

Summary of Product Characteristics (SmPC)

ERYSTAR-250

(Erythromycin Stearate Tablets 250 mg)

1. Name of the medicinal product

ERYSTAR-250 (Erythromycin Stearate Tablets 250 mg)

2. Composition

Quantity of Erythromycin Stearate BP 250mg.

Excipients of Known effects:

Refer to section 6.1 for the full list of excipients.

3. Pharmaceutical form

Tablet

Reddish pink colored round shapes biconvex film coated tablet.

4. Clinical particulars

4.1 Therapeutic indications

For the prophylaxis and treatment of infections caused by erythromycin-sensitive organisms.

Antibiotic, highly effective in the treatment of a great variety of clinical infections, such as:

- 1) Upper respiratory tract infections: laryngitis, pharyngitis, sinusitis, secondary infections in colds and influenza, tonsillitis, peritonsillar abscess.
- 2) Lower respiratory tract infections: acute and chronic bronchitis, tracheitis, pneumonia (lobar pneumonia, bronchopneumonia, primary atypical pneumonia), bronchiectasis, Legionnaire's disease.
- 3) Eye infections: blepharitis
- 4) Ear infections: otitis media and otitis externa, mastoiditis.
- 5) Oral infections: gingivitis, Vincent's angina.
- 6) Skin and soft tissue infections: boils and carbuncles, abscesses, pustular acne, paronychia, impetigo, cellulitis, erysipelas.
- 7) Gastro-intestinal infections: staphylococcal enterocolitis, cholecystitis
- 8) Other infections: gonorrhoea, syphilis, urethritis, osteomyelitis, lymphogranuloma venereum, diphtheria, prostatitis, scarlet fever.
- 9) Prophylaxis: pre- and post-operative, burns, trauma, rheumatic fever.

4.2 Posology and method of administration

Posology

Adult and CHILD over 8 years:

250 – 500mg every 6 hours or 0.5 – 1g every 12 hours, up to 4g daily in severe infections.

If administration on a twice-daily schedule is desirable in adults or children, one-half of the total daily dose may be given every 12 hours, one hour before meals.

Note: For younger children, infants and babies erythromycin ethylsuccinate suspensions, are normally recommended. The recommended dose for children age 2-8 years, for mild to moderate infections, is 1 gram daily in divided doses. The recommended dose for infants and babies, for mild to moderate infections, is 500 mg daily in divided doses. For severe infections doses may be doubled.

Elderly:

No special dose recommendations.

Method of administration

For oral administration only.

The tablets should be swallowed whole and should not be crushed or chewed.

Summary of Product Characteristics (SmPC)

ERYSTAR-250

(Erythromycin Stearate Tablets 250 mg)

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients.

Concomitant use with simvastatin, tolterodine, mizolastine, amisulpride, astemizole, terfenadine, domperidone, cisapride or pimozide.

Erythromycin should not be given to patients with a history of QT prolongation (congenital or documented acquired QT prolongation) or ventricular cardiac arrhythmia, including torsades de pointes.

Erythromycin should not be given to patients with electrolyte disturbances (hypokalaemia, hypomagnesaemia due to the risk of prolongation of QT interval)

Erythromycin is contraindicated with ergotamine and dihydroergotamine.

4.4 Special warnings and precautions for use

As with other macrolides, rare serious allergic reactions, including acute generalised exanthematous pustulosis (AGEP) have been reported. If an allergic reaction occurs, the drug should be discontinued and appropriate therapy should be instituted. Physicians should be aware that reappearance of the allergic symptoms may occur when symptomatic therapy is discontinued.

Erythromycin is excreted principally in the liver, so caution should be exercised in administering the antibiotic to patients with impaired hepatic function or concomitantly receiving potentially hepatotoxic agents.

Hepatic dysfunction including increased liver enzymes and /or cholestatic hepatitis, with or without jaundice, has been infrequently reported with erythromycin.

Pseudomembranous colitis has been reported with nearly all antibacterial agents, including macrolides, and may range in severity from mild to life-threatening. Clostridium difficile-associated diarrhoea (CDAD) has been reported with use of nearly all antibacterial agents including erythromycin, and may range in severity from mild diarrhoea to fatal colitis. Treatment with antibacterial agents alters the normal flora of the colon, which may lead to overgrowth of C. difficile. CDAD must be considered in all patients who present with diarrhoea following antibiotic use. Careful medical history is necessary since CDAD has been reported to occur over two months after the administration of antibacterial agents.

Cardiovascular Events

Prolongation of the QT interval, reflecting effects on cardiac repolarisation imparting a risk of developing cardiac arrhythmia and torsades de pointes, have been seen in patients treated with macrolides including erythromycin.

