1. PRODUCT NAME

Amoxiclav multichem, powder for injection 600 mg and 1.2 g

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Amoxiclav multichem 600 mg: each vial contains potassium clavulanate 119.15 mg equivalent to clavulanate 100 mg and amoxicillin sodium 530 mg equivalent to amoxicillin 500 mg.

Amoxiclav multichem 1.2 g: each vial contains potassium clavulanate 238.3 mg equivalent to clavulanate 200 mg and amoxicillin sodium 1.06 g equivalent to amoxicillin 1 g.

3. PHARMACEUTICAL FORM

Powder for injection. For reconstitution as an intravenous (IV) injection or infusion.

Glass vials containing sterile white to off-white powder.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Amoxiclav multichem should be used in accordance with local official antibiotic-prescribing guidelines and local susceptibility data.

Amoxiclav multichem is indicated for the 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

Amoxiclav multichem is indicated for 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.

Susceptibility to Amoxiclav multichem will vary with geography and time. Local susceptibility data should be consulted where available, and microbiological sampling and susceptibility testing performed where necessary.

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

4.2 Dose and method of administration

Dose

Children 0-3 months: 30 mg/kg* amoxicillin-clavulanate every 12 hours in infants < 4 kg and 30 mg/kg* amoxicillin-clavulanate every 8 hours in infants >4 kg

Children 3 months - 12 years: Usually 30 mg/kg* amoxicillin-clavulanate 8 hourly. In more serious infections, increase frequency to 6 hourly intervals.

Adults and children 40 kg and over: Usually 1.2 g 8 hourly. In more serious infections, increase frequency to 6 hourly intervals.

*Each 30 mg amoxicillin-clavulanate provides 5 mg clavulanic acid with 25 mg amoxicillin.

Dosage for surgical prophylaxis

Surgical prophylaxis with amoxicillin-clavulanate 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-clavulanate given at induction of anaesthesia. Longer operations require subsequent doses of 1.2 g amoxicillin-clavulanate 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-clavulanate therapy post-operatively.

Special populations

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 below).

Renal impairment

Adults

Dosing adjustments are based on the maximum recommended level of amoxicillin.

Method of administration	Mild Impairment (creatinine clearance >30 mL/min)	Moderate Impairment (creatinine clearance 10-30 mL/min)	Severe Impairment (creatinine clearance <10 mL/min)
Intravenous	No change in dosage	1.2 g IV stat followed by 600 mg IV 12 hourly	1.2 g IV stat followed by 600 mg IV 24 hourly. Dialysis decreases serum concentrations of amoxicillin-clavulanate.

			An additional 600 mg IV dose may need to be supplemented at the end of dialysis

Each 1.2 g vial of Amoxiclav multichem contains 1.0 mmoL of potassium and 2.7 mmoL of sodium.

Each 600 mg vial of Amoxiclav multichem contains 0.5 mmoL of potassium and 1.4 mmoL of sodium.

Children:
Dosing adjustments are based on the maximum recommended level of amoxicillin.

Method of administration	Mild Impairment (creatinine clearance >30 mL/min)	Moderate Impairment (creatinine clearance 10-30 mL/min)	Severe Impairment (creatinine clearance <10 mL/min)
Intravenous	No change in dosage	30 mg/kg 12 hourly	30 mg/kg every 24 hours Dialysis decreases serum concentrations of amoxicillin-clavulanate. 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.

Method of administration
Amoxiclav multichem intravenous may be administered either by intravenous injection or by intermittent infusion. It is not suitable for intramuscular administration.

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

IV infusion: Infuse Amoxiclav multichem over 30-40 minutes and complete within the times stated.

For instructions on reconstitution of the medicine before administration, see section 6.6

4.3 Contraindications

Amoxiclav multichem is contraindicated in patients with a previous history of amoxicillin-clavulanate -associated jaundice/hepatic dysfunction.

Amoxiclav multichem is a penicillin and should not be given to patients with a history of hypersensitivity to beta-lactam antibiotics (e.g. penicillins, cephalosporins).

