

Curam

Amoxicillin Sodium Ph Eur and Potassium Clavulanate Ph Eur, powder for injection, 500/100 mg and 1000/200 mg (as amoxicillin/clavulanic acid)

Presentation

Curam injection is a white or almost white crystalline powder aseptically filled into 20 ml glass vials. Curam Injection 500/100 mg (600 mg) contains sterile Amoxicillin Sodium Ph Eur equivalent to amoxicillin 500 mg and sterile Potassium Clavulanate Ph Eur equivalent to clavulanic acid 100 mg. Curam Injection 1000/200 mg (1.2 g) contains sterile Amoxicillin Sodium Ph Eur equivalent to amoxicillin 1000 mg and sterile Potassium Clavulanate Ph Eur equivalent to clavulanic acid 200 mg.

Uses

Actions

Curam injection is an antibiotic aseptically compounded for parenteral administration from amoxicillin sodium – a beta-lactam antibacterial penicillin and the potassium salt of clavulanic acid - a beta-lactamase inhibitor. Amoxicillin/clavulanic acid has a notably broad spectrum of activity against bacterial pathogens of clinical importance to general practice and secondary/tertiary care.

Pharmacotherapeutic group

J01CR02 – Combinations of penicillins including beta-lactamase inhibitors

Mechanism of action

Refer to [Antibiotic nature and mode of action](#).

Pharmacodynamic effects

Refer to [Antibiotic nature and mode of action](#).

Antibiotic class

Semi-synthetic penicillin compounded with a beta-lactamase inhibitor.

Antibiotic nature and mode of action

Amoxicillin is an aminopenicillin type broad spectrum antibiotic that possesses activity against many Gram-positive and Gram-negative aerobes and anaerobes. Amoxicillin is a bactericidal, cell-wall active agent that inhibits bacterial cell wall synthesis by binding to penicillin binding proteins and inhibits the cross-linking of bacterial peptidoglycan. However, amoxicillin is susceptible to degradation by beta-lactamases so its intrinsic spectrum of activity excludes bacteria producing these enzymes.

Clavulanic acid is a beta-lactam, structurally related to the penicillins. It possesses the ability to inactivate a wide range of beta-lactamase enzymes commonly found in micro-organisms resistant to penicillins and cephalosporins. In particular, it has good activity against the clinically important plasmid mediated beta-lactamases frequently responsible for transferred drug resistance. It is generally less effective against chromosomally-mediated type 1 beta-lactamases. When appropriately combined with amoxicillin, clavulanic acid inhibits the degradation of amoxicillin by beta-lactamase enzymes and effectively extends the antibacterial spectrum of amoxicillin to include many bacteria normally resistant to amoxicillin, other penicillins and cephalosporins.

Susceptibility data

The prevalence of resistance may vary geographically and temporally for selected species. Local resistance information is desirable, particularly when treating severe infections. The following information only provides approximate guidance on the probabilities that micro-organisms will be susceptible to amoxicillin/clavulanic acid.

Susceptible

Susceptible Gram-positive aerobes include: *Bacillus anthracis*[1]; *Corynebacterium* spp.; *Enterococcus faecalis*[1]; *Listeria monocytogenes*; *Nocardia asteroides*; *Staphylococcus aureus*[1]; Coagulase-negative staphylococci[1] (including *Staphylococcus epidermidis*[1]); *Streptococcus* spp.; *Streptococcus pneumoniae*; Group A streptococci (including *Streptococcus pyogenes*); Group B streptococci (including *Streptococcus agalactiae*); Viridans group streptococci.

Susceptible Gram-positive anaerobes include: *Clostridium* spp.; *Peptococcus* spp.; *Peptostreptococcus* spp.

Susceptible Gram-negative aerobes include: *Bordetella pertussis*; *Brucella* spp.; *Gardnerella vaginalis*; *Haemophilus influenzae*[1]; *Helicobacter pylori*; *Legionella* spp.; *Moraxella catarrhalis*[1]; *Neisseria gonorrhoeae*[1]; *Neisseria meningitidis*[1]; *Pasteurella multocida*; *Proteus mirabilis*[1]; *Proteus vulgaris*[1]; *Salmonella* spp.[1]; *Vibrio cholerae*; *Yersinia enterocolitica*[1].

