Professional Information for MYMOX 250 and MYMOX 500

SCHEDULING STATUS

S4

1. NAME OF THE MEDICINE

MYMOX 250 capsules, hard

MYMOX 500 capsules, hard

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

MYMOX 250: Each capsule contains amoxicillin trihydrate equivalent to 250 mg amoxicillin.

MYMOX 500: Each capsule contains amoxicillin trihydrate equivalent to 500 mg amoxicillin.

Sugar free.

Excipients with known effect:

MYMOX 250 and MYMOX 500 capsules contain tartrazine.

MYMOX 500 capsules contain sunset yellow.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Capsules, hard.

MYMOX 250: Size “2” hard gelatine capsules with grey cap and yellow body, containing white to off-white granular powder.

MYMOX 500: Size “0” hard gelatine capsule with golden yellow cap and golden yellow body, containing white granular powder.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

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

- Upper respiratory tract infections.
- Lower respiratory tract infections.
- Otitis media.
- Typhoid fever.
- Upper urinary tract infections.
- Lower urinary tract infections.
- Skin and soft tissue infections.
- Gastrointestinal tract infections.
- Gonorrhoea.
- Non-specific urethritis.

4.2 Posology and method of administration

Posology

Adults

- The average adult dose for MYMOX is 750 mg – 1,5 g/day, but in serious infections up to 6 g daily has been administered.
- 1 x 250 mg capsule three times a day.

Special populations

Paediatric population:

MYMOX capsules are not suitable for breaking to accommodate lower dosing requirements.

Different formulations should be considered for paediatric population.

Renal impairment:

Patients with renal insufficiency may possibly require a reduced dose.

During treatment with high doses of MYMOX, an adequate fluid intake and urinary output must be maintained (see section 4.4).

In-dwelling catheters should be checked regularly for potency since at room temperature high urinary concentration of MYMOX may precipitate out of solution (see section 4.4).

Specific dosages

Indications	**Daily dosages (adults)**	**Duration**
Gastrointestinal tract infections	1 – 2 g	4 – 5 days
Acute typhoid fever	4 g	14 days
Gonorrhoea	2 – 3 g	Stat

Method of administration

MYMOX is for oral use.

Swallow with water without opening the capsule.

The presence of food does not interfere with the absorption of MYMOX. MYMOX may be taken with meals.

4.3 Contraindications

- Hypersensitivity to the penicillins, to any of the cephalosporins or to any of the excipients (see section 6.1).
- Amoxicillin as contained in MYMOX is a penicillin and should not be given to patients with a history of hypersensitivity to beta-lactam antibiotics (e.g. carbapenem or monobactam). Potential cross allergy to other beta-lactams such as cephalosporins should be taken into account.

4.4 Special warnings and precautions for use

Hypersensitivity reactions

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

Serious and occasionally fatal hypersensitivity reactions (including anaphylactoid and severe cutaneous adverse reactions) have been reported in patients receiving beta-lactam antibiotics (see section 4.3). 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 in atopic individuals. 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, MYMOX should be discontinued and the appropriate alternative therapy instituted. Serious anaphylactic reactions may require immediate emergency treatment with epinephrine (adrenaline). Oxygen, intravenous steroids and airway management, including intubation may also be required.

Hypersensitivity reactions can also progress to Kounis syndrome, a serious allergic reaction that can result in myocardial infarction (see section 4.8). Presenting symptoms of such reactions can include chest pain occurring in association with an allergic reaction to amoxicillin. If an allergic reaction occurs, MYMOX therapy must be discontinued and appropriate alternative therapy instituted.

Drug-induced enterocolitis syndrome (DIES) has been reported mainly in children receiving amoxicillin (see section 4.8). DIES is an allergic reaction with the leading symptom of protracted vomiting (1 – 4 hours after medicine intake) in the absence of allergic skin or respiratory symptoms. Further symptoms could comprise abdominal pain, diarrhoea, hypotension or leucocytosis with neutrophilia. There have been severe cases including progression to shock.

Non-susceptible microorganisms

MYMOX 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 MYMOX. This particularly applies when considering the treatment of patients with urinary tract infections and severe infections of the ear, nose and throat.

The use of MYMOX 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.

Since MYMOX 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.

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

The dose should be reduced in patients with renal failure (see section 4.2).

Hepatic impairment

Changes in liver function tests have been observed in some patients receiving MYMOX. It should be used with caution in patients with evidence of hepatic dysfunction.

Transient hepatitis and cholestatic jaundice have been reported.

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, see section 4.8). This reaction requires MYMOX discontinuation and contraindicates any subsequent administration.

MYMOX 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.

MYMOX should preferably not be used in patients with lymphatic leukaemia since they are especially susceptible to amoxicillin induced skin rashes.

Jarisch-Herxheimer reaction

Caution is needed when administering amoxicillin to patients with syphilis, as the Jarisch-Herxheimer reaction may occur in these patients.

