Professional Information

SCHEDULING STATUS

S4

1. NAME OF THE MEDICINE

BETAMOX® 250 capsules

BETAMOX® 500 capsules

BETAMOX® S 125 mg/5 ml suspension

BETAMOX® SF 250 mg/5 ml suspension

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

BETAMOX® 250

Each capsule contains amoxycillin trihydrate equivalent to 250 mg amoxycillin.

Sugar free

BETAMOX® 500

Each capsules contains amoxycillin trihydrate equivalent to 500 mg amoxycillin.

Sugar free

BETAMOX® S

Each 5 ml of the reconstituted suspension contains amoxycillin trihydrate equivalent to 125 mg amoxycillin.

Contains sugar: Sucrose (Pharmagrade sugar) 3,031 g

BETAMOX® SF

Each 5 ml of the reconstituted suspension contains amoxycillin trihydrate equivalent to 250 mg amoxycillin.

Contains sugar: Sucrose (Castor sugar) 2,873 g

For full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

BETAMOX® 250

Capsules

Size 2 capsule, with an opaque maroon cap and an opaque flesh coloured body. The name BETAMOX 250 mg is imprinted on the flesh body, and the Be-Tabs logo on the maroon cap.

BETAMOX® 500

Capsules

Size 0 capsule, with an opaque maroon cap and an opaque flesh coloured body. The name BETAMOX 500 mg is imprinted on the flesh body, and the Be-Tabs logo on the maroon cap.

BETAMOX® S

Suspension

Free-flowing, slightly pink powder, purple suspension when reconstituted.

BETAMOX® SF

Suspension

Free-flowing, slightly pink powder, purple suspension when reconstituted.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

BETAMOX® is indicated for the treatment of ~~i~~nfections caused by susceptible, non-penicillinase-producing organisms including:

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

4.2 Posology and method of administration

The average adult dose for **BETAMOX®** is 750 mg to 1,5 g per day.

General dosages

Adults: 250 mg (1 X 250 mg capsule or 5 ml of 250 mg/5 ml suspension) three times a day.

Children 2 to 10 years: 125 mg (5 ml of 125 mg/5 ml suspension) three times a day.

Children 6 months to 2 years: 125 mg (5 ml of 125 mg/5 ml suspension) three times a day.

Infants 0 to 6 months: 62,5 mg (2,5 ml of 125 mg/5 ml suspension) three times a day.

To reconstitute 75 ml suspension, add 44 ml of water, invert the bottle and shake well until all the powder is dispersed.
To reconstitute 100 ml suspension, add 57 ml of water, invert the bottle and shake well until all the powder is dispersed.

Specific dosages

Gastrointestinal tract infections:

Adults: 1 to 2 g daily for 4 to 5 days.

Acute typhoid fever:

Adults: 4 g daily for 14 days.

Children: 100 mg/kg daily for 21 days.

Gonorrhoea:

Adults: 2 to 3 g stat.

4.3 Contraindications

- Hypersensitivity to penicillins (e.g. amoxycillin) or to another beta-lactam agent (e.g. cephalosporin, carbapenem or monobactam), or to any of the excipients listed in section 6.1.
- Patients with infectious mononucleosis since they are especially susceptible to amoxycillin induced skin rashes.
- Patients with lymphatic leukaemia.

- Patients with hyperuricaemia being treated with allopurinol may also be at an increased risk of developing skin rashes.

4.4 Special warnings and precautions for use

Hypersensitivity reactions

Before initiating therapy with any penicillin, careful enquiry should be made concerning previous hypersensitivity reactions to penicillins, cephalosporins, or other beta-lactam agents (see section 4.3 and 4.8).

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 persons with a history of hypersensitivity to beta-lactam antibiotics and in atopic individuals. If an allergic reaction occurs, amoxycillin therapy must be discontinued and appropriate alternative therapy instituted.

