NEW ZEALAND DATA SHEET

E-MYCIN®

1. Product Name

E-Mycin (erythromycin) 200 mg/5 mL and 400 mg/5 mL granules for oral suspension.

E-Mycin (erythromycin) 400 mg film coated tablet.

2. Qualitative and Quantitative Composition

E-Mycin 200 granules for oral suspension, containing erythromycin ethylsuccinate 234 mg per 5 mL, equivalent to 200 mg per 5 mL of erythromycin.

E-Mycin 400 granules for oral suspension, containing erythromycin ethylsuccinate 468 mg per 5 mL, equivalent to 400 mg per 5 mL of erythromycin.

Excipients with known effect (granules): Sodium benzoate, aspartame and sorbitol.

Allergen declaration: Contains benzoates, aspartame and sorbitol (12.5 g in 40 mL for E-Mycin 200 mg/5 mL, and 5.1 g in 20 mL for E-Mycin 400 mg/5 mL).

Each E-Mycin film-coated tablet contains erythromycin ethylsuccinate 482 mg, equivalent to 400 mg of erythromycin.

Excipients with known effect (tablet): Maize starch and sorbic acid.

Allergen declaration: Contains sulfites and sorbates.

For the full list of excipients, see section 6.1.

3. Pharmaceutical Form

E-Mycin 200: Granules for oral suspension. Free flowing pink granules which when mixed with the stated quantity of water provide a cherry flavoured suspension containing erythromycin ethylsuccinate.

E-Mycin 400: Granules for oral suspension. Free flowing pink granules which when mixed with the stated quantity of water provide a cherry flavoured suspension containing erythromycin ethylsuccinate.

E-Mycin tablet oval, normal convex, flesh pink film-coated tablet debossed "E-N" on one side and "α" on the other.

4. Clinical Particulars

4.1 Therapeutic Indications

Streptococcus pyogenes (Group A beta-haemolytic streptococcus)

Upper and lower respiratory tract, skin and soft tissue infections of mild to moderate severity. When oral medication is preferred for treatment of streptococcal pharyngitis and in long term prophylaxis of rheumatic fever, erythromycin is an alternate drug of choice.

When oral medication is given, the importance of strict adherence by the patient to the prescribed dosage regimen must be stressed. A therapeutic dose should be administered for at least 10 days.

Prevention of Initial Attacks of Rheumatic Fever

Penicillin is considered to be the drug of choice in the prevention of initial attacks of rheumatic fever (treatment of Group A beta-haemolytic streptococcal infections of the upper respiratory tract e.g. tonsillitis or pharyngitis). Erythromycin is indicated for the treatment of penicillin-allergic patients. The therapeutic dose should be administered for 10 days.

Prevention of Recurrent Attacks of Rheumatic Fever

Penicillin or sulphonamides are considered to be the drugs of choice in the prevention of recurrent attacks of rheumatic fever. In patients who are allergic to penicillin and sulphonamides, oral erythromycin is recommended in the long term prophylaxis of streptococcal pharyngitis (for the prevention of recurrent attacks of rheumatic fever).

Prevention of Bacterial Endocarditis

Although no controlled clinical efficacy trials have been conducted, oral erythromycin has been recommended for prevention of bacterial endocarditis in penicillin-allergic patients with prosthetic cardiac valves, most congenital cardiac malformations, surgically constructed systemic pulmonary shunts, rheumatic or other acquired valvular dysfunction, idiopathic hypertrophic subaortic stenosis (IHSS), previous history of bacterial endocarditis or mitral valve prolapse with insufficiency when they undergo dental procedures or surgical procedures of the upper respiratory tract.

Alpha-haemolytic streptococci (viridans group)

Although no controlled clinical efficacy trials have been conducted, oral erythromycin has been suggested for use in a regimen for prophylaxis against bacterial endocarditis in patients hypersensitive to penicillin who have congenital heart disease, or rheumatic or other acquired valvular heart disease when they undergo dental procedures or surgical procedures of the upper respiratory tract. Erythromycin is not suitable prior to genitourinary or gastrointestinal tract surgery.

Staphylococcus aureus

Acute infections of skin and soft tissue of mild to moderate severity. Resistant organisms may emerge during treatment.

Streptococcus pneumoniae (Diplococcus pneumoniae)

Upper respiratory tract infections (e.g. otitis media, pharyngitis) and lower respiratory tract infections (e.g. pneumonia) of mild to moderate degree.

Mycoplasma pneumoniae (Eaton agent, PPLO)

For respiratory infections due to this organism.

Haemophilus influenzae

For upper respiratory tract infections of mild to moderate severity. Not all strains of this organism are susceptible to erythromycin at concentrations achieved with usual therapeutic doses; resistant strains may require concomitant therapy with sulphonamides.

