



E.E.S. Granules are intended for reconstitution with water. Each 5-mL teaspoonful of reconstituted cherry-flavored suspension contains erythromycin ethylsuccinate equivalent to 200 mg of erythromycin.

The pleasant tasting, fruit-flavored liquids are supplied ready for oral administration.

E.E.S. 200 Liquid: Each 5-mL teaspoonful of fruit-flavored suspension contains erythromycin ethylsuccinate equivalent to 200 mg of erythromycin.

E.E.S. 400 Liquid: Each 5-mL teaspoonful of orange-flavored suspension contains erythromycin ethylsuccinate equivalent to 400 mg of erythromycin.

Granules and ready-made suspensions are intended primarily for pediatric use but can also be used in adults.

E.E.S. 400<sup>®</sup> Filmtab<sup>®</sup> Tablets: Each tablet contains erythromycin ethylsuccinate equivalent to 400 mg of erythromycin.

The Filmtab<sup>®</sup> tablets are intended primarily for adults or older children.

### ***Inactive Ingredients:***

E.E.S. 200 Liquid: FD&C Red No. 40, methylparaben, polysorbate 60, propylparaben, sodium citrate, sucrose, water, xanthan gum and natural and artificial flavors.

E.E.S. 400 Liquid: D&C Yellow No. 10, FD&C Yellow No. 6, methylparaben, polysorbate 60, propylparaben, sodium citrate, sucrose, water, xanthan gum and natural and artificial flavors.

E.E.S. Granules: Citric acid, FD&C Red No. 3, magnesium aluminum silicate, sodium carboxymethylcellulose, sodium citrate, sucrose and artificial flavor.

E.E.S. 400 Filmtab Tablets: Cellulosic polymers, confectioner's sugar (contains corn starch), corn starch, D&C Red No. 30, D&C Yellow No. 10, FD&C Red No. 40, magnesium stearate, polyacrilin potassium, polyethylene glycol, propylene glycol, sodium citrate, sorbic acid, and titanium dioxide.

### **CLINICAL PHARMACOLOGY**

Orally administered erythromycin ethylsuccinate suspensions and Filmtab tablets are readily and reliably absorbed. Comparable serum levels of erythromycin are achieved in the fasting and nonfasting states.

Erythromycin diffuses readily into most body fluids. Only low concentrations are normally achieved in the spinal fluid, but passage of the drug across the blood-brain barrier increases in meningitis. In the presence of normal hepatic function, erythromycin is concentrated in the liver and excreted in the bile; the effect of hepatic dysfunction on excretion of erythromycin by the liver into the bile is not known. Less than 5 percent of the orally administered dose of erythromycin is excreted in active form in the urine.

Erythromycin crosses the placental barrier, but fetal plasma levels are low. The drug is excreted in human milk.

### **Microbiology:**

Erythromycin acts by inhibition of protein synthesis by binding 50 S ribosomal subunits of susceptible organisms. It does not affect nucleic acid synthesis. Antagonism has been demonstrated *in vitro* between erythromycin and clindamycin, lincomycin, and chloramphenicol.

Many strains of *Haemophilus influenzae* are resistant to erythromycin alone but are susceptible to erythromycin and sulfonamides used concomitantly.

Staphylococci resistant to erythromycin may emerge during a course of therapy.

Erythromycin has been shown to be active against most strains of the following microorganisms, both *in vitro* and in clinical infections as described in the **INDICATIONS AND USAGE** section.

**Gram-positive Organisms:**

*Corynebacterium diphtheriae*  
*Corynebacterium minutissimum*

*Listeria monocytogenes*

*Staphylococcus aureus* (resistant organisms may emerge during treatment)  
*Streptococcus pneumoniae*  
*Streptococcus pyogenes*

**Gram-negative Organisms:**

*Bordetella pertussis*  
*Legionella pneumophila*  
*Neisseria gonorrhoeae*

**Other Microorganisms:**

*Chlamydia trachomatis*  
*Entamoeba histolytica*  
*Mycoplasma pneumoniae*  
*Treponema pallidum*  
*Ureaplasma urealyticum*

The following *in vitro* data are available, **but their clinical significance is unknown.**

Erythromycin exhibits *in vitro* minimal inhibitory concentrations (MIC's) of 0.5 µg/mL or less against most ( ≥90%) strains of the following microorganisms; however, the safety and effectiveness of erythromycin in treating clinical infections due to these microorganisms have not been established in adequate and well controlled clinical trials.

**Gram-positive Organisms:**

*Viridans group streptococci*

**Gram-negative Organisms:**

*Moraxella catarrhalis*

**Susceptibility Tests:**

Dilution Techniques:

Quantitative methods are used to determine antimicrobial minimum inhibitory concentrations (MIC's). These MIC's provide estimates of the susceptibility of bacteria to antimicrobial compounds. The MIC's should be determined using a standardized procedure. Standardized procedures are based on a dilution method<sup>1</sup> (broth or agar) or equivalent with standardized inoculum concentrations and standardized concentrations of erythromycin powder. The MIC values should be interpreted according to the following criteria:

**MIC (µg/mL)**

**Interpretation**

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≤0.5	Susceptible (S)
1-4	Intermediate (I)
≥8	Resistant (R)

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.

Standardized susceptibility test procedures require the use of laboratory control microorganisms to control the technical aspects of the laboratory procedures. Standard erythromycin powder should provide the following MIC values:

Microorganism	MIC (µg/mL)
<i>S. aureus</i> ATCC 25923	0.12-0.5
<i>E. faecalis</i> ATCC 29212	1-4

#### Diffusion Techniques:

Quantitative methods that require measurement of zone diameters also provide reproducible estimates of the susceptibility of bacteria to antimicrobial compounds. One such standardized procedure<sup>2</sup> requires the use of standardized inoculum concentrations. This procedure uses paper disks impregnated with 15-µg erythromycin to test the susceptibility of microorganisms to erythromycin.