Susceptible Gram-negative anaerobes include: *Bacteroides* spp.[1] (including *Bacteroides fragilis*); *Fusobacterium* spp.[1].

Other susceptible pathogens include: *Borrelia burgdorferi*; *Chlamydiae* spp.; *Leptospira icterohaemorrhagiae*; *Treponema pallidum*.

Intermediate

Partially susceptible Gram-positive aerobes include *Enterococcus faecium*[1].

Partially susceptible Gram-negative aerobes include: *Escherichia coli*[1]; *Klebsiella* spp.[1]; *Klebsiella pneumoniae*[1]; *Klebsiella oxytoca*[1]; *Salmonella hadar*[1]; *Salmonella typhimurium*[1]; *Shigella* spp.[1].

Notes:

[1] some members of these species of bacteria produce beta-lactamase, rendering them insensitive to amoxicillin alone.

Resistance

Although, amoxicillin/clavulanic acid may exhibit *in vitro* activity against methicillin/oxacillin resistant *Staphylococcus aureus* (MRSA) and coagulase-negative staphylococci (MRS) it is not clinically effective and isolates should therefore be considered resistant. Rare beta-lactamase negative, ampicillin resistant (BLNAR) strains of *H. influenzae* should also be considered resistant to amoxicillin/clavulanic acid despite the apparent *in vitro* susceptibility of some BLNAR strains.

Resistant Gram-positive aerobes include *Staphylococcus aureus* (MRSA) and Coagulase-negative staphylococci (MRS).

Resistant Gram-negative aerobes include: *Acinetobacter* spp.; *Citrobacter* spp.; *Enterobacter* spp.; *Haemophilus influenzae* (BLNAR); *Morganella morganii*; *Providencia* spp.; *Pseudomonas aeruginosa*; *Serratia* spp.; *Stenotrophomonas maltophilia*.

Other resistant pathogens include *Mycoplasma* spp. and *Rickettsia* spp.

Clinically relevant MIC ranges

According to the US National Committee on Clinical Laboratory Standards (NCCLS) in 2001, the following breakpoints have been defined for amoxicillin/clavulanic acid:

Enterobacteriaceae: NMT 8/4 mcg/ml susceptible, 16/8 mcg/ml intermediate, NLT 32/16 mcg/ml resistant;

Staphylococcus spp. and *Haemophilus* spp.: NMT 4/2 mcg/ml susceptible, NLT 8/4 mcg/ml resistant;
Streptococcus pneumoniae: NMT 2/1 mcg/ml susceptible, 4/2 mcg/ml intermediate, NLT 8/4 mcg/ml resistant;

Anaerobic bacteria: NMT 4/2 mcg/ml susceptible, 8/4 mcg/ml intermediate, NLT 16/8 mcg/ml resistant.

No NCCLS breakpoint is stipulated for *Vibrio cholerae*, however, ampicillin susceptibility (NMT 8 mcg/ml susceptible, 16 mcg/ml intermediate, NLT 32 mcg/ml resistant) is representative for amoxicillin/clavulanic acid.

For *Enterococcus* spp. penicillin and ampicillin susceptibility (NMT 8 mcg/ml susceptible, NLT 16 mcg/ml resistant) may be used to predict the susceptibility to amoxicillin/clavulanic acid.

Pharmacokinetics

Absorption

Amoxicillin and clavulanic acid are not lipophilic. The sodium salt of amoxicillin and the potassium salt of clavulanic acid fully dissociate in aqueous solution at physiological pH.

Mean pharmacokinetic parameters of amoxicillin and clavulanic acid were measured after administration of amoxicillin/clavulanic acid injection in two different doses to healthy volunteers.

Following a 600 mg bolus injection containing amoxicillin 500 mg and clavulanic acid 100 mg: the mean peak plasma concentrations were 32.2 mcg/ml for amoxicillin and 10.5 mcg/ml for clavulanic acid; the mean half lives were 1.07 hours for amoxicillin and 1.12 hours for clavulanic acid; the mean AUC values were 25.5 h.mg/l for amoxicillin and 9.2 h.mg/l for clavulanic acid; the urinary recovery rates in 0 to 6 hours were 66.5% for amoxicillin and 46.0% for clavulanic acid.

