ERYTHROMYCIN

Introduction

Erythromycin is a **macrolide** antibiotic, which can be given orally or intravenously.

It is often prescribed for people who have an allergy to the penicillins or the cephalosporins.

Oral preparations tend to cause more GIT upset compared to other macrolide antibiotics.

IV erythromycin must be diluted and given slowly.

It is on the World Health Organization's List of Essential Medicines, a list of the most important medications needed in a basic health system.

Chemistry

Erythromycin is produced by a strain of ***Streptomyces erythreus***

It is very difficult to produce synthetically.

Classification

The macrolide antibiotics include:

- **Azithromycin**
- **Clarithromycin**
- **Erythromycin**
- **Roxithromycin**

The newer macrolides have more reliable absorption and longer half-lives (azithromycin > roxithromycin > clarithromycin > erythromycin) allowing less frequent dosing.

They attain high intracellular concentrations that confer theoretical benefits in the treatment of infections due to intracellular pathogens.

Preparation

Capsules:

- As erythromycin base

  250 mg (enteric coated)

Tablets:

- As erythromycin **ethyl-succinate** or erythromycin **stearate.**

  250 mg.

Liquid suspension:

- 40 mg/mL (powder for reconstitution)

  80 mg/mL (powder for reconstitution)

Ampoules:

- As erythromycin **lactobionate.**

  This is a soluble salt of erythromycin suitable for intravenous administration

  1 gram (as powder for reconstitution)

Topical gel:

- 2 % gel (for acne).

Mechanism of Action

The macrolides including roxithromycin are **bacteriostatic** agents, (as opposed to bactericidal agents). Bacteriostatic agents inhibit bacterial reproduction, without necessarily killing them. Once inhibited from reproducing the body's natural immune system can kill the organism. Bactericidal agents directly kill bacteria.

The macrolides inhibit **bacterial protein synthesis** by binding to the **50S ribosomal subunit** and preventing translocation of peptides.

They also have some immunomodulatory and anti-inflammatory effects.

Pharmacokinetics

Absorption:

- Erythromycin can be given **orally** or **intravenously.**

Oral formulations of erythromycin have variable absorption and are often poorly tolerated due to gastrointestinal upset. [1]

Furthermore, poor adherence is likely due to the four times daily dosing schedule.

These factors limit the use of erythromycin in practice

Distribution:

- Erythromycin diffuses readily into most body fluids with the exception of cerebrospinal fluid, synovial fluid and vitreous humour.
- Erythromycin appears in breast milk
- Plasma protein binding is approximately 75%.

Metabolism and excretion:

- Up to 15 percent of an intravenously administered dose of erythromycin is excreted in the urine unchanged.

  A substantial proportion is presumably metabolized by the liver , but the exact biochemical pathways are uncertain.

Pharmacodynamics

The macrolides in general have a wide spectrum of antibiotic activity that includes: [1]

1. Gram-positive cocci
2. Gram-negative cocci
3. Anaerobes (both Gram-positive and Gram-negative
4. They also have activity against many so-called "atypical" organisms including:
   - *Legionella*
   - *Corynebacteria*
   - *Mycoplasma*
   - *Chlamydia*
   - *Bordetella*.

The macrolides do **not** have significant activity against:

- Enteric Gram-negative rods.
- Pseudomonas aeruginosa

Azithromycin is less active than erythromycin against Gram-positive pathogens, but has activity against a few Gram-negative bacteria, some anaerobes, non-tuberculous mycobacteria including MAC, and also against some parasites (e.g. *Toxoplasma gondii*). [1]

Indications

Indications (either alone or in combination with other agents) include: [2]

1. Upper respiratory tract infections
2. Lower respiratory tract infections:
    - Including empirical treatment of "atypical" pneumonias.
3. Skin infections.
4. Legionnaires' disease
5. Rheumatic fever prophylaxis (in penicillin allergy)
6. Coral cuts
7. Chlamydial infections
8. Lymphogranuloma venereum (LGV)
9. Prevention and treatment of pertussis
10. *Campylobacter* enteritis
11. Some skin conditions:
    - Acne
    - Rosacea (severe cases or failure of topical treatment).

Note that, as for all antibiotics, the prevalence of bacterial resistance may vary geographically and over time for selected species and local information on resistance is also important, particularly when treating severe infections.

Contraindications/ Precautions

These include:

1. Known hypersensitivity

2. Caution in those with risk factors for prolonged QT interval.

3. Macrolides or lincosamides allergy:

    - There is often cross-resistance between macrolides and lincosamides (clindamycin and lincomycin).

4. Severe hepatic dysfunction.

5. Myasthenia gravis:

    - Erythromycin may aggravate the weakness of patients with myasthenia gravis.

Pregnancy

Erythromycin is classified as a category A drug with respect to pregnancy.

Category A drugs are those drugs which have been taken by a large number of pregnant women and women of childbearing age without any proven increase in the frequency of malformations or other direct or indirect harmful effects on the fetus having been observed.

Breast feeding

Safe in breast feeding; but may cause loose bowel actions in the infant.

Adverse Effects

These include:

1. Allergic reactions (uncommon)

2. Dermatologic hypersensitivity reactions:

    - Including serious reactions such as Stevens-Johnson syndrome and toxic epidermal necrolysis.

3. GIT upset:

    - Nausea, vomiting, diarrhoea, abdominal pain and cramps

      Oral erythromycin has a higher incidence of GIT adverse effects (5 - 30%) than the other macrolides.

- *Clostridium difficile* associated diarrhoea:
    - Antibiotic associated pseudomembranous colitis has been reported with many antibiotics.

4. Cardiac:

- **IV** erythromycin may prolong the QT interval and increase the risk of arrhythmias.

  Both erythromycin and clarithromycin can increase the QT interval and cause torsades de pointes.

  Azithromycin and roxithromycin have also been associated with these adverse effects however the evidence is less compelling. [1]

5. Ototoxicity:

- Rare; but may be some risk with rapid administration of high IV doses in those with renal impairment.

6. Thrombophlebitis when given IV

- Preferable to use larger veins where possible. Avoid extravasation

7. Hepatic:

- Hepatic dysfunction, including increased liver enzymes and hepatocellular and/or cholestatic hepatitis with or without jaundice.

8. Drug interactions:

- Erythromycin (and clarithromycin) are potent inhibitors of the cytochrome P450 (CYP3A4) enzyme system, so they can have significant drug interactions with drugs that are metabolized by these this enzyme system.

  Azithromycin and roxithromycin cause less inhibition of the cytochrome P450 (CYP3A4) enzyme system.

Dosing

Exact dosing and the duration of dosing depends on the condition being treated as well as the severity of the condition and illness.

See latest Antibiotic Therapeutic Guidelines for full prescribing details.

In general terms:

Oral:

- 250 - 500 mg every 6 - 8 hours. (Maximum 4 grams daily).

IV:

- 0.5 - 1 grams every 6 hours.

  Dilute to 1 - 5 mg/mL and infuse over at least **60 minutes** (or slowly via a central vein where possible) to minimise the risk of thrombophlebitis and arrhythmias. [3]

  No less than **100 mL** of intravenous diluent should be used

References

1. eTG - November 2014

   - Antibiotic Therapeutic Guidelines 15th ed 2014

2. Erythromycin in Australian Medicines Handbook Website, Accessed August 2014.

3. Erythromycin in MIMs 1 March 2014.

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