Fatalities have been reported.

Carefully consider the balance of benefits and risks before prescribing erythromycin for any patients taking hydroxychloroquine or chloroquine, because of the potential for an increased risk of cardiovascular events and cardiovascular mortality.

Erythromycin should be used with caution in the following;

Patients with coronary artery disease, severe cardiac insufficiency, conduction disturbances or clinically relevant bradycardia.

Patients concomitantly taking other medicinal products associated with QT prolongation.

Elderly patients may be more susceptible to drug-associated effects on the QT interval.

Epidemiological studies investigating the risk of adverse cardiovascular outcomes with macrolides have shown variable results. Some observational studies have identified a rare short term risk of arrhythmia, myocardial infarction and cardiovascular mortality associated with macrolides including erythromycin. Consideration of these findings should be balanced with treatment benefits when prescribing erythromycin.

Summary of Product Characteristics (SmPC)

ERYSTAR-250

(Erythromycin Stearate Tablets 250 mg)

There have been reports suggesting erythromycin does not reach the foetus in adequate concentrations to prevent congenital syphilis. Infants born to women treated during pregnancy with oral erythromycin for early syphilis should be treated with an appropriate penicillin regimen.

There have been reports that erythromycin may aggravate the weakness of patients with myasthenia gravis.

Erythromycin interferes with the fluorometric determination of urinary catecholamines.

Rhabdomyolysis with or without renal impairment has been reported in seriously ill patients receiving erythromycin concomitantly with statins.

There have been reports of infantile hypertrophic pyloric stenosis (IHPS) occurring in infants following erythromycin therapy. Epidemiological studies including data from meta-analyses suggest a 2-3-fold increase in the risk of IHPS following exposure to erythromycin in infancy. This risk is highest following exposure to erythromycin during the first 14 days of life. Available data suggests a risk of 2.6% (95% CI: 1.5 -4.2%) following exposure to erythromycin during this time period. The risk of IHPS in the general population is 0.1-0.2%. Since erythromycin may be used in the treatment of conditions in infants which are associated with significant mortality or morbidity (such as pertussis or chlamydia), the benefit of erythromycin therapy needs to be weighed against the potential risk of developing IHPS. Parents should be informed to contact their physician if vomiting or irritability with feeding occurs.

4.5 Interaction with other medicinal products and other forms of interaction

Increases in serum concentrations of the following drugs metabolised by the cytochrome P450 system may occur when administered concurrently with erythromycin: acenocoumarol, alfentanil, astemizole, bromocriptine, carbamazepine, cilostazol, ciclosporin, digoxin, dihydroergotamine, disopyramide, ergotamine, hexobarbitone, methylprednisolone, midazolam, omeprazole, phenytoin, quinidine, rifabutin, sildenafil, tacrolimus, terfenadine, domperidone, theophylline, tolterodine, triazolam, valproate, vinblastine, and antifungals e.g. fluconazole, ketoconazole and itraconazole. Appropriate monitoring should be undertaken and dosage should be adjusted as necessary. Particular care should be taken with medications known to prolong the QTc interval of the electrocardiogram.

Drugs that induce CYP3A4 (such as rifampicin, phenytoin, carbamazepine, phenobarbital, St John's Wort) may induce the metabolism of erythromycin. This may lead to sub-therapeutic levels of erythromycin and a decreased effect. The induction decreases gradually during two weeks after discontinued treatment with CYP3A4 inducers. Erythromycin should not be used during and two weeks after treatment with CYP3A4 inducers.

HMG-CoA Reductase Inhibitors: erythromycin has been reported to increase concentrations of HMG-CoA reductase inhibitors (e.g. lovastatin and simvastatin).

Rare reports of rhabdomyolysis have been reported in patients taking these drugs concomitantly.

Contraceptives: some antibiotics may in rare cases decrease the effect of contraceptive pills by interfering with the bacterial hydrolysis of steroid conjugates in the intestine and thereby reabsorption of unconjugated steroid. As a result of this plasma levels of active steroid may decrease.

Antihistamine H1 antagonists: care should be taken in the coadministration of erythromycin with H1 antagonists such as terfenadine, astemizole and mizolastine due to the alteration of their metabolism by erythromycin.

Erythromycin significantly alters the metabolism of terfenadine, astemizole and pimozide when taken concomitantly. Rare cases of serious, potentially fatal, cardiovascular events

Summary of Product Characteristics (SmPC)

ERYSTAR-250

(Erythromycin Stearate Tablets 250 mg)

including cardiac arrest, torsade de pointes and other ventricular arrhythmias have been observed.

