ERITROTEX INJECTION 500MG
Erythromycin Lactobionate 500mg

Product Description
Dry powder for reconstitution in clear glass vials. The powder is white to slightly yellow in colour.

Composition
Each vial contains 744.1 mg of Erythromycin Lactobionate equal to 500mg of Erythromycin.

Pharmacodynamic
Erythromycin binds to the ribosomes of bacteria and affects protein synthesis without affecting nucleic acid synthesis. Erythromycin does not bind to cytoplasmic membranes of the host cells. This is a possible explanation of its low toxicity and safety record.
Erythromycin is bacteriostatic and bactericidal depending on its concentration and the type of organism. It inhibits protein synthesis by binding to ribosmal subunits, inhibiting translocation of aminocyl transfer RNA and inhibiting polypeptide synthesis without causing any alteration in the nucleic acid cycle.

Pharmacokinetics
Distribution:
The apparent volume of distribution of Erythromycin is around 45% of body weight in normal subjects. This large distribution volume is consistent with the extensive tissue penetration of erythromycin.
Erythromycin diffuses readily into most body fluids, except the cerebrospinal fluid. However, in cases of meningeal inflammation, higher concentrations are apparent.

Metabolism:
In studies using rabbit microsomes it has been shown that erythromycin is demethylated to des-N-methyl Erythromycin and formaldehyde.

Excretion:
In the presence of normal hepatic function, Erythromycin is concentrated in the liver and excreted in the bile; the effect of hepatic dysfunction on excretion of Erythromycin by the liver is not known.
From 12% to 15% of intravenously administered Erythromycin is excreted in active form in the urine.
The drug is also excreted in the faeces.

Half-Life:
The plasma elimination half-life in patients with normal renal function is about 2 hours. In severe renal impairment the half-life may be prolonged to between 4 and 7 hours.

Indications
Erythromycin Lactobionate injection is indicated for treatment of upper respiratory tract infections (tonsillitis, pharyngitis, sinusitis, secondary bacterial infections). Lower respiratory tract infections (pneumonia, bronchitis, primary atypical pneumonia, Legionnaire's disease). Skin and soft tissue infections (furunculosis, erysipelas). Other infections - diphtheria carriers and cases as an adjunct to antitoxin, syphilis and gonorrhoea (in cases of penicillin allergy), subacute bacterial endocarditis, otitis media.

Recommended Dosage

Erythromycin Lactobionate injection administered by Intravenous.

Adults
The usual adult dose is the equivalent of 25-50 mg/kg per day in divided doses of Erythromycin, by intravenous infusion every 6 hours, or the equivalent of 1 to 2 g of Erythromycin daily by intermittent intravenous infusion over 20 to 60 minutes every 6 hours or by infusion over 24 hours. The equivalent of 4 gram daily has been recommended for severe infections.
Small volume intravenous infusion, minimum volume 100 ml, is the preferred method so as to minimise venous irritation.

Children
25-50 mg per kg by intravenous injection, daily in divided doses.

Elderly
Use adult dosage with care, taking into consideration any impairments in liver or biliary functions.

Patients with impaired hepatic function
In the presence of normal hepatic function, Erythromycin is concentrated in the liver and excreted in the bile. Although the effect of hepatic dysfunction on the excretion of Erythromycin and its half-life in such patients is not known, caution should be exercised in administering the antibiotic in such cases.

Patients with impaired renal function
The low proportion of renal excretion would suggest that dosage modification in patients with impaired renal function may not be necessary. In severely impaired patients however, toxicity has been reported and dosage adjustment in these cases may be warranted.

Instruction for use
Intravenous administration of Erythromycin is suitable to patients who are unable to tolerate oral medication or when it is necessary to produce a high blood concentration to control severe infections. Oral administration should replace parenteral administration as soon as practicable.
Due to the local irritative effects of Erythromycin as well as reports of QT interval prolongation and ventricular arrhythmias (some of which have been fatal) being associated with elevated serum concentrations of Erythromycin, the drug must not be administered rapidly by direct intravenous injection (intravenous push).
For continuous intravenous infusion the concentrated solution should be diluted to a concentration of 1 mg per ml. If required, solution strengths up to 5 mg/ml (0.5% solution) may be used, but should not be exceeded. Higher concentrations may result in pain along the vein. Bolus injection is not recommended.
For intermittent intravenous infusion the appropriate daily dose can be given as 4 doses once every 6 hours. The Erythromycin concentration should not exceed 5mg per ml and the infusion should be administered over 60 minutes, as a rapid infusion is more likely to be associated with arrhythmias or hypotension. A longer period of infusion should be used in patients with risk factors or previous evidence of arrhythmias. Not less than 100ml of diluent should be used for preparing intermittent intravenous solutions.
Intravenous therapy should be replaced by oral administration at the appropriate time

