Approved Professional Information for Medicines for Human Use:

STELLACELEN

SCHEDULING STATUS

S4

1. NAME OF THE MEDICINE

STELLACELEN 250 mg capsules

STELLACELEN 500 mg capsules

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

STELLACELEN 250 mg capsules

Each capsule contains amoxicillin trihydrate equivalent to 250 mg amoxicillin.

STELLACELEN 500 mg capsules

Each capsule contains amoxicillin trihydrate equivalent to 500 mg amoxicillin.

Sugar free.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Hard gelatin capsules (capsules).

STELLACELEN 250 mg capsules

Hard gelatin capsules size “2” maroon cap with yellow coloured body, printed with “AMOXY 250” in black ink on the body and caps in circular manner, containing white to off white granular powder.

STELLACELEN 500 mg capsules

Hard gelatin capsules size “0” maroon cap with yellow coloured body, printed with “AMOXY 500” in black ink on the body and caps in circular manner, containing white to off white granular powder.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Infections caused by susceptible, non-penicillinase-producing organisms including:

- Respiratory tract infections (upper and lower): sinusitis, pharyngitis, epiglottitis, acute and chronic bronchitis, and acute typical pneumonia.
- Otitis media.
- Urinary tract infections.
- Uncomplicated gonococcal infections.
- Meningitis (sensitivity tests must be performed).
- Gastrointestinal infections including salmonella and typhoid.
- Uncomplicated gastro enteritis and enteric fever.
- Miscellaneous: Skin and soft tissue infections, bacteraemia and as adjunct in the treatment of sepsis caused by gram-negative bacteria.

4.2 Posology and method of administration

Posology

Adults and children over 12 years

250 mg of amoxycillin three times a day; 500 mg of amoxycillin may be required in some severe infections.

In gonorrhoea the usual dose is the equivalent of 3 g given as a single dose, usually combined with 1 g probenecid.

Method of administration

For oral use.

4.3 Contraindications

- Hypersensitivity to amoxicillin or to any of the excipients of STELLACELEN listed in section 6.1.
- Patients known to be sensitive to penicillins or cephalosporins.
- Should not be given to patients with infectious mononucleosis, since they are especially susceptible to amoxycillin-induced skin rashes, patients with lymphatic leukaemia and patients with hyperuricaemia being treated with allopurinol, may be at increased risk of developing skin rashes.

4.4 Special warnings and precautions for use

Hypersensitivity reactions

Before initiating therapy with STELLACELEN, careful enquiry should be made concerning previous hypersensitivity reactions to penicillins, cephalosporins or other beta-lactam medicines.

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 and in atopic individuals. If an allergic reaction occurs, STELLACELEN therapy must be discontinued, and appropriate alternative therapy instituted.

Non-susceptible microorganisms

Amoxicillin is not suitable for the treatment of some types of infection unless the pathogen is already documented and known to be susceptible or there is a very high likelihood that the pathogen would be suitable for treatment with amoxicillin. This particularly applies when considering the treatment of patients with urinary tract infections and severe infections of the ear, nose, and throat.

Convulsions

Convulsions may occur in patients with impaired renal function or in those receiving high doses or in patients with predisposing factors (e.g. history of seizures, treated epilepsy or meningeal disorders.

Renal impairment

In patients with renal impairment, the dose should be adjusted according to the degree of impairment.

Skin reactions

The occurrence at the treatment initiation of a feverish generalised erythema associated with pustules may be a symptom of acute generalised exanthemous pustulosis (AGEP). This reaction requires STELLACELEN discontinuation and contra-indicates any subsequent administration

STELLACELEN 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.

Jarisch-Herxheimer reaction

The Jarisch-Herxheimer reaction has been seen following amoxicillin treatment of Lyme disease. It results directly from the bactericidal activity of amoxicillin on the causative bacteria of Lyme disease, the spirochaete *Borrelia burgdorferi*. Patients should be reassured that this is a common and usually self-limiting consequence of antibiotic treatment of Lyme disease.

Overgrowth of non-susceptible microorganisms

Prolonged use may occasionally result in overgrowth of non-susceptible organisms.

Antibiotic-associated colitis has been reported with nearly all antibacterial medicines and may range in severity from mild to life threatening. Therefore, it is important to consider this diagnosis in patients who present with diarrhoea during, or subsequent to, the administration of any antibiotics. Should antibiotic-associated colitis occur, STELLACELEN should immediately be discontinued, a medical practitioner consulted, and an appropriate therapy initiated. Anti-peristaltic medicines are contraindicated in this situation.

Prolonged therapy

Periodic assessment of organ system functions; including renal, hepatic and haematopoietic function is advisable during prolonged therapy. Elevated liver enzymes and changes in blood counts have been reported.

Anticoagulants

Prolongation of prothrombin time has been reported in patients receiving amoxicillin. Appropriate monitoring should be undertaken when anticoagulants are prescribed concomitantly. Adjustments in the dose of oral anticoagulants may be necessary to maintain the desired level of anticoagulation.

