

Total daily dosage of 750 mg to 3 g administered in divided doses. Maximum recommended dose: 6 g/day in divided doses.

Respiratory tract infections: 500 mg administered 8 hourly.

Lyme disease: 4 g/day in isolated erythema chronicum migrans and 6 g/day in the case of generalized manifestations, both for a minimum of 12 days.

Gonorrhoea: **3 g with 1 g probenecid**

Eradication of Helicobacter pylori: 750 mg – 1 g in combination treatment given 12 hourly for the eradication of established *H pylori* infection associated with duodenal ulceration for seven days.

Children under 40 kg

20-50 mg/kg/day in divided doses.

Maximum recommended dose: 150 mg/kg/day in divided doses.

Lyme disease: 20-50 mg/kg/day in isolated erythema chronicum migrans and 100 mg/kg/day in the case of generalized manifestations, both for a minimum of 12 days.

Elderly

No adjustment needed: as for adults unless there is evidence of severe renal impairment (see below).

Renal impairment:

Glomerular filtration rate	>30 ml/min:	No adjustment needed.
Glomerular filtration rate	10-30 ml/min:	Maximum 500 mg 12 hourly.
Glomerular filtration rate	<10 ml/min:	Maximum 500 mg daily.

In patients receiving peritoneal dialysis: Maximum 500 mg daily

SIDE EFFECTS

Side effects:

Frequent: Diarrhoea, nausea, vomiting, indigestion, abdominal pain, skin rashes, urticaria and erythema multiforme, vaginitis, abnormal taste, headache, dizziness, tiredness and hot flushes.

The following adverse reactions have been reported and may occur with AMOXYCILLIN AUSTELL

Hypersensitivity reactions

Less frequent: Skin rashes, pruritus and urticaria, serum sickness-like syndrome, erythema multiforme, cases of Stevens-Johnson syndrome, hypersensitivity vasculitis and bullous exfoliative dermatitis and toxic epidermal necrolysis have been reported. Whenever such reactions occur, AMOXYCILLIN AUSTELL should be discontinued. Serious and occasional fatal hypersensitivity (anaphylactic) reactions and angioneurotic oedema can occur with oral penicillin (see Warnings).

Interstitial nephritis.

Hepatic effects

Less frequent: Hepatitis and cholestatic jaundice have been reported. The events may be severe, and occur predominantly in adult or elderly patients. Signs and symptoms usually occur during or shortly after treatment, but in some cases may not become apparent until several weeks after treatment has ceased.

The hepatic effects are usually reversible. However, in extremely rare circumstances, death has been reported. These have almost always been cases associated with serious underlying disease or concomitant medication.

A moderate raise in Aspartate transaminase (AST) and/or Alanine transaminase (ALT) has been noted in patients treated with AMOXYCILLIN AUSTELL**,** but the significance of these findings is unknown.

Renal effects

Less frequent: Crystalluria has been reported.

Haematological effects

Less frequent: Haemolytic anaemia, reversible thrombocytopenia, thrombocytopenic purpura, eosinophilia, reversible leucopenia and agranulocytosis have been reported. These reactions are usually reversible on discontinuation of therapy and are believed to be hypersensitivity phenomena. A slight thrombocytosis was noted in less than 1 % of the

Patients treated with AMOXYCILLIN AUSTELL Prolongation of bleeding time and prothrombin time have also been reported. Appropriate monitoring should be undertaken when anticoagulants are prescribed concomitantly.

Nervous System

Less frequent: CNS effects have been seen. These include reversible hyperactivity, dizziness, headache and convulsions. Convulsions may occur with impaired renal function or in those receiving high doses.

Miscellaneous

Less frequent: Superficial tooth discolouration has been reported. It can usually be removed by brushing.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT

Overdosage with AMOXYCILLIN AUSTELL is usually asymptomatic. However, gastro-intestinal effects such as nausea, vomiting and diarrhoea may be evident and symptoms of water and electrolyte imbalance should be treated symptomatically.

Adequate fluid intake and urinary output must be maintained to minimise the possibility of crystalluria.

AMOXYCILLIN AUSTELL may be removed from the circulation by haemodialysis.

IDENTIFICATION

AMOXYCILLIN 250 mg AUSTELL:

White to creamish white in powder/plug form enclosed in red / buff hard gelatin capsule size ‘2’ with “AMOXY 250” printing in black ink.

AMOXYCILLIN 500 mg AUSTELL:

White to creamish white in powder/plug form enclosed in red / buff hard gelatin capsule of size ‘0’ with “AMOXY 500” printing in black.

PRESENTATION

AMOXYCILLIN 250 mg AUSTELL:

Blister pack (Clear PVC film, Aluminium foil) of 1 x 15, 1 x 21, 3 x 10, 2 x 15 and 10 x 10 capsules.

Container of 500 capsules packed in HDPE bags.

AMOXYCILLIN 500 mg AUSTELL:

Blister pack (Clear PVC film, Aluminium foil) of 1 x 15, 1 x 21, 3 x 10, 2 x 15 and 10 x 10 capsules.

Container of 500 capsules packed in HDPE bags.

STORAGE INSTRUCTIONS

Store below 25 °C. Protect from light.

Keep the blister pack in the carton until required for use.

Keep the container well closed.

KEEP OUT OF REACH OF CHILDREN.

REGISTRATION NUMBER:

AMOXYCILLIN 250 mg AUSTELL: 37/20.1.2/0003

AMOXYCILLIN 500 mg AUSTELL: 37/20.1.2/0004

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION

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