PRODUCT MONOGRAPH

INCLUDING PATIENT MEDICATION 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

ATC code: J01FA

Amdipharm Limited,
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Dublin, Dublin 4, Ireland

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RECENT MAJOR LABEL CHANGES

Warnings and Precaution, Immune (7)	AUG, 2018
Adverse Reactions, Adverse Reaction Overview (8.1)	AUG, 2018
Patient Medication Information, Serious side effects and what to do about them	AUG, 2018
Contraindications (2)	JUN, 2020
Serious Warnings & Precautions (3)	JUN, 2020
Warnings And Precautions, Gastrointestinal (7)	JUN, 2020
Adverse Reactions, Adverse Reaction Overview (8.1)	JUN, 2020
Drug Interactions, Drug-Drug Interactions (9.3)	JUN, 2020
Patient Medication Information, Serious Warnings and Precautions	JUN, 2020
Patient Medication Information, Do not use ERYTROCIN® I.V. if	JUN, 2020
Patient Medication Information, Serious side effects and what to do about them	JUN,2020

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PART I: HEALTH PROFESSIONAL INFORMATION

1. 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**).

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."

1.1 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**)

1.2 Geriatrics

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.

2. 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, STRENGTHS, 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**).

- 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**)

- 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)** 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.

3. 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**).
.
. 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**).

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

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.

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

4. DOSAGE AND ADMINISTRATION

4.1 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.

4.2 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.

> 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 (1 month to 18 years): 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)**.

4.3 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 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.

4.4 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 15ºC to 25ºC. 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.

4.5 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.

5. OVERDOSAGE

Symptoms and treatment of overdosage

Symptoms
Hearing loss, severe nausea, vomiting and diarrhoea 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.

6. 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.

7. WARNINGS AND PRECAUTIONS

Please see the Serious Warnings and Precautions Box at the beginning of Part I: Health Professional Information.

Susceptibility/resistance

Development of Drug Resistant Bacteria

Prescribing ERYTHROCIN® I.V. (erythromycin lactobionate for injection) in the absence of a proven or strongly suspected bacterial infection is unlikely to provide benefit to the patient and risks the development of drug-resistant bacteria.

General
There have been post-marketing reports of colchicine toxicity with concomitant use of erythromycin and colchicine (see **DRUG INTERACTIONS**).

Carcinogenesis, Mutagenesis, Impairment of Fertility
Long-term (two-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 tumorigenicity. Mutagenicity studies conducted did not show any genotoxic potential, and there was no apparent effect on male or female fertility in rats treated with erythromycin base by oral gavage at 700 mg/kg/day.

Driving and Operating Machinery

Due caution should be exercised when driving or operating a vehicle or potentially dangerous machinery.

Gastrointestinal

Clostridium difficile-associated disease
Clostridium difficile-associated disease (CDAD) has been reported with use of many antibacterial agents, including ERYTHROCIN® I.V. (erythromycin lactobionate for injection). CDAD may range in severity from mild diarrhea to fatal colitis. It is important to consider this diagnosis in patients who present with diarrhea, or symptoms of colitis, pseudomembranous colitis, toxic megacolon, or perforation of colon subsequent to the administration of any

antibacterial agent. CDAD has been reported to occur over 2 months after the administration of antibacterial agents.

Treatment with antibacterial agents may alter the normal flora of the colon and may permit overgrowth of Clostridium difficile. C. difficile produces toxins A and B, which contribute to the development of CDAD. CDAD may cause significant morbidity and mortality. CDAD can be refractory to antimicrobial therapy.

If the diagnosis of CDAD is suspected or confirmed, appropriate therapeutic measures should be initiated. Mild cases of CDAD usually respond to discontinuation of antibacterial agents not directed against Clostridium difficile. In moderate to severe cases, consideration should be given to management with fluids and electrolytes, protein supplementation, and treatment with an antibacterial agent clinically effective against Clostridium difficile. Surgical evaluation should be instituted as clinically indicated, as surgical intervention may be required in certain severe cases. (see **ADVERSE REACTIONS**).

Pseudomembranous colitis has been reported with nearly all antibacterial agents, including macrolides, and may range in severity from mild to life-threatening (see **ADVERSE REACTIONS**).

There have been reports of infantile hypertrophic pyloric stenosis (IHPS) occurring in infants following erythromycin therapy. Epidemiological studies including data from meta-analyses suggest a 2-3-fold increase in the risk of IHPS following exposure to erythromycin in infancy. This risk is highest following exposure to erythromycin during the first 14 days of life. Available data suggests a risk of 2.6% (95% CI: 1.5 -4.2%) following exposure to erythromycin during this time period. The risk of IHPS in the general population is 0.1-0.2%. 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. Parents should be informed to contact their physician if vomiting or irritability with feeding occurs.

Hepatic/Biliary/Pancreatic
Hepatic dysfunction, including increased liver enzymes and hepatocellular and/or cholestatic hepatitis, with or without jaundice, has been infrequently reported with erythromycin. If findings suggestive of significant hepatic dysfunction occur, therapy with erythromycin products should be discontinued.

Since erythromycin is principally excreted by the liver, caution should be exercised when erythromycin is administered to patients with impaired hepatic function.