Amoxiclav multichem is contraindicated in patients who have had previous experience of a major allergy or anaphylaxis to a cephalosporin or penicillin.

Hypersensitivity to any of the excipients.

4.4 Special warnings and precautions for use

Before initiating therapy with Amoxiclav multichem, careful enquiry should be made concerning previous hypersensitivity reactions to penicillins, cephalosporins, or other allergens.

Serious and occasionally fatal hypersensitivity reactions (including anaphylactoid and severe cutaneous adverse reactions) have been reported in patients on penicillin therapy. These reactions are more likely to occur in individuals with a history of penicillin hypersensitivity. If an allergic reaction occurs, amoxicillin-clavulanate Amoxiclav multichem therapy should be discontinued and appropriate alternative therapy instituted. Serious anaphylactoid reactions require immediate emergency treatment with adrenaline. Oxygen, intravenous steroids and airway management, including intubation may also be required.

Amoxicillin-clavulanate 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 also occasionally result in overgrowth of non-susceptible organisms.

Pseudomembranous colitis has been reported with the use of antibiotics and may range in severity from mild to life-threatening. Therefore, it is important to consider its diagnosis in patients who develop diarrhoea during or after antibiotic use. If prolonged or significant diarrhoea occurs or the patient experiences abdominal cramps, treatment should be discontinued immediately and the patient investigated further.

In general amoxicillin-clavulanate 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.

Abnormal prolongation of prothrombin time (increased INR) has been reported rarely in patients receiving amoxicillin and oral anticoagulants. Appropriate monitoring should be undertaken when anticoagulation treatment is prescribed concomitantly. Adjustment in the dose of oral anticoagulants may be necessary to maintain the desired level of anticoagulation.

Amoxiclav multichem should be used with caution in patients with evidence of hepatic dysfunction.

Amoxiclav multichem should be given with caution to patients who have experienced symptoms of allergy associated with a cephalosporin or penicillin.

Massive doses of Amoxiclav multichem can cause hypokalaemia and sometimes hypernatraemia. Use of a potassium-sparing diuretic may be helpful. In patients undergoing high-dose treatment for more than 5 days, electrolyte balance, blood counts and renal functions should be monitored.

Hepatic events have been reported predominantly in males and elderly patients and may be associated with prolonged treatment. These events have been very rarely reported in children.

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. These are usually reversible. Hepatic events may be severe and in extremely rare circumstances, deaths have been reported. These have almost always occurred in patients with serious underlying disease or taking concomitant medications known to have the potential for hepatic effects.

In patients with renal impairment, dosage should be adjusted according to the degree of impairment (see section 4.2).

Convulsions may occur in patients with impaired renal function or in those receiving high doses.

The occurrence at treatment initiation of a feverish generalised erythema associated with pustule may be a symptom of acute generalised exanthemous pustulosis (AEGP). This reaction requires Amoxiclav multichem discontinuation and is a contraindication to subsequent administration of amoxicillin.

The presence of clavulanic acid in Amoxiclav multichem may cause a non-specific binding of IgG and albumin by red cell membranes leading to a false positive Coombs test.

If the parenteral administration of high doses is necessary, the sodium content must be taken into account in patients on a sodium restricted diet.

In patients with reduced urine output crystalluria has been observed very rarely, predominantly with parenteral therapy. During 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 (see section 4.9).

4.5 Interaction with other medicines and other forms of interaction

Concomitant use of probenecid is not recommended. Probenecid decreases the renal tubular secretion of amoxicillin. Concomitant use with amoxicillin-clavulanate may result in increased and prolonged blood levels of amoxicillin, but not of clavulanic acid.

Concomitant use of allopurinol during treatment with amoxicillin can increase the likelihood of allergic skin reactions. There are no data on the concomitant use of amoxicillin-clavulanate and allopurinol.

In common with other antibiotics, amoxicillin-clavulanate may affect the gut flora, leading to lower oestrogen reabsorption and reduced efficacy of combined oral contraceptives.

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.

