Summary of product characteristics

1. Name of the medicinal product:
E-mox capsules – Dry mix.

2. Qualitative and quantitative composition:

Each dosage unit contains:	**Capsule**	**Suspension** (5 ml)
Amoxicillin (as trihydrate)	500 mg	125 mg or 250 mg

For excipients, see 6.1

3. Pharmaceutical form:
E-MOX 125 mg/5 ml:
Before reconstitution Milky white mix of fine & crystalline powder.
After reconstitution: milky white to yellowish white suspension.
E-MOX 250 mg/5 ml:
Before reconstitution: Yellowish white mix of fine & crystalline powder.
After reconstitution: milky white to yellowish white suspension.
E-MOX 500 mg: Hard gelatin capsules of red cap and white body containing white to creamy white powder.

4. Clinical particulars:
4.1 Therapeutic indications:
E-MOX is indicated for the treatment of the following infections in adults and children:
Acute otitis media.
Acute bacterial sinusitis.
Acute streptococcal tonsillitis and pharyngitis.
Acute exacerbations of chronic bronchitis.
Community acquired pneumonia.
Acute cystitis.
Asymptomatic bacteriuria in pregnancy.
Acute pyelonephritis.
Typhoid and paratyphoid fevers.
Dental abscess with spreading cellulitis.
Prosthetic joint infections.
Helicobacter pylori eradication.
Lyme disease.
E-MOX Capsules and Dry Mix are also indicated for the prophylaxis of endocarditis.
Consideration should be given to official guidance on the appropriate use of antibacterial agents.

4.2 Posology and method of administration:
Dosage:
The dose of **E-MOX** that is selected to treat an individual infection should take into account:
- The expected pathogens and their likely susceptibility to antibacterial agents.
- The severity and the site of the infection.
- The age, weight and renal function of the patient; as shown below.

The duration of therapy should be determined by the type of infection and the response of the patient, and should generally be as short as possible. Some infections require longer periods of treatment.
Adults and Children ≥ 40 kg:

Indication*	**Dose***
Acute bacterial sinusitis.	250 mg - 500 mg every 8 hours or

Asymptomatic bacteriuria in pregnancy.	750 mg - 1 g every 12 hours.
Acute pyelonephritis.	**For severe infections:**
Dental abscess with spreading cellulitis.	750 mg - 1 g every 8 hours.
Acute cystitis.	Acute cystitis may be treated with 3 g twice daily for one day.
Acute otitis media.	500 mg every 8 hours or
Acute streptococcal tonsillitis and pharyngitis.	750 mg - 1 g every 12 hours. **For severe infections:**
Acute exacerbations of chronic bronchitis.	750 mg - 1 g every 8 hours for 10 days.
Community acquired pneumonia.	500 mg - 1 g every 8 hours.
Typhoid and paratyphoid fevers.	500 mg - 2 g every 8 hours.
Prosthetic joint infections.	500 mg - 1 g every 8 hours.
Prophylaxis of endocarditis.	2 g orally, single dose, 30 to 60 minutes before procedure.
Helicobacter pylori eradication	750 mg - 1 g twice daily in combination with a proton pump inhibitor (e.g. omeprazole, lansoprazole) and another antibiotic (e.g. clarithromycin, metronidazole) for 7 days.
Lyme disease	**Early stage:** 500 mg - 1 g every 8 hours, up to a maximum of 4 g/day in divided doses, for 14 days (10 to 21 days). **Late stage (systemic involvement):** 500 mg - 2 g every 8 hours, up to a maximum of 6 g/day in divided doses, for 10 to 30 days.
*****Consideration should be given to the official treatment guidelines for each indication.	

Children < 40 kg:

Children may be treated with **E-MOX** capsules or suspensions.

Children weighing 40 kg or more should be prescribed the adult dosage.

Recommended Doses:

Indication[+]	**Dose**[+]
Acute bacterial sinusitis.	20 - 90 mg/kg/day in divided doses.*****
Acute otitis media.	
Community acquired pneumonia.	
Acute cystitis.	
Acute pyelonephritis.	
Dental abscess with spreading cellulitis.	
Acute streptococcal tonsillitis and pharyngitis.	40 - 90 mg/kg/day in divided doses.*****
Typhoid and paratyphoid fevers.	100 mg/kg/day in three divided doses.
Prophylaxis of endocarditis.	50 mg/kg orally, single dose 30 - 60 minutes before procedure.
Lyme disease.	**Early stage:** 25 - 50 mg/kg/day in three divided doses, for 10 to 21 days. **Late stage (systemic involvement):**

	100 mg/kg/day in three divided doses, for 10 to 30 days.
+ Consideration should be given to the official treatment guidelines for each indication. *****Twice daily dosing regimens should only be considered when the dose is in the upper range.	