Non-susceptible microorganisms

BETAMOX® 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 **BETAMOX®**. 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 (see section 4.8).

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 pustula may be a symptom of acute generalised exanthemous pustulosis (AGEP, see section 4.8). This reaction requires **BETAMOX®** discontinuation and contraindicates any subsequent administration.

BETAMOX® 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 amoxycillin.

Jarisch-Herxheimer reaction

BETAMOX® should be used with caution in patients with syphilis, as the Jarisch-Herxheimer reaction may occur (see section 4.8).

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 agents and may range in severity from mild to life-threatening (see section 4.8). 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, **BETAMOX®** should immediately be discontinued, a doctor consulted and an appropriate therapy initiated. Anti-peristaltic medicinal products 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 (see section 4.8).

Anticoagulants

Prolongation of prothrombin time has been reported rarely in patients receiving amoxycillin. 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 (see sections 4.5 and 4.8).

Crystalluria

In patients with reduced urine output, crystalluria has been observed very rarely, predominantly with parenteral therapy. During the administration of high doses of amoxycillin, it is advisable to maintain adequate fluid intake and urinary output in order to reduce the possibility of amoxycillin crystalluria. In patients with bladder catheters, a regular check of patency should be maintained (see section 4.8).

Interference with diagnostic tests

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

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

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

Excipients

BETAMOX® suspension contains sucrose which may have an effect on the glycaemic control of patients with diabetes mellitus and may be harmful to the teeth when intended for chronic use, e.g. for two weeks or more. Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption orsucrase-isomaltase insufficiency should not take **BETAMOX®** suspension.

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 **BETAMOX®**. Concomitant use of probenecid may result in increased and prolonged blood levels of **BETAMOX®**.

Allopurinol

Concurrent administration of allopurinol during treatment with **BETAMOX®** can increase the likelihood of allergic skin reactions.

Tetracyclines

Tetracyclines and other bacteriostatic medicines may interfere with the bactericidal effects of **BETAMOX®**.

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 amoxycillin. If co-administration is necessary, the prothrombin time or international normalised ratio should be carefully monitored with the addition or withdrawal of **BETAMOX®**. Moreover, adjustments in the dose of oral anticoagulants may be necessary (see sections 4.4 and 4.8).

Methotrexate

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

Oral contraceptives

BETAMOX® may decrease the efficacy of oestrogen-containing oral contraceptives.

Other

BETAMOX® may affect the absorption of other medicines, due to its effect on the gastrointestinal flora.

4.6 Fertility, pregnancy and lactation

Pregnancy

Reported animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity. Limited data on the use of amoxycillin during pregnancy in humans do not indicate an increased risk of congenital malformations.

Breastfeeding

Amoxycillin 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 breastfeeding might have to be discontinued.

Fertility

There are no reported data on the effects of amoxycillin on fertility in humans. Reported reproductive studies in animals have shown no effects on fertility.

4.7 Effects on the ability to drive and use machines

BETAMOX® may cause an allergic reaction, dizziness or convulsions, which may influence the ability to drive and use machines (see section 4.8).

4.8 Undesirable effects

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

Body System	**Frequent**	**Less Frequent**	**Frequency Unknown**

Infections and infestations		Mucocutaneous candidiasis	
Blood and lymphatic system disorders		Reversible leucopenia (including severe neutropenia and agranulocytosis) Reversible thrombocytopenia Haemolytic anaemia Prolongation of bleeding time and prothrombin time (see section 4.4)	
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)
Nervous system disorders		Hyperkinesia Dizziness	

		Convulsions (see section 4.4)	
Gastrointestinal disorders	Diarrhoea Nausea	Vomiting Antibiotic-associated colitis (including pseudomembranous colitis and haemorrhagic colitis see section 4.4) Black hairy tongue Superficial tooth discolouration[#]	
Hepatobiliary disorders		Hepatitis Cholestatic jaundice A moderate rise in AST and/or ALT	
Skin and subcutaneous tissue disorders	Skin rash	Urticaria Pruritus Erythema multiforme Stevens-Johnson syndrome Toxic epidermal necrolysis Bullous and exfoliative dermatitis	