Crystalluria

In patients with reduced urine output, crystalluria has been observed, predominantly with parenteral therapy. During the administration of high doses of amoxicillin, it is advisable to maintain adequate fluid intake and urinary output in order to reduce the possibility of STELLACELEN crystalluria. In patients with bladder catheters, a regular check of patency should be maintained.

Interference with diagnostic tests

Elevated serum and urinary levels of amoxicillin are likely to affect certain laboratory tests. Due to the high urinary concentrations of amoxicillin, false positive readings are common with chemical methods.

It is recommended that when testing for the presence of glucose in urine during amoxicillin treatment, enzymatic glucose oxidase methods should be used.

The presence of amoxicillin may distort assay results for oestriol in pregnant women.

4.5 Interaction with other medicines and other forms of interaction

Probenecid

Concomitant use of probenecid is not recommended. Probenecid decreases the renal tubular secretion of amoxicillin. Concomitant use of probenecid may result in increased and prolonged blood levels of amoxicillin.

Allopurinol

Concurrent administration of allopurinol during treatment with amoxicillin can increase the likelihood of allergic skin reactions.

Tetracyclines

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

Oral anticoagulants

Oral anticoagulants and penicillin antibiotics have been widely used in practice without reports of interaction. However, in the literature there are 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. Moreover, adjustments in the dose of oral anticoagulants may be necessary.

Methotrexate

Penicillins may reduce the excretion of methotrexate causing a potential increase in toxicity.

Oral contraceptives

Amoxicillin may decrease the efficacy of oestrogen-containing oral contraceptives.

4.6 Fertility, pregnancy and lactation

Pregnancy

Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity. Limited data on the use of amoxicillin during pregnancy in humans do not indicate an

increased risk of congenital malformations. STELLACELEN may be used with caution in pregnancy.

Breastfeeding

Amoxicillin is excreted into breast milk in small quantities with the possible risk of sensitisation. Consequently, diarrhoea and fungus infection of the mucous membranes are possible in the breast-fed infant, so that breast-feeding might have to be discontinued. STELLACELEN should be used with caution during breastfeeding.

Fertility

There are no data on the effects of amoxicillin on fertility in humans. Reproductive studies in animals have shown no effects on fertility.

4.7 Effects on ability to drive and use machines

No studies on the effects of 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.

4.8 Undesirable effects

a) Summary of the safety profile

The most commonly reported adverse drug reactions (ADRs) are diarrhoea, nausea and skin rash.

b) Tabulated list of adverse reactions

The ADRs derived from clinical studies and post-marketing surveillance with amoxicillin, presented by MedDRA System Organ Class are listed below.

System Organ Class	**Frequency**		
	Frequent	**Less Frequent**	**Not known**
Infections and infestations		mucocutaneous candidiasis	

Blood and lymphatic system disorders		reversible leukopenia (including severe neutropenia or agranulocytosis), reversible thrombocytopenia and haemolytic anaemia, prolongation of bleeding time and prothrombin time (see section 4.4)	pancytopenia
Immune system disorders		severe allergic reactions, including angioneurotic oedema, anaphylaxis, serum sickness and hypersensitivity vasculitis (see section 4.4)	Jarisch-Herxheimer reaction (see section 4.4)
Psychiatric disorders			auditory and visual hallucinations
Nervous system disorders		hyperkinesia, dizziness and convulsions (see section 4.4).	

Gastrointestinal disorders	diarrhoea and nausea*	vomiting*, antibiotic associated colitis (including pseudomembraneous colitis and haemorrhagic colitis see section 4.4), black hairy tongue	
Hepatobiliary disorders		hepatitis and cholestatic jaundice, a moderate rise in AST and/or ALT.	
Skin and subcutaneous tissue disorders	skin rash*	urticaria and pruritus*	skin reactions such as erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis, bullous and exfoliative dermatitis, acute generalised exanthematous pustulosis (AGEP), and drug reaction with eosinophilia and systemic symptoms (DRESS), photosensitivity

Renal and urinary disorders		interstitial nephritis, crystalluria (see sections 4.4 and 4.9 Overdose)	

* The incidence of these AEs was reportedly derived from clinical studies involving a total of approximately 6000 adults and paediatric patients taking amoxicillin.

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 “6.04 Adverse Drug Reaction Reporting Form”, found online under SAHPRA’s publications: https://www.sahpra.org.za/Publications/Index/8

4.9 Overdose

Signs and symptoms of overdose

Gastrointestinal symptoms (such as nausea, vomiting and diarrhoea) and disturbance of the fluid and electrolyte balances may be evident. Amoxicillin crystalluria, in some cases leading to renal failure, has been observed. Convulsions may occur in patients with impaired renal function or in those receiving high doses.

