NEW ZEALAND DATA SHEET
CURAM® (AMOXICILLIN/CLAVULANIC ACID) POWDER FOR INJECTION

1. PRODUCT NAME

Curam 500/100 powder for injection

Curam 1000/200 powder for injection

Curam 2000/200 powder for injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Curam 500/100 powder for injection: Each vial contains amoxicillin sodium equivalent to 500 mg amoxicillin and potassium clavulanate equivalent to 100 mg clavulanic acid. Each vial contains 0.5 mmoL (19.6 mg) of potassium and 1.4 mmoL (31.4 mg) of sodium.

Curam 1000/200 powder for injection: Each vial contains amoxicillin sodium equivalent to 1000 mg amoxicillin and potassium clavulanate equivalent to 200 mg clavulanic acid. Each vial contains 1.0 mmoL (39.3 mg) of potassium and 2.7 mmoL (62.9 mg) of sodium.

Curam 2000/200 powder for injection: Each vial contains amoxicillin sodium equivalent to 2000 mg amoxicillin and potassium clavulanate equivalent to 200 mg clavulanic acid. Each vial contains 1.0 mmoL (39.3 mg) of potassium and 5.5 mmoL (125.9 mg) of sodium.

Curam contains no excipients.

3. PHARMACEUTICAL FORM

Powder for injection.

Vials containing a sterile white to off-white powder.

4. CLINICAL PARTICULARS

4.1. THERAPEUTIC INDICATIONS

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

Curam is indicated for the short term treatment of common bacterial infections in adults and children 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

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

4.2. DOSE AND METHOD OF ADMINISTRATION

Dosage

Adults and children 40 kg and over: Usually 1.2 g 8 hourly. If higher doses are required, the dosage can be increased to 2000 mg/200 mg every 8 hours. In more serious infections, increase frequency to 6 hourly intervals.

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

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

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

Dosage for 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.

Method of administration

Curam may be administered either by intravenous injection or by intermittent infusion. It is not suitable for intramuscular administration.

IV injection: Curam 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 Curam over 30-40 minutes and complete within the times stated.

For instructions on reconstitution of the medicine before administration, see Section 6.6 Special precautions for disposal and other handling.

Dosage adjustment in:

- renal impairment

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

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

Each 1.2 g vial of Curam contains 1.0 mmoL of potassium and 2.7 mmoL of sodium (approx.).

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

	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/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 Section 4.2 Dose and method of administration – Renal impairment).

4.3. CONTRAINDICATIONS

In patients with a history of hypersensitivity to beta-lactams, e.g. penicillins and cephalosporins.

Curam is contraindicated in patients with a previous history of amoxicillin/clavulanic acid-associated jaundice/hepatic dysfunction.

4.4. SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Before initiating therapy with amoxicillin/clavulanic acid, 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/clavulanic acid therapy should be discontinued and appropriate alternative therapy instituted. Serious anaphylactic reactions require immediate emergency treatment with adrenaline. Oxygen, intravenous steroids and airway management, including intubation may also be required.

amoxicillin/clavulanic acid 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/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.

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

Amoxicillin/clavulanic acid should be used with caution in patients with evidence of hepatic dysfunction.

Use in hepatic impairment

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.

Use in renal impairment

In patients with renal impairment, dosage should be adjusted according to the degree of impairment (see Section 4.2 Dose and method of administration).

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 amoxicillin/clavulanic acid discontinuation and is a contraindication to subsequent administration of amoxicillin.

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 Overdose).

Use in the elderly

No data available.

Paediatric use

No data available.

Effects on laboratory tests

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

4.5. INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

Probenecid

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

Allopurinol

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/clavulanic acid and allopurinol.

Oral contraceptives

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

Oral anticoagulants

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.

Laboratory testings

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

Mycophenolate mofetil

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 pre- dose level may not accurately represent changes in overall MPA exposure.

4.6. FERTILITY, PREGNANCY AND LACTATION

Effects on fertility

There are no data on the effects of amoxicillin sodium/potassium clavulanate on fertility in humans.

Use in pregnancy

Reproduction studies in animals (mice and rats at doses up to 10 times the human dose) with orally and parentally administered amoxicillin/clavulanic acid 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/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

Amoxicillin/clavulanic acid 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.

