# ERYthromycin ethylsuccinate (Oral) 2021

## Newborn use only

<table>
<tr><td>Alert</td><td>Risk of infantile hypertrophic pyloric stenosis is significantly higher in neonates treated with erythromycin.[16]</td></tr>
<tr><td>Indication</td><td>1. Pertussis – post-exposure prophylaxis and treatment (azithromycin is recommended).<br>2. Chlamydial conjunctivitis and pneumonia<br>3. Treatment of other susceptible bacterial infections in penicillin-allergic infants<br>4. Prokinetic agent for gastrointestinal dysmotility (routine use not recommended)</td></tr>
<tr><td>Action</td><td>Inhibits protein synthesis by attaching to the 50S subunit of the bacterial ribosome in susceptible organisms.<br>Motilin receptor agonist.</td></tr>
<tr><td>Drug type</td><td>Macrolide antibiotic.</td></tr>
<tr><td>Trade name</td><td>E-Mycin Syrup, EES Granules</td></tr>
<tr><td>Presentation</td><td>200 mg/5 mL suspension (granules for reconstitution)<br>400 mg/5 mL suspension (granules for reconstitution)</td></tr>
<tr><td>Dose</td><td>Pertussis – post-exposure prophylaxis and treatment[1] Use erythromycin only if azithromycin is not available.<br><br>Chlamydia infection (conjunctivitis, pneumonia)[2]<br><br>Non-chlamydial, susceptible bacterial infection in penicillin-allergic infants[3]
<table>
<tr><th>Condition</th><th>Postnatal age</th><th>Weight</th><th>Dose mg/kg/dose</th><th>Frequency</th><th>Duration</th></tr>
<tr><td>Pertussis</td><td></td><td></td><td>10</td><td>6 hourly</td><td>5-14 days<br>(14 days preferred)</td></tr>
<tr><td>Chlamydia infection</td><td></td><td></td><td>12.5</td><td>6 hourly</td><td>14 days</td></tr>
<tr><td rowspan="4">Non-chlamydial infection</td><td>≤14 days</td><td><1 kg</td><td>10</td><td>12 hourly</td><td></td></tr>
<tr><td>>14 days</td><td>< 1kg</td><td>10</td><td>8 hourly</td><td></td></tr>
<tr><td>≤7 days</td><td>≥1 kg</td><td>10</td><td>12 hourly</td><td></td></tr>
<tr><td>>7 days</td><td>≥1 kg</td><td>10</td><td>8 hourly</td><td></td></tr>
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Prokinetic dose for gastrointestinal dysmotility:[9,10,11,12,18,19] Routine use not recommended as inconsistent evidence for its efficacy and safety
<table>
<tr><th>Condition</th><th>Dose</th><th>Frequency</th><th>Duration</th></tr>
<tr><td>Gastrointestinal dysmotility</td><td></td><td></td><td></td></tr>
<tr><td>Low dose option one[10]</td><td>2.5 mg/kg/dose</td><td>6-hourly</td><td>up to 10 days</td></tr>
<tr><td>Low dose option two[11]</td><td>5 mg/kg/dose</td><td>8-hourly</td><td>7–14 days</td></tr>
<tr><td>High dose[12]</td><td>10–12.5 mg/kg/dose</td><td>6-hourly</td><td>7–14 days</td></tr>
</table></td></tr>
<tr><td>Dose adjustment</td><td></td></tr>
<tr><td>Maximum dose</td><td></td></tr>
<tr><td>Total cumulative dose</td><td></td></tr>
<tr><td>Route</td><td>Oral</td></tr>
<tr><td>Preparation</td><td>Add 77 mL of sterile water to granules in small volumes and shake vigorously until no lumps are visible.<br>Suspension expires 10 days after reconstitution.</td></tr>
<tr><td>Administration</td><td>Oral, preferably with feeds.[15]<br>For prokinetic effect administered 30 minutes prior to feed.</td></tr>
<tr><td>Monitoring</td><td>Liver function.</td></tr>
<tr><td>Contraindications</td><td>Hypersensitivity to erythromycin or any component of the product.<br>Concomitant therapy with pimozide, cisapride, ergotamine or dihydroergotamine, terfenadine, astemizole, lovastatin or simvastatin.</td></tr>
<tr><td>Precautions</td><td>Use with caution in hepatic impairment.<br>QT interval prolongation.<br>Uncorrected hypokalaemia, hypomagnesemia.<br>Class 1A and Class 3 antiarrhythmic agents.</td></tr>
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| **Drug interactions** | QT interval prolonging drugs: Cisapride, fluconazole, octreotide, cotrimoxazole, verapamil, Class 1A and Class 3 antiarrhythmic agents.<br>Drugs that may increase toxicity of erythromycin: Ketoconazole.<br>Drugs that may reduce erythromycin plasma concentration: Carbamazepine, theophylline.<br>Erythromycin may increase plasma concentrations of following drugs: Carbamazepine, digoxin, theophylline, warfarin, midazolam. |
