

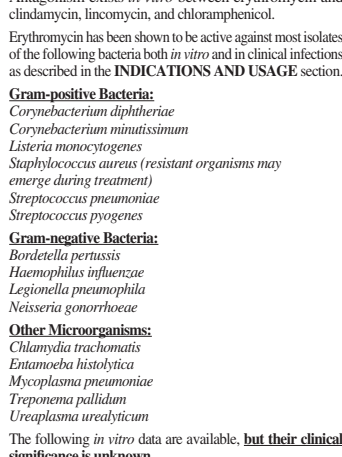


(Nos. 6326 and 6227) XX-XXXX-R1 Rev. July 2013 ERYTHROMYCIN TABLETS, USP Film-coated Tablets Only

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

**DESCRIPTION** Erythromycin Tablets (erythromycin tablets, USP) are an antibacterial product containing erythromycin, USP, in a unique, nonerect, film coating for oral administration. Erythromycin Tablets are available in two strengths containing either 250 mg or 500 mg of erythromycin base.



**Inactive Ingredients** Colloidal silicon dioxide, croscarmellose sodium, crospovidone, D&C Red No. 30 Aluminum Lake, hydroxypropyl cellulose, hypromellose, hydroxypropyl methylcellulose phthalate, magnesium stearate, microcrystalline cellulose, povidone, polyethylene glycol, propylene glycol, sodium citrate, sodium hydroxide, stibic acid, sorbitan monooleate, talc, and titanium dioxide.

**CLINICAL PHARMACOLOGY** Orally administered erythromycin base and its salts are readily absorbed in the microbially active form. Interindividual variations in the absorption of erythromycin are, however, observed, and some patients do not achieve optimal serum levels. Erythromycin is largely bound to plasma proteins.

**Mechanism of Action** Erythromycin acts by inhibition of protein synthesis by binding 50S ribosomal subunits of susceptible organisms. It does not affect nucleic acid synthesis.

**Mechanism of Resistance** The major route of resistance is modification of the 23S rRNA in the 50S ribosomal subunit or sensitivity while others can also be significant.

**Interactions with Other Antibiotics** Antagonism exists *in vitro* between erythromycin and clindamycin, lincomycin, and chloramphenicol.

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

**Gram-positive Bacteria:** *Corynebacterium diphtheriae*, *Corynebacterium minutissimum*, *Listeria monocytogenes*, *Staphylococcus aureus* (resistant organisms may emerge during treatment), *Streptococcus pneumoniae*, *Streptococcus pyogenes*

**Gram-negative Bacteria:** *Bordetella pertussis*, *Haemophilus influenzae*, *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. At least 90% of the following bacteria exhibit *in vitro* minimum inhibitory concentration (MIC) less than or equal to the susceptible breakpoint for erythromycin. However, the efficacy of erythromycin in treating clinical infections due to these bacteria has not been established in adequate and well controlled clinical trials.

**Gram-positive Bacteria:** *Viridans group streptococci*

**Gram-negative Bacteria:** *Moraxella catarrhalis*

**Susceptibility Test Methods** When available the clinical microbiology laboratory should provide the results of *in vitro* susceptibility test results for antimicrobial drug products used in resident hospitals to the physician as periodic reports that describe the susceptibility profile of nosocomial and community-acquired pathogens. These reports should aid the physician in selecting an antibacterial drug product for treatment.

**Dilution Techniques** Quantitative methods are used to determine antimicrobial minimum inhibitory concentrations (MICs). These MICs provide estimates of the susceptibility of bacteria to antimicrobial compounds. The MICs should be determined using a standardized test method (2 broth and/or agar). The MIC values should be interpreted according to criteria provided in Table 1.

**Diffusion techniques** Quantitative methods that require measurement of zone diameters can also provide reproducible estimates of the susceptibility of bacteria to antimicrobial compounds. The zone size provides an estimate of the susceptibility of bacteria to antimicrobial compounds. The zone size should be determined using a standardized test method (2). This procedure uses paper disks impregnated with 15 mcg erythromycin to test the susceptibility of microorganisms to erythromycin. The disc diffusion interpretive criteria are provided in Table 1.

Table 1. In Vitro Susceptibility Test Interpretive Criteria for Erythromycin

Pathogen	Minimum Inhibitory Concentrations (mcg/mL)		Disk Diffusion (zone diameters in mm)	
	S	I	S	I
Staphylococcus aureus	≤0.5	1-4	≥8	≥23
Streptococcus pneumoniae	≤0.25	0.5	≥21	≥21
Streptococcus pyogenes	≤0.25	0.5	≥21	≥16

A report of "Susceptible" indicates that the antimicrobial is likely to inhibit growth of the pathogen if the antimicrobial compound reaches the concentrations at the site of infection necessary to inhibit growth of the pathogen. 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 product 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 antimicrobial is not likely to inhibit growth of the pathogen if the antimicrobial compound reaches the concentrations usually achievable at the infection site; other therapy should be selected.