Following a 1200 mg bolus injection containing amoxicillin 1000 mg and clavulanic acid 200 mg: the mean peak plasma concentrations were 105.4 mcg/ml for amoxicillin and 28.5 mcg/ml for clavulanic acid; the mean half lives were 0.9 hours for amoxicillin and 0.9 hours for clavulanic acid; the mean AUC values were 76.3 h.mg/l for amoxicillin and 27.9 h.mg/l for clavulanic acid; the urinary recovery rates in 0 to 6 hours were 77.4% for amoxicillin and 63.8% for clavulanic acid.

Distribution

Intravenous administration of the prescribed dose of amoxicillin/clavulanic acid provides therapeutic levels of both constituents in the tissues and interstitial fluids including gall bladder, skin, abdominal, adipose and muscle tissues, synovial and peritoneal fluids, bile and pus. Neither amoxicillin nor clavulanic acid is highly bound to plasma proteins and studies demonstrate that about 13% to 25% of the total plasma drug content of each compound binds to protein. From animal studies there is no evidence to suggest that either compound accumulates in any organ.

Low levels of amoxicillin and residual levels of clavulanic acid are detectable in breast milk. With the exception of the risk of sensitisation associated with this excretion, there are no known detrimental effects for the breastfed infant.

While amoxicillin and clavulanic acid cross the placenta, no adverse effects have been observed in animal reproduction studies.

Biotransformation

Amoxicillin is partly metabolised with between 10 and 25% of the initial dose found in the urine as the inactive penicilloic acid. Clavulanic acid is extensively metabolised. The inactive metabolites 2,5-dihydro-4-(2-hydroxyethyl)-5-oxo-1H-pyrrole-3-carboxylic acid and 1-amino-4-hydroxy-butan-2-one are eliminated by urinary and biliary excretion. Approximately 27% of a parenterally administered dose of clavulanic acid is completely metabolised *in vivo* to carbon dioxide and eliminated in expired air and water.

Elimination

Renal excretion is the major elimination pathway for amoxicillin, while clavulanate is eliminated by both renal and non-renal mechanisms. Approximately 60 to 70% of the amoxicillin and approximately 40 to 65% of the clavulanic acid content are excreted unchanged in urine during the first 6 hours after administration of a single bolus intravenous injection of amoxicillin/clavulanic acid 600 mg or 1.2 g.

Indications

Short term treatment of common bacterial infections such as: upper respiratory tract infections (including ENT): e.g. tonsillitis, sinusitis, otitis media; lower respiratory tract infections: e.g. acute exacerbations of chronic bronchitis, lobar and broncho-pneumonia; genito-urinary tract infections: e.g. cystitis, urethritis, pyelonephritis, female genital infections; skin and soft tissue infections; bone and joint infections: e.g. osteomyelitis; other infections: e.g. septic abortion, puerperal sepsis, intra-abdominal sepsis, septicaemia, peritonitis, post-surgical infections.

Prophylaxis against infection which may be associated with major surgical procedures such as gastro-intestinal, pelvic, head and neck, cardiac, renal, joint replacement and biliary tract surgery.

Infections caused by amoxicillin susceptible organisms are amenable to amoxicillin/clavulanic acid treatment due to its amoxicillin content. Mixed infections caused by amoxicillin susceptible organisms in conjunction with amoxicillin/clavulanic acid susceptible beta-lactamase-producing organisms may therefore be treated by amoxicillin/clavulanic acid.

Dosage and administration

Dosage

Each 30 mg amoxicillin/clavulanic acid provides 5 mg clavulanic acid with 25 mg amoxicillin.

Children 0 to 3 months

30 mg/kg amoxicillin/clavulanic acid every 12 hours in infants <4 kg and 30 mg/kg amoxicillin/clavulanic acid every 8 hours in infants >4 kg.