Immune

Erythromycin should be administered with caution to any patient who has demonstrated some form of allergy to drugs. If an allergic reaction to erythromycin occurs, administration of the drug should be discontinued. Serious hypersensitivity reactions may require epinephrine, antihistamines, or corticosteroids.

Prolonged or repeated use of erythromycin may result in an overgrowth of non-susceptible bacteria or fungi and organisms initially sensitive to erythromycin. If superinfection occurs, erythromycin should be discontinued and appropriate therapy instituted.

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.

Monitoring and Laboratory Tests
Erythromycin interferes with the fluorometric determination of urinary catecholamines.

Musculoskeletal
Rhabdomyolysis with or without renal impairment has been reported in seriously ill patients receiving erythromycin concomitantly with lovastatin.

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

Ophthalmologic
There is a risk of 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.

7. 1 Special Populations

7.1.1 Pregnant Women:

Pregnancy

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 should not be used by women during pregnancy unless clearly needed. Erythromycin has been reported to cross the placental barrier in humans, but fetal plasma levels are generally low.

No evidence of teratogenecity or embryotoxicity was observed in the following studies in animals:

Reproductive toxicity in rats with 350 mg/kg/day (7 times the human dose) and 700 mg/kg/day (14 times the human dose) of erythromycin base prior to and during mating, during gestation, and through weaning.

Reproductive toxicity in Swiss Webster mice with 700 mg/kg/day (14 times the human dose) of erythromycin base during the period of embryo-fetal organogenesis (gestational day 6-15).

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

Labour and Delivery

The effect of erythromycin on labour and delivery is unknown.

7.1.2 Breast-feeding

The safety of erythromycin for use during breast feeding has not been established. Erythromycin is excreted in breast milk.

7.1.3 Pediatrics

(*Neonates):* No data are available to Health Canada; therefore, Health Canada has not authorized an indication for use in neonates
(***1 month*-18 years of age**): See **DOSAGE AND ADMINISTRATION**

7.1.4 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.

8. ADVERSE REACTIONS

8.1 Adverse Reaction Overview

Blood and lymphatic system disorders: Eosinophilia

Immune system disorders: Hypersensitivity, Anaphylactic reaction

Psychiatric disorders: Hallucinations

Nervous system disorders: dizziness, central nervous system side effects including seizures, Confusional state, convulsions, and vertigo have been reported occasionally in patients; however, a cause and effect relationship has not been established. There have also been rare reports of convulsions.

Eye disorders: Visual Impairment **(**see **WARNING AND PRECAUTIONS*)***

Ear and labyrinth disorders: Deafness, tinnitus***.*** Occasionally there have been reports of reversible hearing loss occurring chiefly in patients with renal insufficiency and patients receiving high doses of erythromycin.

Cardiac disorders: Occasional case reports of cardiac arrhythmias such as ventricular tachycardia have been documented in patients receiving erythromycin therapy. There have been isolated reports of other cardiovascular symptoms such as chest pain, and palpitations; however, a cause and effect relationship has not been established. As with other macrolides, Electrocardiogram QT prolonged, ventricular tachycardia, and Torsades de Pointes have been reported with erythromycin (see **CONTRAINDICATIONS**).

Cardiac arrest, ventricular fibrillation (frequency not known)

Vascular disorders: Hypotension.

Gastrointestinal disorders: Abdominal discomfort, nausea, vomiting, diarrhea anorexia and infantile hypertrophic pyloric stenosis are also observed but less frequently. Pseudomembranous colitis has been occasionally reported to occur in association with erythromycin therapy (see **WARNINGS).** There have been rare reports of pancreatitis. There has also been a report of a case of erythromycin-induced pancreatitis following erythromycin overdose.

Hepatobiliary disorders: Symptoms of hepatitis, Hepatitis cholestatic, jaundice, Hepatic function abnormal, Hepatomegaly, hepatic failure, hepatic dysfunction and/or Liver function test abnormal results may occur (see **WARNINGS**)

Skin and subcutaneous tissue disorders: Rash, pruritus, uticaria, mild skin eruptions Skin reactions ranging from mild eruptions to erythema multiform, Stevens-Johnson syndrome and toxic epidermal necrolysis have rarely been reported.
Not known: Acute generalised exanthematous pustulosis (AGEP)
During prolonged or repeated therapy, there is a possibility of overgrowth of non-susceptible bacteria or fungi and organisms initially sensitive to erythromycin (e.g. *Staphylococcus aureus*, *Hemophilus influenzae*). If such infections occur, erythromycin should be discontinued and appropriate therapy instituted.

Musculoskeletal and connective tissue disorders: Rhabdomyolysis (see **CONTRAINDICATIONS AND DRUG INTERACTIONS**).

Renal and urinary disorders: There have been reports of Tubulointerstitial nephritis coincident with erythromycin use.

General disorders and administration site conditions: Phlebitis has been encountered occasionally during intravenous administration of erythromycin. If the infusion is given slowly, in dilute solution, preferably by continuous intravenous infusion or intermittent infusion over no less than 20 to 60 minutes, pain and vessel trauma are minimized.