4.7. EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

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

4.8. UNDESIRABLE EFFECTS

Tabulated list of adverse reactions

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 $\geq$ 1/10

common $\geq$ 1/100 and < 1/10

uncommon $\geq$ 1/1000 and < 1/100

rare $\geq$ 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: 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 Special warnings and precautions for use) are less likely to occur after parenteral administration.

In all populations, nausea is more often associated with higher oral dosages. If gastrointestinal reactions are evident, they may be reduced by taking amoxicillin/clavulanic acid at the start of a meal.

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 Special warnings and precautions for use)

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 systemic 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 Overdose)

Reporting suspected adverse effects

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 Special warnings and precautions for use).

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

Amoxicillin/clavulanic acid can be removed from the circulation by haemodialysis.

A prospective study of 51 paediatric patients at a poison control centre suggested that overdosages 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: Combinations of penicillins, incl. beta-lactamase inhibitors; ATC code: J01CR02.

Chemical structure

Amoxicillin sodium

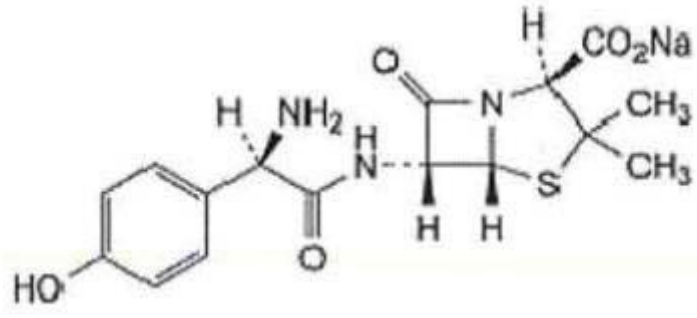

Figure 1: Chemical Structure of Amoxicillin sodium

Chemical name: sodium (2*S*,5*R*,6*R*)-6-[[(2R)-2-amino-2-(4-hydroxyphenyl)acetyl]amino]-3,3-dimethyl-7-oxo-4-thia-1 azabicyclo[3.2.0]heptane-2- carboxylate

Molecular formula: $C_{16}H_{18}N_3NaO_5S$

Molecular weight: 387.4

Potassium clavulanate

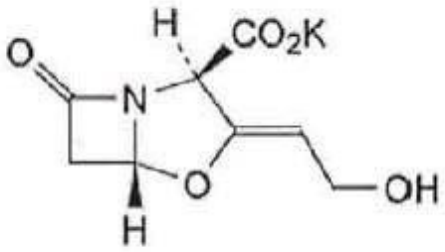

Figure 2: Chemical Structure of Potassium clavulanate

Chemical name: potassium (2*R*,3*Z*,5*R*)-3-(2- hydroxyethylidene)-7-oxo-4-oxa-1-azabicyclo[3.2.0]heptane-2-carboxylate

Molecular formula: $C_8H_8KNO_5$

Molecular weight: 237.3

CAS number

Amoxicillin sodium

34642-77-8

Potassium clavulanate

61177-45-5

Mechanism of action

Amoxicillin/clavulanic acid (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 Curam 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 amoxicillin/clavulanic acid 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 asteroides* *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 cholerae
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.

Clinical trials

No data available.

5.2. PHARMACOKINETIC PROPERTIES

Absorption

The two components of Curam, amoxicillin and clavulanic acid are fully dissociated in aqueous solution at physiological pH. The pharmacokinetic results for studies in which amoxicillin/clavulanic acid 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.

	Mean Pharmacokinetic Parameters				
		Mean Peak Serum Conc	T ½ hours	AUC hours	Urinary recovery

	Mean Pharmacokinetic Parameters				
Drug Administration		mcg/mL		h.mg/L	0 – 6 hrs%
Amoxicillin	Amox dose				
Amoxicillin/clavulanic acid 500/100 mg	500 mg	32.2	1.07	25.5	66.5
Amoxicillin/clavulanic acid 1000/200 mg	1 g	105.4	0.9	76.3	77.4

	Mean Pharmacokinetic Parameters				
		Mean Peak Serum Conc	T ½ hours	AUC hours	Urinary recovery
Drug Administration		mcg/mL		h.mg/L	0 – 6 hrs%
Clavulanic acid	CVA dose				
Amoxicillin/clavulanic acid 500/100 mg	100 mg	10.5	1.12	9.2	46.0
Amoxicillin/clavulanic acid 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 500/125mg 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 Interactions with other medicines and other forms of interactions).

