PROFESSIONAL INFORMATION SANDOZ CO-AMOXYCLAV S and SANDOZ CO-AMOXYCLAV SF

SCHEDULING STATUS: S4

PROPRIETARY NAME AND DOSAGE FORM:

Sandoz® Co-amoxyclav S (powder for suspension)

Sandoz® Co-amoxyclav SF (powder for suspension)

COMPOSITION:

Sandoz® Co-amoxyclav S: Each 5 mℓ of reconstituted suspension contains amoxycillin trihydrate equivalent to 125 mg amoxycillin and potassium clavulanate equivalent to 31,25 mg clavulanic acid.

Sandoz® Co-amoxyclav SF: Each 5 mℓ of the reconstituted suspension contains amoxycillin trihydrate equivalent to 250 mg amoxycillin and potassium clavulanate equivalent to 62,5 mg clavulanic acid.

Excipients:

Lemon flavouring (powdered), peach-apricot flavouring (powdered), citric acid anhydrous, trisodium citrate anhydrous, aspartame, talc, orange flavouring (powdered), guar galactomannan, silicon dioxide.

Sandoz® Co-amoxyclav S contains sugar (0,025 g guar galactomannan per 5 mℓ suspension) and artificial sweetener (0,0085 g aspartame per 5 mℓ suspension).

Sandoz® Co-amoxyclav SF contains sugar (0,025 g guar galactomannan per 5 mℓ suspension) and artificial sweetener (0,0085 g aspartame per 5 mℓ suspension).

PHARMACOLOGICAL CLASSIFICATION:

A 20.1.2 Penicillins

PHARMACOLOGICAL ACTION:

Pharmacodynamic properties:

SANDOZ CO-AMOXYCLAV is a combination preparation consisting of amoxycillin, a bactericidal for both Gram-negative and Gram-positive bacteria and clavulanic acid, an irreversible β-lactamase inhibitor.

Bacteriology:

Spectrum:

Potassium clavulanate is a potent progressive irreversible inhibitor of β-lactamases produced by: *Staphylococcus aureus*, *Escherichia coli*, *Klebsiella pneumoniae*, *Proteus mirabilis*, *Proteus vulgaris*, *Haemophilus influenzae, Neisseria gonorrhoeae* and *Bacteroides fragilis*. Clavulanic acid can permeate bacterial cell walls and can therefore inactivate both extracellular enzymes and those that are bound to the cell.

Potassium clavulanate does not inactivate the chromosomal mediated (Sykes Type 1 Cephalosporinase) β-lactamase produced by Acinobacter species, Citrobacter species, Enterobacter, indole positive Proteus, Providencia species and *Serratia marcescens*. Clavulanic acid consequently enhances the activity of penicillins against many resistant strains of bacteria.

Bacterial action:

The amoxycillin component of the formulation exerts a bactericidal action against many strains of Gram-positive and Gram-negative organisms. The clavulanic acid component has very little bactericidal action. It does, however, by inactivation of susceptible β-lactamases, protect amoxycillin from degradation by a large number of β-lactamase enzymes produced by penicillin resistant strains of organisms.

Pharmacokinetic properties:

Absorption:

The pharmacokinetics of amoxycillin and clavulanic acid are closely allied and neither are adversely affected by the presence of food in the stomach. Amoxycillin is resistant to inactivation by the acid of gastric secretion.

Excretion:

Probenecid retards renal excretion of amoxycillin and has no significant effect in the renal excretion of the clavulanic acid component of the formulation.

INDICATIONS:

Amoxycillin / clavulanic acid combinations are indicated for the treatment of infections caused by amoxycillin resistant organisms producing β-lactamases sensitive to clavulanic acid, namely:

- Upper respiratory tract infections, such as sinusitis, otitis media, tonsillitis.
- Lower respiratory tract infections, such as bronchitis, (caused by amoxycillin resistant β-lactamase producing *Escherichia coli*, *Haemophilus influenzae* and *Haemophilus para-influenzae*), pneumonia.
- Urinary tract infections.
- Skin and soft tissue infections.
- SANDOZ CO-AMOXYCLAV is also indicated in certain situations that require specified dosages like otitis media in children and bronchitis in adults caused by amoxycillin resistant β-lactamase producing *E.coli, Haemophilus influenzae* and *Haemophilus para-influenzae.*

Amoxycillin / clavulanic acid combinations will also be effective in the treatment of infections caused by amoxycillin sensitive organisms at the appropriate amoxycillin dosage, since in this situation the clavulanic acid component does not contribute to the therapeutic effect.