Investigations: Hepatic enzyme increased

9. DRUG INTERACTIONS

9.1 Serious Drug Interactions Box

Serious Drug Interactions

- Concomitant administration of erythromycin with astemizole*, terfenadine*, cisapride*, pimozide*, and ergotamine or dihydroergotamine is contraindicated. (see **CONTRAINDICATIONS**)
- The use of terfenadine* and astemizole* is contraindicated in conjunction with erythromycin due to the occurrence of rare life threatening cardiovascular adverse events including death, cardiac arrest, torsade de pointes and other ventricular arrhythmias. Quinide, disopyramide and verapamil have been associated with rare instances of cardiac adverse events and should be used with caution in combination with erythromycin
- Erythromycin is an inhibitor of the CYP 3A4 and CYP 1A2 isoenzymes. Concurrent administration of erythromycin and drugs metabolised by either of these two isoenzymes may lead to an increase in the plasma concentrations of the co-administered drug which could result in clinically significant safety concerns.

*No longer marketed in Canada

9.2 Overview

Many categories of drugs are metabolized by CYP3A4 or CYP1A2. Some drugs may inhibit or induce the activities of these two isoenzymes. Administration of such inhibitors or inducers may impact upon the metabolism of co-administered medication(s). In some cases serum concentrations may be increased and in others decreased. Care must therefore be exercised when co administering such drugs.

Effects of erythromycin on other drugs
Erythromycin is an inhibitor of the cytochrome P450 isoenzymes CYP1A2 and CYP3A4. This inhibition may lead to increased or prolonged serum levels of those drugs metabolized by either of these two isoenzymes when co-administered with erythromycin. For such drugs the monitoring of their serum concentration may be necessary.

Erythromycin should be used with caution in patients receiving treatment with other drugs known to be CYP3A4 and/or CYP1A2 substrates, especially if the substrate has a narrow safety margin and/or the substrate is extensively metabolized by CYP3A4 or CYP1A2.

Dosage adjustments may be considered, and when possible, serum concentrations of these drugs should be monitored closely in patients concurrently receiving erythromycin.
Effects of other drugs on erythromycin
Drugs that induce CYP3A4 (such as rifampicin, phenytoin, carbamazepine, phenobarbital, 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 during two weeks after discontinued treatment with CYP3A4 inducers. Erythromycin should not be used during and two weeks after treatment with CYP3A4 inducers.

9.3 Drug-Drug Interactions

The drugs listed in this table are based on either drug interaction case reports or studies, or potential interactions due to the expected magnitude and seriousness of the interaction (i.e., those identified as contraindicated).

Table 3. Established or Potential Drug-Drug Interactions

Proper name	Ref	Effect	Clinical comments
CYP3A4 inducers			
Rifabutin	T	↓erythromycin levels	Rifabutin is an inducer of the cytochrome P450 isoenzyme CYP3A4. Rifabutin may therefore affect the pharmacokinetic behaviour of drugs metabolised by the enzymes belonging to this subfamily. Studies with the macrolide antibiotic clarithromycin demonstrated that the level of clarithromycin was reduced by approximately half when the medicines were concomitantly administered. An upward adjustment of the dose of clarithromycin and other antibiotics in the macrolide class (e.g. erythromycin) may be required when the medicines are administered in combination with rifabutin.
CYP3A4 substrates			
Alfentanil	CT	↑alfentanil levels	Alfentanil is metabolised in the liver by cytochrome P450 isoenzyme CYP3A4. Increased blood concentrations of alfentanil have been reported in patients co-administered erythromycin. This may increase the risk of prolonged or delayed respiratory depression.
Astemizole*	C	↑astemizole levels	Astemizole is metabolised in the liver by the cytochrome P450 isoenzyme CYP3A4. Concomitant administration of astemizole with erythromycin is contraindicated because erythromycin is known to impair the cytochrome P450 enzyme system which also influences astemizole metabolism. Erythromycin significantly alters the metabolism of astemizole when taken concomitantly. Rare cases of serious cardiovascular adverse events including cardiac arrest, torsade de pointes and other ventricular arrhythmias have been observed. (see **CONTRAINDICATIONS and ADVERSE REACTIONS**).

Bromocriptine	CT	↑bromocriptine levels	Bromocriptine is metabolised in the liver by cytochrome P450 isoenzyme CYP3A4. Increased blood concentrations of bromocriptine have been reported in patients co-administered erythromycin. This appears to be a result of decreased hepatic metabolism of bromocriptine due to the inhibition of CYP3A4 by erythromycin.
Carbamazepine	C	↑carbamazepine levels	Carbamazepine is a substrate of CYP3A4 and macrolides such as erythromycin have been reported to cause substantial elevations of serum concentrations of carbamazepine and symptoms of carbamazepine toxicity.
Cilostazol	CT		Cilostazol is metabolised in the liver by cytochrome P450 isoenzyme CYP3A4. Increased blood concentrations of cilostazol have been reported in patients co-administered erythromycin. This appears to be a result of decreased hepatic metabolism of cilostazol due to the inhibition of CYP3A4 by erythromycin.
Cisapride*	C	↑cisapride levels	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.
Colchicine	C	↑colchicine levels	There have been post-marketing reports of colchicine toxicity with concomitant use of erythromycin and colchicine.
Cyclosporin	C	↑cyclosporin levels	Cyclosporin is metabolised in the liver by cytochrome P450 isoenzyme CYP3A4. Increased blood concentrations of cyclosporin have been reported in patients co-administered erythromycin. This appears to be a result of decreased hepatic metabolism of cyclosporin due to the inhibition of CYP3A4 by erythromycin.