Ureaplasma urealyticum

For the treatment of urethritis caused by these organisms in adult males.

Neisseria gonorrhoeae

ERA-IV (erythromycin lactobionate for injection) in conjunction with erythromycin orally, as an alternative drug in treatment of acute pelvic inflammatory disease caused by *N. gonorrhoeae* in female patients with a history of sensitivity to pencillin. Before treatment of gonorrhoea, patients who are suspected of also having syphilis should have a microscopic examination for *T. pallidum* (by immunofluorescence or darkfield) before receiving erythromycin, and monthly serologic tests for a minimum of 4 months thereafter.

Chlamydia trachomatis

Erythromycin is indicated for treatment of the following infections caused by Chlamydia trachomatis; conjunctivitis of the newborn, pneumonia of infancy and urogenital infections during pregnancy (see section 4.4). When tetracyclines are contraindicated or not tolerated, erythromycin is indicated for the treatment of uncomplicated urethral, endocervical or rectal infections in adults due to Chlamydia trachomatis.

Treponema pallidum

Erythromycin is an alternate choice of treatment for primary syphilis in patients allergic to the penicillins. In treatment of primary syphilis, spinal fluid examinations should be done before treatment and as part of follow-up therapy. Erythromycin should not be used for the treatment of syphilis in pregnancy because it cannot be relied upon to cure an infected foetus.

Corynebacterium diphtheriae

As an adjunct to antitoxin, to prevent establishment of carriers, and to eradicate the organism in carriers.

Corynebacterium minutissimum

For the treatment of erythrasma.

Entamoeba histolytica

In treatment of intestinal amoebiasis only. Extra-enteric amoebiasis requires treatment with other agents.

Listeria monocytogenes

Infections due to this organism.

Bordetella pertussis

Erythromycin is effective in eliminating the organism from the nasopharynx of infected individuals, rendering them non-infectious. Some clinical studies suggest that erythromycin may be helpful in the prophylaxis of pertussis in exposed susceptible individuals.

Legionnaire's Disease

Clinical evidence suggests that erythromycin is the preferred antibiotic for treating Legionnaire's Disease.

4.2 Dose and method of administration

Dose

Adults

400 mg erythromycin (as erythromycin ethylsuccinate) every 6 hours is the usual dose. Dosage may be increased up to 4 g per day according to the severity of the infection. If twice-a-day dosage is desired, one-half of the total daily dose may be given every 12 hours. Doses may also be given three times daily by administering one-third of the total daily dose every 8 hours.

In the treatment of streptococcal infections, a therapeutic dosage of erythromycin (as erythromycin ethylsuccinate) should be administered for at least 10 days. In continuous prophylaxis against recurrences of streptococcal infections in persons with a history of rheumatic heart disease, the usual dosage is 400 mg twice a day.

For prophylaxis against bacterial endocarditis in patients with congenital heart disease, or rheumatic or other acquired valvular heart disease when undergoing dental procedures or surgical procedures of the upper respiratory tract, give 1.6 g (20 mg/kg for children) orally 1.5 to 2 hours before the procedure, and then 800 mg (10 mg/kg for children) orally every 6 hours for 8 doses.

For treatment of urethritis due to *C. trachomatis* or *U. urealyticum* 800 mg every 6 to 8 hours for 7 days or 400 mg every 6 to 8 hours for 14 days.

For treatment of primary syphilis: Adults 48 to 64 g given in divided doses over a period of 10 to 15 days.

For intestinal amoebiasis: Adults 400 mg four times daily for 10 to 14 days. Children 30 to 50 mg/kg/day in divided doses for 10 to 14 days.

For use in pertussis: Although optimal dosage and duration have not been established, doses of erythromycin utilized in reported clinical studies were 40 to 50 mg/kg/day, given in divided doses for 5 to 14 days.

For treatment of Legionnaire's Disease: Although optimal doses have not been established, doses utilized in reported clinical data were 1.6 to 4 g daily in divided doses.

Special Populations

Paediatric

Age, weight, and severity of the infection are important factors in determining the proper dosage. In mild to moderate infections the usual dosage of erythromycin (as erythromycin ethylsuccinate) for children is 30 to 50 mg/kg/day in equally divided doses every six hours. For more severe infections this dosage may be doubled.

If twice-a-day dosage is desired one-half of the total daily dose may be given every 12 hours. Doses may also be given three times daily if desired by administering one-third of the total daily dose every 8 hours.

The following dosage schedule is suggested for mild to moderate infections

Body weight	Total daily dose (erythromycin base)
<4.5kg	30-50 mg/kg/day
4.5 - 6.8kg	200 mg
6.8 - 11kg	400 mg
11 – 23kg	800 mg
23 - 45kg	1200 mg
Over 45kg	1600 mg

Method of Administration

E-Mycin suspensions and tablets may be administered without regard to meals.