CONTRAINDICATIONS:

SANDOZ CO-AMOXYCLAV should not be administered to patients allergic to penicillins and cephalosporins. It is contra-indicated in patients with a previous history of amoxycillin/clavulanic acid - associated jaundice or hepatic dysfunction. Safety in pregnancy has not been established. Safety in children under 6 months of age has not been established.

WARNINGS AND SPECIAL PRECAUTIONS:

Serious and occasionally fatal hypersensitivity (anaphylactoid) reactions have been reported in patients on penicillin therapy. 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.

Before initiating therapy with any penicillin, careful inquiry should be made concerning previous hypersensitivity reactions to penicillins, cephalosporins or other allergens. If an allergic reaction occurs, SANDOZ CO-AMOXYCLAV should be discontinued and appropriate therapy instituted: adrenaline, corticosteroids and antihistamines.

Transient hepatitis and cholestatic jaundice have been reported. SANDOZ CO-AMOXYCLAV should be used with caution in patients with evidence of hepatic dysfunction.

SANDOZ CO-AMOXYCLAV should be discontinued if a skin rash occurs. It should preferably not be given to patients with infectious mononucleosis since they are especially susceptible to amoxycillin - induced skin rashes; patients with lymphatic leukaemia or possibly HIV infection may also be at increased risk of developing skin rashes. (Periodic assessment of organ system functions, including renal, hepatic and haematopoietic function, is advisable during prolonged therapy). Since SANDOZ CO-AMOXYCLAV contains amoxycillin, an aminopenicillin, it is not the treatment of choice in patients presenting with sore throat or pharyngitis because of the possibility of underlying cause of infectious mononucleosis.

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.

Changes in liver function tests have been observed in some patients receiving SANDOZ CO-AMOXYCLAV. It should be used with care in patients with evidence of severe hepatic dysfunction.

In patients with moderate to severe renal impairment SANDOZ CO-AMOXYCLAV dosage should be adjusted.

Amoxycillin is excreted in the breast milk, there is no data on the excretion of clavulanic acid in human milk. Therefore, caution should be exercised when SANDOZ CO-AMOXYCLAV is administered to a nursing woman.

SANDOZ CO-AMOXYCLAV contains guar galatomannan. Patients with the rare hereditary conditions of galactose intolerance e.g. galactosaemia, or glucose-galactose malabsorption, should not take SANDOZ CO-AMOXYCLAV. Guar galactomannan contains galactose, which may have an effect on the glycaemic control of patients with diabetes.

SANDOZ CO-AMOXYCLAV contains aspartame, which is metabolised to phenylalanine and should be used with caution in patients with phenylketonuria.

INTERACTIONS:

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

The concurrent administration of allopurinol and amoxycillin substantially increases the incidence of rashes in patients receiving both agents as compared to patients receiving amoxycillin alone. It is not known whether this potentiation of amoxycillin rashes is due to allopurinol or the hyperuricaemia present

in these patients. There is no data on SANDOZ CO-AMOXYCLAV and allopurinol administered concurrently.

No information is available about the concurrent use of SANDOZ CO-AMOXYCLAV and alcohol. However, the ingestion of alcohol whilst being treated with some other β-lactam antibiotics has precipitated a disulfiram like reaction in some patients. Therefore, the ingestion of alcohol should be avoided during and for several days after treatment with SANDOZ CO-AMOXYCLAV.

Following administration of ampicillin to pregnant women a transient decrease in plasma concentration of total conjugate oestriol, oestriolglucuronide, conjugated oestrone and oestradiol has been noted. This effect may also occur with amoxycillin and therefore SANDOZ CO-AMOXYCLAV may reduce the efficacy of oral contraceptives and patients should be warned accordingly.

