1. **NAME OF THE MEDICINAL PRODUCT**

Emmox Dispersible Tablet 250mg

2. **QUALITATIVE AND QUANTITATIVE COMPOSITION**

The Emmox Dispersible Tablet contain amoxicillin 250mg. See for excipients section 6.1.

3. **PHARMACEUTICAL FORM**

Dispersible tablet.

Description: oblong, biconvex, white to yellowish-with tablet, 10 x 22 mm, scored

4. **CLINICAL PARTICULARS**

4.1. **Therapeutic indications**

Emmox Dispersible Tabletis indicated for the oral treatment of the following bacterial infections caused by amoxicillin-susceptible gram-positive and gram-negative pathogens (see section 5.1):

* Infections of the upper respiratory tract, including infections of the ears, nose and throat: Acute otitis media, acute sinusitis and bacterial pharyngitis

* Infections of the lower respiratory tract: Acute exacerbation of chronic bronchitis, community-acquired pneumonia

* Infections of the lower urinary tract: Cystitis

* Prophylaxis of endocarditis in patients at risk i.e. surgery in the oral cavity or upper airways

Consideration should be given to official local guidance (e.g. national recommendations) on the appropriate use of antibacterial agents.

Susceptibility of the causative organism to the treatment should be tested (if possible), although therapy may be initiated before the results are available.

4.2. **Posology and method of administration**

The dosage of amoxicillin is dependent on age, bodyweight and renal function of the patient, on the seriousness and localisation of the infection and on the expected or proved causative agent. The tablets can be used in two ways. First disperse in water, then drink, or take directly with water. The tablets may be broken to ease the swallowing.

Emmox Dispersible Tabletcan be taken either before, during or after meals.

Treatment of infections:

In general the therapy should be continued for 2 to 3 days following the disappearance of symptoms. In beta- haemolytic streptococcal infections the duration of therapy should be at least 10 days in order to achieve eradication of the organism.

Parenteral therapy is indicated if the oral route is considered impracticable or unsuitable, and particularly for the urgent treatment of severe infection

Adults (including elderly) and children above 12 years of age

The usual dosage covers a range from 750 mg to 3g amoxicillin daily in divided doses. In some areas 1500 mg amoxicillin daily in divided doses are recommended as the upper usual dose.

Special dosage recommendation

Acute exacerbation of chronic bronchitis in adults: 2 x 1 g per day

Elderly

Dosage as for adults, unless an impaired renal function exists.

Dosage in impaired renal function

The dose should be reduced in patients with severe renal function impairment. In patients with a renal clearance of less than 30 ml/min an increase in the dosage interval or a reduction in the subsequent doses is recommended (see section 4.4).

Short course treatments with a single dose of 3 g cannot be given in case of renal failure.

Adults (including elderly patients): Creatinine clearance ml/min	Dose	Interval between administration
> 30	No adjustment necessary.	
10 – 30	500 mg	12 h
< 10	500 mg	24 h

In case of hemodialysis: 500 mg should be administered at the end of the procedure. Prophylaxis for endocarditis

For the prevention of endocarditis, in patients not having general anaesthetic, 3 g amoxicillin are given in the hour preceding the surgical procedure, followed by (6 hours later) a further 3 g dose, if considered necessary.

For children a dose of 50 mg amoxicillin/kg body weight is recommended.

For further details and description of risk patients local official guidelines for the prevention of endocarditis should be consulted.

4.3. **Contra-indications**

MP-Amoxicillin disper is contraindicated in patients with:

• Hypersensitivity to penicillin; a cross-allergy to β-lactams such as cephalosporins should be taken into account.

• Hypersensitivity to any of the other ingredients in the product.

4.4. **Special warnings and precautions for use**

Before initiating therapy with amoxicillin, careful enquiry should be made concerning previous hypersensitivity reactions to penicillins and cephalosporins. The possibility of cross-hypersensitivity (10 % - 15 %) with cephalosporins should be taken into account.

Serious and occasionally fatal hypersensitivity (anaphylactoid) reactions have been reported in patients on penicillin therapy. These reactions are more likely to occur in individuals with a history of hypersensitivity to beta-lactam antibiotics.

Patients suffering from severe gastrointestinal disturbances with diarrhoea and vomiting should not be treated with Amoxicilline Sandoz disper, due to the risk of reduced absorption. In these cases a parenteral treatment with amoxicillin is advisable.

Emmox Dispersible Tabletshould be used with caution in patients with allergic diathesis and asthma.

In patients with renal impairment the excretion of amoxicillin will be delayed and, depending on the degree of the impairment, it may be necessary to reduce the total daily dosage (see section 4.2)

The prolonged use of amoxicillin may occasionally result in an overgrowth of non-susceptible organisms or yeasts. Patients should therefore carefully be watched for superinfections.