Disopyramide	C	↑disopyramide levels	Disopyramide is metabolised in the liver by cytochrome P450 isoenzyme CYP3A4. Increased blood concentrations of disopyramide have been reported in patients co-administered erythromycin. This appears to be a result of decreased hepatic metabolism of disopyramide due to the inhibition of CYP3A4 by erythromycin.
Ergotamine/ Dihydroergotamine	C	↑ergotamine/ dihydroergotamine	There are reports that ischemic reactions may occur when erythromycin is given concurrently with ergotamine-containing drugs. Post-marketing reports indicate that co-administration of erythromycin with ergotamine or dihydroergotamine has been associated with acute ergot toxicity characterized by vasospasm and ischemia of the extremities and other tissues including the central nervous system. (see C**ONTRAINDICATIONS**).
HMG-CoA Reductase Inhibitors	C,CT	↑statin levels	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 erythromycin concomitantly with HMG-CoA Reductase inhibitors.
Phenytoin	T	↑phenytoin levels	The metabolism of phenytoin is complex and is believed to be mediated by several cytochrome enzymes, particularly cytochrome P450 CYP2C9 and to a lesser extent the CYP 2C19 and CYP3A4 isoenzymes. Increased blood concentrations of phenytoin have been reported in patients co-administered erythromycin. This appears to be a result of decreased hepatic metabolism of phenytoin due to the inhibition of CYP3A4 by erythromycin.
Pimozide*	T	↑pimozide levels	Pimozide is a substrate for cytochrome P450 isoenzyme CYP3A4. Elevated pimozide levels have been observed with concomitant administration with clarithromycin, another macrolide antiobiotic. This may result in QT prolongation and cardiac arrhythmias including ventricular tachycardia, ventricular fibrillation and torsade de pointes.

Quinidine	C	↑quinidine levels	Quinidine is metabolised in the liver by cytochrome P450 isoenzyme CYP3A4. Increased blood concentrations of quinidine have been reported in patients co-administered erythromycin. This appears to be a result of decreased hepatic metabolism of quinidine due to the inhibition of CYP3A4 by erythromycin.
Sildenafil	C	↑sildenafil levels	Sildenafil is metabolised in the liver by cytochrome P450 isoenzyme CYP3A4. Increased blood concentrations of sildenafil have been reported in patients co-administered erythromycin. This appears to be a result of decreased hepatic metabolism of sildenafil due to the inhibition of CYP3A4 by erythromycin.
Tacrolimus	C	↑tacrolimus levels	Tacrolimus is metabolised in the liver by cytochrome P450 isoenzyme CYP3A4.Increased blood concentrations of tacrolimus have been reported in patients co-administered erythromycin.
Terfenadine*	C	↑terfenadine levels	Terfenadine undergoes metabolism in the liver by the specific cytochrome P450 isoenzyme, CYP3A4. This metabolic pathway may be impaired in patients who are taking erythromycin, an inhibitor of this isoenzyme. Interference with this enzyme can lead to elevated terfenadine plasma levels which may be associated with QT prolongation. Rare cases of serious cardiovascular adverse events including death, cardiac arrest, torsades de pointes and other ventricular arrhythmias (such as ventricular tachycardia, and ventricular fibrillation) have been observed. (see **CONTRAINDICATIONS** and **ADVERSE REACTIONS**).
Triazolobenzodiazepines (such as tria-zolam and alprazolam) and related benzodiazepines	C	↑triazolobenzodiazepines	Erythromycin has been reported to decrease the clearance of triazolam and related benzodiazepines, and thus may increase the pharmacologic effects of these benzodiazepines.

Verapamil	C	↑verapamil levels	Verapamil is metabolised in the liver by cytochrome P450 isoenzyme CYP3A4. Increased blood concentrations of verapamil have been reported in patients co-administered erythromycin. This appears to be a result of decreased hepatic metabolism of verapamil due to the inhibition of CYP3A4 by erythromycin. Hypotension, bradyarrhythmias, and lactic acidosis have been observed in patients receiving concurrent verapamil, belonging to the calcium channel blockers drug class.
Vinblastine	T	↑vinblastine levels	Vinblastine is metabolised in the liver by cytochrome P450 isoenzyme CYP3A4. Concomitant administration of vinblastine and erythromycin has been demonstrated to increase the toxicity of vinblastine. This appears to be a result of decreased hepatic metabolism of vinblastine due to the inhibition of CYP3A4 by erythromycin.
Zopiclone levels	CT	↑zopiclone	Erythromycin has been reported to decrease the clearance of zopiclone and thus may increase the pharmacodynamic effects of this drug.
CYP1A2 substrates			
Theophylline	CT	↑theophylline levels	Recent data from studies of erythromycin in patients reveal that its 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 concurrently with theophylline there is a significant decrease in erythromycin serum concentrations. This decrease could result in subtherapeutic concentrations of erythromycin.
Other drug interactions			
Digoxin	C	↑digoxin levels	There have been reports that there is a rise in plasma digoxin levels during concomitant administration of erythromycin

