Approved Professional Information for Medicines for Human Use:

AUSTELL CO-AMOXICLAV 375/625 mg Tablets

SCHEDULING STATUS

S4

1. NAME OF THE MEDICINE

Austell Co-Amoxiclav 375 mg Tablets

Austell Co-Amoxiclav 625 mg Tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Austell Co-Amoxiclav 375 mg Tablets

Each tablet contains amoxicillin trihydrate equivalent to 250 mg amoxicillin and potassium clavulanate equivalent to 125 mg clavulanic acid.

Austell Co-Amoxiclav 625 mg Tablets

Each tablet contains amoxicillin trihydrate equivalent to 500 mg amoxicillin and potassium clavulanate equivalent to 125 mg clavulanic acid.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablets

Austell Co-Amoxiclav 375 mg Tablets

White to off-white oval shaped film coated tablets with ‘R375’ embossing on one side.

Austell Co-Amoxiclav 625 mg Tablets

White to off-white oval shaped film coated tablets with ‘R625’ embossing on one side.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Austell Co-Amoxiclav tablets are indicated for the treatment of infections caused by amoxicillin resistant organisms producing beta-lactamases sensitive to clavulanic acid:

Upper respiratory tract infections, such as sinusitis, recurrent otitis media, tonsillitis. Lower respiratory tract infections, such as bronchitis and bronchopneumonia. Genito-urinary tract infections, such as cystitis, urethritis, pyelonephritis. Skin and soft tissue infections.

Austell Co-Amoxiclav will also be effective in the treatment of infections caused by amoxicillin sensitive organisms at the appropriate amoxicillin dosage since in this situation the clavulanic acid component does not contribute to the therapeutic effect.

4.2 Posology and method of administration

Posology

Tablets should be taken immediately before a meal.

Dosages:

General Information: For infections caused by amoxicillin sensitive organisms the dosage is that approved for amoxicillin as the clavulanic acid component does not contribute to the therapeutic effect.

Adult:

The adult dose for Austell Co- Amoxiclav is one Austell Co- Amoxiclav 375 mg tablet every eight hours at the start of a meal. For more severe infections and infection of the respiratory tract, the dose should be one Austell Co- Amoxiclav 625 mg tablet every eight hours at the start of a meal.

Since Austell Co- Amoxiclav 375 mg and 625 mg tablets contain the same amount of clavulanic acid (125 mg as the potassium salt), two Austell Co- Amoxiclav 375 mg tablets are not equivalent to one Austell Co- Amoxiclav 625 mg tablet**.**

Therefore, two Austell Co- Amoxiclav 375 mg tablets should not be substituted for one Austell Co- Amoxiclav 625 mg tablet.

Special populations

Impaired renal function:

Both amoxicillin and clavulanic acid are excreted by the kidneys and the serum half-life of each increases in patients with renal failure. Therefore, the dose may need to be reduced or the interval extended. Dosage adjustments are based on the maximum recommended level of amoxicillin.

The following schedule is proposed:

Austell Co-Amoxiclav 375 mg and 625 mg Tablets:

Mild impairment (creatinine clearance greater than 30 ml/minute): no change in dosage.

Moderate impairment (creatinine clearance 10 to 30 ml/minute): 1 tablet every twelve hours.

Severe impairment (creatinine clearance less than 10 ml/minute): half a tablet every twelve hours.

Haemodialysis decreases serum concentrations of both amoxicillin and clavulanic acid and an additional dose should be administered at the end of dialysis.

Dosage Guide:

Amoxicillin-Sensitive Organisms

Product	**Upper Respiratory Tract Infection**	**Lower Respiratory Tract Infection**	**Urinary Tract infection**	**Skin and soft Tissue Infections**

Austell-Co Amoxiclav 375 mg Tablets	1 tablet 8 hourly	-	1 tablet 8 hourly	1 tablet 8 hourly
Austell-Co Amoxiclav 625 mg Tablets	1 tablet 8 hourly	1 tablet 8 hourly	1 tablet 8 hourly	1 tablet 8 hourly

Amoxicillin-Resistant Organisms

Product	Upper Respiratory Tract Infection (otitis media)	Lower Respiratory Tract Infection (bronchitis)	Urinary Tract infection	Skin and soft Tissue Infections
Austell-Co Amoxiclav 375 mg Tablets	-	-	1 tablet 8 hourly	1 tablet 8 hourly
Austell-Co Amoxiclav 625 mg Tablets	1 tablet 8 hourly	1 tablet 8 hourly	1 tablet 8 hourly	1 tablet 8 hourly

Paediatric population

The dose of Austell Co-Amoxiclav in children is 25-50 mg/kg/day of the 4 parts amoxicillin, 1 part clavulanic acid preparations (which corresponds to a daily dosage of the equivalent of 20-40 mg/kg of amoxicillin and 5–10 mg/kg of clavulanic acid) to be taken in divided doses every eight hours, at the start of a meal.

