Package Insert for Reconstitution, Administration and Dosage
See Product Monograph for complete product information

Pr ERYTHROCIN® I.V.

(erythromycin lactobionate for injection)
Powder for solution
500 mg and 1 g erythromycin/vial
For Intravenous (i.v.) use only
Antibiotic

INDICATIONS

ERYTHROCIN® I.V. (erythromycin lactobionate for injection) should be used in the treatment of patients when oral administration is not possible or when it is desirable to obtain higher serum levels of erythromycin than achievable with orally administered preparations. Intravenous erythromycin should be replaced by an oral form of erythromycin as soon as possible.

ERYTHROCIN® I.V. (erythromycin lactobionate for injection) is indicated for:

- the treatment of infections caused by susceptible strains of the designated microorganisms in the diseases listed below:

- **Lower respiratory tract infections** of mild to moderate severity caused by *S. pyogenes* (Group A beta-hemolytic streptococci), *S. pneumoniae* and *M. pneumoniae*.
- **Skin and soft tissue infections** of mild to moderate severity caused by *S.pyogenes* and *S. aureus*.
  N.B. Resistance of staphylococci may emerge during treatment.
- **Legionnaires' disease** caused by *L. pneumophila*. Although no controlled clinical efficacy studies have been conducted, *in vitro* and limited clinical data suggest that erythromycin can be effective in treating Legionnaires' disease. Clinical evidence suggests that erythromycin is the preferred antibiotic for treating Legionnaires' Diseases.
- Erythromycin should not be used for the treatment of syphilis in pregnancy because it cannot be relied upon to cure an infected fetus (see **PRECAUTIONS, Pregnancy in Product Monograph**).

Specimens for bacteriologic culture should be obtained prior to therapy in order to isolate and identify the causative organisms and to determine their susceptibility to erythromycin. Therapy may be instituted before results of susceptibility studies are known; however, antibiotic treatment should be re-evaluated when the results become available or if the clinical response is not adequate.

To reduce the development of drug-resistant bacteria and maintain the effectiveness of ERYTHROCIN® I.V. (erythromycin lactobionate for injection) and other antibacterial drugs, ERYTHROCIN® I.V. (erythromycin lactobionate for injection) should be used only to treat 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."

Pediatrics

Pediatrics <Neonates>: Based on the data submitted and reviewed by Health Canada, the safety and efficacy of ERYTHROCIN® I.V in Neonates has not been established; therefore, Health Canada has not authorized an indication for Neonates use. (See **DOSAGE AND ADMINISTRATION**)

Pediatrics <1 month-18 years of age >: Based on the data submitted and reviewed by Health Canada, the safety and efficacy of ERYTHROCIN® I.V in pediatric patients has been established; therefore, Health Canada has authorized an indication for pediatric use.(see **DOSAGE AND ADMINISTRATION**)

Geriatrics:

(> 65 years of age): There is no specific information available for comparing use of erythromycin in elderly with use in other age groups. Nevertheless, special care is advised in this age group due to age associated changes such as the decrease in renal function and alteration of hematological parameters.

an acceptable method of administration.

Continuous infusion of erythromycin lactobionate is preferable due to the slow infusion rate and lower concentration of erythromycin; however, intermittent infusion at intervals not greater than every 6 hours may also be used.

Continuous Intravenous Infusion: For slow continuous infusion, erythromycin lactobionate solutions should be diluted to give a final concentration of 1 g per litre (1 mg/mL).

Intermittent Intravenous Infusion: One-fourth of the total daily dose of erythromycin lactobionate should be administered by intravenous infusion in 20 to 60 minutes at intervals not greater than every 6 hours. The erythromycin lactobionate solutions should be diluted to give a final concentration of 1 to 5 mg/mL. No less than 100 mL of i.v. diluent should be used. Infusion should be sufficiently slow to minimize pain along the vein.

Reconstitution

Vial Reconstitution

Reconstitute with Sterile Water for Injection USP only as indicated in Table 1. Use of other diluents may cause precipitation during reconstitution. Do not use diluents containing preservatives or inorganic salts.