Reports from the laboratory providing results of the standard single-disk susceptibility test with a 15-µg erythromycin disk should be interpreted according to the following criteria:

Zone Diameter (mm)	Interpretation
≥23	Susceptible (S)
14-22	Intermediate (I)
≤13	Resistant (R)

Interpretation should be as stated above for results using dilution techniques. Interpretation involves correlation of the diameter obtained in the disk test with the MIC for erythromycin.

As with standardized dilution techniques, diffusion methods require the use of laboratory control microorganisms that are used to control the technical aspects of the laboratory procedures. For the diffusion technique, the 15-µg erythromycin disk should provide the following zone diameters in these laboratory test quality control strains:

Microorganism	Zone Diameter (mm)
<i>S. aureus</i> ATCC 25923	22-30

#### INDICATIONS AND USAGE

To reduce the development of drug-resistant bacteria and maintain the effectiveness of E.E.S<sup>®</sup> and other antibacterial drugs, E.E.S should be used only to treat or prevent infections that are proven or

strongly suspected to be caused by susceptible bacteria. When culture and susceptibility information are available, they should be considered in selecting or modifying antibacterial therapy. In the absence of such data, local epidemiology and susceptibility patterns may contribute to the empiric selection of therapy.

E.E.S. is indicated in the treatment of infections caused by susceptible strains of the designated organisms in the diseases listed below:

Upper respiratory tract infections of mild to moderate degree caused by *Streptococcus pyogenes*, *Streptococcus pneumoniae*, or *Haemophilus influenzae* (when used concomitantly with adequate doses of sulfonamides, since many strains of *H. influenzae* are not susceptible to the erythromycin concentrations ordinarily achieved). (See appropriate sulfonamide labeling for prescribing information.)

Lower-respiratory tract infections of mild to moderate severity caused by *Streptococcus pneumoniae* or *Streptococcus pyogenes*.

Listeriosis caused by *Listeria monocytogenes*.

Pertussis (whooping cough) caused by *Bordetella pertussis*. Erythromycin is effective in eliminating the organism from the nasopharynx of infected individuals rendering them noninfectious. Some clinical studies suggest that erythromycin may be helpful in the prophylaxis of pertussis in exposed susceptible individuals.

Respiratory tract infections due to *Mycoplasma pneumoniae*.

Skin and skin structure infections of mild to moderate severity caused by *Streptococcus pyogenes* or *Staphylococcus aureus* (resistant staphylococci may emerge during treatment).

Diphtheria: Infections due to *Corynebacterium diphtheriae*, as an adjunct to antitoxin, to prevent establishment of carriers and to eradicate the organism in carriers.

Erythrasma: In the treatment of infections due to *Corynebacterium minutissimum*.

Intestinal amebiasis caused by *Entamoeba histolytica* (oral erythromycins only). Extraenteric amebiasis requires treatment with other agents.

Acute pelvic inflammatory disease caused by *Neisseria gonorrhoeae*: As an alternative drug in treatment of acute pelvic inflammatory disease caused by *N. gonorrhoeae* in female patients with a history of sensitivity to penicillin. Patients should have a serologic test for syphilis before receiving erythromycin as treatment of gonorrhea and a follow-up serologic test for syphilis after 3 months.

Syphilis caused by *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 after therapy.

Erythromycins are indicated for the treatment of the following infections caused by *Chlamydia trachomatis*: conjunctivitis of the newborn, pneumonia of infancy, and urogenital infections during pregnancy. 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*.

When tetracyclines are contraindicated or not tolerated, erythromycin is indicated for the treatment of nongonococcal urethritis caused by *Ureaplasma urealyticum*.

Legionnaires' Disease caused by *Legionella pneumophila*. Although no controlled clinical efficacy studies have been conducted, *in vitro* and limited preliminary clinical data suggest that erythromycin may be effective in treating Legionnaires' Disease.

### **Prophylaxis:**

Prevention of Initial Attacks of Rheumatic Fever: Penicillin is considered by the American Heart Association to be the drug of choice in the prevention of initial attacks of rheumatic fever (treatment of *Streptococcus pyogenes* infections of the upper respiratory tract, e.g., tonsillitis or pharyngitis).

Erythromycin is indicated for the treatment of penicillin-allergic patients.<sup>3</sup> The therapeutic dose should be administered for 10 days.

Prevention of Recurrent Attacks of Rheumatic Fever: Penicillin or sulfonamides are considered by the American Heart Association to be the drugs of choice in the prevention of recurrent attacks of rheumatic fever. In patients who are allergic to penicillin and sulfonamides, oral erythromycin is recommended by the American Heart Association in the long-term prophylaxis of streptococcal pharyngitis (for the prevention of recurrent attacks of rheumatic fever).<sup>3</sup>

## CONTRAINDICATIONS

Erythromycin is contraindicated in patients with known hypersensitivity to this antibiotic.

Erythromycin is contraindicated in patients taking terfenadine, astemizole, pimozone, or cisapride. (See **PRECAUTIONS - Drug Interactions.**)

## WARNINGS

There have been reports of hepatic dysfunction, including increased liver enzymes, and hepatocellular and/or cholestatic hepatitis, with or without jaundice, occurring in patients receiving oral erythromycin products.

There have been reports suggesting that erythromycin does not reach the fetus in adequate concentration 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.

**Pseudomembranous colitis has been reported with nearly all antibacterial agents, including erythromycin, and may range in severity from mild to life threatening. Therefore, it is important to consider this diagnosis in patients who present with diarrhea subsequent to the administration of antibacterial agents.**

Treatment with antibacterial agents alters the normal flora of the colon and may permit overgrowth of clostridia. Studies indicate that a toxin produced by *Clostridium difficile* is a primary cause of "antibiotic-associated colitis".

After the diagnosis of pseudomembranous colitis has been established, therapeutic measures should be initiated. Mild cases of pseudomembranous colitis usually respond to discontinuation of the drug alone. In moderate to severe cases, consideration should be given to management with fluids and electrolytes, protein supplementation, and treatment with an antibacterial drug clinically effective against *Clostridium difficile* colitis.