Lincomycin, Clindamycin, Chloramphenicol	T	↓effect of coadministered	Erythromycin should be used with caution if administered concomitantly with these drugs. In vitro experiments have demonstrated that binding sites for erythromycin, lincomycin, clindamycin and chloramphenicol overlap and competitive inhibition may occur.
Methylprednisolone	CT	↑methylprednisolone levels	Concurrent administration of erythromycin and methylprednisolone has been shown to decrease the clearance of methylprednisolone and increase the half-life. The mechanistic basis of this interaction is uncertain, but may involve enzymes in the Cytochrome P450 system.
Oral Anticoagulants	C	↑prothrombin time	Published reports indicate that caution should be observed when erythromycin and oral anticoagulants (e.g. rivaroxaban) are used concurrently since prothrombin time may by prolonged.
Valproate	C	↑valproate levels	Increased blood concentrations of valproate have been reported in patients co-administered erythromycin. The mechanistic basis of this interaction is uncertain, but may involve enzymes in the Cytochrome P450 system.

Legend: C = Case Study; CT = Clinical Trial; T = Theoretical

*No longer marketed in Canada.

9.4 Drug-Food Interactions

Interactions with food have not been established.

9.5 Drug-Herb Interactions

Interactions with herbal products have not been established.

9.6 Drug-Laboratory Interactions

Erythromycin interferes with the fluorometric determination of urinary catecholamines.

10. ACTION AND CLINICAL PHARMACOLOGY

10. 1 Mechanism of Action

Erythromycin exerts its antibacterial action by binding to the 50S ribosomal subunit of susceptible bacteria and suppressing protein synthesis. Erythromycin is usually bacteriostatic but may be bactericidal in high concentrations or against highly susceptible organisms.

Intravenous infusion of 500 mg erythromycin lactobionate at a constant rate over 1 hour in fasting adults produced a mean serum erythromycin level of approximately 7 µg/mL at 20

minutes, 10 µg/mL at 1 hour, 2.6 µg/mL at 2.5 hours, and 1 µg/mL at 6 hours.

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.

10. 2 Pharmacodynamics

(see MICROBIOLOGY)

Pharmacotherapeutic group: Macrolides

10. 3 Pharmacokinetics

Absorption:
Erythromycin base is unstable in gastric acid, and absorption is therefore variable and unreliable. Consequently, the base is usually given in film- or enteric-coated preparations, or one of the more acid-stable salts or esters is used. Food may reduce absorption of the base or the stearate, although this depends to some extent on the formulation; the esters are generally more reliably and quickly absorbed and their absorption is little affected by food, so that the timing of doses in relation to food intake is unimportant.

Distribution:

Erythromycin is widely distributed throughout body tissues and fluids, although it does not cross the blood-brain barrier well and concentrations in CSF are low. Relatively high concentrations are found in the liver and spleen, and some is taken up into polymorphonuclear lymphocytes and macrophages. Erythromycin is largely bound to plasma proteins (over 70% to 75%), but after doses as the estolate the propionate ester is stated to be about 95% protein bound. Erythromycin crosses the placenta: fetal plasma concentrations are variously stated to be 5 to 20% of those in the mother. It is distributed into breast milk.

Metabolism:

Erythromycin is partly metabolised in the liver by the cytochrome P450 isoenzyme CYP3A4 via N-demethylation to inactive, unidentified metabolites.

Elimination:

In the presence of normal hepatic function, erythromycin is concentrated in the liver and is excreted in the bile and undergoes intestinal reabsorption. The effect of hepatic dysfunction on biliary excretion of erythromycin is not known. About 2 to 5% of an oral dose is excreted unchanged in the urine and as much as 12 to 15% of an intravenous dose may be excreted unchanged by the urinary route. The half-life of erythromycin is usually reported to be about 1.5 to 2.5 hours, although this may be slightly longer in patients with renal impairment and has been reported to be between 4 to 7 hours in severe impairment.
Erythromycin is not removed by haemodialysis or peritoneal dialysis.

11. 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.

12. SPECIAL HANDLING INSTRUCTIONS

There are no special handling instructions.

PART II: SCIENTIFIC INFORMATION

13. PHARMACEUTICAL INFORMATION

Drug Substance

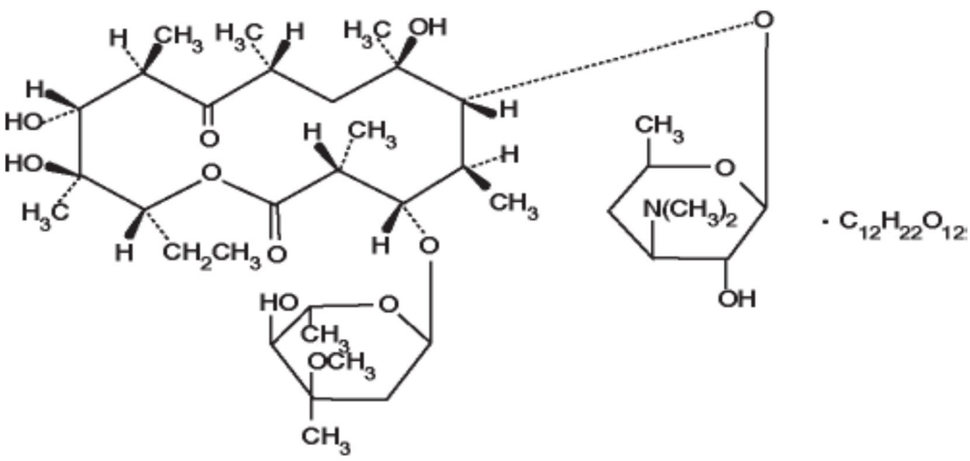
Erythromycin is produced by a strain of Streptomyces erythraeus and belongs to the macrolide group of antibiotics.

