

## Erythromycin\*

### Class: Macrolide

#### Overview

Erythromycin, a naturally occurring macrolide, is derived from *Streptomyces erythrus*. This macrolide is a member of the 14-membered lactone ring group. Erythromycin is predominantly erythromycin A, but B, C, D and E forms may be included in preparations. These forms are differentiated by characteristic chemical substitutions on structural carbon atoms and on sugars. Although macrolides are generally bacteriostatic, erythromycin can be bactericidal at high concentrations. Eighty percent of erythromycin is metabolically inactivated, therefore very little is excreted in active form. Erythromycin can be administered orally and intravenously. Intravenous use is associated with phlebitis.

Toxicities are rare for most macrolides and hypersensitivity with rash, fever and eosinophilia is rarely observed, except with the estolate salt. Erythromycin is well absorbed when given orally. Erythromycin, however, exhibits poor bioavailability, due to its basic nature and destruction by gastric acids. Oral formulations are provided with acid-resistant coatings to facilitate bioavailability; however these coatings can delay therapeutic blood levels. Additional modifications produced better tolerated and more conveniently dosed newer macrolides, such as azithromycin and clarithromycin. Erythromycin can induce transient hearing loss and, most commonly, gastrointestinal effects evidenced by cramps, nausea, vomiting and diarrhea. The gastrointestinal effects are caused by stimulation of the gastric hormone, motilin, which activates receptors in the small intestine that initiate peristalsis. Enteric coatings do not reduce risk of these gastrointestinal sequelae. Erythromycin estolate may be hepatotoxic, resulting in cholestasis and is no longer widely recommended for use in medicine. The ethylsuccinate salt is used in oral suspensions in lieu of estolate. Erythromycin and clarithromycin are microsomal enzyme inhibitors that depress the metabolism of some drugs, such as theophylline, phenytoin, cyclosporine, digoxin, carbamazepine, benzodiazepines, ergot alkaloids, lovastatin, pimozide, simvastatin, tacrolimus, warfarin and corticosteroids. Concurrent use with terfenadine or astemizole is contraindicated due to cardiac toxicity.

#### Resistance

See also the discussion of resistance in the general overview of *Macrolides* (on the Webpage). Resistance to erythromycin can develop rapidly. Resistance can be due to alteration of ribosomal targets, the 50S and the 23 S ribosomal receptor sites, or through loss of affinity for the chemical. This erythromycin resistance, and resistance to macrolides in general, can be intrinsic, induced by plasmids or chromosomally constitutive. Increasing resistance to group B streptococci has been observed for several years. Resistance to *Enterococcus* species and *S. pneumoniae* has also been observed. In fact macrolide monotherapy for community acquired pneumonia is no longer

recommended due to a rate of resistance in *S. pneumoniae* estimated between 20% and 25%. The mechanism for this increase in resistance is the presence of genes that encode for methylation of the erythromycin binding nucleotide target or of those that code for drug efflux.

### Effectiveness

See also the general overview of *Macrolides* (on the Webpage). Erythromycin is effective against streptococci, including group A  $\beta$ -hemolytic streptococci and *S. pneumoniae*, methicillin susceptible staphylococci, *Moraxella catarrhalis*, *Treponema pallidum*, *Ureaplasma urealyticum*, *Mycoplasma pneumoniae*, *Legionella* species, *Listeria* species, *Chlamydia* species, some rickettsiae, *Neisseria meningitides*, *Bordetella pertussis* and *Campylobacter jejuni*. In human medicine, erythromycin is the drug of choice for *Mycoplasma pneumoniae*, *Legionella pneumophila*, diphtheria, *Chlamydia trachomatis* pneumonia or conjunctivitis and bacillary angiomatosis. At one time erythromycin was the first line agent of choice in treating pertussis and *Chlamydia* infections in newborn infants, however due to erythromycin's association with hypertrophic pyloric stenosis, azithromycin is often used in lieu of the parent compound. In children, erythromycin and sulfasoxazole can be used in combination to treat otitis media caused by *S. pneumoniae*, non-typable *H. influenzae* and *Moraxella* species.

**\*References available by request. Call the Infectious Disease Epidemiology Section, Office of Public Health, Louisiana Department of Health and Hospitals (504-219-4563)**