Elderly:
No dose adjustment is considered necessary.
Renal impairment:

GFR (ml/min)	Adults and Children ≥ 40 kg	Children < 40 kg[#]
Greater than 30	No adjustment necessary.	No adjustment necessary.
10 - 30	Maximum 500 mg twice daily.	15 mg/kg given twice daily; (maximum 500 mg twice daily).
Less than 10	Maximum 500 mg/day.	15 mg/kg given as a single daily dose; (maximum 500 mg).
[#] In the majority of cases, parenteral therapy is preferred.		

In patients receiving Haemodialysis:
Amoxicillin may be removed from the circulation by haemodialysis.

	Haemodialysis
Adults and Children over 40 kg	500 mg every 24 hours. Prior to haemodialysis, one additional dose of 500 mg should be administered. In order to restore circulating drug levels, another dose of 500 mg should be administered after haemodialysis.
Children under 40 kg	15 mg/kg/day given as a single daily dose (maximum 500 mg). Prior to haemodialysis, one additional dose of 15 mg/kg should be administered. In order to restore circulating drug levels, another dose of 15 mg/kg should be administered after haemodialysis.

In patients receiving Peritoneal dialysis:
Amoxicillin maximum 500 mg/day.
Hepatic impairment:
Dose with caution and monitor hepatic function at regular intervals.
Administration:
E-MOX is for oral use.
Absorption of **E-MOX** is unimpaired by food.
Therapy can be started parenterally according to the dosing recommendations of the intravenous formulation and continued with an oral preparation.
Swallow capsule with water without opening capsule.
Instructions on Reconstitution of the Medicinal product Before Administration:
Check cap seal is intact before use.
Invert and shake bottle to loosen powder.
To prepare add potable water and shake until all contents are dispersed.
Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

4.3 Contraindications:
Hypersensitivity to the active substance, to any of the penicillins or to any of the excipients.
History of a severe immediate hypersensitivity reaction (e.g. anaphylaxis) to another beta-lactam agent (e.g. a cephalosporin, carbapenem or monobactam).

4.4 Special warnings and precautions for use:
Hypersensitivity reactions:
Severe cutaneous adverse reactions (SCARs), including Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), drug reaction with eosinophilia and systemic symptoms (DRESS), and acute generalised exanthematous pustulosis (AGEP) have been reported in association with beta lactam antibiotics .

Before initiating therapy with **E-MOX**, careful enquiry should be made concerning previous hypersensitivity reactions to penicillins, cephalosporins or other beta-lactam agents.
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, **E-MOX** therapy must be discontinued and appropriate alternative therapy instituted.
Non-susceptible microorganisms:
E-MOX 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 pustula may be a symptom of acute generalised exanthemous pustulosis. This reaction requires amoxicillin discontinuation and contraindicates any subsequent administration.
E-MOX 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 agents 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 antibiotic. Should antibiotic-associated colitis occur, **E-MOX** should immediately be discontinued, a physician consulted and an appropriate therapy initiated. Anti-peristaltic medicinal products are contra-indicated 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 rarely 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 very rarely, 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 amoxicillin 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 **E-MOX** treatment, enzymatic glucose oxidase methods should be used.
The presence of amoxicillin may distort assay results for oestriol in pregnant women.
E-MOXDry Mix contains sucrose and lactose. Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrose-isomaltase insufficiency, should not take this medicine.

Clostridioides difficile Associated Diarrhea (CDAD) has been reported with nearly all antibacterial agents, including amoxicillin, and may range in severity from mild diarrhea to fatal colitis

4.5 Interaction with other medicinal products:

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 **E-MOX**.

Allopurinol:

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

Tetracyclines:

Tetracyclines and other bacteriostatic drugs 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 **E-MOX**. 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 Typhoid vaccine:

The oral typhoid vaccine is inactivated by antibacterials.

4.6 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. **E-MOX** may be used in pregnancy when the potential benefits outweigh the potential risks associated with treatment.

Lactation:

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 breastfed infant, so that breastfeeding might have to be discontinued. **E-MOX** should only be used during breastfeeding after benefit/risk assessment by the physician in charge.

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 to use machines:

No studies on the effects on the ability to drive and to use machines have been performed. However, undesirable effects may occur (e.g. allergic reactions, dizziness, convulsions), which may influence the ability to drive and to use machines.

4.8 Undesirable effects:

Clostridioides difficile-Associated Diarrhea (CDAD).

The most commonly reported adverse drug reactions (ADRs) are diarrhoea, nausea and skin rash.
The ADRs derived from clinical studies and post-marketing surveillance with amoxicillin, presented by Medical Dictionary for Regulatory Activities (MedDRA) System Organ Class are listed below.
The following terminologies have been used in order to classify the occurrence of undesirable effects:
Very common (≥1/10).
Common (≥1/100 to <1/10).
Uncommon (≥1/1,000 to <1/100).
Rare (≥1/10,000 to <1/1,000).
Very rare (<1/10,000).
Not known (cannot be estimated from the available data).

Infections and Infestations:

Very rare: Mucocutaneous candidiasis.