The presence of clavulanic acid in Amoxiclav multichem may cause a non-specific binding of IgG and albumin by red cell membranes leading to a false positive Coombs test.

In patients receiving mycophenolate mofetil, reduction in pre-dose concentration of the active metabolite mycophenolic acid of approximately 50% has been reported following commencement of oral amoxicillin plus clavulanic acid. The change in predose level may not accurately represent changes in overall MPA exposure.

The efficacy of oral contraceptives may be impaired under concomitant administration of Amoxiclav multichem, which may result in unwanted pregnancy. Women taking oral contraceptives should be aware of this and should be informed about alternative methods of contraception.

Penicillins reduce the excretion of methotrexate thereby increasing the risk of methotrexate toxicity.

Penicillins may interfere with:

- urinary glucose test
- Coomb's tests
- tests for urinary or serum proteins
- tests which use bacteria e.g. Guthrie test

4.6 Fertility, pregnancy and lactation

Fertility

No fertility data available.

Pregnancy

Reproduction studies in animals (mice and rats at doses up to 10 times the human dose) with orally and parentally administered amoxicillin-clavulanate have shown no teratogenic effects. In a single study in women with preterm, premature rupture of the foetal membrane (pPROM), it was reported that prophylactic treatment with amoxicillin-clavulanate 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.

Lactation

Amoxiclav multichem may be administered during the period of lactation. With the exception of the risk of sensitisation, associated with the excretion of trace quantities in breast milk, there are no known detrimental effects for the breastfed infant.

Trace quantities of penicillin can be detected in breast milk with the potential for hypersensitivity reactions (e.g. drug rashes) or gastrointestinal disorders (e.g. diarrhea or candidosis) in the breast-fed infant. Consequently, breastfeeding might have to be discontinued.

4.7 Effects on ability to drive and use machines

Adverse effects on the ability to drive or operate machinery have not been observed.

During treatment with Amoxiclav multichem undesirable effects may occur (e.g. allergic reactions, dizziness, convulsions) which may influence the ability to drive and use machines. Patients should be cautious when driving or operating machinery.

4.8 Undesirable effects

Data from large clinical trials was used to determine the frequency of very common to rare undesirable effects. The frequencies assigned to all other undesirable effects (i.e., those occurring at <1/10,000) were mainly determined using post-marketing data and refer to a reporting rate rather than a true frequency.

The following convention has been used for the classification of frequency:

very common ≥1/10

common ≥1/100 and <1/10

uncommon >1/1000 and <1/100

rare ≥1/10,000 and <1/1000

very rare <1/10,000

Infections and infestations:

Common: Mucocutaneous candidiasis

Blood and lymphatic system disorders:

Rare: Reversible leucopenia (including neutropenia) and thrombocytopenia

Very rare: Reversible agranulocytosis and haemolytic anaemia. Prolongation of bleeding time and prothrombin time

Immune system disorders:

Very rare: Angioneurotic oedema, anaphylaxis, serum sickness-like syndrome, hypersensitivity vasculitis

Nervous system disorders:

Uncommon: Dizziness, headache

Very rare: Aseptic meningitis, reversible hyperactivity and convulsions. Convulsions may occur in patients with impaired renal function or in those receiving high doses.

Vascular disorders:

Rare: Thrombophlebitis at the site of injection

Gastrointestinal disorders following intravenous administration:

Common: Diarrhoea

Uncommon: Nausea, vomiting, indigestion

Very rare: Antibiotic-associated colitis (including pseudomembranous colitis and haemorrhagic colitis) (see section 4.4) are less likely to occur after parenteral administration.

Hepatobiliary disorders:

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

Very rare: Hepatitis and cholestatic jaundice. These events have been noted with other penicillins and cephalosporins (see section 4.4).

Skin and subcutaneous tissue disorders:

Uncommon: Skin rash, pruritus, urticaria

Rare: Erythema multiforme

Very rare: Stevens-Johnson syndrome, toxic epidermal necrolysis, bullous exfoliative-dermatitis, acute generalised exanthemous pustulosis (AGEP), and drug reaction with eosinophilia and systematic symptoms (DRESS).