Treatment of intoxication

Treatment is symptomatic and supportive. Amoxicillin can be removed from the circulation by haemodialysis.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Category and Class: A 20.1.2 Penicillins

Pharmacotherapeutic group: Penicillins with extended spectrum

ATC Code: J01CA04

Amoxycillin is a penicillinase-susceptible semisynthetic penicillin (beta-lactam antibiotic) that inhibits one or more enzymes in the biosynthetic pathway of bacterial peptidoglycan, which is an integral structural component of the bacterial cell wall. Inhibition of peptidoglycan synthesis leads to weakening of the cell wall, which is usually followed by cell lysis and death. It is bactericidal *in vitro* against a broad spectrum of gram-positive and gram-negative pathogens.

Inherently resistant organisms

Most species of the following organisms are resistant to STELLACELEN:

Gram-positive aerobes

Enterococcus faecium

Gram-negative aerobes

Acinetobacter spp.

Enterobacter spp.

Klebsiella spp.

Pseudomonas spp.

Serratia spp.

Gram-negative anaerobes

Indole-positive *Proteus* spp.

Bacteroides spp. (many strains of *Bacteroides fragilis* are resistant)

Others

Chlamydia spp.

Mycoplasma spp.

Legionella spp.

5.2 Pharmacokinetic properties

Absorption

Amoxicillin fully dissociates in aqueous solution at physiological pH. It is rapidly and well absorbed by the oral route of administration. Following oral administration, amoxicillin is approximately 70 % bioavailable. The time to peak plasma concentration (t_{max}) is approximately one hour.

Distribution

About 18 % of total plasma amoxicillin is bound to protein and the apparent volume of distribution is around 0,3 to 0,4 L/kg.

Following intravenous administration, amoxicillin has been found in gall bladder, abdominal tissue, skin, fat, muscle tissues, synovial and peritoneal fluids, bile and pus. Amoxicillin does not adequately distribute into the cerebrospinal fluid.

From animal studies there is reportedly no evidence for significant tissue retention of drug-derived material. Amoxicillin, like most penicillins, can be detected in breast milk (see section 4.6).

Amoxicillin has been shown to cross the placental barrier (see section 4.6).

Biotransformation

Amoxicillin is partly excreted in the urine as the inactive penicilloic acid in quantities equivalent to up to 10 to 25 % of the initial dose.

Elimination

The major route of elimination for amoxicillin is via the kidney.

Amoxicillin has a mean elimination half-life of approximately one hour and a mean total clearance of approximately 25 L/hour in healthy subjects. Approximately 60 to 70 % of the amoxicillin is excreted unchanged in urine during the first 6 hours after administration of a single 250 mg or 500 mg dose of amoxicillin. Various studies have found the urinary excretion to be 50 – 85 % for amoxicillin over a 24 hour period.

Concomitant use of probenecid delays amoxicillin excretion (see section 4.5).

Haemodialysis can be used for elimination of amoxicillin.

Linearity/non-linearity

In the range 250 to 3000 mg the bioavailability of amoxicillin is linear in proportion to dose (measured as C_{max} and AUC).

Age

The elimination half-life of amoxicillin is similar for children aged around 3 months to 2 years and older children and adults. For very young children (including preterm newborns) in the first week of life the interval of administration should not exceed twice daily administration due to immaturity of the renal pathway of elimination. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and it may be useful to monitor renal function.

Gender

Following oral administration of amoxicillin to healthy males and female subjects, gender has no significant impact on the pharmacokinetics of amoxicillin.

Renal impairment

The total serum clearance of amoxicillin decreases proportionately with decreasing renal function (see sections 4.2 and 4.4).

Hepatic impairment

Hepatically impaired patients should be dosed with caution and hepatic function monitored at regular intervals.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Capsule content

Sodium lauryl sulfate

Purified talc

Magnesium stearate

Capsule shell

Gelatin

Methylparaben

Propylparaben

Sodium lauryl sulfate

Titanium dioxide (E171)

Carmoisine (E122)

Sunset yellow (E110)

Indigo carmine (E132)

Iron oxide yellow (E172)

Printing ink

Shellac (E904)

Dehydrated alcohol (E1510)

Isopropyl alcohol

Butyl alcohol

Propylene glycol (E1520)

Black iron oxide (E172)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

LDPE Patient Ready Pack (PRP) Pouch: 24 months

HDPE Container with cap: 36 months

6.4 Special precautions for storage

Store tightly closed in a dry place at or below 30 °C. Protect from light.

6.5 Nature and contents of container

Patient Ready Pack (PRP)

15 capsules are packed in LDPE PRP pouch. 50 PRPs are packed in a printed carton, along with patient information leaflet (PIL).

Bulk/Jar Pack

500 capsules are packed in a HDPE jar, jar is sealed with aluminium seal and closed with cap. PIL is affixed on cap of jar.

Not all pack sizes may be marketed.

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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Parktown

JOHANNESBURG

2193

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Tel: 0860287835

8. REGISTRATION NUMBERS

STELLACELEN 250 mg: 55/20.1.2/0508.506

STELLACELEN 500 mg: 55/20.1.2/0509.507

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

06 December 2022

10. DATE OF REVISION OF THE TEXT