		Acute generalised exanthematous pustulosis (AGEP) (see section 4.4) Drug reaction with eosinophilia and systemic symptoms (DRESS)	
Renal and urinary tract disorders		Interstitial nephritis Crystalluria (see section 4.4)	
[#]For suspensions: Superficial tooth discolouration has been reported in children. Good oral hygiene may help to prevent tooth discolouration as it can usually be removed by brushing.			

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. Health care providers 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

See section 4.4 and 4.8.

Treatment is symptomatic and supportive.

Should a serious anaphylactic reaction occur, **BETAMOX®** should be discontinued and the patient treated with adrenalin, corticosteroids and antihistamines.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Category and class: A 20.1.2 Penicillins

Pharmacotherapeutic group: penicillins with extended spectrum; ATC code J01CA04.

Mechanism of action

Amoxycillin is a semisynthetic, broad-spectrum, beta-lactam penicillin antibiotic that inhibits one or more enzymes (often referred to as penicillin-binding proteins, PBPs) 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.

Amoxycillin is susceptible to degradation by beta-lactamases produced by resistant bacteria and therefore the spectrum of activity of amoxycillin alone does not include organisms which produce these enzymes.

Amoxycillin exhibits *in vitro* bactericidal activity against a wide range of Gram-negative and Gram-positive organisms including: (*in vitro* sensitivity does not necessarily imply *in vivo* efficacy):

- Gram-positive bacteria: **Staphylococcus aureus* (Penicillin-sensitive)*, Streptococcus pyogenes,* **Streptococcus viridans*, **Streptococcus faecalis*, **Streptococcus pneumonia*, *Corynebacterium species, *Clostridium species, **Bacillus anthracis*

- Gram-negative bacteria: *Neisseria gonorrhoeae*, *Neisseria meningitides*, *Haemophilus influenzae* (except type B-strains causing meningitis in children), *Bordetella pertussis*, **Escherichia coli*, *Salmonella typhi*, Salmonella species, Shigella species, Brucella species, Proteus mirabilis

Amoxycillin may also have some effect against the following organisms:

*Bacteroides fragilis**, *Proteus mirabilis** and Nocardia*.

*Sensitivity tests must be formed.

Most species of the following organisms are resistant to amoxycillin:

Enterobacter, Pseudomonas, Klebsiella, Serratia, Acinetobacter and indole-positive Proteus.

5.2 Pharmacokinetic properties

Absorption

Amoxycillin is well absorbed orally. After oral administration, there is no significant difference between the peak serum levels in fasting and non-fasting subjects. The presence of food does not interfere with the absorption of amoxycillin and may therefore, be taken with meals.

Distribution

There is a linear/dose response in peak serum levels after oral administration.

There is insufficient evidence at present to show that amoxycillin penetrates into the cerebro spinal fluid in therapeutic quantities and it should, therefore, not be used in the treatment of cerebro spinal infections.

Biotransformation

Amoxycillin 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

Approximately 60 % of an oral dose of amoxycillin is excreted unchanged in the active form into the urine within six hours.

Age

The elimination half-life of amoxycillin 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 amoxycillin to healthy males and female subjects, gender has no significant impact on the pharmacokinetics of amoxycillin.

Renal impairment

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

Hepatic impairment

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

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on studies of safety pharmacology, repeated dose toxicity, genotoxicity and toxicity to reproduction and development.