The use of this antibiotic 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.

The possibility of a prolonged bleeding time following oral treatment with a broad spectrum medicine like amoxycillin should be born in mind in patients receiving anticoagulants.

DOSAGE AND DIRECTIONS FOR USE:

To be taken immediately before meals.

Directions for reconstituting into suspension:

Fill the bottle with potable water to just below the ring mark and shake well at once. Then add water to the ring mark and shake vigorously again.

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

Adults:

Antibacterial

Pneumonia and other severe infections:

SANDOZ CO-AMOXYCLAV SF *10 mℓ (2 medicine measures) every 8 hours*

Other infections:

SANDOZ CO-AMOXYCLAV SF *10 mℓ (2 medicine measures) every 12 hours or 5 mℓ every 8 hours*

NB: Adults who have difficulty swallowing may be given the SANDOZ CO-AMOXYCLAV SF or S in place of the 500 mg tablet

Children:

Antibacterial

Dosage is based on the amoxycillin component.

Neonates and infants up to 12 weeks (3 months) of age:

Oral 15 mg of amoxycillin per kg every 12 hours.

Infants 3 months of age and older, and children up to 40 kg of body weight:

Acute otitis media, pneumonia, sinusitis and other severe infections:

13,3 mg of amoxycillin per kg of body weight.

Less severe infections:

6,7 mg per kg of body weight every 8 hours.

Children weighing more than 40 kg of body weight, see adult dose.

Impaired renal function:

Patients with impaired renal function generally do not require dosage adjustment unless the renal impairment is severe. Adults and adolescents with severely impaired renal function may receive 500 mg or 250 mg with the dosing interval increased as follows:

Impairment	*Creatinine clearance (mℓ/minute)*	*Dosing interval (hours)*
Mild	**30 / 0,5**	**8**
Moderate	**10 - 30 /0,17 - 0,5**	**12**
Severe	**< 10 /< 0,17**	**24**

Patients on haemodialysis should receive 500 mg or 250 mg every 24 hours, depending on the severity of the infection. They should receive an additional dose both during and at the end of dialysis. Haemodialysis decreases serum concentrations of both amoxycillin and clavulanic, and an additional dose should be administered at the end of dialysis.

SIDE EFFECTS:

The most frequently reported adverse effects following oral administration are diarrhoea, nausea, vomiting, indigestion, abdominal pain, skin rashes, urticaria and erythema multiforme, vaginitis, abnormal taste, headache, dizziness, tiredness and hot flushes.
The incidence and severity of adverse effects, particularly nausea and diarrhoea, can be minimised by administering the agent at the start of a meal.

Hepatitis and cholestatic jaundice have been reported, and the clavulanic acid component has been implicated. 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. The hepatic events are usually reversible. However, in extremely rare circumstances, death has been reported. These have almost always been cases associated with serious underlying disease or concomitant medication.

A moderate rise in aspartate transaminase and or alanine transaminase has been noted in patients treated with SANDOZ CO-AMOXYCLAV.

The following adverse reactions have been reported for ampicillin class antibiotics and may occur with SANDOZ CO-AMOXYCLAV:

Gastrointestinal: gastritis, stomatitis, glossitis, black "hairy tongue", enterocolitis and pseudomembranous colitis. If gastrointestinal reactions are evident, they may be reduced by taking SANDOZ CO-AMOXYCLAV at the start of a meal.

Hypersensitivity: Skin rashes, urticaria, erythema multiforme (including the Stevens-Johnson syndrome), and less frequently exfoliative dermatitis and toxic epidermal necrolysis, have been reported. Whenever such reactions occur, SANDOZ CO-AMOXYCLAV should be discontinued. Serious and occasional fatal hypersensitivity (anaphylactic) reactions and angioneurotic oedema can occur with oral penicillin (see "WARNINGS AND SPECIAL PRECAUTIONS"). Nephropathy and interstitial nephritis can occur less frequently

Haematopoietic and lymphatic: Anaemia, thrombocytopenia, thrombocytopenic purpura, eosinophilia, leucopenia and agranulocytosis have been reported during therapy with penicillins. These reactions are usually reversible on discontinuation of therapy and are believed to be hypersensitivity phenomena.
A slight thrombocytosis was noted in less than 1 % of the patients treated with SANDOZ CO-AMOXYCLAV. Prolongation of bleeding time and prothrombin time and defective platelet function have also been reported less frequently. Appropriate monitoring should be undertaken when anticoagulants are prescribed concomitantly.