| **Adverse reactions** | Infantile hypertrophic pyloric stenosis (IHPS): Risk of developing IHPS following erythromycin exposure is 0.4 % (95% CI 0.3–0.5%) in those receiving erythromycin at any time and 2.6 % (95% CI 1.5–4.2%) in those receiving erythromycin in the first 14 days.[16]<br>COMMON: Nausea, vomiting and abdominal pain. The incidence of GI reactions may vary with the erythromycin salt preparation and/or dosing regimen. Diarrhoea may occur due to increased gastrointestinal motility caused by erythromycin.<br>LESS FREQUENT OR RARE: Pancreatitis, pyloric stenosis, ileus, pseudomembranous colitis, sensorineural hearing loss, cholestasis, acute hepatitis, hepatic failure, agranulocytosis, thrombocytopenia, haemolytic anaemia, hypothermia, hypovolaemic shock and hypotension, leukocytoclastic vasculitis, acute respiratory distress following an allergic reaction, Schonlein-Henoch syndrome, candidal esophagitis, gingival hyperplasia, contact dermatitis, fixed drug eruptions, toxic pustuloderma, toxic epidermal necrolysis, interstitial nephritis, glomerulonephritis. |
| **Compatibility** | Not applicable |
| **Incompatibility** | Not applicable |
| **Stability** | After reconstituting granules, refrigerate and use within 10 days. |
| **Storage** | Store granules below 25°C. Reconstituted suspension should be refrigerated at 2–8°C and used within 10 days; do not freeze. |
| **Excipients** | |
| **Special comments** | Readily absorbed.<br>Hepatic metabolism by cytochrome P450 enzymes. |
| **Evidence** | **Efficacy**<br><u>Pertussis – post-exposure prophylaxis and treatment[1,4]</u><br>Systematic review of eradicating *B. pertussis* from the nasopharynx found short-term antibiotics (azithromycin for 3–5 days, or clarithromycin or erythromycin for 7 days) were as effective as long-term (erythromycin for 10 to 14 days) (risk ratio (RR) 1.01; 95% CI 0.98 to 1.04), but had fewer side effects (RR 0.66; 95% CI 0.52 to 0.83).[4]<br>The Centers for Disease Control and Prevention recommends oral azithromycin 10 mg/kg/day daily for 5 days. Azithromycin has the advantage of once daily dosing and shorter duration of therapy.[1]<br>Erythromycin may be used if azithromycin is unavailable: 40 mg/kg per day in 4 divided doses for 14 days.[1]<br><br><u>*Chlamydia* prophylaxis in infants born to mothers who have chlamydial infection[2]</u><br>Infants born to mothers who have untreated chlamydia are at high risk for infection. However, prophylactic antibiotic treatment is not indicated and the efficacy of such treatment is unknown. Infants should be monitored to ensure appropriate diagnosis and treatment if symptoms develop.<br><br><u>Treatment of chlamydial conjunctivitis and pneumonia[2]</u><br>*C. trachomatis* infection in neonates is most frequently recognised by conjunctivitis that develops 5 to 12 days after birth. *C. trachomatis* also can cause a subacute, afebrile pneumonia with onset at ages 1 to 3 months. RCTs reported chlamydial conjunctivitis or pneumonia is eradicated after systemic treatment with oral erythromycin 50 mg/kg/day for 14 days with few treatment failures and is more effective than topical treatment for chlamydia conjunctivitis. [5-8]<br>Recommendation: The Centers for Disease Control and Prevention recommends oral erythromycin 50 mg/kg per day given orally in four divided doses for 14 days for either chlamydial conjunctivitis or pneumonia. Alternative regimen is azithromycin 20 mg/kg/day, once daily for 3 days. Topical antibiotic therapy alone is inadequate and is unnecessary when systemic treatment is administered. [2]<br><br><u>Prokinetic agent in preterm infants</u><br>Systematic review evaluated the efficacy of erythromycin for prophylaxis or treatment of feeding intolerance in preterm infants. Ng and Shah 2008 [9] reviewed 10 randomised, controlled studies using |