4.3 Contraindications

Erythromycin is contraindicated in the case of:

- Hypersensitivity to erythromycin, or any of the excipients in the formulation
- Hypersensitivity to other antibiotics from the macrolide family.
- Severely impaired hepatic function
- Congenital or acquired QT interval prolongation
- Concurrent treatment with ergotamine or dihydroergotamine (see Section 4.5)
- Disturbances of the electrolyte balance (especially in the case of hypokalaemia and hypomagnesaemia)
- Clinically relevant cardiac arrhythmias (e.g. ventricular arrhythmias) or in severe congestive heart failure (NYHA IV)
- Concomitant intake of medicinal products, which can lead to prolongation of the QT interval and under some circumstances to life-threatening ventricular arrhythmia (torsade de pointes) e.g. terfenadine, astemizole, domperidone, cisapride, pimozide, class IA and III antiarrhythmics (e.g. disopyramide), certain neuroleptics, tri- and tetracyclic antidepressants, arsenic trioxide, methadone, budipine, certain fluoroquinolones, imidazole anti-mycotics and anti-malarials (e.g. pentamidine i.v.) (see section 4.5)
- Concomitant use of simvastatin, lovastatin or atorvastatin. Treatment with these agents should be interrupted while taking erythromycin (see Section 4.5)
- Concomitant administration of lomitapide (see Section 4.5).

4.4 Special warnings and precautions for use

QTc prolongation

Prolongation of the QT interval and development of ventricular arrhythmias (some of which have been fatal), including atypical ventricular tachycardia (torsades de pointes), have been reported with the administration of erythromycin. Therefore, use of erythromycin is contraindicated in patients with high risk factors for cardiac arrhythmia (see Section 4.3 CONTRAINDICATIONS) and should be used with caution in patients with coronary artery disease, severe cardiac insufficiency, conduction disturbances or clinically relevant bradycardia.

If during therapy with erythromycin symptoms such as palpitations, dizziness or syncope occur which can be signs of arrhythmia, an investigation of the patient including electrocardiogram and determination of the QT interval should be initiated immediately.

Electrolyte disturbances promote the probability of cardiac arrhythmia. In the case of risk factors for electrolyte disturbances (such as diuretic/laxative medication, vomiting, diarrhoea, use of insulin in emergency situations, renal diseases or anorectic conditions), adequate laboratory tests and if necessary an adequate electrolyte balance should be carried out.

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.

Musculature and nervous system

Rhabdomyolysis with or without renal impairment has been reported in seriously ill patients receiving erythromycin concomitantly with simvastatin, lovastatin or atorvastatin (see Section 4.5). The concomitant use of these medicines with erythromycin is contraindicated (see section 4.3).

Patients taking other statins and erythromycin concomitantly should be instructed by the physician to pay attention to signs of myopathy (e.g. inexplicable muscle pain or weakness or dark coloured urine). If myopathy occurs, the intake of the statin has to be stopped immediately.

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

Clostridium difficile-associated diseases

The use of erythromycin can lead to the development of severe colitis as a result of colonisation with *Clostridium difficile*, a toxin-producing organism. Colitis, which may or may not be accompanied by the formation of a pseudomembrane in the colon, can range in severity from mild diarrhoea to fatal colitis. If significant diarrhoea occurs, erythromycin should be discontinued (diarrhoea may, however, begin up to several weeks to over two months after cessation of antibiotic therapy). This may be sufficient treatment in the early stages although colestyramine orally may help by binding the toxin in the colonic lumen. In moderate to severe cases appropriate therapy with a suitable oral antibacterial agent effective against *Clostridium difficile* should be considered.

Drugs which delay peristalsis, e.g. opiates and diphenoxylate with atropine may prolong and/or worsen the condition and should not be used.

Allergic reactions

With the administration of erythromycin, severe, life-threatening allergic reactions may occur, e.g. severe skin reactions such as erythema multiforme, Stevens-Johnson syndrome or toxic epidermal necrolysis (especially in children of all ages), as well as angioneurotic oedema or anaphylaxis. A cross allergy in patients with hypersensitivity to macrolide antibiotics can exist, so in patients with known hypersensitivity to macrolides or related substances (e.g. ketolides), special caution is recommended. At first signs of hypersensitivity, erythromycin has to be stopped immediately and necessary symptomatic emergency measures initiated.

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.

Prolonged or repeated therapy

Overgrowth of non-susceptible bacteria or fungi may occur during prolonged or repeated therapy. If superinfection occurs, erythromycin should be discontinued and appropriate therapy instituted.