Children 3 months to 12 years

Usually 30 mg/kg amoxicillin/clavulanic acid given 8 hourly. In more serious infections, increase the dosing frequency to 6 hourly intervals.

Adults and children 40 kg and over

Usually 1.2 g given 8 hourly. In more serious infections, increase the dosing frequency to 6 hourly intervals.

Surgical prophylaxis

Surgical prophylaxis with amoxicillin/clavulanic acid should aim to protect the patient for the period of risk of infection. Accordingly, procedures in adults lasting for less than 1 hour are successfully covered by 1.2 g amoxicillin/clavulanic acid intravenous given at induction of anaesthesia. Longer operations require subsequent doses of 1.2 g amoxicillin/clavulanic acid IV (up to 4 doses in 24 hours), and this regime can be continued for several days if the procedure has significantly increased the risk of infection. Clear clinical signs of infection at operation will require a normal course of IV or oral amoxicillin/clavulanic acid therapy post-operatively.

Renal impairment

Intravenous dosing adjustments are based on the maximum recommended level of amoxicillin.

Adults

Mild impairment (creatinine clearance >30 ml/min) requires no change in dosage. For moderate impairment (creatinine clearance 10 to 30 ml/min) give 1.2 g IV stat followed by 600 mg IV 12 hourly. For severe impairment (creatinine clearance <10 ml/min) give 1.2 g IV stat followed by 600 mg IV 24 hourly. Dialysis decreases serum concentrations of amoxicillin/clavulanic acid. An additional 600 mg IV dose may need to be supplemented at the end of dialysis

Children

Mild impairment (creatinine clearance >30 ml/min) requires no change in dosage. For moderate impairment (creatinine clearance 10 to 30 ml/min) give 30 mg/kg 12 hourly. For severe impairment

(creatinine clearance <10 ml/min) give 30 mg/kg every 24 hours. Dialysis decreases serum concentrations of amoxicillin/clavulanic acid. An additional 15 mg/kg may need to be supplemented at the end of dialysis, then 30 mg/kg/day.

Hepatic impairment

Dose with caution; monitor hepatic function at regular intervals for both adults and children. There are as yet insufficient data on which to base a dosage recommendation.

Elderly

No adjustment needed, dose as for adults. If there is evidence of renal impairment, dose should be adjusted as for renally impaired adults (see above).

Administration

Curam injection may be administered either by intravenous injection or by intermittent infusion. It is not suitable for intramuscular administration. Each 1.2 g vial contains approximately 1.0 mmol potassium and 3.1 mmol sodium.

To reconstitute the 600 mg vial, dissolve contents in Water for Injections BP 10 ml to give a final volume of 10.5 ml.

To reconstitute the 1.2 g vial, dissolve contents in Water for Injections BP 20 ml to give a final volume of 20.9 ml.

Curam injection should be given by slow intravenous injection over a period of 3 to 4 minutes and within 20 minutes of reconstitution. It may be injected directly into the vein or via a drip tube.

To prepare amoxicillin/clavulanate for intravenous infusion, add without delay 600 mg reconstituted solution to 50 ml infusion fluid or 1.2 g reconstituted solution to 100 ml infusion fluid (e.g. using a mini-bag or in-line burette). Infuse over 30 to 40 minutes and complete within the times stated.

Satisfactory antibiotic concentrations are retained at 5°C and at room temperature (25°C) in the recommended volumes of the following infusion fluids. If reconstituted and maintained at room temperature, infusions should be completed within the time stated.

Amoxicillin/clavulanic acid intravenous infusion is stable for 4 hours at 25°C when prepared in the following diluents: Water for Injections BP; Sodium Chloride Intravenous infusion BP (0.9% w/v); Sodium Lactate Intravenous infusion BP (M/6).

Amoxicillin/clavulanic acid intravenous infusion is stable for 3 hours at 25°C when prepared in the following diluents: Compound Sodium Chloride Injection BPC 1959 (Ringer's); Compound Sodium Lactate Intravenous Infusion BP (Ringer-Lactate: Hartmann's); Potassium Chloride and Sodium Chloride Intravenous Infusion BP.