The occurrence of anaphylactic shock and other severe allergic reactions is rare following the oral administration of amoxicillin. However, if such reactions occur, appropriate emergency treatment measures must be taken: I.v. administration of epinephrine, followed by antihistaminic drugs, volume substitution and administration of glucocorticoids. Patients should be kept under close observation, and further therapeutic measures (artificial respiration, oxygen) should be administered as required.

The presence of high urinary concentrations of amoxicillin can cause precipitation of the product in urinary catheters. Therefore, catheters should be visually inspected at intervals.

At high doses, adequate fluid intake and urinary output must be maintained to minimise the possibility of amoxicillin crystalluria.

Emmox Dispersible Tabletshould be used with caution in patients with viral infections, acute lymphatic leukaemia, or infectious mononucleosis (due to an increased risk of erythematous skin rashes).

Pseudomembranous colitis should be borne in mind if severe persistent diarrhoea occurs (in most cases caused by Clostridium difficile). In this case Emmox Dispersible Tabletshould be discontinued and an adequate therapy (e.g.: vancomycin 4 x 250 mg p.o.) has to be started.

All Emmox Dispersible Tablettablets contain aspartame (E951) and should be used with care in patients with phenylketonuria. In homozygotic patients with phenylketonuria, the amount of phenylalanine that is supplied by aspartame must be included in the calculation for the dietary regulations.

A dose adjustment of digoxin may be necessary on concurrent administration with amoxicillin (see section 4.5). A dose adjustment of anticoagulants may be necessary on concurrent administration with amoxicillin (see section 4.5).

Serum methotrexate levels should be carefully monitored on concurrent administration with amoxicillin (see section 4.5).

4.5. **Interaction with other medicinal products and other forms of interaction Concomitant use not recommended**

Allopurinol

Concomitant administration of allopurinol may promote the occurrence of allergic cutaneous reactions and is therefore not advised.

Digoxin

An increase in the absorption of digoxin is possible on concurrent administration with amoxicillin. A dose adjustment of digoxin may be necessary. (see section 4.4)

Disulfiram

Simultaneous administration of disulfiram is contraindicated.

Anticoagulants

Concomitant administration of amoxicillin and anticoagulants, from the coumarin class, may prolong the bleeding time. A dose adjustment of anticoagulants may be necessary. (see section 4.4)

Probenicid

By inhibiting the renal elimination of amoxicillin the concomitant administration of probenecid leads to an increase in the concentrations of amoxicillin in serum and bile.

Other antibiotics

In general amoxicillin should not be combined with bacteriostatic chemotherapeutics/antibiotics (like tetracyclines, macrolids, sulfonamids or chloramphenicol), because in vitro antagonism is observed.When used simultaneously with aminoglycosides a synergistic effect may occur.

Methotrexate

Interaction between amoxicillin and methotrexate leading to methotrexate toxicity has been reported. Serum methotrexate levels should be closely monitored in patients who receive amoxicillin and methotrexate simultaneously. Amoxicillin decreases the renal clearance of methotrexate, probably by competition at the common tubular secretion system. (see section 4.4)

Caution is recommended when amoxicillin is given concomitantly with:

Oral hormonal contraceptives

Administration of amoxicillin can transiently decrease the plasma level of estrogens and progesterone, and may reduce the efficacy of oral contraceptives. It is therefore recommended to take supplemental non-hormonal contraceptive measures.

Other forms of interactions:

• Forced diuresis leads to a reduction in blood concentrations by increased elimination of amoxicillin.

• The occurrence of diarrhoea may impair the absorption of other medicaments and consequently adversely affect the efficacy.

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

• Amoxicillin may decrease the amount of urinary estriol in pregnant women.

• At high risk concentrations, amoxicillin may diminish the results of serum glycemia levels

• Amoxicillin may interfere with protein testing when colormetric methods are used

4.6. **Pregnancy and lactation**

Amoxicillin passes the placenta and foetal plasma concentrations are approximately 25-30% of the maternal plasma concentrations.

Data on a limited number of exposed pregnancies indicate no adverse effects of amoxicillin on pregnancy or on the health of the foetus/new-born child. To date, no other relevant epidemiological data are available. Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonal/foetal development, parturition or postnatal development.

Caution should be exercised when prescribing to pregnant women.

Amoxicillin diffuses into the breast milk (approx. 10% of the corresponding serum concentration) and in rare cases this can lead to diarrhoea and/or fungal colonisation of the mucosa in the infant. The possibility of sensitisation of the infant to beta-lactam drugs should also be considered.

4.7. **Effects on ability to drive and use machines**

No effects on the ability to drive and to use machines have been observed.