Table 1 - Reconstitution

Vial Size	Volume of Diluent to be Added to Vial	Nominal Concentration per mL
500 mg	10 mL	50 mg/mL
1 g	20 mL	50 mg/mL

Stability and Storage Recommendation for stock solution:
The reconstituted stock solution is stable under refrigeration for 96 hours, or for 24 hours between 15°C to 25°C. The stock solution must be diluted before use (see Dilution).

Dilution:

For Continuous Intravenous Infusion dilute the reconstituted stock solution in 0.9% Sodium Chloride Injection USP, Lactated Ringer's Injection USP, or NORMOSOL-R* to give a concentration of approximately 1 mg/mL.

For Intermittent Intravenous Infusion dilute the reconstituted stock solution to a final concentration of 1 to 5 mg/mL in 0.9% Sodium Chloride Injection USP, Lactated Ringer's Injection USP, or NORMOSOL-R*.

The following solutions may also be used for continuous or intermittent intravenous infusion provided they are first buffered by the addition of 1 mL of 4% sodium bicarbonate per 100 mL of solution.

- 5% Dextrose Injection USP
- 5% Dextrose and Lactated Ringer's Injection
- 5% Dextrose and 0.9% Sodium Chloride Injection USP

Sodium bicarbonate must be added to these solutions so that their pH is in the optimum range for erythromycin lactobionate stability. Acidic solutions of erythromycin are unstable and lose their potency rapidly. A pH of at least 5.5 is desirable for the final diluted solution of erythromycin lactobionate.

No drug or chemical agent should be added to an ERYTHROCIN® I.V. (erythromycin lactobionate for injection) fluid admixture unless its effect on the chemical and physical stability of the solution has first been determined.

The pH of intravenous solutions in plastic containers tends to be lower than that of the same solutions in glass containers. The concurrent use of additives that will result in an erythromycin lactobionate admixture with a pH below 5.5 should be avoided.

Stability of Diluted Solution:
The final diluted solution of erythromycin lactobionate is not suitable for storage and should be completely administered within 8 hours in order to assure proper potency.

Missed Dose

If a dose is missed, it should be taken as soon as remembered unless it is almost time for the next dose. The dose should not be doubled to make up for a missed dose.

CONTRAINDICATIONS

Erythromycin lactobionate for injection is contraindicated in patients who are hypersensitive to erythromycin, clarithromycin, other macrolide antibacterial agents or to any ingredient in the formulation, including any non-medicinal ingredient, or component of the container. For a complete listing, see the **DOSAGE FORMS, COMPOSITION AND PACKAGING** section of the product monograph.

- Erythromycin is also contraindicated as concurrent therapy with astemizole*, terfenadine*, cisapride*, pimozide* and ergotamine or dihydroergotamine (see **Drug Interactions in Product Monograph**).
- Erythromycin should not be given to patients with a history of QT prolongation (congenital or documented acquired QT prolongation) or ventricular cardiac arrhythmia, including torsades de pointes (see **WARNINGS AND PRECAUTIONS** and **DRUG INTERACTIONS in Product Monograph**)
- Erythromycin should not be given to patients with electrolyte disturbances (hypokalaemia, hypomagnesaemia due to the risk of prolongation of QT interval)
- Erythromycin should not be used concomitantly with HMG-CoA reductase inhibitors (statins) that are extensively metabolized by CYP3A4 (lovastatin or simvastatin), due to the increased risk of myopathy, including rhabdomyolysis (see **DRUG INTERACTIONS and ADVERSE REACTIONS in Product Monograph**)

ERYTHROCIN® I.V. (erythromycin lactobionate for injection) must be administered by continuous or intermittent intravenous infusion only. I.V. bolus/push is an unacceptable route of administration.

*Astemizole, terfenadine, cisapride and pimozide are no longer marketed in Canada

SERIOUS WARNINGS AND PRECAUTIONS BOX

Serious Warnings and Precautions

Cardiovascular Events

Prolongation of the QT interval, reflecting effects on cardiac repolarisation imparting a risk of developing cardiac arrhythmia and torsades de pointes, have been seen in patients treated with macrolides including erythromycin (see **CONTRAINDICATIONS, DRUG INTERACTIONS** and **ADVERSE REACTIONS in the Product Monograph**).