Proper name: Erythromycin Lactobionate

Chemical Name: erythromycin mono (4-O-beta-D- galactopyranosyl-D-glucinate)

Molecular formula and molecular mass: $C_{37}H_{67}NO_{13}•C_{12}H_{22}O_{12}$
1092.23

Structural formula:



Physicochemical properties:
It is basic and readily forms salts with acids. It occurs as white or slightly yellow, odourless or almost odourless, slightly hygroscopic crystals or powder with a bitter taste. It is freely soluble in methanol, ethanol, acetone and chloroform. It is soluble in water at 2 mg/mL. The melting point is 135 to 140°C. Erythromycin lactobionate is a white amorphous salt of erythromycin freely soluble in methanol and ethanol. It is soluble in water at 200 mg/mL.

15. MICROBIOLOGY

Many strains of Hemophilus influenzae are resistant to erythromycin alone.
Staphylococci resistant to erythromycin may emerge during a course of erythromycin therapy. Culture and sensitivity testing should be performed prior to and during therapy.

Erythromycin is usually bacteriostatic but may be bactericidal in high concentrations or against highly susceptible organisms. The bactericidal activity is greatest against a small number of rapidly dividing microorganisms and increases markedly as the pH of the medium is raised over the range of pH 5.5 to 8.5.
Biochemical tests demonstrate that erythromycin inhibits protein synthesis of the pathogen without directly affecting nucleic acid synthesis. Antagonism has been demonstrated between clindamycin, lincomycin and chloramphenicol and erythromycin.

16. NON-CLINICAL TOXICOLOGY

Susceptibility Testing

Disc Susceptibility Tests: Quantitative methods that require measurement of zone diameters give the most precise estimates of antibiotic susceptibility[1,212.] One recommended procedure uses erythromycin class discs for testing susceptibility; interpretations correlate zone diameters of this disc test with MIC values for erythromycin. With this procedure, a report from the laboratory of "susceptible" indicates that the infecting organism is likely to respond to therapy. A report of "resistant" indicates that the infecting organism is not likely to respond to therapy. A report of "intermediate susceptibility" suggests that the organism would be susceptible if higher doses were used.

NOTE: Many strains of *Hemophilus 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.
The standard single disc susceptibility test (using the 15 µg erythromycin disc) and the dilution susceptibility test[3]should be interpreted according to the criteria in Table 4

Table 4
Criteria for Interpreting Standard Single Disc Susceptibility Test and The Dilution Susceptibility Test

	Zone Diameter (mm)	Approximate MIC Correlate (mg/L)
Susceptible	≥ 23	≤ 0.5
Intermediate*	14-22	1-4
Resistant	≤ 13	≥ 8
* Indicates that the test results are equivocal; therefore, dilution tests may be indicated. N.B.: These criteria and the definition are in agreement with NCCLS Order Code M2A3.		

Control limits for monitoring erythromycin susceptibility tests are given in Table 5.

Table 5
Control Limits for Monitoring Erythromycin Susceptibility Tests

	Zone Diameter (mm)	MIC (mg/L)
S. aureus ATCC 29213	22-30	0.12 - 0.5
S. faecalis ATCC 29212		1.0 - 4.0

[1] Clinical and Laboratory Standards Institute. Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically; Approved Standard-9th Edition. Clinical and Laboratory Standards Institute document M07-A9. Clinical and Laboratory Standards Institute, 950 West Valley Road, Suite 2500, Wayne, Pennsylvania 19087-1898 USA, 2012.

[2] Clinical and Laboratory Standards Institute. Performance Standards for Antimicrobial Disk Susceptibility Tests; Approved Standard-11th Edition. Clinical and Laboratory Standards Institute document M02-A11. Clinical and Laboratory Standards Institute, 950 West Valley Road, Suite 2500, Wayne, Pennsylvania 19087-1898 USA, 2012.

[3] Clinical and Laboratory Standards Institute. Performance Standards for Antimicrobial Susceptibility Testing; 22nd Informational Supplement. CLSI document M100-S22. Clinical and Laboratory Standards Institute, 950 West Valley Road, Suite 2500, Wayne, Pennsylvania 19087-1898 USA, 2012.