Incompatibilities
Erythromycin should not be reconstituted with inorganic salt solution. Use only Water for Injection.

Subsequent dilution into infusion fluids should be made prior to administration. Recommended fluids are Sodium Chloride Injection B.P. 0.9% Dextrose 5% Injection B.P. The stability of solutions of Erythromycin Lactobionate is adversely affected below pH 5.5. 5ml of sterile 8.4% sodium bicarbonate solution will neutralize 1 litre of Glucose Injection B.P. 5% and should be added to the bag prior to addition of Erythromycin Lactobionate.

Contraindications

Patients with known hypersensitivity to Erythromycin.

Erythromycin is contraindicated with astemizole, terfenadine, cisapride or pimozide. The concurrent administration of these drugs with Erythromycin has been associated with increased blood levels of astemizole, terfenadine, cisapride or pimozide, with an increased risk of life threatening cardiac arrhythmias.

Prolongation of the QT interval and development of ventricular arrhythmias (some of which have been fatal), including atypical ventricular tachycardia (torsades de pointes) have been reported with the intravenous administration of Erythromycin. Limited data suggest that these adverse effects may be associated with abnormally elevated serum Erythromycin concentrations following rapid administration. Erythromycin therefore must not be administered rapidly by direct intravenous injection (intravenous push).

Concomitant use of Erythromycin and simvastatin or lovastatin is contraindicated see warning and interaction with other medicament)

Warning and Precautions

Allergic reactions ranging from urticaria to anaphylaxis have been reported with intravenous Erythromycin.

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

Superinfection may occur with prolonged use, giving rise to overgrowth of non susceptible organisms.

Erythromycin is excreted principally via the liver and caution should be exercised when using Erythromycin in patients with a degree of hepatic impairment.

In severe renal impairment the half life may be prolonged to 4-7 hours requiring a dose modification.

Reports of rhabdomyolysis in patients administered Erythromycin concomitantly with lovastatin or simvastatin have been received and so such concomitant use is contraindicated. Caution should also be exercised in patients receiving other statins concomitantly with Erythromycin.

There have been reports of infantile hypertrophic pyloric stenosis (IHPS) occuringin infants following erythromycin therapy. In one cohort of 157 newborns who were given erythromycin for pertussis prophylaxis, seven neonates (5%) developed symptoms of non-billious vomiting or irritability with feeding and were subsequently diagnosed as having IHPS requiring surgical pyloromyotomy. 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 and caregivers should be informed to contact their physician if vomiting and/or irritability with feeding occurs.

In the event of severe acute hypersensitivity reactions, such as anaphylaxis, severe cutaneous adverse reactions (SCARs) [e.g. Stevens-Johnson Syndrome (SJS), toxic epidermal necrolysis (TEN), drug reaction with eosinophilia and systemic symptoms (DRESS) & acute generalised exanthematous pustulosis (AGEP)], [product name] should be discontinued immediately and appropriate treatment should be urgently initiated.

Interaction with Other Medicaments

Penicillin: Erythromycin, in low bacteriostatic concentrations, may inhibit the actions of bactericidal drugs. In high concentrations, Erythromycin may act synergistically with penicillin.