4.8. **Undesirable effects**

In this section undesirable effects are defined as follows: Common: 10%, or less, but greater than 1% Uncommon: 1%, or less, but greater than 0.1%

Rare: 0.1% or less, but greater than 0.01% Very rare, including isolated cases: 0.01% or less

Infections and infestations

Uncommon

Prolonged and repeated use of the preparation can result in superinfections and colonization with resistant organisms or yeasts such as oral and vaginal candidiasis**.**

Blood and the lymphatic system disorders

Rare

Eosinophilia and haemolytic anaemia have been reported rarely.

Very rare

There have been isolated reports of leucopenia, granulocytopenia, thrombocytopenia, pancytopenia, anaemia, myelosuppression, agranulocytosis, prolongation of bleeding time, and prolongation of prothrombin time. However, these changes were reversible on discontinuation of therapy.

Immune system disorders

Rare

Laryngeal oedema, serum sickness, allergic vasculitis and anaphylactic shock may occur in rare cases.

Nervous system disorders

Rare

CNS effects have been seen rarely. They include hyperkinesia, dizziness and convulsions. Convulsions may occur in patients with impaired renal function or in those receiving high doses.

Gastrointestinal disorders:

Common

Gastric complaints, nausea, loss of appetite, vomiting, flatulence, soft stools, diarrhoea, enanthemas (particularly in the region of the mouth), dry mouth, taste disturbances. These effects on the gastrointestinal system are mostly mild and frequently disappear either during the treatment or very soon after completion of therapy. The occurrence of these side-effects can generally be reduced by taking amoxicillin during meals.

If severe and persistent diarrhoea occurs, the very rare possibility of pseudomembranous colitis should be considered. The administration of anti-peristaltic drug is contraindicated.

Rare

A superficial discoloration of the teeth (especially in case of the suspension) is rare. Usually the discoloration can be removed by teeth brushing.

Very rare

Development of a black tongue.

Hepato-biliary disorders:

Uncommon

Moderate and transient increase of liver enzymes. Rare reports of hepatitis and cholestatic jaundice.

Skin and subcutaneous tissue disorders:

Common

Cutaneous reactions such as exanthema, pruritus, urticaria; the typical morbilliform exanthema occurs 5 - 11 days after start of therapy. Immediate appearance of urticaria indicates an allergic reaction to amoxicillin and therapy should therefore be discontinued.

Rare: (see also section 4.4)

Angioneurotic oedema (Quincke's oedema) Erythema multiforme exudativum

Acute generalized pustulosis Stevens-Johnson syndrome Toxic epidermal necrolysis

Bullous and exfoliative dermatitis

Renal disorders

Rare:

Acute interstitial nephritis may occur in rare cases.

General disorders and administration site conditions

Rare:

In rare cases drug fever has been reported.

4.9. **Overdose**

Symptoms of overdose:

Amoxicillin is not generally associated with acute toxic effects, even when accidentally consumed in high doses. Overdosage can lead to symptoms such as gastrointestinal disturbances and fluid and electrolyte imbalance. In patients with severely impaired renal function, large overdoses can result in signs of renal toxicity; crystalluria is possible.

Management of overdose:

There is no specific antidote for an overdose of amoxicillin.

Treatment consists primarily of administration of activated charcoal (a gastric lavage is usually not necessary), or symptomatic measures. Particular attention should be paid to the water and electrolyte balance of the patients. Amoxicillin can be eliminated via haemodialysis.

5. **PHARMACOLOGICAL PROPERTIES**

ATC-Code: J01CAO4

5.1. **Pharmacodynamic properties (microbiology)**

General Properties

Amoxicillin is an aminobenzyl penicillin that has a bactericidal action due to its inhibition of the synthesis of the bacterial cell wall.

Breakpoints

Enterobacteriaceae: S ≤ 8 µg/ml; I = 16 µg/ml; R ≥ 32 µg/ml Staphylococcus spp.: S ≤ 4 µg/ml; R ≥ 8 µg/ml

Haemophilus spp.: S ≤ 1 µg/ml; R ≥ 4 µg/ml

Str. pneumoniae: S ≤ 2 µg/ml; I = 4 µg/ml; R ≥ 8 µg/ml

Susceptibility:

The prevalence of resistance may vary geographically and with time for selected species and local information on resistance is desirable, particularly when treating severe infections. As necessary, expert advice should be sought when the local prevalence of resistance is such that the utility of the agent in at least some types of infections is questionable. This information gives only an approximate guidance on probabilities whether microorganisms will be susceptible to amoxicillin or not.