Method of administration

Austell Co-Amoxiclav is for oral administration.

4.3 Contraindications

- Hypersensitivity to the amoxicillin trihydrate and potassium clavulanate or to any of the excipients listed in section 6.1.
- Hypersensitivity to penicillins or to cephalosporins. Cross- sensitivity between penicillins and cephalosporins is well documented.

Austell Co-Amoxiclav is contra-indicated in patients with a previous history of amoxicillin/clavulanic –associated jaundice/hepatic dysfunction.

4.4 Special warnings and precautions for use

Serious and occasionally fatal hypersensitivity (anaphylactic) reactions have been reported in patients on penicillin therapy. Before initiating therapy with Austell Co-Amoxiclav 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, Austell Co-Amoxiclav 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.

Austell Co-Amoxiclav should be avoided if infectious mononucleosis is suspected since the occurrence of 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 Austell Co-Amoxiclav. Appropriate monitoring should be undertaken when anticoagulants are prescribed concurrently.

Transient hepatitis and cholestatic jaundice has been reported. Austell Co-Amoxiclav 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.

Periodic assessment of organ system functions, including renal, hepatic and haematopoietic function, is advisable during prolonged therapy. Since Austell Co-Amoxiclav 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.

Austell Co-Amoxiclav 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 (usually involving *Aerobacter, Pseudomonas or Candida*), 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 Austell Co-Amoxiclav. It should be used with care in patients with evidence of severe hepatic dysfunction.

Impaired renal function:
In patients with moderate or severe renal impairment Austell Co-Amoxiclav dosage should be adjusted. (See section 4.2)

Austell Co-Amoxiclav contains sodium

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

4.5 Interaction with other medicines and other forms of interaction

Probenecid decreases the renal tubular secretion of amoxicillin, but does not affect clavulanic acid excretion. Concurrent use with Austell Co-Amoxiclav may result in increased and prolonged blood levels of amoxicillin, but not of clavulanic acid.

Austell Co-Amoxiclav may reduce the efficacy of oral contraceptives and the 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 hyperuricaemia present in these patients.

Tetracyclines and other bacteriostatic drugs may interfere with the bactericidal effects of amoxicillin.

Interaction with Laboratory tests:

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

4.6 Fertility, pregnancy and lactation

Pregnancy

The safety of Austell Co-Amoxiclav in pregnancy has not been established.

Breastfeeding

Austell Co-Amoxiclav is distributed into breast milk. Although significant problems in humans have not been documented, the use of amoxicillin by breast feeding mothers may lead to sensitisation, diarrhoea, candidiasis and skin rash in the infant.

Amoxicillin is excreted in the milk; there is no data on the excretion of clavulanic acid in human milk. Therefore, caution should be exercised when Austell Co-Amoxiclav is administered to a nursing woman.

The use of Austell Co-Amoxiclav 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.

4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed. However, undesirable effects may occur (e.g. allergic reactions, dizziness, convulsions), which may influence the ability to drive and use machines (see section 4.8).

4.8 Undesirable effects

Tabulated list of adverse reactions

The table below shows all adverse drug reactions (ADRs) observed during clinical trials and postmarket spontaneous reports with amoxicillin trihydrate and potassium clavulanate.