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

PATIENT MEDICATION INFORMATION

[Pr] ERYTHROCIN® I.V.
(erythromycin lactobionate for injection)

Read this carefully before you start taking **ERYTHROCIN® I.V.** and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **ERYTHROCIN® I.V.**

Serious Warnings and Precautions

Talk to your healthcare professional before you take Erythrocin® I.V if you:

- have heart problems such as an irregular or slow heartbeat, or previous heart failure. Death has been reported.
- are taking other medicines which are known to cause serious changes in heart rhythm

What is ERYTHROCIN® I.V. used for?
ERYTHROCIN® I.V. is an antibiotic. ERYTHROCIN® I.V. is used to treat bacterial infections such as:

- Chest infections like bronchitis or pneumonia.
- Skin and tissue infections.

ERYTHROCIN® I.V. is typically used when your condition requires that your medication be delivered directly into the bloodstream. ERYTHROCIN® I.V. may also be used if you are unable to swallow pills.

Antibiotics medications like ERYTHROCIN® I.V treat only bacterial infections. They do not treat viral infections. Although you may feel better early in your treatment, ERYTHROCIN® I.V should be used exactly as directed. Misuse or overuse of ERYTHROCIN® I.V could lead to the growth of bacteria that will not be killed by ERYTHROCIN® I.V (resistance). This means that ERYTHROCIN® I.V may not work for you in the future. Do not share your medicine.

How does ERYTHROCIN® I.V. work?
Erythromycin is in a class of antibiotics called macrolides. ERYTHROCIN® I.V. works by killing or stopping the growth of bacteria which cause infections.

What are the ingredients in ERYTHROCIN® I.V.?

Medicinal ingredients:
Erythromycin lactobionate

Non-medicinal ingredients:
Acid Lactobionic (Lactobionate powder source)
Charcoal activated
Nitrogen
Water for Injection

ERYTHROCIN® I.V. comes in the following dosage forms:
ERYTHROCIN® I.V. comes as a sterile Powder.
Each vial of ERYTHROCIN® I.V. contains**:** 500mg or 1g of Erythromycin (as erythromycin lactobionate)

Do not use ERYTHROCIN® I.V. if:

- you are allergic to :
    - erythromycin
    - any of the other ingredients of ERYTHROCIN® I.V. (see What are the ingredients in **ERYTHROCIN® I.V.?**).
    - other macrolides antibiotics from the same group such as clarithromycin and azithromycin.
- you are taking a medication called:
    - *Astemizole or *terfenadine (used for hay fever and allergies),
    - *Cisapride (used for stomach problems) or *pimozide (used for mental illness
    - Ergotamine or dihydroergotamine (used for migraine headaches)
    - Simvastatin or lovastatin (used to lower cholesterol). Abnormal muscle breakdown (rhabdomyolysis) may occur.

  (see **Taking other medicines with ERYTHROCIN® I.V.)**
- You have abnormally low levels of potassium or magnesium in your blood (hypomagnesaemia or hypokalaemia)
- You or someone in your family has a history of heart rhythm conditions (Called QT prolongation). This includes conditions called ventricular cardiac arrhythmia or torsades de pointes.

*No longer marketed in Canada

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take ERYTHROCIN® I.V. Talk about any health conditions or problems you may have, including if you:

- Please see the Serious Warnings and Precautions Box at the beginning of PATIENT MEDICATION INFORMATION.
- are elderly
- have liver problems
- are suffering from an inherited form of vision loss (Leber's hereditary optic neuropathy or autosomal dominant optic atrophy). There is a risk of having visual problems after receiving erythromycin.
- have or have ever had colitis (inflammation of the large intestine) or other conditions that affect your stomach or intestines
- suffer from a condition called myasthenia gravis (characterized by muscle weakness)

Other warnings you should know about:
Call your healthcare professional if:

- your child become irritable (fussy) or vomit when fed during treatment with ERYTHROCIN® I.V (See Serious side effects and what to do about them).

Breast-feeding and pregnancy:
Tell your healthcare professional if you:

- are breast-feeding.
- are pregnant.
- think you might be pregnant.
- are planning to have a baby.

Driving and using machines:
Give yourself time after receiving ERYTHROCIN® I.V. to see how you feel before driving a vehicle or using machinery.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

Serious Drug Interactions

Do not take ERYTHROCIN® I.V. with the following:

- *Astemizole and *terfenadine (used to treat allergies such as hayfever);
- *Cisapride (used to treat stomach problems);
- *Pimozide (used to treat mental illness);
- Ergotamine/Dihydroergotamine (used for migraine headaches)
- Disopyramide and quinidine (used to treat heart problems);
- Verapamil (used to treat high blood pressure and chest pain).

The following may interact with ERYTHROCIN® I.V.:

- Rifampicin, rifabutin, clindamycin, lincomycin, chloramphenicol (medicines used to treat different types of bacterial infection);
- Phenytoin, carbamazepine, valproate (used to control epilepsy);
- Phenobarbital (used as sedatives);
- St John's Wort (a herbal medicine used to treat depression);
- Alfentanil (a medicine used to provide pain relief);
- Bromocriptine (used to treat Parkinson's disease);
- Cilostazol (a medicine used to treat conditions that affects blood vessels in the legs or arm)
- Colchicine (used to treat gout and arthritis);
- Cyclosporin and tacrolimus (used following organ transplants)
- Digoxin, procainamide, dofetilide, amiodarone and sotalol (used to treat heart problems);
- Lovastatin and simvastatin (used to lower cholesterol)
- Sildenafil (used to treat erectile dysfunction; inability to get or keep an erection);
- Zopiclone, triazolam and alprazolam (used to help you sleep or relieve states of anxiety);
- Vinblastine (used to treat certain types of cancer);
- Theophylline (used to treat asthma and other breathing problems);
- Methylprednisolone (used to help suppress the body's immune system-this is useful in treating a wide range of conditions);
- Oral Anticoagulants (Blood thinner medicines) e.g. warfarin, acenocoumarol and rivaroxaban.