SUSCEPTIBLE:

Gram-positive aerobes *Bacillus anthracis Corynebacterium* spp § *Enterococcus faecalis* § *Listeria monocytogenes*

Staphylococcus aureus (MSSA) beta-lactamase negative

Streptococcus agalactiae Streptococcus bovis

Frequency of resistance ranges in EU (if > 10%) (extreme values)

*Streptococcus pneumoniae # * 4.6 – 51.4 %*

*Streptococcus pyogenes # * Streptococcus viridans* § **Gram-negative aerobes:** *Brucella* spp #

*Escherichia coli * 46.7 %*

*Haemophilus influenzae * 2 – 31.7 %*

Haemophilus para-influenzae 15.3%

*Helicobacter pylori **

Neisseria gonorrhoeae § 12 – 80%

Neisseria meningitidis #

Proteus mirabilis 34.1 %

Salmonella spp § *Shigella* spp § *Vibrio cholerae* **Anaerobes**

Bacteroides melaninogenicus §

Clostridium spp *Fusobacterium spp.*§ *Peptostreptococci*

RESISTANT

Gram-positive aerobes

Staphylococcus (β-lactamase producing strains)

Gram-negative aerobes *Acinetobacter* spp *Citrobacter* spp *Enterobacter* spp *Klebsiella* spp *Moraxella catarrhalis **

Proteus spp (indol positive) *Proteus vulgaris Providencia* spp *Pseudomonas* spp

Serratia spp **Anaerobes** *Bacteroides fragilis* ***Others***

Chlamydia Mycoplasma Rickettsia

No β-lactamase producers have as yet been reported for these bacterial species

§ inconstantly susceptible; susceptibility is therefore unpredictable in the absence of susceptibility testing

* Clinical efficacy has been demonstrated for susceptible isolates in approved clinical indications

Other information:

Bacteria may be resistant to amoxicillin (and, thus, ampicillin) due to production of chromosomal or R-plasmide coded beta-lactamases which hydrolyse aminopenicillins, due to alteration in penicillin-binding proteins, due to impermeability to the drug, or due to drug efflux pumps. One or more of these mechanisms may co-exist in the same organism, leading to a variable and unpredictable cross-resistance to other beta-lactams such as cephalosporins and to antibacterial drugs of other classes.

5.2 **Pharmacokinetic properties**

Absorption:

The absolute bioavailability of amoxicillin depends on the dose and ranges between 75 and 90%. In the dose range between 250 mg and 750 mg the bioavailability (parameters: AUC and/or recovery in urine) is linearly proportional to the dose. At higher doses the extent of absorption decreases. The absorption is not affected by concomitant food intake. Oral administration of a single dose of 500 mg amoxicillin results in plasma concentrations of 6 - 11 mg/l. After administration of a single dose of 3 g amoxicillin, the plasmaconcentrations reach 27 mg/l. Peak plasma concentrations are present about 1-2 hours after administration.

Distribution:

Protein binding for amoxicillin is approximately 17%. Therapeutic drug levels are rapidly achieved in serum, lung tissue, bronchial secretions, middle ear fluid, bile and urine. In healthy meninges amoxicillin diffuses badly in the liquor cerebrospinalis. In inflamed meninges the concentration can reach approximately 20 % of the concentration in blood. Amoxicillin crosses the placenta and a small percentage is excreted into the breast milk.

Biotransformation and elimination:

The main route of excretion of amoxicillin is the kidney. About 60-80% of an oral dose of amoxicillin are excreted in unchanged active form in the urine within 6 hours of administration, and a small fraction is excreted in the bile. Approximately 7 - 25% of the administered dose is metabolised to inactive penicilloic acid. The serum half-life in patients with normal renal function is approximately 1 – 1,5 hour. In patients with end-stage renal failure the half-life ranges between 5 to 20 hours. The substance is haemodialysable.

5.3 **Preclinical safety data**

Preclinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity and toxicity to reproduction.

6. **PHARMACEUTICAL PARTICULARS**

6.1. **List of excipients**

Peach-Apricot Flavouring, powdered Orange Flavouring, powdered Magnesium Stearate E470B Aspartame E951

Croscarmellose Sodium Mannitol E421

Talc E553b

Silica, colloidal anhydrous E551 Cellulose, microcrystalline E460 Malto dextrin

Starch, soluble Titanium dioxide E171

6.2. **Incompatibilities**

Not applicable.

6.3. **Shelf life**

3 years

6.4. **Special precautions for storage**

Not applicable

6.5. **Nature and contents of container**

Packs of 2, 8, 10, 12, 14, 16, 20, 30, 100 and 1000 tablets in PVC/PVDC/Al blisters.

6.6. **Instructions for use and handling**

No special requirements.

7 NAME AND PERMANENT ADDRESS OR REGISTERED PLACE OF BUSINESS OF THE HOLDER OF THE MARKETING AUTHORISATION

Emzor Pharmaceutical Industries Limited.

Sagamu/Benin Expressway, Makun, Sagamu Local Govt, Ogun state.

8 **MARKETING AUTHORISATION NUMBER**

N/A

9. **DATE OF FIRST AUTHORISATION/RENEWAL OF AUTHORISATION**

N/A

10 DATE OF REVISION OF THE TEXT

N/A