System Organ Class	**Frequency**		
	Frequent	**Less Frequent**	**Not known**
Infections and infestations	Mucocutaneous candidosis		Overgrowth of non-susceptible organisms
Blood and lymphatic system disorders		Reversible leucopenia (including neutropenia), thrombocytopenia	Reversible agranulocytosis, haemolytic anaemia, prolongation of bleeding time and prothrombin time
Immune system disorders			Angioneurotic oedema, anaphylaxis, serum sickness-like syndrome, hypersensitivity vasculitis,

Nervous system disorders		Dizziness, headache	Reversible hyperactivity, convulsions, aeseptic meningitis
Cardiac disorders			Risk of kounis syndrome
Gastrointestinal disorders	Diarrhoea, nausea, vomiting	Indigestion	Antibiotic-associated colitis, drug-induced enterocolitis syndrome, pancreatitis acute, black hairy tongue
Hepatobiliary disorders		Rises in AST and/or ALT	Hepatitis, cholestatic jaundice
Skin and subcutaneous tissue disorders		Skin rash, pruritus, urticaria, erythema multiforme	Stevens-Johnson syndrome, toxic epidermal necrolysis, bullous exfoliative-dermatitis, acute generalised exanthemous pustulosis (AGEP),

			drug reaction with eosinophilia and systemicsymptoms (DRESS), linear IgA disease
Renal and urinary disorders			Interstitial nephritis, crystalluria (including acute renal injury)

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 to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website.

Suspected adverse reactions can also be reported directly to the HCR via medsafety@austell.co.za

4.9 Overdose

Signs and symptoms

Overdosage with amoxicillin 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.

Amoxicillin may be removed from circulation by haemodialysis. The molecular weight, degree of protein binding and pharmacokinetic profile of clavulanic acid together with information from a single patient with renal insufficiency all suggest that this compound may also be removed by haemodialysis.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Category and Class: A.20.1.2 Penicillins

Pharmacotherapeutic group: Combinations of penicillins, incl. beta-lactamase inhibitors

ATC Code: J01CR02

Austell Co- Amoxiclav tablets is a combination of amoxicillin and clavulanic acid.

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.*

Clavulanic acid has been shown *in vitro* to be an irreversible inhibitor of beta-lactamases produced by: *Staphylococcus aureus*, *Escherichia coli, Klebsiella pneumoniae, Proteus mirabilis, Proteus vulgaris, Haemophilus influenzae, Neisseria gonorrhoea* and *Bacteroides fragilis*. Clavulanic acid does not inactivate the chromosomally mediated (Sykes Type 1 Cephalosporinase) beta-lactamases produced by *Acinetobacter species, Citrobacter species, Enterobacter, Indole positive Proteus, Providencia species and Serratia marcescens*. *In vitro* the formulation showed synergism against amoxicillin-resistant organisms, with no evidence of antagonism and the activity was not reduced in the presence of serum. (*In vitro* activity does not necessarily imply *in vivo* efficacy.) The clavulanic acid component has very little bactericidal action.

5.2 Pharmacokinetic properties

Absorption

Amoxicillin is stable in the presence of acidic gastric secretions. Peak blood levels are achieved 1-2 hours after administration. There is a linear dose response in peak serum levels.

The pharmacokinetics of amoxicillin and clavulanic acid are closely allied and neither are adversely affected by the presence of food in the stomach.

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.

Elimination

The elimination half –life of amoxicillin is approximately 1 hour. Co-administration of probenecid has little effect on the excretion of the clavulanic acid component of the formulation. Small amounts of amoxicillin are also excreted in the faeces and bile.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Core Tablets

Microcrystalline cellulose

Colloidal silicon dioxide

Croscannellose Sodium

Magnesium Stearate

Film-coating

Hydroxypropyl methyl cellulose (HPMC- 15cps)

Dibutyl Phthalate

Purified Talc

Titanium Dioxide

Isopropyl alcohol

Methylene chloride

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

24 months

6.4 Special precautions for storage

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

Keep strip packs in carton until required for use.

This medicine does not require any special storage conditions.

KEEP OUT OF REACH OF CHILDREN

6.5 Nature and contents of container

Austell Co-Amoxiclav 375 mg Tablets:

Aluminium strip pack of 5X3's.

Austell Co-Amoxiclav 625 mg Tablets:

Aluminium strip pack of 5X3's.

6.6 Special precautions for disposal and other handling

No special requirements

7. HOLDER OF CERTIFICATE OF REGISTRATION

Austell Pharmaceuticals (Pty) Ltd

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8. REGISTRATION NUMBERS

Austell Co-Amoxiclav 375 mg Tablets: A39/20.1.2/0488

Austell Co-Amoxiclav 625 mg Tablets: A39/20.1.2/0489

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

11 August 2006

10. DATE OF REVISION OF THE TEXT

19 August 2026