5.3. PRECLINICAL SAFETY DATA

Genotoxicity

No data available.

Carcinogenicity

No data available.

6. PHARMACEUTICAL PARTICULARS

6.1. LIST OF EXCIPIENTS

Curam powder for injection contain no excipients. Refer to Section 2 Qualitative and quantitative composition.

6.2. INCOMPATIBILITIES

Curam powder for injection should not be mixed with blood products, other proteinaceous fluids such as protein hydrolysates or with intravenous lipid emulsions.

Amoxicillin/clavulanic acid 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 3-4 minutes.

For information on interactions with other medicines and other forms of interactions, refer to Section 4.5 Interactions with other medicines and other forms of interactions.

6.3. SHELF LIFE

Dry powder: 2 years.

Reconstituted solution: see Section 6.6 Special precautions for disposal and other handling.

6.4. SPECIAL PRECAUTIONS FOR STORAGE

Store below 25°C.

For storage conditions after reconstitution of the medicine, see Section 6.3 Shelf life.

6.5. NATURE AND CONTENTS OF CONTAINER

Curam 500 mg/100 mg, 1000 mg/200 mg and 2000 mg/200 mg powder for injection are presented in single dose, type II colourless glass vials with a normal capacity of 20 mL closed with rubber stopper and flip off cap.

Curam 500 mg/100 mg, 1000 mg/200 mg and 2000 mg/200 mg powder for injection are available in packs of 1, 5, 10, 20 or 50 vials.

Not all presentations may be distributed in New Zealand.

6.6. SPECIAL PRECAUTIONS FOR DISPOSAL AND OTHER HANDLING

Reconstitution of powder

500 mg/100 mg vial: To reconstitute dissolve in 10 mL of Water for Injections B.P. (Final volume 10.0 mL).

1000 mg/200 mg vial: To reconstitute dissolve in 20 mL of Water for Injections B.P. (Final volume 20.25 mL).

2000 mg/200 mg vial: To reconstitute dissolve in 20 mL of Water for injections B.P. (Final volume 21.6 mL).

After dissolution in water for injection, a transient pink colour may occur; the solution will become clear again rapidly afterwards.

The reconstituted solution for injection should be administered within 15 minutes if stored at 25^0C and the reconstituted solution for infusion within 60 minutes if stored at 25^0C.

Preparation of infusion

Add without delay the 500 mg/100 mg reconstituted solution to 50 mL of infusion fluid or the 1000 mg/200 mg and 2000 mg/200 mg reconstituted solutions to 100mL infusion fluid (e.g. using a minibag or in-line burette).

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 times stated.

Intravenous Infusion	**Stability Period 25°C**	**Storage Period 5°C**
Water for Injections B.P.	4 hours	8 hours
Sodium Chloride Intravenous infusion B.P. (0.9% w/v)	4 hours	8 hours
Sodium Lactate Intravenous Infusion (M/6)	4 hours	
Compound Sodium Chloride Injection (Ringer's Solution)	3 hours	
Compound Sodium Lactate Intravenous Infusion B.P. (Hartmann's solution; Ringer-Lactate solution)	3 hours	
Potassium Chloride and Sodium Intravenous Infusion B.P.	3 hours	

For storage at 5°C, the reconstituted solutions 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 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 3-4 minutes.

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

Curam vials are not suitable for multi-dose use. Product is for single use in one patient only. Discard any residue. Any unused medicine or waste material should be disposed of in accordance with local requirements.

7. MEDICINE SCHEDULE

Prescription Medicine

8. SPONSOR

Sandoz New Zealand Limited

12 Madden Street

Auckland 1010

New Zealand

Telephone: 0800 726 369

9. DATE OF FIRST APPROVAL

10/09/2020

10. DATE OF REVISION OF THE TEXT

20/03/2023

SUMMARY TABLE OF CHANGES

Section Changed	Summary of new information
8	Change in sponsor details