In the case of a treatment duration longer than 3 weeks, it is recommended that whole blood count and hepatic and renal function tests be performed at regular intervals.

Eye disorder

There is a risk for developing visual impairments after exposure to erythromycin. For some patients, a pre-existing dysfunction in mitochondrial metabolism from genetic causes such as Leber's hereditary optic neuropathy (LHON) and autosomal dominant optic atrophy (ADOA) might play a contributing role.

Pneumonia

Due to very common resistance of *Streptococcus pneumoniae* against macrolides, erythromycin is not the first choice therapy in case of ambulant acquired pneumonia. In hospital acquired pneumonia, erythromycin should only be used in combination with other antibiotics.

Oral erythromycin is not considered to be the antibiotic of choice in critically ill patients.

When indicated, incision or drainage or other surgical procedures should be performed in conjunction with antibiotic therapy.

Vomiting and diarrhoea

Use of erythromycin can cause vomiting and diarrhoea (see Section 4.8) impairing the efficacy of this and other concomitantly taken medicines.

Use in hepatic impairment

There have been reports of hepatic dysfunction, including increased liver enzymes, hepatomegaly and hepatocellular and/or cholestatic hepatitis, with or without jaundice, occurring in patients receiving oral erythromycin products (see Section 4.8). Patients should be informed to terminate the therapy and seek medical advice if signs and symptoms of liver disease such as loss of appetite, jaundice, dark colouring of the urine and itching or pressure sensitivity of the stomach develop.

Since erythromycin is principally excreted by the liver, caution should be exercised when erythromycin is administered to patients with impaired hepatic function. Erythromycin in contraindicated in severe hepatic impairment (see Section 4.3).

Patients with existing liver damage and allergies may be at higher risk of intrahepatic cholestasis and cholestatic jaundice due to sensitisation, resulting in colicky abdominal pain, nausea, vomiting, urticaria, eosinophilia and fever. Although these reactions can occur after initial administration, the risk increases with repeated administration and therapy lasting longer than 10 days (see Section 4.8).

Use in the elderly

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

Paediatric use

To avoid liver damage due to overdose in infants and toddlers, dosing should be dependent on the clinical picture and the course of the disease.

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. A possible dose-response effect was described with an absolute risk of IHPS of 5.1% for infants who took erythromycin for 8 to 14 days and 10% for infants who took erythromycin for 15 to 21 days. 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 trachomatis*), 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.

Laboratory tests

Erythromycin interferes with the fluorometric determination of urinary catecholamines.

For erythromycin 200 mg/5 mL and 400 mg/5 mL granules for oral suspension, which contains sorbitol, propylene glycol, aspartame and benzoate

Sorbitol

Patients with hereditary fructose intolerance (HFI) should not be given this medicine, as sorbitol may cause gastrointestinal discomfort and mild laxative effects.

Propylene glycol

Co-administration with any substrate for alcohol dehydrogenase such as ethanol may induce serious adverse effects in neonates.

Aspartame

Aspartame is a source of phenylalanine. It may be harmful in case of phenylketonuria (PKU), a rare genetic disorder in which phenylalanine builds up because it cannot be eliminated from the body properly.

Benzoate

May increase jaundice in newborn babies up to 4 weeks old.

4.5 Interaction with other medicines and other forms of interaction

Theophylline

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 that when oral erythromycin is given concomitantly with theophylline there is a significant decrease in erythromycin serum concentrations. This decrease could result in subtherapeutic concentrations of erythromycin.

Carbamazepine

Erythromycin administration in patients receiving carbamazepine has been reported to cause increased serum levels of carbamazepine with subsequent development of signs of carbamazepine toxicity.

Digoxin

Concomitant administration of erythromycin and digoxin has been reported to result in elevated digoxin serum levels. In approximately 10% of the patients treated with digoxin, glycoside is reduced to inactive dihydro metabolites of the bacterial flora. Antibiotic treatment can reduce this degradation and thereby increase plasma concentrations.

Oral anticoagulants

Erythromycin can inhibit the metabolism of warfarin leading to enhanced effects. There have been reports of increased anticoagulant effects when erythromycin and oral anticoagulants (e.g. warfarin, rivaroxaban) were used concomitantly.

Medicines that prolong the QTc interval

Erythromycin has been shown to prolong the QTc interval and is associated with case reports of torsade de pointes in some patients. Patients with uncorrected electrolyte disorders particularly hypokalaemia; known prolongation of the QTc interval, or those concurrently receiving medicines that prolong the QTc interval, in particular Class IA (e.g. quinidine, procainamide) or Class III (amiodarone, sotalol) antiarrhythmics, certain neuroleptics, tri- and tetracyclic antidepressants, ebastine, arsenic trioxide, methadone, budipine, certain fluoroquinolones, imidazole anti-mycotics and anti-malarial medicines (e.g. pentamidine i.v.), are at increased risk of ventricular arrhythmias. As these predisposing conditions may increase the risk for ventricular arrhythmias, erythromycin should not be used in patients with ongoing proarrhythmic conditions (see Section 4.3).