Rhabdomyolysis with or without renal impairment has been reported in seriously ill patients receiving erythromycin concomitantly with lovastatin. Therefore, patients receiving concomitant lovastatin and erythromycin should be carefully monitored for creatine kinase (CK) and serum transaminase levels. (See package insert for lovastatin.)

## PRECAUTIONS

*General:* Prescribing E.E.S. in the absence of a proven or strongly suspected bacterial infection or a prophylactic indication is unlikely to provide benefit to the patient and increases the risk of the development of drug-resistant bacteria.

Since erythromycin is principally excreted by the liver, caution should be exercised when erythromycin is administered to patients with impaired hepatic function. (See **CLINICAL PHARMACOLOGY** and **WARNINGS** sections.)

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

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 8-14 days and 10% for infants who took erythromycin for 15-21 days.<sup>4</sup> Since erythromycin may be used in the treatment of conditions in infants which are associated with significant mortality or morbidity (such as pertussis or neonatal *Chlamydia trachomatis* infections), 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.

Prolonged or repeated use of erythromycin may result in an overgrowth of nonsusceptible bacteria or fungi. If superinfection occurs, erythromycin should be discontinued and appropriate therapy instituted.

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

*Information for Patients:* Patients should be counseled that antibacterial drugs including E.E.S. should only be used to treat bacterial infections. They do not treat viral infections (e.g., the common cold). When E.E.S. is prescribed to treat a bacterial infection, patients should be told that although it is common to feel better early in the course of therapy, the medication should be taken exactly as directed. Skipping doses or not completing the full course of therapy may (1) decrease the effectiveness of the immediate treatment and (2) increase the likelihood that bacteria will develop resistance and will not be treatable by E.E.S. or other antibacterial drugs in the future.

*Drug Interactions:* 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.

Concomitant administration of erythromycin and digoxin has been reported to result in elevated digoxin serum levels.

There have been reports of increased anticoagulant effects when erythromycin and oral anticoagulants were used concomitantly. Increased anticoagulation effects due to interactions of erythromycin with various oral anticoagulants may be more pronounced in the elderly.

Erythromycin is a substrate and inhibitor of the 3A isoform subfamily of the cytochrome p450 enzyme system (CYP3A). Coadministration of erythromycin and a drug primarily metabolized by CYP3A may be associated with elevations in drug concentrations that could increase or prolong both the therapeutic and adverse effects of the concomitant drug. Dosage adjustments may be considered, and when possible, serum concentrations of drugs primarily metabolized by CYP3A should be monitored closely in patients concurrently receiving erythromycin.

The following are examples of some clinically significant CYP3A based drug interactions. Interactions with other drugs metabolized 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 characterized by severe peripheral vasospasm and dysesthesia.

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

*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.

*Sildenafil (Viagra)*: Erythromycin has been reported to increase the systemic exposure (AUC) of sildenafil. Reduction of sildenafil dosage should be considered. (See Viagra package insert.)

There have been spontaneous or published reports of CYP3A based interactions of erythromycin with cyclosporine, carbamazepine, tacrolimus, alfentanil, disopyramide, rifabutin, quinidine, methylprednisolone, cilostazol, vinblastine, and bromocriptine.

Concomitant administration of erythromycin with cisapride, pimozone, astemizole, or terfenadine is contraindicated. (See **CONTRAINDICATIONS**.)

In addition, there have been reports of interactions of erythromycin with drugs not thought to be metabolized by CYP3A, including hexobarbital, phenytoin, and valproate.

Erythromycin has been reported to significantly alter the metabolism of the nonsedating antihistamines terfenadine and astemizole when taken concomitantly. Rare cases of serious cardiovascular adverse events, including electrocardiographic QT/QT<sub>c</sub> interval prolongation, cardiac arrest, torsades de pointes, and other ventricular arrhythmias have been observed. (See **CONTRAINDICATIONS**.) In addition, deaths have been reported rarely with concomitant administration of terfenadine and erythromycin.

There have been post-marketing reports of drug interactions when erythromycin is coadministered with cisapride, resulting in QT prolongation, cardiac arrhythmias, ventricular tachycardia, ventricular fibrillation, and torsades de pointes, most likely due to inhibition of hepatic metabolism of cisapride by erythromycin. Fatalities have been reported. (See **CONTRAINDICATIONS**.)

*Drug/Laboratory Test Interactions*: Erythromycin interferes with the fluorometric determination of urinary catecholamines.

*Carcinogenesis, Mutagenesis, Impairment of Fertility*: Long-term (2-year) oral studies in rats with erythromycin ethylsuccinate and erythromycin base did not provide evidence of tumorigenicity. Mutagenicity studies have not been conducted. There was no apparent effect on male or female fertility in rats fed erythromycin (base) at levels up to 0.25% of diet.

*Pregnancy: Teratogenic Effects. Pregnancy Category B*: There is no evidence of teratogenicity or any other adverse effect on reproduction in female rats fed erythromycin base (up to 0.25% of diet) prior to and during mating, during gestation, and through weaning of two successive litters. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

*Labor and Delivery*: The effect of erythromycin on labor and delivery is unknown.

*Nursing Mothers*: Erythromycin is excreted in human milk. Caution should be exercised when erythromycin is administered to a nursing woman.

*Pediatric Use*: See **INDICATIONS AND USAGE** and **DOSAGE AND ADMINISTRATION** sections.

*Geriatric Use*: Elderly patients, particularly those with reduced renal or hepatic function, may be at increased risk for developing erythromycin-induced hearing loss. (See **ADVERSE REACTIONS** and **DOSAGE AND ADMINISTRATION**.)

Elderly patients may be more susceptible to the development of torsades de pointes arrhythmias than younger patients. (See **ADVERSE REACTIONS**.)

Elderly patients may experience increased effects of oral anticoagulant therapy while undergoing treatment with erythromycin. (See **PRECAUTIONS**, Drug Interactions.)

E.E.S.<sup>®</sup> Granules contains 25.9 mg (1.1 mEq) of sodium per individual dose.