Blood and Lymphatic System disorders:

Very rare: Reversible leucopenia (including severe neutropenia or agranulocytosis), reversible thrombocytopenia and haemolytic anaemia, prolongation of bleeding time and prothrombin time.

Immune System disorders:

Very rare: Severe allergic reactions, including angioneurotic oedema, anaphylaxis, serum sickness and hypersensitivity vasculitis.
Not known: Jarisch-Herxheimer reaction.

Nervous System disorders:

Very rare: Hyperkinesia, dizziness and convulsions.

Gastrointestinal disorders:

Clinical Trial Data:

*****Common: Diarrhoea and nausea.
*****Uncommon: Vomiting.

Post-marketing Data:

Very rare: Antibiotic associated colitis (including pseudomembraneous colitis and haemorrhagic colitis), black hairy tongue, superficial tooth discolouration[#] (with Oral Suspensions).

Hepatobiliary disorders:

Very rare: Hepatitis, cholestatic jaundice, a moderate rise in AST and/or ALT.
Skin and Subcutaneous tissue disorders:
Clinical Trial Data:
*****Common: Skin rash.
*****Uncommon: Urticaria and pruritus.
Post-marketing Data:
Very rare: 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).
Renal and Urinary tract disorders:
Very rare: Interstitial nephritis, crystalluria.
***** The incidence of these AEs was derived from clinical studies involving a total of approximately 6,000 adult and pediatric patients taking amoxicillin.
 # With Oral 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.

4.9 Overdose:
Symptoms and Signs 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:
Gastrointestinal symptoms may be treated symptomatically, with attention to the water/electrolyte balance. Amoxicillin can be removed from the circulation by haemodialysis.

5. Pharmacological properties:
5.1 Pharmacodynamic properties:
Pharmacotherapeutic group: Penicillins with extended spectrum.
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 weakening 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.
Pharmacokinetic/Pharmacodynamic relationship:
The time above the minimum inhibitory concentration (T>MIC) is considered to be the major determinant of efficacy for amoxicillin.
In vitro susceptibility of micro-organisms to Amoxicillin:
Commonly Susceptible Species:
Gram-positive aerobes:
Enterococcus faecalis.
Beta-hemolytic streptococci (Groups A, B, C and G).
Listeria monocytogenes.
Species for which acquired resistance may be a problem:
Gram-negative aerobes:
Escherichia coli.
Haemophilus influenzae.
Helicobacter pylori.

Proteus mirabilis.
Salmonella typhi.
Salmonella paratyphi.
Pasteurella multocida.
Gram-positive aerobes:
Coagulase negative staphylococcus.
Staphylococcus aureus£.
Streptococcus pneumoniae.
Viridans group streptococcus.
Gram-positive anaerobes:
Clostridium spp..
Gram-negative anaerobes:
Fusobacterium spp..
Other:
Borrelia burgdorferi.
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.
£ Almost all *S. aureus* are resistant to amoxicillin due to production of penicillinase. In addition, all methicillin-resistant strains are resistant to amoxicillin.

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.
In the range 250 to 3000 mg, the bioavailability is linear in proportion to dose (measured as C_{max} and AUC). The absorption is not influenced by simultaneous food intake.
Haemodialysis can be used for elimination of amoxicillin.
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 no evidence for significant tissue retention of drug-derived material.
Amoxicillin, like most penicillins, can be detected in breast milk.
Amoxicillin has been shown to cross the placental barrier.

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.
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 male 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.
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:

Capsules: Maize starch, Microcrystalline cellulose PH101, Talc purified, Magnesium stearate, colloidal silicon dioxide.
Red Capsule shell : gelatin, titanium dioxide, brilliant blue, carmosine red, ponceau red , quinolone yellow
White body : Gelatin , titanium dioxide.
Dry Mix: Sucrose, carboxymethylcellulose sodium, caramel oil, banana flavour oil, lactose monohydrate, vanillin, sodium citrate anhydrous, colloidal silicon dioxide, sodium benzoate.

6.2 Incompatibilities:

None known.

6.3 Shelf life:

3 years.

6.4 Special precautions for storage:

Store at a temperature not exceeding 25˚C.

6.5 Nature and contents of container:

E-Mox 500 mg Capsules: A carton box contain 1 or 2 Blisters each of 8 capsules and pamphlet.

E-Mox 125 mg Dry Mix: A carton box contain a glass bottle of 80 ml or 100 ml suspension after reconstitution and pamphlet.
E-Mox 250 mg Dry Mix: A carton box contain a glass bottle of 60 ml or 80 ml or 100 ml suspension after reconstitution and pamphlet.

6.6 Special precautions for disposal and other handling:
Any unused medicinal product or waste material should be disposed of in accordance with local requirements

7. Marketing authorisation holder:
Egyptian international pharmaceutical industries company (EIPICO)

8. MARKETING AUTHORISATION NUMBER(S)
06649/07600/REN/2020

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
19-10-2021

10.Date of revision of the text:
March 2016