Carcinogenicity studies have not been conducted with amoxycillin.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

BETAMOX® 250 and BETAMOX® 500

Capsule contents:

Magnesium stearate, purified talc and sodium lauryl sulphate

Capsule shell:

Flesh opaque body: erythrosine (CI no. 45430), gelatin, quinoline yellow (CI no. 47005), titanium dioxide (CI no. 77891)

Maroon cap: brilliant blue (CI no. 42090), erythrosine (CI no. 45430), gelatin, sunset yellow (CI no. 15985), titanium dioxide (CI no. 77891)

Capsule printing ink:

Yellow printing ink: butyl alcohol, dehydrated alcohol, isopropyl alcohol, propylene glycol, shellac, strong ammonia solution, yellow iron oxide (CI no. 77492)

Black printing ink: absolute alcohol, black iron oxide (CI no. 77499), butyl alcohol, isopropyl alcohol, propylene glycol, shellac

BETAMOX® S

Hexacol grape A B 100 concentration (grape colour): hexacol brilliant blue FCF supra (CI no. 42090) and hexacol carmoisine (red) (CI no. 14720), sodium acid citrate, sodium carboxymethyl cellulose, sodium citrate, sucrose (pharmagrade sugar), Trusil grape concord (F1526) (grape flavour)

BETAMOX® SF

Castor sugar (starch free), Hexacol grape A B 100 concentration (grape colour): hexacol brilliant blue FCF supra (CI no. 42090) and hexacol carmoisine (red) (CI no. 14720), sodium acid citrate, sodium carboxymethyl cellulose, sodium citrate, sucrose (pharmagrade sugar), Trusil grape concord (F1526) (grape flavour)

6.2 Incompatibilities

Not applicable

6.3 Shelf life

BETAMOX® 250

36 months

15 months (for Patient Ready Packs)

BETAMOX® 500

48 months (for the 500's pack size packed in amber PVC bottle)

60 months (for 15's and 100's packed a in white polypropylene securitainer and 500's packed in an opaque white HDPE jar with a white HDPE screw on cap)

15 months (Patient Ready Packs)

BETAMOX® S

60 months (for powder packed in a glass bottle)

24 months (for powder packed in a HDPE bottle)

BETAMOX® SF

60 months (for powder packed in a glass bottle)

6.4 Special precautions for storage

Store at or below 25 °C, in a dry place.

The reconstituted suspension must be used within 14 days if stored in a refrigerator or within 7 days if stored below 25 °C.

6.5 Nature and contents of container

BETAMOX® 250

Canisters containing 15, 100 or 500 X 250 mg amoxycillin capsules.

Patient ready packs of different pack sizes.

BETAMOX® 500

Canisters containing 15, 100 or 500 X 500 mg amoxycillin capsules.

Patient ready packs of different pack sizes.

BETAMOX® S

Bottles containing powder for reconstitution to 75 ml and to 100 ml of 125 mg / 5 ml suspension.

BETAMOX® SF

Bottles containing powder for reconstitution to 100 ml of 250 mg/5 ml suspension.

6.6 Special precautions for disposal and other handling

Return all unused medicine to your pharmacist.

Do not dispose of unused medicine in drains or sewerage systems (e.g. toilets).

7. HOLDER OF CERTIFICATE OF REGISTRATION

Ranbaxy Pharmaceuticals (Pty) Ltd

14 Lautre Road

Stormill Ext. 1

Roodepoort 1724

South Africa

8. REGISTRATION NUMBER(S)

BETAMOX® 250

Y/20.1.2/127 (S.A.)

Botswana: S2 BOT0500765

Namibia: NS2 04/20.1.2/1625

BETAMOX® 500

Y/20.1.2/128 (S.A.)

Namibia: NS2 04/20.1.2/1626

BETAMOX® S

Y/20.1.2/129 (S.A.)

Botswana: S2 BOT0500763

Namibia: NS2 04/20.1.2/1623

BETAMOX® SF

Y/20.1.2/130 (S.A.)

Botswana: S2 BOT0500764

Namibia: NS2 04/20.1.2/1624

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

May 1991

10. DATE OF REVISION OF THE TEXT

30 April 2021