

PROKINETIC DRUGS

WHAT IS PROKINETIC?

Prokinetic is stimulating movement or motility, such as a drug that promotes gastrointestinal motility. The bottom line is that a **prokinetic** helps keep things moving throughout the gastrointestinal (GI) tract⁽¹⁾

WHAT ARE PROKINETIC DRUGS USED FOR?

Prokinetic agents, or **prokinetics**, are **medications** that help control acid reflux. **Prokinetics** help strengthen the lower esophageal sphincter (LES) and cause the contents of the stomach to empty faster. This allows less time for acid reflux to occur.⁽¹⁾

Prokinetic Drugs

Drug	Prokinetic action	Dose	Notes
Motilin agonist: Erythromycin	<ul style="list-style-type: none"> prokinetic action due to agonism at motilin receptors⁽¹⁾ chronotropic effect on neuronal receptors⁽¹⁾ enhances motilin release from enterochromaffin cells in duodenum⁽¹⁾ enhanced contractile effects on gastric antrum and duodenum⁽¹⁾ 	<p>Prokinetic (GI motility) agent:</p> <p>Adult : IV: 70 or 200 mg IV as single dose, 200 mg IV every 12 hours for 7 days, or 250 mg IV every 6 hours for at least 24 to 48 hours⁽¹⁾</p> <p>Infants, Children, and Adolescents:</p> <p>Diagnosis: gastric emptying study (provocative testing): IV: 2.8 mg/kg infused over 20 minutes; maximum dose: 250 mg⁽⁴⁾</p> <p>Treatment: Oral: base/stearate/ Ethylsuccinate: 3 mg/kg/dose QID; may increase as needed to effect; maximum dose: 10 mg/kg or 250 mg⁽⁴⁾</p> <p>Neonate: 2mg/kg TDS⁽¹²⁾ Low-dose regimens: 2.5 mg/kg/dose 6-hourly up to 10 days. 10 or 5 mg/kg/dose 8-hourly (7–14 days)¹¹ High dose regimens: Doses up to 10–12.5 mg/kg/dose 6-hourly for 7–14 days have been used.¹²⁻¹⁴ Post-op intestinal atresia: 3 mg/kg/dose 6-hourly⁽¹³⁾</p> <p>Gastroparesis (off-label use): Adult: IV: 3 mg/kg administered over 45 minutes TDS.⁽⁴⁾ Oral: Patients refractory/intolerant to other prokinetic agents (eg, metoclopramide, domperidone): 250 to 500 mg (base) TDS before meals. Limit duration of therapy, tachyphylaxis may occur after 4 weeks.⁽⁴⁾</p>	<ul style="list-style-type: none"> adverse effects: prolonged QT, hepatic dysfunction, overgrowth of non-susceptible organisms and clostridium difficile, possibly antibiotic resistance⁽¹⁾ most effective single agent, but is limited by tachyphylaxis (over 2-7 days)⁽¹⁾ dose dependent effects⁽¹⁾ combination with metoclopramide is more effective than either alone⁽¹⁾ the suspension form of erythromycin is recommended when this drug is used as a prokinetic agent. Erythromycin suspension should be administered 15–60 min prior to a meal. This should result in optimal prokinetic effects of the drug.⁽¹⁴⁾