## ADVERSE REACTIONS

The most frequent side effects of oral erythromycin preparations are gastrointestinal and are dose-related. They include nausea, vomiting, abdominal pain, diarrhea and anorexia. Symptoms of hepatitis, hepatic dysfunction and/or abnormal liver function test results may occur. (See **WARNINGS**.)

Onset of pseudomembranous colitis symptoms may occur during or after antibiotic treatment. (See **WARNINGS**.)

Erythromycin has been associated with QT prolongation and ventricular arrhythmias, including ventricular tachycardia and torsades de pointes.

Allergic reactions ranging from urticaria to anaphylaxis have occurred. Skin reactions ranging from mild eruptions to erythema multiforme, Stevens-Johnson syndrome, and toxic epidermal necrolysis have been reported rarely.

THERE HAVE BEEN RARE REPORTS OF PANCREATITIS AND CONVULSIONS.

THERE HAVE BEEN ISOLATED REPORTS OF REVERSIBLE HEARING LOSS OCCURRING CHIEFLY IN PATIENTS WITH RENAL INSUFFICIENCY AND IN PATIENTS RECEIVING HIGH DOSES OF ERYTHROMYCIN.

## OVERDOSAGE

In case of overdosage, erythromycin should be discontinued. Overdosage should be handled with the prompt elimination of unabsorbed drug and all other appropriate measures should be instituted.

Erythromycin is not removed by peritoneal dialysis or hemodialysis.

## DOSAGE AND ADMINISTRATION

Erythromycin ethylsuccinate suspensions and Filmtab tablets may be administered without regard to meals.

CHILDREN: 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 ETHYLSUCCINATE FOR CHILDREN IS 30 TO 50 MG/KG/DAY IN EQUALLY DIVIDED DOSES EVERY 6 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 BY ADMINISTERING ONE THIRD OF THE TOTAL DAILY DOSE EVERY 8 HOURS.

THE FOLLOWING DOSAGE SCHEDULE IS SUGGESTED FOR MILD TO MODERATE INFECTIONS:

<b>Body Weight</b>	<b>Total Daily Dose</b>
<b>Under 10 lbs</b>	30-50 mg/kg/day 15-25 mg/kg/q 12 h
10 to 15 lbs	200 mg
16 to 25 lbs	400 mg
26 to 50 lbs	800 mg
51 to 100 lbs	1200 mg
over 100 lbs	1600 mg

Adults: 400 mg 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.

For adult dosage calculation, use a ratio of 400 mg of erythromycin activity as the ethylsuccinate to 250 mg of erythromycin activity as the stearate, base or estolate.

In the treatment of streptococcal infections, a therapeutic dosage of 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 treatment of urethritis due to *C. trachomatis* or *U. urealyticum*: 800 mg three times a day for 7 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 amebiasis: 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 Legionnaires' Disease: Although optimal doses have not been established, doses utilized in reported clinical data were those recommended above (1.6 to 4 g daily in divided doses.)

#### HOW SUPPLIED

E.E.S. 200 LIQUID (erythromycin ethylsuccinate oral suspension, USP) is supplied in 1 pint bottles (NDC 0074-6306-16) and in 100-mL bottles (NDC 0074-6306-13).

E.E.S. 400<sup>®</sup> LIQUID (erythromycin ethylsuccinate oral suspension, USP) is supplied in 1 pint bottles (NDC 0074-6373-16) and in 100-mL bottles (NDC 0074-6373-13).

Both liquid products require refrigeration to preserve taste until dispensed. Refrigeration by patient is not required if used within 14 days.

E.E.S. GRANULES (erythromycin ethylsuccinate for oral suspension, USP) is supplied in 100-mL (NDC 0074-6369-02) and 200-mL (NDC 0074-6369-10) size bottles.

E.E.S. 400 Filmtab tablets (erythromycin ethylsuccinate tablets, USP) 400 mg, are supplied as pink tablets imprinted with the Abbott logo, , and two letter Abbo-Code designation, EE, in bottles of 100 (NDC 0074-5729-13), 500 (NDC 0074-5729-53) and 1000 (NDC 0074-5729-19) and in ABBO-PAC unit dose strip packages of 100 (NDC 0074-5729-11).

Recommended storage: Store tablets below 86°F (30°C).

Store granules, prior to mixing, below 86°F (30°C). After mixing, refrigerate and use within 10 days.

#### REFERENCES

1. National Committee for Clinical Laboratory Standards, *Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria that Grow Aerobically*, Third Edition. Approved Standard NCCLS Document M7-A3, Vol. 13, No. 25. NCCLS, Villanova, PA, December 1993.
2. National Committee for Clinical Laboratory Standards, *Performance Standards for Antimicrobial Disk Susceptibility Tests*, Fifth Edition. Approved Standard NCCLS Document M2-A5, Vol. 13, No. 24. NCCLS, Villanova, PA, December 1993.
3. Committee on Rheumatic Fever, Endocarditis, and Kawasaki Disease of the Council on Cardiovascular Disease in the Young, the American Heart Association: Prevention of Rheumatic Fever. *Circulation*. 78(4): 1082-1086, October 1988.
4. Honein, M.A., et. al.: Infantile hypertrophic pyloric stenosis after pertussis prophylaxis with erythromycin: a case review and cohort study. *The Lancet* 1999; 354 (9196): 2101-5.

Filmtab—Film-sealed tablets, Abbott.

Revised: NEW

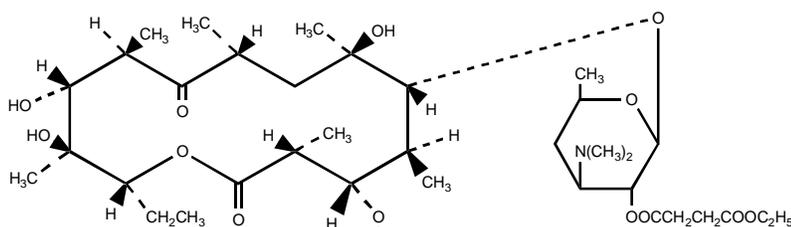
## Ery-Ped<sup>®</sup> (ERYTHROMYCIN ETHYLSUCCINATE, USP)

### R<sub>x</sub> only

To reduce the development of drug-resistant bacteria and maintain the effectiveness of EryPed and other antibacterial drugs, EryPed should be used only to treat or prevent infections that are proven or strongly suspected to be caused by bacteria.

