ERYGEN-125 ORAL SUSPENSION

(ERYTHROMYCIN ETHYL SUCCINATE FOR ORAL SUSPENSION USP 125 MG/5 ML)

1.3 Product Information

1.3.1 Summary of product characteristics

SUMMARY OF PRODUCT CHARACTERISTICS (SPC)

1. NAME OF THE MEDICINAL PRODUCT

P-ONE ERYTHROMYCIN 125 ORAL SUSPENSION
(ERYTHROMYCIN ETHYL SUCCINATE FOR ORAL SUSPENSION USP 125 MG/5 ML)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Sr. No.	Ingredients	Spec	Mg/ 5 ml	Ovg. (%)	Std.batch qty (Kg)
1	*Erythromycin Ethyl Succinate Equivalent to Erythromycin	USP	161.400	2%	32.280
2	Sucrose	BP	1310.600	--	262.120
3	Kyron T 112 B	IHS	485.000	--	97.000
4	Flavour Orange (IFF)	IHS	35.000	--	7.000
5	Aspartame	BP	8.000	--	1.600
	Total		**2000.000**		

Note:
* Erythromycin Ethyl Succinate is taken as per as is basis
Average weight per Bottle: 40 gm ± 5%
USP: United States Pharmacopoeia
BP: British Pharmacopoeia
IHS: In House Specification

3. PHARMACEUTICAL FORM
Suspension

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

i) Antibiotic for treatment of infections caused by erythromycin sensitive organisms especially gram positive pyogenic cocci and some gram-negative bacteria. It may be used in a wide variety of clinical infections.
ii) Erythromycin is an appropriate alternative to penicillin in hypersensitive patients especially in pre or post operative patients.
iii) Respiratory Tract Infections:

Acute and chronic bronchitis, legionnaires disease, tracheitis, bronchiectasis, pneumonia.
iv) Skin and Soft Tissue Infections:
Acute infections of skin and soft tissue which are mild to moderately severe
v) Eye/Ear Infections:
Otitis media and otitis externa mastoiditis, chlamydial conjunctivitis, blepharitis
vi) Oral Infections:
Gingivitis, vincent's angina
vii) Gastro-Intestinal Infections:
Staphylococcal enterocolitis, cholecystitis, campylobacter infections
viii) Other Infections:
Gonorrhoea, Syphilis, Urethritis, Diphtheria, Pertussis

4.2 Posology and Method of Administration

Adults and children over 8 years: 2g/day in divided doses. For severe infections up to 4g/day in divided doses.
Children 2-8 years: 30 mg/kg/day in divided doses. For severe infections up to 50 mg/kg/day in divided doses.
Normal dose: 250mg four times a day or 500mg twice daily.
Children up to 2 years: 30mg/kg/day in divided doses. For severe infections up to 50mg/kg/day in divided doses.
Normal dose: 125mg four times a day or 250mg twice daily.
Presentations are available for adults and children over 8 years, children aged 2-8 years, and for children under 2 years.

Contraindications

Known hypersensitivity to erythromycin.
Erythromycin is contraindicated in patients taking simvastatin, tolterodine, mizolastine, amisulpride, astemizole, terfenadine, domperidone, cisapride or pimozide.
Erythromycin is contraindicated with ergotamine and dihydroergotamine.

4.4 Special Warnings and Precautions for use

Erythromycin is excreted principally by 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.
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.
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.
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. In one cohort of 157 newborns who were given erythromycin for pertussis prophylaxis, seven neonates (5%) developed symptoms of non-bilious vomiting or irritability with feeding and were subsequently diagnosed as having IHPS requiring surgical pyloromyotomy. 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, cyclosporin, digoxin, dihydroergotamine, disopyramide, ergotamine, hexobarbitone, methylprednisolone, midazolam, omeprazole, phenytoin, quinidine, rifabutin, sildenafil, tacrolimus, terfenadine, domperidone, theophylline, 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.
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 including cardiac arrest, torsade de pointes and other ventricular arrhythmias have been

observed (see sections 4.3 and 4.8).
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) 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.
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 Pregnancy and Lactation

There are no adequate and well-controlled studies in pregnant women. However, observational studies in humans have reported cardiovascular malformations after exposure to medicinal products containing erythromycin during early pregnancy.
Erythromycin has been reported to cross the placental barrier in humans, but foetal plasma levels are generally low.
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).
Erythromycin can be excreted into breast-milk. Caution should be exercised when administering erythromycin to lactating mothers due reports of infantile hypertrophic pyloric stenosis in breast-fed infants.

4.7 Effects on ability to drive and use machines

None known

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.

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 disfunction, 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

Eye disorders
Mitochondrial Optic Neuropathy

Renal and urinary disorders
Interstitial nephritis

Skin and subcutaneous tissue disorders
Skin eruptions, prurituls, urticaria, exanthema, angioedema, Stevens-Johnson syndrome, toxic

epidermal necrolysis, erythema multiforme.
Not known: acute generalised exanthematous pustulosis (AGEP)

Vascular disorders
Hypotension.

4.9 Overdose

Symptoms: hearing loss, severe nausea, vomiting and diarrhoea.
Treatment: gastric lavage, general supportive measures.

5.1 Pharmacodynamic Properties

Pharmacotherapeutic group: Macrolide Antibiotic

ATC code: J01F A

Mechanism of action:
Erythromycin is a Macrolide antibiotic which acts by interfering with bacterial protein synthesis and is bacteriostatic or bactericidal depending on its concentration and the type of organism. Sensitive organisms include:
i) Gram - positive bacteria such as staph aureus, staph epidermis, strep pyogenes, strep pneumoniae, strep viridans, corynebacterium diptheriae and listeria monocytogenes;
ii) Gram - negative bacteria such as h influenzae, n meningitidis, n gonorrhoea, b pertussis, campylobacter strains and legionella pneumophila; treponema pallidum ; mycoplasma pneumoniae ;
chlamydia trachomatis

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

Not applicable

6. PHARMACEUTICAL PARTICULARS

6.1 List of Excipients

1.	Sucrose	BP
2.	Kyron T 112 B	IHS
3.	Flavour Orange (IFF)	IHS
4.	Aspartame	BP

6.2 Incompatibilities

None

6.3 Shelf Life

24 months

6.4 Special Precautions for Storage

Store at a temperature below 30°C.Do not freeze. Keep the bottle tightly closed .The suspension should be used within 14 days of preparation and stored in cool dry place preferably in a refrigerator
Keep all medicines out of reach of children.

6.5 Nature and contents of container

Bottle Pack of 100 ml

6.6 Special precautions for disposal and other handling

No special requirement

10. DATE OF REVISION OF THE TEXT

As per revision