Central nervous system effects:

CNS effects have been seen less frequently. These include reversible hyperactivity, dizziness, headache and convulsions. Convulsions may occur with impaired renal functions or in those receiving high doses.

Some patients with syphillis and other spirochaete infection may experience a Jarisch-Herxheimer reaction shortly after starting treatment. Symptoms include fever, chills, headache and reaction at the

site of the lesions. The reaction can be dangerous in cardiovascular syphillis or where there is a serious risk of increased local damage such as with optic atrophy.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:

Nausea, vomiting and diarrhoea may occur with overdosing. Treatment is symptomatic. Amoxycillin 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.

IDENTIFICATION:

Sandoz® Co-amoxyclav S: Off-white powder, and off-white ready-to-use suspension (reconstituted suspension) with a fruity odour, characteristic of the active ingredient, and a bitter sweet taste.

Sandoz® Co-amoxyclav SF: Off-white powder, and off-white ready-to-use suspension (reconstituted suspension) with a fruity odour, characteristic of the active ingredient, and a bitter sweet taste.

PRESENTATION:

60 mℓ or 100 mℓ amber glass bottles with screw closure, containing powder for reconstitution to suspension.

STORAGE INSTRUCTIONS:

Dry powder: Store at or below 25 °C, protect from light and moisture.

Reconstituted suspension: Store in a refrigerator (2 to 8 °C) and use within 7 days.

The product will only retain its stability if stored in the refrigerator.

KEEP OUT OF THE REACH OF CHILDREN.

REGISTRATION NUMBER:

Sandoz® Co-amoxyclav S: 34/20.1.2/0394

Sandoz® Co-amoxyclav SF: 34/20.1.2/0395

PROFESSIONAL INFORMATION SANDOZ CO-AMOXYCLAV S and SANDOZ CO-AMOXYCLAV SF

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION:

Sandoz SA (Pty) Ltd[1]

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1619

South Africa

DATE OF PUBLICATION OF THIS PROFESSIONAL INFORMATION:

Date of registration (Sandoz Co-Amoxyclav S): 5 September 2003

Date of registration (Sandoz Co-Amoxyclav SF): 27 July 2003

Date of most recent approval of professional information: 19 November 2015

Additional countries registration details:

Country	*Product name*	*Scheduling status (or Category of distribution)*	*Registration number*
Botswana	Sandoz® Co-amoxyclav S (60 mℓ)	S2	BOT1302473A
	Sandoz® Co-amoxyclav S (100 mℓ)	S2	BOT1302473B
	Sandoz® Co-amoxyclav S (120 mℓ)	S2	BOT1302473C
	Sandoz® Co-amoxyclav SF (60 mℓ)	S2	BOT1302474A
	Sandoz® Co-amoxyclav SF (100 mℓ)	S2	BOT1302474B
	Sandoz® Co-amoxyclav SF (120 mℓ)	S2	BOT1302474C
Namibia	Sandoz® Co-Amoxiclav S	NS2	05/20.1.2/0322
	Sandoz® Co-Amoxiclav SF	NS2	05/20.1.2/0321
Zambia	Sandoz® Co-Amoxiclav S	POM	039/014
	Sandoz® Co-Amoxiclav SF	POM	039/015
Zimbabwe	Sandoz® Co-Amoxiclav S	P.P	2014/7.1.2/4907

Sandoz® Co-Amoxiclav SF	P.P	2014/7.1.2/4891

ATC code: J01CR02 – Beta-Lactam Antibacterials, Penicillins

Pharmacological classification: 7.1.2 Beta-lactamase Resistant Penicillins

(Zimbabwe)

Name and address of manufacturer:

Sandoz GmbH

Biochemiestraβe 10

A-6250 Kundl

Austria

[1] Company Reg. No.: 1990/001979/07