If any hypersensitivity dermatitis reaction occurs, treatment should be discontinued.

Renal and urinary disorders:

Very rare: Interstitial nephritis, crystalluria (see section 4.9).

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions https://nzphvc.otago.ac.nz/reporting/

4.9 Overdose

Gastrointestinal symptoms and disturbance of the fluid and electrolyte balances may be evident. They may be treated symptomatically, with attention to the water/electrolyte balance.

Amoxicillin crystalluria, in some cases leading to renal failure, has been observed (see section 4.4).

Amoxicillin has been reported to precipitate in bladder catheters after intravenous administration of large doses. A regular check of patency should be maintained.

Amoxicillin-clavulanate can be removed from the circulation by haemodialysis.

A prospective study of 51 paediatric patients at a poison control centre suggested that overdoses of less than 250 mg/kg of amoxicillin are not associated with significant clinical symptoms and do not require gastric emptying.

Drug abuse and dependence
Drug dependency, addiction and recreational abuse have not been reported as a problem with this compound.

For advice on the management of overdose please contact the National Poisons Centre on 0800 POISON (0800 764766).

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Amoxicillin and enzyme inhibitor. ATC code: JO1CR02.

Mechanism of action
Amoxiclav multichem (beta-lactam antibacterial penicillin co-formulated with a beta-lactamase inhibitor) is an antibiotic agent with a notably broad spectrum of activity against the commonly occurring bacterial pathogens in general practice and hospital. The beta-lactamase inhibitory action of clavulanate extends the spectrum of amoxicillin to embrace a wider range of organisms, including many resistant to other beta-lactam antibiotics.

Amoxicillin is a semisynthetic antibiotic with a broad spectrum of antibacterial activity against many gram-positive and gram-negative micro-organisms. Amoxicillin is, however susceptible to degradation by beta-lactamases and therefore the spectrum of activity of amoxicillin alone does not include organisms which produce these enzymes.

Clavulanic acid is a beta-lactam, structurally related to the penicillins, which 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.

The presence of clavulanic acid in Amoxiclav multichem formulations protects amoxicillin from degradation by beta-lactamase enzymes and effectively extends the antibacterial spectrum of amoxicillin to include many bacteria normally resistant to amoxicillin and other penicillins and cephalosporins. Thus Amoxiclav multichem possesses the distinctive properties of a broad spectrum antibiotic and a beta-lactamase inhibitor.

Pharmacodynamic effects

In the list below, organisms are categorised according to their in vitro susceptibility to amoxicillin-clavulanate.

In vitro susceptibility of micro-organisms to amoxicillin-clavulanate Where clinical efficacy of amoxicillin-clavulanate has been demonstrated in clinical trials this is indicated with an asterisk (*). Organisms that do not produce beta-lactamase are identified (with †). If an isolate is susceptible to amoxicillin, it can be considered susceptible to amoxicillin-clavulanate.
Commonly susceptible species
Gram-positive aerobes: *Bacillius anthracis* *Enterococcus faecalis* *Gardnerella vaginalis* *Listeria monocytogenes* *Nocardia asteroids* *Streptococcus pneumoniae*†* *Streptococcus pyogenes*†* *Streptococcus agalactiae*†* *Viridans group streptococcus†* *Streptococcus spp.* (other β-hemolytic)**†* *Staphylococcus aureus (methicillin susceptible)** *Staphylococcus saprophyticus* (methicillin susceptible) *Coagulase negative staphylococcus* (methicillin susceptible)
Gram-negative aerobes: *Bordetella pertussis* *Haemophilus influenzae**