For storage at 5°C, the reconstituted solution should be added to pre-refrigerated infusion bags which may be stored for up to 8 hours. Thereafter, the infusion should be administered immediately after reaching room temperature. Amoxicillin/clavulanic acid intravenous infusion is stable for 8 hours at 5°C when prepared in the following diluents: Water for Injections BP; Sodium Chloride Intravenous infusion BP (0.9% w/v).

Amoxicillin/clavulanic acid injection is less stable in infusions containing glucose, dextran or bicarbonate. Reconstituted solution should, therefore, not be added to such infusions but may be injected into the drip tubing over a period of 3 to 4 minutes.

Any residual antibiotic solutions should be discarded. Curam injection vials are not suitable for multi-dose use.

Amoxicillin/clavulanic acid injection should not be mixed with blood products, other proteinaceous fluids such as protein hydrolysates or with intravenous lipid emulsions.

Contraindications

Hypersensitivity to one of the constituents of the medicine.

Hypersensitivity to other beta-lactam antibiotics such as penicillins and cephalosporins.

Previous history of jaundice or hepatic dysfunction associated with amoxicillin/clavulanic acid.

Warnings and precautions

Before initiating amoxicillin/clavulanic acid therapy it is imperative to determine if the patient is hypersensitive to penicillins, cephalosporins or other allergens. Serious and occasionally fatal cases of hypersensitivity (anaphylactoid reactions) have been reported in patients receiving penicillin therapy. These reactions are more likely to occur in individuals with a history of penicillin hypersensitivity. If an allergic reaction occurs, discontinue amoxicillin/clavulanic acid immediately and replace with an appropriate alternative therapy. Serious anaphylactoid reactions require immediate emergency treatment with adrenaline or epinephrine. Oxygen, intravenous steroids and airway management including intubation may also be required. There is cross-resistance and cross-hypersensitivity with the other penicillins and sometimes also with cephalosporins.

Avoid amoxicillin/clavulanic acid if infectious mononucleosis is suspected since the incidence of a morbilliform rash has been associated with this condition following amoxicillin treatment.

In general, amoxicillin/clavulanic acid is well tolerated and possesses the characteristic low toxicity of the penicillin group of antibiotics. Periodic assessment of organ system functions, including renal, hepatic and haematopoietic function is advisable during prolonged therapy.

As with other broad spectrum antibiotics, superinfections due to non-susceptible micro-organisms may occur, particularly in patients with chronic disorders and/or impaired immune defence mechanisms. Mucocutaneous candida infections have been reported.

Prolonged use may also occasionally result in the overgrowth of non-susceptible organisms in the intestinal tract. If severe diarrhoea occurs, the diagnosis of pseudomembranous colitis should be considered. In this case, appropriate measures should be taken. Likewise, appropriate measures should be taken in the event of haemorrhagic colitis.

During high-dose therapy, maintaining adequate fluid intake and urinary output is necessary to minimise the risk of amoxicillin crystalluria. Bladder catheters should be checked regularly for patency since some medicines, including amoxicillin, may precipitate in the urine at room temperature if they are present in high concentrations.

In patients with moderate or severe renal impairment, the dosage should be adjusted according to the degree of impairment (refer to [Dosage and administration](#)).

Amoxicillin/clavulanic acid should be administered with caution to patients presenting hepatic dysfunction. Liver function should also be monitored regularly. Currently, there is insufficient information to make a dosage recommendation.

Prolongation of prothrombin time has been reported rarely. If anticoagulants are prescribed concomitantly, it may be necessary to monitor the patient.

If the parenteral administration of high doses is necessary, the sodium content must be considered for patients on a sodium-restricted diet.

Pregnancy and lactation

Use in pregnancy

Assigned Category B1 by the Australian Drug Evaluation Committee. This category includes medicines which have been taken by only a limited number of pregnant women and women of childbearing age, without an increase in the frequency of malformation or other direct or indirect harmful effects on the human foetus having been observed.

Reproduction studies in animals (mice and rats at doses up to 10 times the human dose) with orally and parenterally administered amoxicillin/clavulanic acid have shown no teratogenic effects. In a single study in women presenting preterm, premature rupture of the foetal membrane (pPROM), it was reported that prophylactic treatment with amoxicillin/clavulanic acid may be associated with an increased risk of necrotising enterocolitis in neonates. As with all medicines, use should be avoided in pregnancy, unless considered essential by the physician.