### DESCRIPTION

Erythromycin is produced by a strain of *Saccharopolyspora erythraea* (formerly *Streptomyces erythraeus*) and belongs to the macrolide group of antibiotics. It is basic and readily forms salts with acids. The base, the stearate salt, and the esters are poorly soluble in water. Erythromycin ethylsuccinate is an ester of erythromycin suitable for oral administration. Erythromycin ethylsuccinate is known chemically as erythromycin 2'-(ethyl succinate). The molecular formula is C<sub>43</sub>H<sub>75</sub>NO<sub>16</sub> and the molecular weight is 862.06. The structural formula is:



ERYPED 200 AND ERYPED DROPS (ERYTHROMYCIN ETHYLSUCCINATE FOR ORAL SUSPENSION) WHEN RECONSTITUTED WITH WATER, FORMS A SUSPENSION CONTAINING ERYTHROMYCIN ETHYLSUCCINATE EQUIVALENT TO 200 MG ERYTHROMYCIN PER 5 ML (TEASPOONFUL) OR 100 MG PER 2.5 ML (DROPPERFUL) WITH AN APPEALING FRUIT FLAVOR. ERYPED 400 WHEN RECONSTITUTED WITH WATER, FORMS A SUSPENSION CONTAINING ERYTHROMYCIN ETHYLSUCCINATE EQUIVALENT TO 400 MG OF ERYTHROMYCIN PER 5 ML (TEASPOONFUL) WITH AN APPEALING BANANA FLAVOR.

These products are intended primarily for pediatric use but can also be used in adults.

### **Inactive Ingredients:**

EryPed 200, EryPed 400 and EryPed Drops: Caramel, polysorbate, sodium citrate, sucrose, xanthan gum and artificial flavors.

### CLINICAL PHARMACOLOGY

Orally administered erythromycin ethylsuccinate suspension is readily and reliably absorbed under both fasting and nonfasting conditions.

Erythromycin diffuses readily into most body fluids. Only low concentrations are normally achieved in the spinal fluid, but passage of the drug across the blood-brain barrier increases in meningitis. In the presence of normal hepatic function, erythromycin is concentrated in the liver and excreted in the bile; the effect of hepatic dysfunction on excretion of erythromycin by the liver into the

bile is not known. Less than 5 percent of the orally administered dose of erythromycin is excreted in active form in the urine.

Erythromycin crosses the placental barrier, but fetal plasma levels are low. The drug is excreted in human milk.

**Microbiology:**

Erythromycin acts by inhibition of protein synthesis by binding 50 S ribosomal subunits of susceptible organisms. It does not affect nucleic acid synthesis. Antagonism has been demonstrated *in vitro* between erythromycin and clindamycin, lincomycin, and chloramphenicol.

Many strains of *Haemophilus influenzae* are resistant to erythromycin alone but are susceptible to erythromycin and sulfonamides used concomitantly.

Staphylococci resistant to erythromycin may emerge during a course of therapy.

Erythromycin has been shown to be active against most strains of the following microorganisms, both *in vitro* and in clinical infections as described in the **INDICATIONS AND USAGE** section.

**Gram-positive Organisms:**

*Corynebacterium diphtheriae*

*Corynebacterium minutissimum*

*Listeria monocytogenes*

*Staphylococcus aureus* (resistant organisms may emerge during treatment)

*Streptococcus pneumoniae*

*Streptococcus pyogenes*

**Gram-negative Organisms:**

*Bordetella pertussis*

*Legionella pneumophila*

*Neisseria gonorrhoeae*

**Other Microorganisms:**

*Chlamydia trachomatis*

*Entamoeba histolytica*

*Mycoplasma pneumoniae*

*Treponema pallidum*

*Ureaplasma urealyticum*

The following *in vitro* data are available, **but their clinical significance is unknown**.

Erythromycin exhibits *in vitro* minimal inhibitory concentrations (MIC's) of 0.5 µg/mL or less against most (≥ 90%) strains of the following microorganisms; however, the safety and effectiveness of erythromycin in treating clinical infections due to these microorganisms have not been established in adequate and well-controlled clinical trials.

**Gram-positive Organisms:**

Viridans group streptococci

**Gram-negative Organisms:**

*Moraxella catarrhalis*

**Susceptibility Tests:**

**Dilution Techniques:**

Quantitative methods are used to determine antimicrobial minimum inhibitory concentrations (MIC's). These MIC's provide estimates of the susceptibility of bacteria to antimicrobial compounds. The MIC's should be determined using a standardized procedure. Standardized procedures are based on a dilution method<sup>1</sup> (broth or agar) or equivalent with standardized inoculum concentrations and standardized concentrations of erythromycin powder. The MIC values should be interpreted according to the following criteria:

MIC (µg/mL)	Interpretation
≤0.5	Susceptible (S)
1-4	Intermediate (I)
≥8	Resistant (R)

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.

STANDARDIZED SUSCEPTIBILITY TEST PROCEDURES REQUIRE THE USE OF LABORATORY CONTROL MICROORGANISMS TO CONTROL THE TECHNICAL ASPECTS OF THE LABORATORY PROCEDURES. STANDARD ERYTHROMYCIN POWDER SHOULD PROVIDE THE FOLLOWING MIC VALUES:

Microorganism	MIC (µg/mL)
<i>S. aureus</i> ATCC 29213	0.12-0.5
<i>E. faecalis</i> ATCC 29212	1-4

#### Diffusion Techniques:

Quantitative methods that require measurement of zone diameters also provide reproducible estimates of the susceptibility of bacteria to antimicrobial compounds. One such standardized procedure<sup>2</sup> requires the use of standardized inoculum concentrations. This procedure uses paper disks impregnated with 15-µg erythromycin to test the susceptibility of microorganisms to erythromycin.