**Quality Control:** Standardized susceptibility test procedures require the use of laboratory controls to monitor and ensure the accuracy and precision of supplies and reagents used in the assay, and the techniques of the individuals performing the test. Standard erythromycin powder should provide the following range of MIC values noted in Table 2. For the diffusion technique using the 15 mcg disk, the criteria in Table 2 should be achieved.

Table 2. Acceptable Quality Control Ranges for Erythromycin

QC Strain	Minimum Inhibitory Concentrations (mcg/mL)	Disk Diffusion (zone diameters in mm)
<i>Staphylococcus aureus</i>	0.25-1	NA
ATCC 29213		
<i>Staphylococcus aureus</i>	NA	22-30
ATCC 25923		
<i>Enterococcus faecalis</i>	1-4	NA
ATCC 29212		
<i>Streptococcus pneumoniae</i>	0.03-0.12	25-30
ATCC 49619		

**INDICATIONS AND USAGE** To reduce the development of drug-resistant bacteria and maintain the effectiveness of Erythromycin Tablets, USP and other antibacterial drugs, Erythromycin Tablets, USP 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 antibiologic use. In the absence of such data, local epidemiology and susceptibility patterns may contribute to the empiric selection of therapy.

Erythromycin Tablets, USP are indicated in the treatment of infections caused by susceptible strains of the designated microorganisms in the diseases listed below:

**Upper respiratory tract infections of mild to moderate degree caused by *Streptococcus pneumoniae*, *Streptococcus pneumoniae*, *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 degree caused by *Streptococcus pyogenes* or *Streptococcus pneumoniae*.**

**Listeriosis caused by *Listeria monocytogenes*.**

**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 organisms may emerge during treatment).**

**Pertussis (whooping cough) caused by *Bordetella pertussis*.** Erythromycin is effective in eliminating the organism from the nasopharynx of infected children, but does not prevent noninfectious. Some clinical studies suggest that erythromycin may be helpful in the prophylaxis of pertussis in exposed susceptible individuals.

**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 erythromycin only). Extraintestinal amebiasis requires treatment with other agents.

**Acute pelvic inflammatory disease caused by *Neisseria gonorrhoeae*:** Erythromycin Lactobionate-LV, erythromycin lactobionate for injection, USP followed by erythromycin base 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 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.

Erythromycin is indicated for treatment of the following infections caused by *Chlamydia trachomatis*: conjunctivitis of the newborn, pneumonia of infants, and ureteral 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* at the following dosages:

When tetracyclines are contraindicated or not tolerated, erythromycin is indicated for the treatment of nongonococcal urethritis caused by *Treponema pallidum*. Erythromycin (oral forms only) is an alternative choice of treatment for primary syphilis in patients allergic to the penicillins. In treatment of primary syphilis, spinal fluid should be examined before treatment and as part of the follow-up after therapy.

**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** Penicillin is Initial Attack 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. The therapeutic dose should be administered for ten 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).

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

Erythromycin is contraindicated in patients taking tetradenine, sisomicin, cisapride, pimozide, ergotamine, or dihydroergotamine. (See PRECAUTIONS - Drug Interactions.)

**Warnings** **Hepatotoxicity** 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.

**QT Prolongation** Erythromycin has been associated with prolongation of the QT interval and infrequent cases of arrhythmias. Cases of torsades de pointes have been spontaneously reported during postmarketing surveillance in patients receiving erythromycin. Fatalities have been reported. Erythromycin should be avoided in patients with known prolongation of the QT interval, patients with ongoing arrhythmias, conditions such as uncorrected hypokalemia or hypomagnesemia, clinically significant bradycardia, and in patients receiving Class IA (quinidine, procainamide) or Class III (dofetilide, amiodarone, sotalolol) antiarrhythmic agents. Elderly patients may be more susceptible to drug-associated effects on the QT interval.

**Thyroiditis in Pregnancy** There has 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.

**Clotrimazole Difficile Associated Diarrhea (CDAD)** has been reported with use of nearly all antibacterial agents, including Erythromycin Tablets, and may range in severity from mild diarrhea to fatal colitis. Treatment with antibacterial agents alters the normal flora of the colon leading to overgrowth of *C. difficile*.

*C. difficile* produces toxins A and B which contribute to the development of CDAD. Hypertoxic producing strains of *C. difficile* cause increased morbidity and mortality, as these infections can be refractory to antimicrobial therapy and may require colectomy. CDAD must be considered in all patients who present with diarrhea following antibiotic use. Careful medical history is necessary since CDAD has been reported to occur over two months after the administration of antibacterial agents.

If CDAD is suspected or confirmed, ongoing antibiotic use not directed against *C. difficile* may need to be discontinued. Appropriate fluid and electrolyte management, protein supplementation, antibiotic therapy, and surgical evaluation should be instituted as clinically indicated.

**Drug Interactions** Serious adverse reactions have been reported in patients taking erythromycin concomitantly with CYP3A4 substrates. These include colchicine toxicity with colchicine; thalidomide toxicity with simvastatin, lovastatin, and atorvastatin; and hypotension with calcium channel blockers (metabolized by CYP3A4 (e.g., verapamil, anhalazine, diltiazem)). (See PRECAUTIONS - Drug Interactions.)

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