Medicines metabolised by the cytochrome P450 system

Erythromycin is a substrate and inhibitor of the 3A isoform subfamily of the cytochrome P450 system (CYP3A) and P-glycoprotein, and also inhibits isoenzyme CYP1A2. Co-administration of erythromycin and a drug primarily metabolised by CYP3A may be associated with elevations in drug concentrations that could increase or prolong both the therapeutic or adverse effects of the concomitant medicine e.g. ciclosporin, phenytoin, felodipine, hexobarbital, carbamazepine, alfentanil, disopyramide, bromocriptine, valproate, methylprednisolone, vinblastine, sildenafil, cilostazol, quinidine, tacrolimus, rifabutin, verapamil, diltiazem, acenocoumarol, astemizole, digoxin, dihydroergotamine, ergotamine, midazolam, omeprazole, terfenadine, mizolastine, domperidone, theophylline, triazolam, buspirone, clozapine, lomitapide and antifungals (e.g. fluconazole, ketoconazole and itraconazole). Dosage adjustments may be considered, and when possible, serum concentrations of medicines primarily metabolised by CYP3A4 should be monitored closely in patients receiving erythromycin.

Erythromycin has been shown to prolong the QTc interval and is associated with case reports of torsades de pointes in some patients. In one published study patients who used both oral erythromycin and strong CYP3A inhibitors (azole antifungal medicines [ketoconazole, itraconazole and fluconazole, all administered systemically], diltiazem, verapamil, troleandomycin, mibefradil, nefazodone) had a risk of sudden death from cardiac causes that was five times as great as that among patients who had not used these medicines. Many of the medicines that are known to block CYP3A4 also have direct effects on repolarisation, which may cause a dramatic lengthening of the QT interval. Given that there are alternatives to erythromycin and these listed CYP3A inhibitors, the use of these combinations should be avoided.

Hypotension, bradyarrhythmia and lactic acidosis have been observed in patients receiving concurrent verapamil.

Medicines that induce CYP3A (such as rifampicin, rifabutin, phenytoin, carbamazepine, phenobarbital (phenobarbitone), 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 after discontinuing treatment with CYP3A4 inducers. Erythromycin should not be used during, or for two weeks after stopping treatment, with CYP3A4 inducers.

The following are examples of some clinically significant CYP3A based drug interactions. Interactions with other medicines metabolised by the CYP3A isoform are also possible. The following CYP3A based drug interactions have been observed with erythromycin products in post-marketing experience:

Ergotamine / dihydroergotamine

Concurrent use of erythromycin and ergotamine or dihydroergotamine has been associated in some patients with acute ergot toxicity characterised by severe peripheral vasospasm and dysaesthesia (see Section 4.3).

Triazolobenzodiazepines (such as triazolam and alprazolam) and related benzodiazepines

Triazolam plasma concentrations may approximately double when erythromycin is co-administered, due to a reduction in clearance and increase in elimination half-life but drug accumulation has not been observed with repeated dosing. Therefore consideration of dose reduction may be appropriate in patients treated concurrently with triazolam and erythromycin.

HMG-CoA Reductase Inhibitors

Erythromycin has been reported to increase concentrations of HMG-CoA reductase inhibitors (e.g., lovastatin, simvastatin or atorvastatin). Rare reports of rhabdomyolysis have been reported in patients taking these medicines concomitantly (see Section 4.3).

Sildenafil (e.g. Viagra)

Erythromycin has been reported to increase the systemic exposure (AUC) of sildenafil. Reduction of sildenafil dosage should be considered.

Zopiclone

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

Cisapride

Elevated cisapride levels have been reported in patients receiving erythromycin and cisapride concomitantly. This may result in QT prolongation and cardiac arrhythmias including ventricular tachycardia, ventricular fibrillation and torsade de pointes. Similar effects have been observed in patients taking pimozide and clarithromycin, another macrolide antibiotic. Concomitant administration of erythromycin with cisapride or pimozide is contraindicated (see section 4.3).

Colchicine

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

Cimetidine

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

Protease inhibitors

Protease inhibitors (e.g. ritonavir) has been reported to increase the level of effect of erythromycin by altering drug metabolism.

Anti-bacterial agents

Antagonism has been demonstrated in vitro between erythromycin and clindamycin, lincomycin and chloramphenicol. Same interaction is applicable with streptomycin, tetracyclines, colistin and bactericidal beta-lactam antibiotics (e.g. penicillin, cephalosporin).