- Fatalities have been reported.

Erythromycin should be used with caution in the following:

Patients with coronary artery disease, severe cardiac insufficiency, conduction disturbances or clinically relevant bradycardia.

Patients concomitantly taking other medicinal products associated with QT prolongation (see **CONTRAINDICATIONS** and **DRUG INTERACTIONS in the Product Monograph**).

Elderly patients may be more susceptible to drug-associated effects on the QT interval (see **ADVERSE REACTIONS in the Product Monograph**).

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.

DOSAGE AND ADMINISTRATION

Dosing Considerations

ERYTHROCIN® I.V. (erythromycin lactobionate for injection) should be used in the treatment of patients when oral administration is not possible or when it is desirable to obtain higher serum levels of erythromycin than achievable with orally administered preparations. Intravenous erythromycin should be replaced by an oral form of erythromycin as soon as possible.

Recommended Dose and Dosage Adjustment

The doses are expressed in terms of the base.

Adults: The recommended intravenous dose is 15 to 20 mg/kg/day. In severe infections, doses of up to 4 g of erythromycin may be given daily in divided doses.

*Astemizole, terfenadine, cisapride and pimozide are no longer marketed in Canada.

For treatment of Legionnaires' Disease: Optimal dosages have not been established; however, the larger doses (eg. 4 g daily) should be considered for known or suspected Legionella infections. Doses utilized in reported clinical data were 1 to 4 grams daily in divided doses.

Children: Age, weight, and severity of the infection are important factors in determining the proper dosage. The recommended dose is 15 to 20 mg/kg/day.

Health Canada has not authorized an indication for neonates use. (See **INDICATIONS**).

Administration

ERYTHROCIN® I.V. (erythromycin lactobionate for injection) must be administered by continuous or intermittent intravenous infusion only. Due to the irritative properties of ERYTHROCIN® I.V. (erythromycin lactobionate for injection), intravenous push is not

OVERDOSAGE

Symptoms and treatment of overdosage

Symptoms

Hearing loss, severe nausea, vomiting and diarrhea may occur.

Recently there has been a report of a case of erythromycin-induced pancreatitis following erythromycin overdose.

Treatment

There is no specific treatment for overdosage. Erythromycin should be discontinued, and gastric lavage considered, if appropriate; otherwise, the treatment should be symptomatic.

Erythromycin is not removed by peritoneal dialysis or hemodialysis.

For management of a suspected drug overdose, contact your regional poison control centre.

DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

Table 2 – Dosage Forms, Strengths, Composition and Packaging.

Route of Administration	Dosage Form / Strength/Composition	Non-medicinal Ingredients
Intravenous	Powder for Solution 500 mg and 1 g	Acid Lactobionic (Lactobionate powder source) Charcoal activated Nitrogen Water for Injection

Each vial contains 500 mg or 1 g erythromycin base in the form of erythromycin lactobionate for injection as sterile lyophilized powder. ERYTHROCIN® I.V. (erythromycin lactobionate for injection) vials contain a soluble salt of erythromycin without preservative suitable for intravenous administration.

ERYTHROCIN® I.V. (erythromycin lactobionate for injection) are available in packages of 10 vials.

ADVERSE REACTIONS

Please refer to the section in complete Product Monograph.

STORAGE, STABILITY AND DISPOSAL

ERYTHROCIN® I.V. (erythromycin lactobionate for injection) powder should be stored between 15°C to 25°C and protected from heat.

Others:

Keep in a safe place out of the reach and sight of children.

SPECIAL HANDLING INSTRUCTIONS

There are no special handling instructions.

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AMDIPHARM
Amdipharm Limited
Temple Chambers
3 Burlington Road
Dublin 4, Ireland

methapharm
Distributed by:
Methapharm Inc.
Brantford, ON
N3S 7X6