Overgrowth of non-susceptible microorganisms

Prolonged use may occasionally result in overgrowth of non-susceptible organisms. Antibiotic-associated *Pseudomembranous* colitis has been reported 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 MYMOX (this may occur up to several weeks after cessation of MYMOX therapy). If prolonged or significant diarrhoea occurs or the patient experiences abdominal cramps, treatment with MYMOX should be discontinued immediately. Antiperistaltic 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 (see section 4.8).

The possibility of superinfections with mycotic or bacterial pathogens should be kept in mind during therapy. If superinfections occur, the medicine should be discontinued and/or appropriate therapy instituted.

Crystalluria

In patients with reduced urine output, crystalluria (including acute renal injury) has been observed, predominantly with parenteral therapy. During the administration of high doses of MYMOX, it is advisable to maintain adequate fluid intake and urinary output in order to reduce the possibility of amoxicillin crystalluria. In patients with bladder catheters, a regular check of patency should be maintained (see sections 4.8 and 4.9).

Anticoagulants

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

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 MYMOX, false positive readings are common with chemical methods.

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

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

MYMOX contains colourants

MYMOX 250 contains tartrazine and MYMOX 500 contains tartrazine and sunset yellow FCF as colourants, which may cause allergic reactions.

4.5 Interaction with other medicines and other forms of interaction

Due to amoxicillin's effect on intestinal flora, the absorption of other medicines may be affected.

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 (INR) in patients maintained on acenocoumarol or warfarin and prescribed a course of amoxicillin, such as MYMOX. If co-administration is necessary, the prothrombin time or INR should be carefully monitored with the addition or withdrawal of MYMOX. Moreover, adjustments in the dose of oral anticoagulants may be necessary (see sections 4.4 and 4.8).

Probenecid

Concomitant use of probenecid is not recommended. Probenecid decreases the renal tubular secretion of MYMOX. Concurrent use with MYMOX may result in increased and prolonged blood concentrations of MYMOX.

Allopurinol

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

Tetracyclines

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

Methotrexate

Penicillins may reduce the excretion of methotrexate causing a potential increase in toxicity. Serum methotrexate levels should be closely monitored in patients who receive MYMOX and methotrexate simultaneously. MYMOX decreases the renal clearance of methotrexate, probably by competition at the common tubular secretion system.

Oral contraceptives

MYMOX may reduce the efficacy of oral contraceptives and patients should be warned accordingly.

4.6 Fertility, pregnancy and lactation

Women of childbearing potential

MYMOX may reduce the efficacy of oral contraceptives and patients should be warned accordingly (see section 4.5).

Pregnancy

The safety of MYMOX in pregnancy has not been established.

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.

Breastfeeding

MYMOX 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 breastfed infant, so that breastfeeding might have to be discontinued.

Fertility

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

4.7 Effects on ability to drive and use machines

MYMOX may cause allergic reactions, dizziness and convulsions (see section 4.8), which may influence the ability to drive and use machines. The patient should be advised not to drive or operate machines until the effects of MYMOX are known.

4.8 Undesirable effects

Summary of the safety profile

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

Tabulated summary of adverse reactions

System organ class	Frequency	Adverse reaction
Infections and infestations	Frequent	Vaginitis.
	Less frequent	Mucocutaneous candidiasis.
Blood and lymphatic system disorders[1]	Less frequent	Reversible leukopenia (including severe neutropenia or agranulocytosis), reversible thrombocytopenia, haemolytic anaemia, thrombocytopenic purpura, eosinophilia, prolongation of bleeding time and prothrombin time (see section 4.4).

Immune system disorders[6]	Frequent	Severe allergic reactions, including angioneurotic oedema, anaphylaxis, serum sickness-like syndrome, hypersensitivity vasculitis (see section 4.4).
	Frequency unknown	Jarisch-Herxheimer reaction (see section 4.4).
Nervous system disorders	Frequent	Abnormal taste, headache, dizziness, tiredness, hot flushes.
	Less frequent	Reversible hyperactivity, hyperkinesia, convulsions (see section 4.4).[2]
	Frequency unknown	Aseptic meningitis.
Cardiac disorders	Frequency unknown	Kounis syndrome.
Gastrointestinal disorders[3]	Frequent	Diarrhoea, nausea, vomiting, indigestion, abdominal pain, gastritis, stomatitis, glossitis, black 'hairy' tongue, enterocolitis, and antibiotic-associated colitis (including pseudomembranous colitis and haemorrhagic colitis, see section 4.4).
	Less frequent	Superficial tooth discolouration.[7]
	Frequency unknown	Drug-induced enterocolitis syndrome.
Hepatobiliary disorders[4]	Less frequent	Hepatitis, cholestatic jaundice. Raise in aspartate transaminase (AST) and/or alanine transaminase (ALT).[5]
Skin and subcutaneous tissue disorders	Frequent	Skin rash, urticaria, pruritus, erythema multiforme.
	Less frequent	Skin reactions such as Stevens Johnson syndrome, toxic epidermal necrolysis, bullous and exfoliative dermatitis, acute generalised exanthematous pustulosis (AGEP) (see section 4.4), and drug reaction with eosinophilia and systemic symptoms (DRESS).
	Frequency unknown	Linear IgA disease.
Renal and urinary tract disorders	Less frequent	Interstitial nephritis, crystalluria (including acute renal injury).