REPORTS FROM THE LABORATORY PROVIDING RESULTS OF THE STANDARD SINGLE-DISK SUSCEPTIBILITY TEST WITH A 15-µG ERYTHROMYCIN DISK SHOULD BE INTERPRETED ACCORDING TO THE FOLLOWING CRITERIA:

Zone Diameter (mm)	Interpretation
≥23	Susceptible (S)
14-22	Intermediate (I)
≤13	Resistant (R)

Interpretation should be as stated above for results using dilution techniques. Interpretation involves correlation of the diameter obtained in the disk test with the MIC for erythromycin.

AS WITH STANDARDIZED DILUTION TECHNIQUES, DIFFUSION METHODS REQUIRE THE USE OF LABORATORY CONTROL MICROORGANISMS THAT ARE USED TO CONTROL THE TECHNICAL ASPECTS OF THE LABORATORY PROCEDURES. FOR THE DIFFUSION TECHNIQUE, THE 15-µG ERYTHROMYCIN DISK SHOULD PROVIDE THE FOLLOWING ZONE DIAMETERS IN THESE LABORATORY TEST QUALITY CONTROL STRAINS:

<b>Microorganism</b>	<b>Zone Diameter (mm)</b>
<i>S. aureus</i> ATCC 25923	22-30

## **INDICATIONS AND USAGE**

To reduce the development of drug-resistant bacteria and maintain the effectiveness of Ery-Ped and other antibacterial drugs, Ery-Ped should be used only to treat or prevent infections that are proven or strongly suspected to be caused by susceptible bacteria. When culture and susceptibility information are available, they should be considered in selecting or modifying antibacterial therapy. In the absence of such data, local epidemiology and susceptibility patterns may contribute to the empiric selection of therapy.

Ery-Ped is indicated in the treatment of infections caused by susceptible strains of the designated organisms in the diseases listed below:

Upper respiratory tract infections of mild to moderate degree caused by *Streptococcus pyogenes*, *Streptococcus pneumoniae*, or *Haemophilus influenzae* (when used concomitantly with adequate doses of sulfonamides, since many strains of *H. influenzae* are not susceptible to the erythromycin concentrations ordinarily achieved). (See appropriate sulfonamide labeling for prescribing information.)

Lower-respiratory tract infections of mild to moderate severity caused by *Streptococcus pneumoniae* or *Streptococcus pyogenes*.

Listeriosis caused by *Listeria monocytogenes*.

Pertussis (whooping cough) caused by *Bordetella pertussis*. Erythromycin is effective in eliminating the organism from the nasopharynx of infected individuals rendering them noninfectious. Some clinical studies suggest that erythromycin may be helpful in the prophylaxis of pertussis in exposed susceptible individuals.

Respiratory tract infections due to *Mycoplasma pneumoniae*.

Skin and skin structure infections of mild to moderate severity caused by *Streptococcus pyogenes* or *Staphylococcus aureus* (resistant staphylococci may emerge during treatment).

Diphtheria: Infections due to *Corynebacterium diphtheriae*, as an adjunct to antitoxin, to prevent establishment of carriers and to eradicate the organism in carriers.

Erythrasma: In the treatment of infections due to *Corynebacterium minutissimum*.

Intestinal amebiasis caused by *Entamoeba histolytica* (oral erythromycins only). Extraenteric amebiasis requires treatment with other agents.

Acute pelvic inflammatory disease caused by *Neisseria gonorrhoeae*: As an alternative drug in treatment of acute pelvic inflammatory disease caused by *N. gonorrhoeae* in female patients with a history of sensitivity to penicillin. Patients should have a serologic test for syphilis before receiving erythromycin as treatment of gonorrhea and a follow-up serologic test for syphilis after 3 months.

Syphilis caused by *Treponema pallidum*: Erythromycin is an alternate choice of treatment for primary syphilis in penicillin-allergic patients. In primary syphilis, spinal fluid examinations should be done before treatment and as part of follow-up after therapy.

Erythromycins are indicated for the treatment of the following infections caused by *Chlamydia trachomatis*: conjunctivitis of the newborn, pneumonia of infancy, and urogenital infections during pregnancy. 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*.

When tetracyclines are contraindicated or not tolerated, erythromycin is indicated for the treatment of nongonococcal urethritis caused by *Ureaplasma urealyticum*.

Legionnaires' Disease caused by *Legionella pneumophila*. Although no controlled clinical efficacy studies have been conducted, *in vitro* and limited preliminary clinical data suggest that erythromycin may be effective in treating Legionnaires' Disease.

## **Prophylaxis:**

Prevention of Initial Attacks of Rheumatic Fever: Penicillin is considered by the American Heart Association to be the drug of choice in the prevention of initial attacks of rheumatic fever (treatment of *Streptococcus pyogenes* infections of the upper respiratory tract, e.g., tonsillitis or pharyngitis). Erythromycin is indicated for the treatment of penicillin-allergic patients.<sup>3</sup> The therapeutic dose should be administered for 10 days.

Prevention of Recurrent Attacks of Rheumatic Fever: Penicillin or sulfonamides are considered by the American Heart Association to be the drugs of choice in the prevention of recurrent attacks of rheumatic fever. In patients who are allergic to penicillin and sulfonamides, oral erythromycin is recommended by the American Heart Association in the long-term prophylaxis of streptococcal pharyngitis (for the prevention of recurrent attacks of rheumatic fever).<sup>3</sup>

## **CONTRAINDICATIONS**

Erythromycin is contraindicated in patients with known hypersensitivity to this antibiotic.

Erythromycin is contraindicated in patients taking terfenadine, astemizole, pimozone, or cisapride. (See **PRECAUTIONS - Drug Interactions.**)

## **WARNINGS**

There have been reports of hepatic dysfunction, including increased liver enzymes, and hepatocellular and/or cholestatic hepatitis, with or without jaundice, occurring in patients receiving oral erythromycin products.

There have been reports suggesting that erythromycin does not reach the fetus in adequate concentration 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.