*No longer marketed in Canada

How to take ERYTHROCIN® I.V.:

Usual dose:

Adults and Children: The recommended dose is 15 to 20 mg per kg of body weight per day. Your healthcare professional will calculate the right dose for you or your child.

Your healthcare professional will also tell you how long to use ERYTHROCIN® I.V as the length of your treatment depends on the type of infection you or your child may have.

ERYTHROCIN® I.V comes as a powder to be mixed with a liquid (Sterile Water for Injection) prior to use. Your healthcare professional will prepare the solution for you.

Your healthcare professional will inject ERYTHROCIN® I.V solution slowly into your vein.

Overdose:

If you think you have received too much ERYTHROCIN® I.V., contact your healthcare professional, hospital emergency department or regional Poison Control Centre immediately, even if there are no symptoms.

The symptoms of over dosage may include hearing loss, severe nausea, vomiting and diarrhoea. The symptoms are generally reversible and disappear normally following discontinuation of erythromycin.

Missed Dose:
If you missed a dose of Erythrocin® I.V., your healthcare professional will decide when you should receive your next dose.

What are possible side effects from using ERYTHROCIN® I.V.?

These are not all the possible side effects you may feel when taking ERYTHROCIN® I.V. If you experience any side effects not listed here, contact your healthcare professional. Please also see **WARNINGS AND PRECAUTIONS.**

Side effects reported include:
- Abdominal cramping and discomfort
- Feeling sick, nausea, vomiting, diarrhea and lack of appetite (anorexia)
- pain and discomfort at the site of the injection
- Low blood pressure (causing dizziness etc.)
- itching or hives

Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare professional		Get immediate medical help
	Only if severe	In all cases	
Convulsions (fits)			✓
Confusion (feel disoriented and have difficulty paying attention, remembering, and making decisions)		✓	
Hallucinations (seeing, hearing or even feeling something that is not really there)		✓	
Hearing loss, tinnitus (ringing in the ears)		✓	
Vertigo (spinning sensation)		✓	
Eosinophilia (a type of blood disorder usually found with blood tests)		✓	
Chest pain		✓	
Palpitations (feeling that your heart is pounding or racing)		✓	
Abnormal heart rhythms including • Fast or slow heart beat: • a life-threatening irregular heart beat called torsades de pointes or abnormal ECG heart tracing • Skipping beats • Lightheadedness or dizziness • Chest pain • Shortness of breath • Sweating • heart stopping (cardiac arrest)			✓
Infantile hypertrophic pyloric stenosis (narrowing of the pylorus, the opening from the stomach into the small intestine in infants): • Vomiting • Abdominal pain • Burping • Constant hunger			✓

• Dehydration (being thirsty, urinating less often) (dehydration gets worse as vomiting gets worse) • Failure to gain weight or weight			
Pancreatitis (inflammation of the pancreas): Severe pain in the upper abdomen, nausea, and vomiting			✓
Rhabdomyolysis (abnormal muscle breakdown) • Dark, red, or cola-colored urine • Urinating less often than usual General weakness • Muscle stiffness or aching (myalgia) • Muscle tenderness • Weakness of the affected muscles			✓
Tubulointerstitial nephritis (kidney problem): • Blood in the urine • Fever • Urinating more or less often than usual Nausea, vomiting			✓
Severe, potentially life-threatening allergic reaction: • Trouble breathing/wheezing • Throat tightness • Swelling of face, lips, tongue or throat • Itching, hives and severe skin rash (red spots on your skin)			✓
Bowel infection (Clostridium difficile colitis): May happen 2 or more months after you have finished ERYTHROCIN® I.V • Diarrhea that does not go away (bloody or watery) with or without: o Fever o stomach cramps			✓
Serious disorders of your skin and mucous membranes (such as eyes, lips or genital area) Conditions known as Stevens Johnson syndrome, toxic epidermal necrolysis and erythema multiforme). flu-like symptoms (fever, headache, cough, body aches) followed by a painful red or purplish rash that spreads and blisters, skin peeling			✓
skin reaction: a red, scaly rash with bumps under the skin and	✓		

blisters (exanthematous pustulosis)			
Various liver or gall-bladder problems, which can cause: • yellowing of the skin and/or eyes (jaundice) • pale stools with dark urine.			✓
Vision problem		✓	

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, talk to your healthcare professional.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: *Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.*

Storage:
Store powder between 15°C and 25°C. Protect from heat.
Keep out of reach and sight of children.

If you want more information about ERYTHROCIN® I.V.:
- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website (https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html); the manufacturer's website https://methapharm.com/products/ or by calling 1-800-287-7686 (Ext. 7804).

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