Drug	Prokinetic action	Dose	Notes
D-2 antagonist: Metoclopramide	<ul style="list-style-type: none"> increased tone of the lower oesophageal sphincter, accelerated gastric contractions, increased small bowel transit time (increased peristalsis in duodenum and jejunum)⁽¹⁾ 	<p>Adult : 10mg QID^(1,2)</p> <p>Administration: IV, PO, IM^(1,2)</p> <p>Infants, Children, and Adolescents: Oral: 0.1 to 0.2 mg/kg/dose TDS-QID; maximum dose: 10 mg/dose^(8,5)</p>	<ul style="list-style-type: none"> adverse effects: sedation, dystonic reactions, dysrhythmias (methemoglobinemia in overdose)⁽¹⁾ not effective in patients with brain injury and may contribute to raised ICP⁽¹⁾
D-2 antagonist: Domperidone	<ul style="list-style-type: none"> Dopaminergic blocking agents—Gastrointestinal emptying (delayed) adjunct; peristaltic stimulant: The gastroprokinetic properties of domperidone are related to its peripheral dopamine receptor blocking properties. Domperidone facilitates gastric emptying and decreases small bowel transit time by increasing esophageal and gastric peristalsis and by lowering esophageal sphincter pressure.⁽³⁾ 	<p>Prokinetic: Adult: 10 TDS</p> <p>Paediatric: 0.1-0.2 mg/kg (maximum 10mg/dose) QID⁽⁶⁾</p> <p>Gastroparesis: Adult: 10-20 mg TDS⁽¹⁰⁾</p>	potential for cardiac side effects based on concerns for QT prolongation and increased risk of ventricular arrhythmias ⁽³⁾
D-2 antagonist: Itopride	It accelerates gastric emptying, improves gastric tension and sensitivity, and has an anti-emetic action ⁽⁶⁾	Adult : 100mg TDS ⁽⁶⁾	Itopride is well tolerated with few minor adverse drug reactions in the form of diarrhea, headache, abdominal pain etc ⁽⁷⁾

References:

- 1) Nickson C. Prokinetics . Retrieved on 13/12/2020 from: <https://litfl.com/prokinetics/>
- 2) Metoclopramide. Retrieved on 13/12/2020 from: <https://www.drugs.com/metoclopramide.html>
- 3) Domperidone (Systemic). Retrieved on 13/12/2020 from: <https://www.drugs.com/mmx/domperidone-maleate.html>
- 4) Erythromycin (systemic): Drug information. UpToDate. Retrieved December 13, 2020 from : <https://www.uptodate.com/contents/erythromycin-systemic-drug-information>
- 5) Tillman EM, Smetana KS, Bantu L, Buckley MG. Pharmacologic Treatment for Pediatric Gastroparesis: A Review of the Literature. J Pediatr Pharmacol Ther. 2016;21(2):120-132. doi:10.5863/1551-6776-21.2.120
- 6) Kim YS, Kim TH, Choi CS, Shon YW, Kim SW, Seo GS, Nah YH, Choi MG, Choi SC. Effect of itopride, a new prokinetic, in patients with mild GERD: a pilot study. World J Gastroenterol. 2005 Jul 21;11(27):4210-4. doi: 10.3748/wjg.v11.i27.4210. PMID: 16015691; PMCID: PMC4615444.
- 7) Gupta S, Kapoor V, Kapoor B. Itopride : A Novel Prokinetic Agent. JK Science 2004; Vol. 6 No. 2, April-June.
- 8) Metoclopramide: Drug information. UpToDate. Retrieved December 13, 2020 from : <https://www.uptodate.com/contents/metoclopramide-drug-information>
- 9) Metoclopramide: Drug information. UpToDate. Retrieved December 13, 2020 from : <https://www.uptodate.com/contents/metoclopramide-drug-information>
- 10) Camilleri M, Grover S. Treatment of gastroparesis. UpToDate. Retrieved December 13, 2020 from : <https://www.uptodate.com/contents/treatment-of-gastroparesis>
- 11) Erythromycin. Retrieved December 24 2020 from <https://www.pdr.net/drug-summary/E-E-S--erythromycin-ethylsuccinate-2472>.
- 12) Frank Shann 2017
- 13) ERYthromycin ethylsuccinate (Oral) Retrieved on Desember 28 2020 https://www.slhd.nsw.gov.au/RPA/neonatal%5Ccontent/pdf/Medications_Neomed/Erythromycin_Oral_NMFv1.0_Full_2019
- 14) Erythromycin. Retrieved December 28 2020 from <https://onlinelibrary.wiley.com/doi/10.1046/j.1365-2036.1998.00302.x>

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