Haemophilus parainfluenzae *Helicobacter pylori* *Moraxella catarrhalis** *Neisseria gonorrhoeae* *Pasteurella multocida* *Vibrio cholera*
Other: *Borrelia burgdorferi* *Leptospira ictterohaemorrhagiae* *Treponema pallidum*
Gram-positive anaerobes: *Clostridium spp.* *Peptococcus niger* *Peptostreptococcus magnus* *Peptostreptococcus micros* *Peptostreptococcus spp.*
Gram-negative anaerobes: *Bacteroides fragilis* *Bacteroides spp.* *Capnocytophaga spp.* *Eikenella corrodens* *Fusobacterium nucleatum* *Fusobacterium spp.* *Porphyromonas spp.* *Prevotella spp.*
Species for which acquired resistance may be a problem
Gram-negative aerobes: *Escherichia coli** *Klebsiella oxytoca* *Klebsiella pneumoniae** *Klebsiella spp.*

Proteus mirabilis *Proteus vulgaris* *Proteus spp.* *Salmonella spp.* *Shigella spp.*
Gram-positive aerobes: *Corynebacterium spp.* *Enterococcus faecium*
Inherently resistant organisms
Gram-negative aerobes: *Acinetobacter spp.* *Citrobacter freundii* *Enterobacter spp.* *Hafnia alvei* *Legionella pneumophila* *Morganella morganii* *Providencia spp.* *Pseudomonas spp.* *Serratia spp.* *Stenotrophomas maltophilia,* *Yersinia enterolitica*
Others: *Chlamydia pneumoniae* *Chlamydia psittaci* *Chlamydia spp.* *Coxiella burnetti* *Mycoplasma spp.*

5.2 Pharmacokinetic properties

Absorption

The two components of Amoxiclav multichem, amoxicillin and clavulanic acid are fully dissociated in aqueous solution at physiological pH. The pharmacokinetic results for studies in which amoxicillin-clavulanate was administered to groups of healthy volunteers as either

500/100 (600 mg) or 1000/200 mg (1.2 g) given as a bolus intravenous injection are presented below.

Amoxicillin component	Mean pharmacokinetic parameters				
	Amoxicillin dose	Mean peak serum conc (mcg/ml)	T½ (hours)	AUC hours (h.mg/L)	Urinary recovery 0 to 6 hours (%)
Amoxicillin-clavulanate 500/100 mg	500 mg	32.2	1.07	25.5	66.5
Amoxicillin-clavulanate 1000/200 mg	1 g	105.4	0.9	76.3	77.4

Clavulanic acid component	Mean pharmacokinetic parameters				
	Clavulanic acid dose	Mean peak serum conc (mcg/ml)	T½ (hours)	AUC hours (h.mg/L)	Urinary recovery 0 to 6 hours (%)
Amoxicillin-clavulanate 500/100 mg	100 mg	10.5	1.12	9.2	46.0
Amoxicillin-clavulanate 1000/200 mg	200 mg	28.5	0.9	27.9	63.8

Distribution

Following intravenous administration therapeutic concentrations of both amoxicillin and clavulanic acid may be detected in the tissues and interstitial fluid. Therapeutic concentrations of both medicines have been found in gall bladder, abdominal tissue, skin, fat, and muscle tissues; fluids found to have therapeutic levels include synovial and peritoneal fluids, bile and pus.

Neither amoxicillin nor clavulanic acid is highly protein bound, studies show that about 13-25% of total plasma drug content of each compound is bound to protein. From animal studies there is no evidence to suggest that either component accumulates in any organ.

Amoxicillin, like most penicillins, can be detected in breast milk. Trace quantities of clavulanate can also be detected 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.

Reproduction studies in animals have shown that both amoxicillin and clavulanic acid penetrate the placental barrier. However, no evidence of impaired fertility or harm to the foetus was detected.

Biotransformation

Amoxicillin is also partly excreted in the urine as the inactive penicilloic acid in quantities equivalent to 10-25% of the initial dose. Clavulanic acid is extensively metabolised in man to 2,5-dihydro-4-(2-hydroxyethyl)-5-oxo-1H-pyrrole-3-carboxylic acid and 1-amino-4-hydroxy-butan-2-one and eliminated in urine and faeces as carbon dioxide in expired air.