Corticosteroids

Caution should be exercised in concomitant use of erythromycin with systemic and inhaled corticosteroids that are primarily metabolized by CYP3A4 due to the potential for increased systemic exposure to corticosteroids. If concomitant use occurs, patients should be closely monitored for systemic corticosteroid undesirable effects.

Hydroxychloroquine and chloroquine

Erythromycin should be used with caution in patients receiving these medicines known to prolong the QT interval due to the potential to induce cardiac arrhythmia and serious adverse cardiovascular events.

Fexofenadine

With concomitant administration, plasma concentrations of fexofenadine increase due to increased absorption.

4.6 Fertility, pregnancy and lactation

Effects on fertility

There was no apparent effect on male or female fertility in rats treated with erythromycin base by oral gavage at 700 mg/kg/day (approximately 9 times the maximum human dose).

Pregnancy

Category A.

Drugs which have been taken by a large number of pregnant women and women of childbearing age without any proven increase in the frequency of malformations or other direct or indirect harmful effects on the foetus having been observed.

No evidence of teratogenicity or embryotoxicity was observed when erythromycin base was given by oral gavage to pregnant rats and mice at 700 mg/kg/day (approximately 9 times the maximum human dose), and to pregnant rabbits at 125 mg/kg/day (approximately 1.5 times the maximum human dose).

A slight reduction in birth weights was noted when female rats were treated prior to mating, during mating, gestation and lactation at an oral dosage of 700 mg/kg/day of erythromycin base; weights of the offspring were comparable to those of the controls by weaning. No evidence of teratogenicity or effects on reproduction were noted at this dosage. When administered during late gestation and lactation periods, this dosage of 700 mg/kg/day

(approximately 9 times the maximum human dose) did not result in any adverse effects on birth weight, growth and survival of offspring.

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. Erythromycin does not reach the foetus in adequate concentration to prevent congenital syphilis. Newborns of mothers treated with oral erythromycin against early syphilis during pregnancy, will require treatment with an appropriate antibiotic, e.g. penicillin.

Erythromycin should be used by women during pregnancy only if clearly needed.

Breastfeeding

Erythromycin is concentrated in breast milk and adverse effects have been seen in breast-fed infants including gastrointestinal disturbances, pyloric stenosis (see section 4.4), sensitisation or colonisation with fungi. Caution should therefore be exercised when erythromycin is administered to a breastfeeding woman.

Effects on the Neonate

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. Patients should be informed to contact their physician if vomiting or irritability with feeding occurs.

4.7 Effects on ability to drive and use machines

Erythromycin has a negligible influence on the ability to concentrate and react. However the occurrence of undesirable effects can negatively influence the ability to drive and use machines.

4.8 Undesirable effects

The most frequent side effects of erythromycin preparations are gastrointestinal, such as abdominal cramping and discomfort, and are dose-related. Nausea, vomiting, and diarrhoea occur infrequently with usual oral doses.

The following adverse effects have been reported for erythromycin. The adverse effects are listed according to the frequency defined as:

- Very common (≥ 1/10)
- Common (≥ 1/100 - < 1/10)
- Uncommon (≥ 1/1000 - < 1/100)
- Rare (> 1/10000 - < 1/1000)
- Very rare (< 1/10000)
- Not known (cannot be estimated from the available data)

Infections and infestations

Uncommon: Overgrowth of non-susceptible bacteria or fungi (e.g. oral and vaginal candidiasis)

Rare: Pseudomembranous colitis

Blood and lymphatic system disorders

Not known: Eosinophilia

Immune system disorders

Uncommon: Hypersensitivity ranging from urticaria and mild rash

Rare: Anaphylactic reaction including anaphylactic shock

Metabolism and nutritional disorders

Very common: Decreased appetite

Psychiatric disorders

Not known: Hallucinations and confusional state

Nervous system disorders

Rare: Seizures

Not known: Headache, somnolence and dizziness

Eye disorders

Not known: Visual impairment including diplopia and vision blurred

Ear and labyrinth disorders

Very rare: Tinnitus, reversible hearing loss and deafness*

Not known: Vertigo

*These disorders are concentration-dependent and are more likely in patients with severe renal and/or hepatic impairment or in high doses or in cases of overdose.