Observational data have shown that co-administration of azithromycin with hydroxychloroquine in patients with rheumatoid arthritis is associated with an increased risk of cardiovascular events and cardiovascular mortality. Because of the potential for a similar risk with other macrolides when used in combination with hydroxychloroquine or chloroquine, careful consideration should be given to the balance of benefits and risks before prescribing erythromycin for any patients taking hydroxychloroquine or chloroquine.

Anti-bacterial agents: an in vitro antagonism exists between erythromycin and the bactericidal beta-lactam antibiotics (e.g. penicillin, cephalosporin). Erythromycin antagonises the action of clindamycin, lincomycin and chloramphenicol. The same applies for streptomycin, tetracyclines and colistin.

Protease inhibitors: in concomitant administration of erythromycin and protease inhibitors, an inhibition of the decomposition of erythromycin has been observed.

Oral anticoagulants: there have been reports of increased anticoagulant effects when erythromycin and oral anticoagulants (e.g. warfarin, rivaroxaban) are used concomitantly.

Triazolobenzodiazepines (such as triazolam and alprazolam) and related benzodiazepines: erythromycin has been reported to decrease the clearance of triazolam, midazolam, and related benzodiazepines, and thus may increase the pharmacological effect of these benzodiazepines.

Post-marketing reports indicate that co-administration of erythromycin with ergotamine or dihydroergotamine has been associated with acute ergot toxicity characterised by vasospasm and ischaemia of the central nervous system, extremities and other tissues.

Elevated cisapride levels have been reported in patients receiving erythromycin and cisapride concomitantly. This may result in QTc prolongation and cardiac arrhythmias including ventricular tachycardia, ventricular fibrillation and torsades de pointes.

Similar effects have been observed with concomitant administration of pimozide and clarithromycin, another macrolide antibiotic.

Erythromycin use in patients who are receiving high doses of theophylline may be associated with an increase in serum theophylline levels and potential theophylline toxicity. In case of theophylline toxicity and/or elevated serum theophylline levels, the dose of theophylline should be reduced while the patient is receiving concomitant erythromycin therapy. There have been published reports suggesting when oral erythromycin is given concurrently with theophylline there is a significant decrease in erythromycin serum concentrations. This decrease could result in sub-therapeutic concentrations of erythromycin.

There have been post-marketing reports of colchicine toxicity with concomitant use of erythromycin and colchicine.

Hypotension, bradyarrhythmias and lactic acidosis have been observed in patients receiving concurrent verapamil, a calcium channel blocker.

Cimetidine may inhibit the metabolism of erythromycin which may lead to an increased plasma concentration.

Erythromycin has been reported to decrease the clearance of zopiclone and thus may increase the pharmacodynamic effects of this drug.

4.6 Fertility, pregnancy and lactation

There is a large amount of data from observational studies performed in several countries on exposure to erythromycin during pregnancy, compared to no antibiotic use or use of another antibiotic during the same period (>24,000 first trimester exposures). While most studies do not suggest an association with adverse fetal effects such as major congenital malformations,

Summary of Product Characteristics (SmPC)

ERYSTAR-250

(Erythromycin Stearate Tablets 250 mg)

cardiovascular malformations or miscarriage, there is limited epidemiological evidence of a small increased risk of major congenital malformations, specifically cardiovascular malformations following first trimester exposure to erythromycin.

Therefore, erythromycin should only be used during pregnancy if clinically needed and the benefit of treatment is expected to outweigh any small increased risks which may exist.

Erythromycin has been reported to cross the placental barrier in humans, but foetal plasma levels are generally low.

Erythromycin is excreted in breast milk, therefore, caution should be exercised when erythromycin is administered to a nursing mother due reports of infantile hypertrophic pyloric stenosis in breast-fed infants.

There have been reports that maternal macrolide antibiotics exposure within 7 weeks of delivery may be associated with a higher risk of infantile hypertrophic pyloric stenosis (IHPS).

4.7 Effects on ability to drive and use machines

Not relevant.

4.8 Undesirable effects

Blood and lymphatic system disorders

Eosinophilia.

Cardiac disorders

QTc interval prolongation, torsades de pointes, palpitations, and cardiac rhythm disorders including ventricular tachyarrhythmias.

Cardiac arrest, ventricular fibrillation (frequency not known)

Ear and labyrinth disorders

Deafness, tinnitus

There have been isolated reports of reversible hearing loss occurring chiefly in patients with renal insufficiency or high doses.

Gastrointestinal disorders

The most frequent side effects of oral erythromycin preparations are gastrointestinal and are dose-related. The following have been reported:

upper abdominal discomfort, nausea, vomiting, diarrhoea, pancreatitis, anorexia, infantile hypertrophic pyloric stenosis.