Use of Erythromycin in patients receiving digoxin, warfarin, carbamazepine or high doses of theophylline may result in potentiation of the effects due to impairment of excretion. A possible interaction between Erythromycin and Vinblastine has been reported in which patients receiving the two agents concurrently may experience myalgia, neutropenia and fever. It is recommended that patients should avoid receiving Erythromycin and vinblastine at the same time.
When administered concurrently with Erythromycin, increases in serum concentrations may occur for the drugs metabolised by the cytochrome P450 system such as alfentanil, bromocriptine, hexobarbitone, midazolam, phenytoin, tacrolimus, triazolam, valproate, acenocoumarol. Appropriate monitoring should be undertaken and dosage should be adjusted as necessary. Concomitant use of simvastatin or lovastatin with Erythromycin is contraindicated (see contraindicated and warning) and Erythromycin can lead to increased serum level of other statins by inhibiting the CYP3A4 isoenzyme.
Increased plasma levels of cyclosporin may occur in patients on Erythromycin.
Ergotism has been reported in patients receiving Erythromycin in combination with ergot.
Concomitant use of Erythromycin with astemizole, terfenadine, cisapride or pimozide is likely to result in an increased risk of cardiotoxicity with these drugs, and is therefore contraindicated (see Contra-indications).
Concomitant use of theophylline and Erythromycin has resulted in increased theophylline levels resulting in toxicity and decreased Erythromycin levels which could lead to subtherapeutic concentrations.
Concomitant use of Erythromycin and medications that cause prolongation of the QT interval has been reported to lead to cardiac toxicity or Torsades de Pointes.
Caution should be used with the concomitant use of Erythromycin with statins.
Interactions between Erythromycin and verapamil or clozapine have been reported.
Laboratory tests used for measurement of urinary catecholamines, SGOT and 17-hydroxycorticosteroids, may be affected if a colorimetric test is used. This interference may complicate interpretation of liver function tests. Suppression of growth of Lactobacillus casei by Erythromycin, may interfere with serum folate measurements.

Pregnancy and Lactation
Erythromycins cross the placenta, resulting in low fetal plasma concentrations (5 to 20% of maternal plasma concentrations). Erythromycin estolate has been associated with an increased risk of reversible, subclinical hepatotoxicity in approximately 10% of pregnant women; its use during pregnancy is not recommended. However, problems with other Erythromycins have not been documented.

There was no evidence of teratogenicity or any other adverse effect on reproduction in female rats fed Erythromycin base (up to 0.25% of their diet) prior to and during mating, during gestation, and through weaning of 2 successive litters.

Erythromycins are distributed into breast milk. However, problems in humans have not been documented

Side Effects
***Hepatic*:** Administration may be followed, in up to 10% of cases, by increases in AST and ALT enzymes, which sometimes recur on challenge.
Cholestatic hepatitis. Jaundice.
***Gastrointestinal*:** Pseudomembranous colitis has been reported rarely with Erythromycin.
Gastrointestinal disturbances such as abdominal discomfort and cramp, nausea, vomiting and diarrhoea are common after both oral and parenteral administration.
Pancreatitis (rare)
***Cardiovascular*:** Thrombophlebitis, venous irritation. Irritation can be reduced by either slow IV injection, or preferably a small volume IV infusion.

Prolongation of the QT interval and development of ventricular arrhythmias (some of which have been fatal), including atypical ventricular tachycardia (torsades de pointes), have been reported with the intravenous administration of Erythromycin. Limited data suggest that these adverse effects may be associated with abnormally elevated serum Erythromycin concentrations following rapid administration.
***Auditory/Vestibular*:** In very high doses, Erythromycin may cause transient perceptive deafness.
***Dermatological*:** Mild allergic reactions, urticaria, skin eruptions, rashes with fever, and reports of erythema multiforme reaction have been noted.
Stevens-Johnson syndrome and toxic epidermal necrolysis have rarely been reported.
Skin and Subcutaneous Tissue Disorders Frequency not known : severe cutaneous adverse reactions (SCARs) including Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), drug reaction with eosinophilia and systemic symptoms (DRESS) & acute generalised exanthematous pustulosis (AGEP).
Post Marketing Experience:
Gastrointestinal Disorders: Infantile hypertrophic pyloric stenosis.

Symptoms and Treatment of Overdose
Since there is no special antidote, treatment of Erythromycin overdose or toxic reactions should be symptomatic and supportive.

Presentation
This injection is available in 500mg.
1 or 10 vials are packed into one folder paperbox.

Storage Condition
Protect from light and store below 30°C. Keep out of reach of children.

Shelf Life
The injections can be used within 36 months from the date of manufacture if kept as recommended. The injection should be freshly prepared and unused portion should be discarded.

Registration number
Eritrotex Injection 500mg– **MAL06051289AZ**

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