Cardiac disorders

Rare: QT interval prolongation, cardiac arrhythmias such as ventricular tachycardia (torsade de pointes), cardiac arrest and palpitation

Vascular disorders

Not known: Hypotension

Respiratory, thoracic and mediastinal disorders

Not known: Dyspnoea (including asthmatic states)

Gastrointestinal disorders

Very common: Nausea, vomiting, abdominal pain, flatulence, soft defecation or diarrhoea

Rare: Pancreatitis

Very rare: Spastic hypertrophic pyloric stenosis in children

Not known: Abdominal discomfort, pseudomembranous colitis

Hepatobiliary disorders

Uncommon:	Elevation of certain liver enzymes (GPT, GPT. LDH, AP, γ-GT)
Rare:	Cholestasis and cholestatic jaundice, bilirubin elevations
Very rare:	Hepatic dysfunction, with or without jaundice, hepatitis, and/or abnormal liver function test results, hepatomegaly and hepatic failure

Skin and subcutaneous tissue disorders

Uncommon:	Erythema, urticarial exanthema, pruritus
Rare:	Erythema multiforme, Stevens-Johnson Syndrome, Toxic Epidermal Necrolysis, allergic oedema/angioedema
Not known:	Acute generalised exanthematous pustulosis (AGEP)

Musculoskeletal and connective tissue disorders

Very common:	Muscle spasms
Rare:	Joint swelling, rhabdomyolysis
Very rare:	Unmasking and worsening of myasthenia gravis

Renal and urinary disorders

Very rare:	Tubulointerstitial nephritis

General disorders and administration site conditions

Rare:	Pyrexia
Not known:	Chest pain, malaise, headache

Infantile hypertrophic pyloric stenosis (IHPS)

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 oral erythromycin for pertussis, seven neonates (5%) developed symptoms of non-bilious vomiting or irritability with feeding and were subsequently diagnosed as having IHPS requiring surgical pyloromyotomy. The relative risk of IHPS was increased 6.8 fold (95% CI=3-16) compared to a retrospective cohort of infants.

Reporting of suspected adverse reactions - Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions https://pophealth.my.site.com/carmreportnz/s/.

4.9 Overdose

Symptoms: ingestion of large amounts of erythromycin can be expected to produce reversible hearing loss, nausea, vomiting, diarrhoea, possible hallucinations, pancreatitis, allergic reactions, liver effects and other adverse effects (see section 4.8). In case of overdosage, erythromycin should be discontinued.

Treatment: Allergic reactions accompanying overdosage should be treated by the prompt elimination of unabsorbed drug and supportive measures. Erythromycin serum levels are not appreciably altered by haemodialysis or peritoneal dialysis.

For risk assessment and advice on the management of overdose please contact the National Poisons Centre on 0800 POISON (0800 764 766).

5. Pharmacological Properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Macrolides, ATC code: J01FA01

Mechanism of action

Microbiology

The mode of action of erythromycin has been well characterized. Erythromycin binds to the 50S ribosomal sub-units of susceptible bacteria and suppresses protein synthesis without affecting nucleic acid synthesis. Erythromycin is usually active *in vitro* against the following Gram positive and Gram negative organisms:

Streptococcus pyogenes
Alpha-haemolytic streptococci (viridans group)
Staphylococcus aureus
Streptococcus pneumoniae
Corynebacterium diphtheriae (as an adjunct to antitoxin)
Corynebacterium
minutissimum Listeria
monocytogenes
Clostridium
tetani Neisseria
gonorrhoeae
Bordetella
pertussis
Haemophilus influenzae (some strains are resistant)
Legionella pneumophila
Treponema pallidum
Chlamydia trachomatis
Mycoplasma pneumoniae
Campylobacter jejuni (in severe or prolonged cases)
Ureaplasma urealyticum

Not all strains of the organism listed above are sensitive and culture and susceptibility testing should be done. Several strains of *Haemophilus influenzae* and *Staphylococci* have been found to be resistant to erythromycin. Some strains of *Haemophilus influenza* are resistant to erythromycin alone, but are susceptible when erythromycin and sulphonamides are administered concurrently. *Staphylococci* resistant to erythromycin may emerge during a course of therapy.

Antagonism has been demonstrated *in vitro* between erythromycin and clindamycin, lincomycin and chloramphenicol. Susceptibility Testing

Dilution or diffusion techniques - either quantitative (MIC) or breakpoint, should be used following a regular updated, recognized and standardised method (e.g. CLSI).

Standardised susceptibility test procedures require the use of laboratory control microorganisms to control the technical aspects of the laboratory procedures.

- A report of "Susceptible" indicates that the pathogen is likely to be inhibited if the antimicrobial compound in the blood reaches the concentrations usually achievable.

- A report of "Intermediate" indicates that the result should be considered equivocal, and if the microorganism is not fully susceptible to alternative clinically feasible drugs, the test should be repeated. This category implies possible clinical applicability in body sites where the drug is physiologically concentrated or in situations where high dosage of drug can be used. This category also provides a buffer zone, which prevents small-uncontrolled technical factors from causing major discrepancies in interpretation.
- A report of "Resistant" indicates that the pathogen is not likely to be inhibited if the antimicrobial compound in the blood reaches the concentrations usually achievable: other therapy should be selected.