Pseudomembranous colitis has been rarely reported in association with erythromycin therapy.

General disorders and administration site conditions

Chest pain, fever, malaise.

Hepatobiliary disorders

Cholestatic hepatitis, jaundice, hepatic dysfunction, hepatomegaly, hepatic failure, hepatocellular hepatitis.

Immune system disorders

Allergic reactions ranging from urticaria and mild skin eruptions to anaphylaxis have occurred.

Investigations

Increased liver enzyme values.

Nervous system disorders

There have been isolated reports of transient central nervous system side effects including confusion, seizures and vertigo; however, a cause and effect relationship has not been established.

Psychiatric disorders

Hallucinations

Summary of Product Characteristics (SmPC)

ERYSTAR-250

(Erythromycin Stearate Tablets 250 mg)

Eye disorders

Mitochondrial Optic Neuropathy

Renal and urinary disorders

Interstitial nephritis

Skin and subcutaneous tissue disorders

Skin eruptions, pruritus, urticaria, exanthema, angioedema, Stevens-Johnson syndrome, toxic epidermal necrolysis, erythema multiforme.

Not known: acute generalised exanthematous pustulosis (AGEP)

Vascular disorders

Hypotension.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions to National Regulatory Authority.

4.9 Overdose

Symptoms: hearing loss, severe nausea, vomiting and diarrhoea.

Treatment: gastric lavage and general supportive measures.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic Group: Macrolides

ATC Code: J01FA01

Erythromycin exerts its antimicrobial action by binding to the 50S ribosomal sub-unit of susceptible microorganisms and suppresses protein synthesis. Erythromycin is usually active against most strains of the following organisms both in vitro and in clinical infections:

Gram positive bacteria - *Listeria monocytogenes*, *Corynebacterium diphtheriae* (as an adjunct to antitoxin), *Staphylococci* spp, *Streptococci* spp (including *Enterococci*).

Gram negative bacteria - *Haemophilus influenzae*, *Neisseria meningitidis*, *Neisseria gonorrhoeae*, *Legionella pneumophila*, *Moraxella* (*Branhamella*) *catarrhalis*, *Bordetella pertussis*, *Campylobacter* spp.

Mycoplasma - *Mycoplasma pneumoniae*, *Ureaplasma urealyticum*.

Other organisms - *Treponema pallidum*, *Chlamydia* spp, *Clostridia* spp, L-forms, the agents causing trachoma and lymphogranuloma venereum.

5.2 Pharmacokinetic properties

Peak blood levels normally occur within 1 hour of dosing of erythromycin ethylsuccinate granules. The elimination half life is approximately 2 hours. Doses may be administered 2, 3 or 4 times a day.

Erythromycin ethylsuccinate is less susceptible than erythromycin to the adverse effect of gastric acid. It is absorbed from the small intestine. It is widely distributed throughout body tissues. Little metabolism occurs and only about 5% is excreted in the urine. It is excreted principally by the liver.

5.3 Preclinical safety data

None Clinical reveal on safety data.

Summary of Product Characteristics (SmPC)

ERYSTAR-250

(Erythromycin Stearate Tablets 250 mg)

6. Pharmaceutical particulars

6.1 List of excipients

Sr. No.	Ingredients
1	Maize Starch
2	P.V.P.K-30
3	Isopropyl Alcohol
4	Talcum
5	Cross Carmellose Sodium
6	Colloidal anhydrous silica
7	HPMC 15 cps
8	Titanium Dioxide
9	Erythrosine
10	Carmoisine
11	Methylene Chloride

6.2 Incompatibilities

None Known

6.3 Shelf life

36 Months

6.4 Special precautions for storage

Store below 30°C. Protect from light & moisture.

6.5 Nature and contents of container

10 tablets packed in one ALU-PVC blister. Such 10 blisters are packed in one carton with insert.

6.6 Special precautions for disposal and other handling

No special requirements

7. MARKETING AUTHORISATION HOLDER AND MANUFACTURER

Marketing Authorisation Holder:

ZAIN PHARMA LTD.

Plot No: 209/13741, Colchester Park,
Go-Down No.1, 2, 3, Off Mombasa Road,
Behind Nice and Lovely House,
P.O. Box: 100167-00101, Nairobi, Kenya

8. Marketing Authorization Number:

CTD11686

9. Date of First <Registration> / Renewal of The <Registration>

Not Applicable

10. Date of Revision of the Text:

Jan 19, 2026

Summary of Product Characteristics (SmPC)
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(Erythromycin Stearate Tablets 250 mg)