**Pseudomembranous colitis has been reported with nearly all antibacterial agents, including erythromycin, and may range in severity from mild to life threatening. Therefore, it is important to consider this diagnosis in patients who present with diarrhea subsequent to the administration of antibacterial agents.**

Treatment with antibacterial agents alters the normal flora of the colon and may permit overgrowth of clostridia. Studies indicate that a toxin produced by *Clostridium difficile* is a primary cause of "antibiotic-associated colitis".

After the diagnosis of pseudomembranous colitis has been established, therapeutic measures should be initiated. Mild cases of pseudomembranous colitis usually respond to discontinuation of the drug alone. In moderate to severe cases, consideration should be given to management with fluids and electrolytes, protein supplementation, and treatment with an antibacterial drug clinically effective against *Clostridium difficile* colitis.

Rhabdomyolysis with or without renal impairment has been reported in seriously ill patients receiving erythromycin concomitantly with lovastatin. Therefore, patients receiving concomitant lovastatin and erythromycin should be carefully monitored for creatine kinase (CK) and serum transaminase levels. (See package insert for lovastatin.)

## **PRECAUTIONS**

*General:* Prescribing Ery-Ped in the absence of a proven or strongly suspected bacterial infection or a prophylactic indication is unlikely to provide benefit to the patient and increases the risk of the development of drug-resistant bacteria.

Since erythromycin is principally excreted by the liver, caution should be exercised when erythromycin is administered to patients with impaired hepatic function. (See **CLINICAL PHARMACOLOGY** and **WARNINGS** sections.)

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

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 8-14 days and 10% for infants who took erythromycin for 15-21 days.<sup>4</sup> Since erythromycin may be used in the treatment of conditions in infants which are associated with significant mortality or morbidity (such as pertussis or neonatal Chlamydia trachomatis infections), 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.

Prolonged or repeated use of erythromycin may result in an overgrowth of nonsusceptible bacteria or fungi. If superinfection occurs, erythromycin should be discontinued and appropriate therapy instituted.

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

*Information for Patients:* Patients should be counseled that antibacterial drugs including Ery-Ped should only be used to treat bacterial infections. They do not treat viral infections (e.g., the common cold). When Ery-Ped is prescribed to treat a bacterial infection, patients should be told that although it is common to feel better early in the course of therapy, the medication should be taken exactly as directed. Skipping doses or not completing the full course of therapy may (1) decrease the effectiveness of the immediate treatment and (2) increase the likelihood that bacteria will develop resistance and will not be treatable by Ery-Ped or other antibacterial drugs in the future.

*Drug Interactions:* 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.

CONCOMITANT ADMINISTRATION OF ERYTHROMYCIN AND DIGOXIN HAS BEEN REPORTED TO RESULT IN ELEVATED DIGOXIN SERUM LEVELS.

There have been reports of increased anticoagulant effects when erythromycin and oral anticoagulants were used concomitantly. Increased anticoagulation effects due to interactions of erythromycin with various oral anticoagulants may be more pronounced in the elderly.

Erythromycin is a substrate and inhibitor of the 3A isoform subfamily of the cytochrome p450 enzyme system (CYP3A). Coadministration of erythromycin and a drug primarily metabolized by CYP3A may be associated with elevations in drug concentrations that could increase or prolong both the therapeutic and adverse effects of the concomitant drug. Dosage adjustments may be considered, and when possible, serum concentrations of drugs primarily metabolized by CYP3A should be monitored closely in patients concurrently receiving erythromycin.

The following are examples of some clinically significant CYP3A based drug interactions. Interactions with other drugs metabolized 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 characterized by severe peripheral vasospasm and dysesthesia.

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

*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.

*Sildenafil (Viagra):* Erythromycin has been reported to increase the systemic exposure (AUC) of sildenafil. Reduction of sildenafil dosage should be considered. (See Viagra package insert.)

There have been spontaneous or published reports of CYP3A based interactions of erythromycin with cyclosporine, carbamazepine, tacrolimus, alfentanil, disopyramide, rifabutin, quinidine, methylprednisolone, cilostazol, vinblastine, and bromocriptine.

Concomitant administration of erythromycin with cisapride, pimozone, astemizole, or terfenadine is contraindicated. (See **CONTRAINDICATIONS.**)

In addition, there have been reports of interactions of erythromycin with drugs not thought to be metabolized by CYP3A, including hexobarbital, phenytoin, and valproate.

Erythromycin has been reported to significantly alter the metabolism of the nonsedating antihistamines terfenadine and astemizole when taken concomitantly. Rare cases of serious cardiovascular adverse events, including electrocardiographic QT/QT<sub>c</sub> interval prolongation, cardiac arrest, torsades de pointes, and other ventricular arrhythmias have been observed. (See **CONTRAINDICATIONS.**) In addition, deaths have been reported rarely with concomitant administration of terfenadine and erythromycin.

There have been post-marketing reports of drug interactions when erythromycin was coadministered with cisapride, resulting in QT prolongation, cardiac arrhythmias, ventricular tachycardia, ventricular fibrillation, and torsades de pointes most likely due to the inhibition of hepatic metabolism of cisapride by erythromycin. Fatalities have been reported. (See **CONTRAINDICATIONS.**)

*Drug/Laboratory Test Interactions:* Erythromycin interferes with the fluorometric determination of urinary catecholamines.

*Carcinogenesis, Mutagenesis, Impairment of Fertility:* Long-term (2-year) oral studies in rats with erythromycin ethylsuccinate and erythromycin base did not provide evidence of tumorigenicity. Mutagenicity studies have not been conducted. There was no apparent effect on male or female fertility in rats fed erythromycin (base) at levels up to 0.25% of diet.

*Pregnancy: Teratogenic Effects. Pregnancy Category B:* There is no evidence of teratogenicity or any other adverse effect on reproduction in female rats fed erythromycin base (up to 0.25% of diet) prior to and during mating, during gestation, and through weaning of two successive litters. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

*Labor and Delivery:* The effect of erythromycin on labor and delivery is unknown.

*Nursing Mothers:* Erythromycin is excreted in human milk. Caution should be exercised when erythromycin is administered to a nursing woman.