Note 1: The prevalence of resistance may vary geographically for selected species and local information on resistance is desirable, particularly when treating severe infections.

Note 2: Many strains of *Haemophilus influenzae* are resistant to erythromycin alone but are susceptible to erythromycin and sulfonamides together. Staphylococci resistant to erythromycin may emerge during a course of erythromycin therapy. Culture and susceptibility testing should be performed.

5.2 Pharmacokinetic properties

Absorption

Erythromycin ethyl succinate is absorbed intact following oral administration, and undergoes hydrolysis to yield the active erythromycin base. Serum levels are comparable when administered to patients in either the fasting or non-fasting state. Individual peak serum levels show considerable variability; the peak after each dose occurs in one to two hours.

Distribution

The extent of plasma protein binding has been variably reported but is probably of the order of around 60 – 80%. Erythromycin diffuses readily into most body fluids with the exception of cerebrospinal fluid, synovial fluid and vitreous humour. Concentrations in tissues are persistently greater than in blood/plasma (especially in pulmonary tissue). Erythromycin passes the blood-brain barrier to a small extent.

Erythromycin appears in breast milk at levels which are approximately 50% of the plasma concentration. It crosses the placenta and fetal plasma levels are usually 5% to 20% of the maternal plasma concentration.

Excretion

In the presence of normal renal function, the plasma half-life is approximately 1.5 to 3 hours. In anuric patients, the half-life may increase to 6 hours, but dosage adjustment is not usually required. Erythromycin is not removed by dialysis.

In the presence of normal hepatic function, erythromycin is concentrated in the liver and high concentrations appear in the bile. However, approximately 1.5% of the absorbed erythromycin can be recovered unchanged in bile over a period of 8 hours. Substantial quantities appear in the faeces and probably represent the unabsorbed drug plus the drug excreted into the bile. After oral administration, approximately 5% appears in the urine. A large proportion of the absorbed drug remains unaccounted for and is presumably metabolised, probably in the liver.

5.3 Preclinical safety data

Carcinogenicity

Long term (2 year) oral studies conducted in rats up to about 400 mg/kg/day and in mice up to about 500 mg/kg/day with erythromycin stearate did not provide evidence of tumourigenicity.

Genotoxicity

Erythromycin was not genotoxic in assays for bacterial and mammalian mutagenicity and for clastogenicity *in vitro*. The clastogenic potential of erythromycin has not been investigated *in vivo*.

---

6. Pharmaceutical Particulars

6.1 List of excipients

E-Mycin tablets also contain:

- Calcium hydrogen phosphate anhydrous
- Maize starch
- Sorbic acid
- Povidone
- Purified talc
- Sodium starch glycollate
- Magnesium stearate
- Polyvinyl alcohol
- Titanium dioxide
- Lecithin
- Iron oxide red
- Xanthan gum

E-Mycin granules for oral suspension also contain:

- Sorbitol
- Sodium citrate dihydrate
- Aspartame
- Propylene glycol alginate
- Silicon dioxide colloidal
- Sodium benzoate
- Erythrosine C145430
- Cherry flavour (contains preservative 320)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

E-Mycin suspension 18 months.

E-Mycin tablets 36 months.

Reconstituted suspension

Reconstituted suspension should be refrigerated at 2° - 8°C and used within 10 days; do not freeze. Discard remaining portion thereafter. Shake well before use.

6.4 Special precautions for storage

Store tablets below 30°C.

Store granules below 25°C.

For storage conditions after reconstitution of the medicine, see section 6.3.

6.5 Nature and contents of container

E-Mycin 200 mg per 5 mL and 400 mg per 5 mL, granules for oral suspension: HDPE bottle with a screw cap. Pack size 100 mL when reconstituted.

E-Mycin 400 mg tablets: HDPE bottle with a screw cap. Pack-size of 100 film-coated tablets.

Not all pack types and sizes may be marketed.

6.6 Special precautions for disposal and other handling

No special requirements for disposal.

Reconstitution of granules

Add 77 mL of water in small volumes and shake vigorously until no lumps are visible.

Any unused medicine or waste material should be disposed of in accordance with local requirements.

7. Medicines Schedule

Prescription Medicine

8. Sponsor Details

Viatris Ltd
PO Box 11-183
Ellerslie
AUCKLAND
www.viatris.co.nz
Telephone 0800 168 169

9. Date of First Approval

24 August 1995

10. Date of Revision of the Text

13 August 2025

Section	Summary of changes
4.4	Addition safety information on the risk of adverse cardiovascular outcomes with macrolides.
4.8	Updated ADR reporting website.
4.9	Minor editorial changes.

E-MYCIN® is a Viatris company trade mark.