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| | both high- and low-dose erythromycin. Meta-analysis on most outcomes couldn't be done. Erythromycin for prevention or treatment demonstrated no consistent effect on time required to achieve full feeds. Three studies using erythromycin at doses between 40 and 50 mg/kg/day reported a statistically significant effect on feeding tolerance as did one study using erythromycin at a slightly smaller dose (but still considered high dose) of 15 mg/kg/day. A single study (Oei 2001) using low-dose erythromycin (10 mg/kg/day) for prevention of feed intolerance reported showed that infants in the erythromycin group achieved full feeds significantly earlier than the placebo group.[10] However, three other studies that used low-dose erythromycin failed to show any significant difference between erythromycin and placebo in the times to establish full feeds in preterm infants <32 weeks' gestation with feeding intolerance. There was no reported effect on other neonatal morbidities including necrotising enterocolitis or sepsis.<br>Conclusion: Although some studies have reported a reduced time to full feeds, the effect is inconsistent, the optimal dose is unclear and there has been no reported consistent effect on other neonatal morbidities.[9] (LOE I, GOR C)<br><br><u>Prokinetic agent in surgical infants</u><br>An RCT comparing erythromycin 3 mg/kg/dose 4 times daily compared with placebo after primary repair of uncomplicated gastroschisis in 62 infants reported no difference in time to achieve full enteral feeding (27.2 v 28.7 days; P =.75), catheter-related sepsis, duration of parenteral nutrition or time to discharge between the 2 groups.[18] An RCT comparing erythromycin 3 mg/kg/dose 4 times daily in 30 neonates undergoing primary anastomosis for congenital small bowel atresia reported neonates receiving oral erythromycin achieved full enteral feeding earlier (13.07 vs. 16.13 days), required PN for a shorter duration (10.53 vs. 13.73 days) and their hospital stay was less (16.2 vs. 18.0 days).[19] Conclusion: There is inconsistent evidence that erythromycin 3 mg/kg/dose 4 times daily may have a beneficial effect in newborn infants with abdominal surgical conditions restricted to infants undergoing repair of small intestinal atresia. (LOE II GOR D)[18,19]<br><br>**Safety**<br>A systematic review of observational data reported an increase in the absolute risk of developing infantile hypertrophic pyloric stenosis (IHPS) following erythromycin exposure of 0.4 % (95% CI 0.3–0.5%) in those receiving erythromycin at any time, and 2.6% (95% CI 1.5–4.2%) in those receiving erythromycin in the first 14 days.[16]<br><br>**Bioavailability**<br>The absorption was lower in infants <1 month of age than in older children. Administration of the drug with feeds considerably increased the absorption of erythromycin ethylsuccinate.[15] |
| **Practice points** | |
| **References** | 1. Centers for Disease Control and Prevention. Recommended Antimicrobial Agents for the Treatment and Postexposure Prophylaxis of Pertussis, 2005. MMWR Recomm Rep. 2005 December 9, 2005 / 54(RR14);1-16.<br>2. Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines, 2015. MMWR Recomm Rep. 2015 Jun 5;64(RR-03):1-137.<br>3. American Academy of Pediatrics (AAP). In: Pickering LK, Baker CJ, Kimberlin DW, Long SS, eds. Red Book: 2012 Report of the Committee on Infectious Diseases. 29th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2012.<br>4. Altunaiji SM, Kukuruzovic RH, Curtis NC, Massie J. Antibiotics for whooping cough (pertussis). Cochrane Database of Systematic Reviews. 2007.<br>5. Heggie AD, Jaffe AC, Stuart LA, Thombre PS, Sorensen RU. Topical sulfacetamide vs oral erythromycin for neonatal chlamydial conjunctivitis. American Journal of Diseases of Children. 1985;139:564-6.<br>6. Sandstrom I. Treatment of neonatal conjunctivitis. Arch Ophthalmol. 1987;105:925-8.<br>7. Stenberg K, Mardh PA. Treatment of chlamydial conjunctivitis in newborns and adults with erythromycin and roxithromycin. J Antimicrob Chemother. 1991;28:301-7.<br>8. Lee PI, Wu MH, Huang LM, Chen JM, Lee CY. An open, randomized, comparative study of clarithromycin and erythromycin in the treatment of children with community-acquired pneumonia. J Microbiol Immunol Infect. 2008;41:54-61. |

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