Elimination

As with other penicillins, the major route of elimination for amoxicillin is via the kidney, whereas for clavulanate it is by both renal and non-renal mechanisms. Approximately 60-70% of the amoxicillin and approximately 40-65% of the clavulanic acid are excreted unchanged in urine during the first 6 hours after administration of a single 500/125 mg tablet or a single 500/100 mg or a single 1000/200 mg bolus intravenous injection.

Concomitant use of probenecid delays amoxicillin excretion but does not delay renal excretion of clavulanic acid (see section 4.5).

5.3 Preclinical safety data

No further information of relevance is available.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Amoxiclav multichem powder for injection contains no excipients.

6.2 Incompatibilities

Amoxicillin-clavulanate should not be mixed with blood products, other proteinaceous fluids such as protein hydrolysates or with intravenous lipid emulsions. If prescribed concomitantly with an aminoglycoside, the antibiotics should not be mixed in the syringe, intravenous fluid container or giving set because of loss of activity of the aminoglycoside under these conditions.

Amoxicillin-clavulanate solutions should not be mixed with infusions containing glucose, dextran or bicarbonate.

6.3 Shelf life

3 years.

For the shelf-life of the reconstituted solution see section 6.6.

6.4 Special precautions for storage

Store below 30°C.

For storage conditions after reconstitution of the medicine, see section 6.3

6.5 Nature and contents of container

Glass vial with synthetic bromobutyl rubber stopper and Al-polypropylene flip-off cap.

Pack size of 10 vials.

Not all strengths may be marketed.

6.6 Special precautions for disposal and other handling

Preparation of intravenous injections

Vial	Water for Injection Diluent (mL)	Displacement Volume (mL)	Final Volume (mL)
600 mg (500/100 mg)	10	0.33	10.33
1.2 g (1000/200 mg)	20	0.97	20.97

Water for Injections B.P. is the normal diluent. A transient pink colouration may or may not develop during reconstitution. Reconstituted solutions are normally colourless or a pale yellow colour.

Amoxiclav multichem should be administered within 20 minutes of reconstitution.

Preparation of intravenous infusions and stability

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).

Intravenous infusions of amoxicillin-clavulanate may be given in a range of different intravenous fluids. 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.

Intravenous Infusion	Stability Period 25°C
Water for Injections B.P.	4 hr
Sodium Chloride Intravenous infusion B.P. (0.9% w/v)	4 hr
Sodium Lactate Intravenous infusion B.P. (M/6)	4 hr
Compound Sodium Chloride Injection B.P.C. 1959 (Ringer's)	3 hr
Compound Sodium Lactate Intravenous Infusion B.P. (Ringer-Lactate: Hartmann's)	3 hr
Potassium Chloride and Sodium Chloride Intravenous Infusion B.P.	3 hr

The stability of amoxicillin-clavulanate intravenous solutions is concentration dependent. In the event that the use of more concentrated solutions is required, the stability period should be adjusted accordingly.

For storage at 5°C, the reconstituted solutions of 1000/200 mg (1.2 g) and 500/100 mg (600 mg) may 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.

Intravenous Infusion	Stability Period 5°C
Water for Injections B.P.	8 hr
Sodium Chloride Intravenous infusion B.P. (0.9% w/v)	8 hr

Amoxicillin-clavulanate is less stable in infusions containing glucose, dextran or bicarbonate.

Reconstituted solutions of Amoxiclav multichem may be injected into the drip tubing over a period of 3-4 minutes.

Amoxiclav multichem vials are not suitable for multi-dose use.

Any residual antibiotic solutions should be discarded.

Any unused medicine should be disposed of in accordance with local requirements.

7. MEDICINE SCHEDULE

Prescription medicine.

8. SPONSOR

Multichem NZ Ltd
Private Bag 93527
Takapuna
AUCKLAND 0740
Telephone: (09) 488 0330

9. DATE OF FIRST APPROVAL

20 September 2006

10. DATE OF REVISION OF THE TEXT

25 March 2020

SUMMARY TABLE OF CHANGES

Section	CHANGE
4.8	Minor editorial changes and addition of aseptic meningitis as a new adverse reaction