*Pediatric Use:* See **INDICATIONS AND USAGE** and **DOSAGE AND ADMINISTRATION** sections.

*Geriatric use:* Elderly patients, particularly those with reduced renal or hepatic function, may be at increased risk for developing erythromycin-induced hearing loss. (See **ADVERSE REACTIONS** and **DOSAGE AND ADMINISTRATION**).

Elderly patients may be more susceptible to development of torsades de pointes arrhythmias than younger patients. (See **ADVERSE REACTIONS.**)

Elderly patients may experience increased effects of oral anticoagulant therapy while undergoing treatment with erythromycin. (See **PRECAUTIONS**, Drug Interactions.)

Ery-Ped 200 contains 117.5 mg (5.1 mEq) of sodium per individual dose.

Ery-Ped 400 contains 117.5 mg (5.1 mEq) of sodium per individual dose.

Based on the 200 mg/5 mL strength, at the usual recommended doses, adult patients would receive a total of 940 mg/day (40.8 mEq) of sodium. Based on the 400 mg/5 mL strength, at the usual recommended doses, adult patients would receive a total of 470 mg/day (20.4 mEq) of sodium. The geriatric population may respond with a blunted natriuresis to salt loading. This may be clinically important with regard to such diseases as congestive heart failure.

ERYPED<sup>®</sup> Drops contains 58.8 mg (2.6 mEq) of sodium per individual dose.

### **ADVERSE REACTIONS**

The most frequent side effects of oral erythromycin preparations are gastrointestinal and are dose-related. They include nausea, vomiting, abdominal pain, diarrhea and anorexia. Symptoms of hepatitis, hepatic dysfunction and/or abnormal liver function test results may occur. (See **WARNINGS** section.)

Onset of pseudomembranous colitis symptoms may occur during or after antibacterial treatment. (See **WARNINGS**.)

Erythromycin has been associated with QT prolongation and ventricular arrhythmias, including ventricular tachycardia and torsades de pointes.

ALLERGIC REACTIONS RANGING FROM URTICARIA TO ANAPHYLAXIS HAVE OCCURRED. SKIN REACTIONS RANGING FROM MILD ERUPTIONS TO ERYTHEMA MULTIFORME, STEVENS-JOHNSON SYNDROME, AND TOXIC EPIDERMAL NECROLYSIS HAVE BEEN REPORTED RARELY. THERE HAVE BEEN RARE REPORTS OF PANCREATITIS AND CONVULSIONS.

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

### **OVERDOSAGE**

In case of overdosage, erythromycin should be discontinued. Overdosage should be handled with the prompt elimination of unabsorbed drug and all other appropriate measures should be instituted.

Erythromycin is not removed by peritoneal dialysis or hemodialysis.

### **DOSAGE AND ADMINISTRATION**

EryPed (erythromycin ethylsuccinate) oral suspensions may be administered without regard to meals.

Children: 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 ethylsuccinate for children is 30 to 50 mg/kg/day in equally divided doses every 6 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 by administering one-third of the total daily dose every 8 hours.

THE FOLLOWING DOSAGE SCHEDULE IS SUGGESTED FOR MILD TO MODERATE INFECTIONS

<b>Body Weight</b>	<b>Total Daily Dose</b>
Under 10 lbs	30-50 mg/kg/day 15-25 mg/lb/day

10 to 15 lbs	200 mg
16 to 25 lbs	400 mg
26 to 50 lbs	800 mg
51 to 100 lbs	1200 mg
over 100 lbs	1600 mg

Adults: 400 mg 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.

For adult dosage calculation, use a ratio of 400 mg of erythromycin activity as the ethylsuccinate to 250 mg of erythromycin activity as the stearate, base or estolate.

In the treatment of streptococcal infections, a therapeutic dosage of 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 treatment of urethritis due to *C. trachomatis* or *U. urealyticum*: 800 mg three times a day for 7 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 amebiasis: Adults: 400 mg four times daily for 10 to 14 days. Children: 30 to 50mg/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 Legionnaires' Disease: Although optimal doses have not been established, doses utilized in reported clinical data were 1.6 to 4 g daily in divided doses.

For the EryPed 200 unit dose, reconstitute with 2.9 mL of water. For the EryPed 400 unit dose, reconstitute with 2.7 mL of water.

## HOW SUPPLIED

EryPed 200 (erythromycin ethylsuccinate for oral suspension, USP) is supplied in bottles of 100 mL (NDC 0074-6302-13), 200 mL (NDC 0074-6302-53), and 5 mL unit dose ABBO-PAC<sup>®</sup> packages of 100 bottles (NDC 0074-6302-05).

EryPed 400 (erythromycin ethylsuccinate for oral suspension, USP) is supplied in bottles of 60 mL (NDC 0074-6305-60), 100 mL (NDC 0074-6305-13), 200 mL (NDC 0074-6305-53), and 5 mL unit dose ABBO-PAC packages of 100 bottles (NDC 0074-6305-05).

EryPed Drops (erythromycin ethylsuccinate for oral suspension) is supplied in 50 mL bottles (NDC 0074-6303-50).

Recommended storage: Store EryPed 200, EryPed 400, and EryPed Drops, prior to mixing, below 86°F (30°C). After reconstitution, EryPed 200, EryPed 400, and EryPed Drops must be stored at or below 77°F (25°C) and used within 35 days; refrigeration is not required.

## REFERENCES

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2. National Committee for Clinical Laboratory Standards, *Performance Standards for Antimicrobial Disk Susceptibility Tests*, Fifth Edition. Approved Standard NCCLS Document M2-A5, Vol. 13, No. 24. NCCLS, Villanova, PA, December 1993.
3. Committee on Rheumatic Fever, Endocarditis, and Kawasaki Disease of the Council on Cardiovascular Disease in the Young, the American Heart Association: Prevention of Rheumatic Fever. *Circulation*. 78(4):1082-1086, October 1988.
4. Honein, M.A., et. al.: Infantile hypertrophic pyloric stenosis after pertussis prophylaxis with erythromycin: a case review and cohort study. *The Lancet* 1999; 354 (9196): 2101-5.