Use in lactation

Administration of amoxicillin/clavulanic acid injection is permitted during lactation. Apart from the risk of sensitisation, associated with the excretion of trace quantities in breast milk, there are no known effects potentially detrimental to the breastfed infant.

Effects on ability to drive and use machines

This medicine is presumed to be safe or unlikely to produce an effect.

Adverse effects

Data from large clinical trials were used to determine the incidence of very common to rare adverse effects. The incidences of all other adverse effects occurring below 1 in 10,000 were mainly determined from post-marketing data and reflect the reporting rate rather than the true incidence.

Common (incidence from 1 in 100 to 1 in 10)

Gastrointestinal tract

Lower gastro-intestinal irritation reactions such as diarrhoea and pruritus ani have been observed. These side-effects are generally of a mild and transitory nature.

Infections and infestations

Mucocutaneous candidiasis.

Skin and subcutaneous tissues

Allergic skin reactions occur significantly more often than with other penicillins and generally are maculopapular in nature. In a small majority of cases, "fifth day rash" (a morbilliform exanthema) is reported. This is dependent on the size of the dose and the patient's condition.

Uncommon (incidence from 1 in 1000 to 1 in 100)

Gastrointestinal tract

Indigestion, nausea and vomiting.

Hepatobiliary tract

A moderate rise in AST and/or ALT values has been noted in patients treated with beta-lactam antibiotics, but the significance of these findings is unknown.

Nervous system

Dizziness, headache.

Skin and subcutaneous tissues

Typical type I allergic reactions such as skin rash, pruritis, urticaria and purpura; angio-oedema and anaphylaxis can occur less frequently.

Rare (incidence from 1 in 10,000 to 1 in 1,000)**Blood and lymphatic system**

Abnormalities of the blood count, usually reversible such as leucopenia (including neutropenia) and thrombocytopenia.

Cardiovascular system

In rare cases, allergies can result in anaphylactic shock.

Skin and subcutaneous tissues

Erythema multiforme.

Vascular

Thrombophlebitis at the site of injection.

Very rare (incidence below 1 in 10,000)**Blood and lymphatic system**

Reversible agranulocytosis and haemolytic anaemia. Prolongation of bleeding and prothrombin time (refer to Warnings and precautions)

Gastrointestinal tract

Antibiotic-associated colitis (including pseudomembranous colitis and haemorrhagic colitis) occur, although at a lower incidence than orally administered amoxicillin/clavulanic acid.

Hepatobiliary tract

Hepatitis and cholestatic jaundice associated with amoxicillin/clavulanic acid and other beta-lactam antibiotics have been reported rarely. Hepatic effects occur predominantly in males and elderly patients, particularly those over 65 years of age. These side-effects are very rarely reported in children. The incidence appears to increase with treatment courses exceeding 14 days. Signs and symptoms usually occur during or shortly after treatment, but in some cases may not become apparent until several weeks after treatment cessation. Hepatic effects are usually transient and reversible. However, they may be severe and in extremely rare cases, a fatal outcome has been reported. These have mostly occurred in patients with a serious underlying disease, or patients taking potentially hepatotoxic agents in addition to amoxicillin/clavulanic acid.

Immune system disorders

Angioneurotic oedema, anaphylaxis, serum sickness-like syndrome, hypersensitivity vasculitis.

Nervous system

Reversible hyperactivity and convulsions. Convulsions may occur in patients with impaired renal function or in those receiving high doses.

Skin and subcutaneous tissues

Stevens-Johnson syndrome, toxic epidermal necrolysis, bullous exfoliative dermatitis, acute generalised exanthematous pustulosis. The appearance of skin hypersensitivity reactions warrants discontinuation of amoxicillin/clavulanic acid treatment.

Urogenital tract

Interstitial nephritis and crystalluria (refer to Overdosage)

Interactions

Other medicines

Amoxicillin/clavulanic acid injection must not be administered concomitantly with bacteriostatic agents, such as tetracyclines, macrolides and chloramphenicol, particularly in acute infections.