[1] These reactions are usually reversible on discontinuation of therapy and are believed to be hypersensitivity phenomena. A slight thrombocytosis (noted in less than 1 % of the patients treated with MYMOX. Appropriate monitoring should be undertaken when anticoagulants are prescribed concomitantly.

[2] Convulsions may occur with impaired renal function or those receiving high doses.

[3] If gastrointestinal reactions are evident, they may be reduced by taking MYMOX at the start of a meal.

[4] The events may be severe, and occur predominantly in adult or elderly patients. 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 effects 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.

[5] A moderate raise in AST and/or ALT has been noted in patients treated with MYMOX, but the significance of these findings is unknown.

[6] Serious and occasional fatal hypersensitivity (anaphylactic) reactions and angioneurotic oedema can occur with oral penicillin (see section 4.4). Whenever such reactions occur, MYMOX should be discontinued.

[7] It can usually be removed by brushing.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of MYMOX is important. It allows continued monitoring of the benefit/risk balance of MYMOX. Health care providers are requested 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's website.

4.9 Overdose

Gastrointestinal effects (such as nausea, vomiting and diarrhoea) and disturbances 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 those receiving high doses (see sections 4.4 and 4.8).

Gastrointestinal symptoms may be treated symptomatically, with attention to the water/electrolyte balance.
MYMOX 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

Mechanism of action

Amoxicillin is a semisynthetic penicillin (beta-lactam 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 wakening of the cell wall, which is usually followed by cell lysis and death. Amoxicillin is susceptible to degradation by beta-lactamases produced by resistant bacteria and therefore the spectrum of activity of amoxicillin alone does not include organisms which produce these enzymes.

Amoxicillin has *in vitro* bactericidal activity against a broad spectrum of non-beta-lactamase-producing Gram-positive and Gram-negative organisms.

Pharmacokinetic/pharmacodynamic relationship

The time above the minimum inhibitory concentration (T > MIC) is considered to be the major determinant of efficacy for amoxicillin.

Mechanisms of resistance

The main mechanisms of resistance to amoxicillin are:

- Inactivation by bacterial beta-lactamases.
- Alteration of PBPs, which reduce the affinity of the antibacterial medicine for the target.

Impermeability of bacteria or efflux pump mechanisms may cause or contribute to bacterial resistance, particularly in Gram-negative bacteria.

Inherently resistant organisms*
Gram-positive aerobes: *Enterococcus faecium*
Gram-negative aerobes: *Acinetobacter* spp. *Enterobacter* spp. *Klebsiella* spp. *Pseudomonas* spp.
Gram-negative anaerobes: *Bacteroides* spp. (many strains of *Bacteroides fragilis* are resistant).
Others: *Chlamydia* spp.

Mycoplasma spp. *Legionella* spp.
* Natural intermediate susceptibility in the absence of acquired mechanism of resistance.

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.

The absorption is not influenced by simultaneous food intake.

Distribution

Approximately 18 % of the total plasma amoxicillin content 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.

Amoxicillin 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 (see section 4.2).

Small amounts of amoxicillin are also excreted in the faeces and bile.

Linearity

There is a linear dose response in peak serum levels.

Special populations

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.

Renal impairment

The total serum clearance of amoxicillin decreases proportionately with decreasing renal function

(see sections 4.2 and 4.4).

Hepatic impairment

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

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Capsule contents:

Magnesium stearate.

Capsule shell:

MYMOX 250:

Brilliant blue (E133)

Gelatine

Tartrazine (E102)

Titanium dioxide.

MYMOX 500:

Gelatine

Sunset yellow FCF (E110)

Tartrazine (E102)

Titanium dioxide.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years.

6.4 Special precautions for storage

Store at or below 25 °C.

Store in a dry place, protected from light.

6.5 Nature and contents of container

MYMOX 250: Clear PVC, aluminium blister pack containing 10 capsules per blister. The blister strips are packed in an outer carton. Each carton contains 3, 10 or 50 blister strips.

MYMOX 500: Clear PVC, aluminium blister pack containing 10 capsules per blister. The blister strips are packed in an outer carton. Each carton contains 3, 10 or 50 blister strips.

6.6 Special precautions for disposal and other handling

No special requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Unichem SA (Pty) Ltd

San Domenico

Ground Floor, Unit G4

10 Church Street

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7551 Cape Town

8. REGISTRATION NUMBERS

MYMOX 250: A38/20.1.2/0462

MYMOX 500: A38/20.1.2/0463

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

25 November 2005

10. DATE OF REVISION OF THE TEXT

28 November 2024