A number of agents can inhibit the renal tubular secretion of amoxicillin but not clavulanic acid. Inhibitors include probenecid, phenylbutazone, oxyphenbutazone and to a lesser extent, acetylsalicylic acid, indomethacin and sulfinpyrazone. As inhibition of renal tubular secretion prolongs the half-life and increases plasma levels of amoxicillin only, concomitant use of probenecid is not recommended.

Concomitant administration with aminoglycosides is possible to provide synergistic activity but refer to [Pharmaceutical precautions](#).

Concomitant use of amoxicillin and oral contraceptives is associated with the incidence of breakthrough bleeding and possibly reduced activity of the oral contraceptives. Amoxicillin/clavulanic acid may affect the gut flora, leading to lower oestrogen reabsorption and reduced efficacy of combined oral contraceptives.

Concomitant use of allopurinol during treatment with amoxicillin can increase the risk of allergic skin reactions. There are no data on the concomitant use of amoxicillin/clavulanic acid and allopurinol.

Amoxicillin can partially eradicate the gastrointestinal flora and therefore potentially increase the absorption of concomitantly administered digoxin.

Concurrent administration of amoxicillin/clavulanic acid and disulfiram is poorly tolerated. Therefore, amoxicillin/clavulanic acid injection should not be used concomitantly with disulfiram.

Laboratory diagnostic tests

Non-enzymatic methods for glucose determination in urine may give false-positive results.

Clavulanic acid may cause a non-specific binding of IgG and albumin by red cell membranes leading to a false positive Coombs test.

Overdosage

Drug dependency, addiction and recreational abuse have not been reported as problems.

Signs and symptoms

Convulsions can occur following parenteral administration of an overdose, particularly in patients with renal dysfunction. This is also possible after intrathecal administration. Gastrointestinal symptoms and disturbance of fluid and electrolyte balances may be evident.

Complications from amoxicillin crystalluria may present in high doses (refer to [Warnings and precautions](#)). Amoxicillin has been reported to precipitate in bladder catheters after intravenous administration of large doses. A regular check of patency should be maintained.

Management

Convulsions can be treated with diazepam. Amoxicillin and clavulanic acid can be removed from the circulation by haemodialysis. Treat other symptoms symptomatically. Gastrointestinal symptoms may be treated symptomatically by attending to the water and electrolyte balance. A prospective study of 51 paediatric patients at a poison control centre suggested that overdoses less than 250 mg/kg of amoxicillin are not associated with significant clinical symptoms and do not require gastric emptying.

Pharmaceutical precautions

Instructions for use/handling

Aseptic techniques in reconstitution and immediate use of the solution are recommended. Aseptic techniques are especially important if the solution is not used immediately. Any unused solution should be discarded.

Water for Injections BP is the normal diluent. Refer to Dosage and administration for the instructions for reconstitution. A transient pink colouration may develop during reconstitution. Reconstituted solutions are normally colourless or a pale straw colour. The stability of amoxicillin/clavulanic acid intravenous solutions is concentration dependent. In the event that the use of more concentrated solutions is required, the stability period should be adjusted accordingly.

Incompatibilities

Reconstituted solutions of amoxicillin/clavulanic acid must not be directly mixed with amino acid solutions, lipid emulsions, blood, protein hydrolysates and solutions containing glucose, dextran or bicarbonate (refer to Dosage and administration).

Amoxicillin inactivates aminoglycosides in solution so avoid mixing these agents during preparation and administration.

Individual vials may appear turbid when the reconstituted contents are mixed with lignocaine or lidocaine solutions. Turbid solutions should be discarded.

Shelf life

Unopened container:

36 months.

After container first opened:

Not applicable.

After dilution or reconstitution:

The product should be used immediately; within 15 minutes as a solution for injection and within 60 minutes as a solution for infusion.

Special precautions for storage

Store at or below 25°C. Protect from light.

Medicine classification

Prescription Medicine.

Package quantities

Packs of 10 vials.

Further information

List of excipients

Nil.

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Date of preparation

11 May 2009