



PROKINETIC AGENTS

Prokinetic agents are drugs that enhance gastrointestinal motility by increasing the rate of luminal transit as well as the force of contraction. Delayed gastric emptying or also known as gastroparesis is a condition where the stomach is unable to contract normally causing food cannot be crushed and propelled into the small intestine properly. It is common in critically ill patients and other causes may include patient with insulin-dependent diabetes, post-surgical patient, chronic pancreatitis or induced by medications. Symptoms of gastroparesis includes nausea, vomiting, early satiety, belching, bloating, and/or upper abdominal pain. **Pharmacologic therapy with prokinetic agent is recommended when initial management with dietary modification, optimizing of glycemic control and hydration failed.**

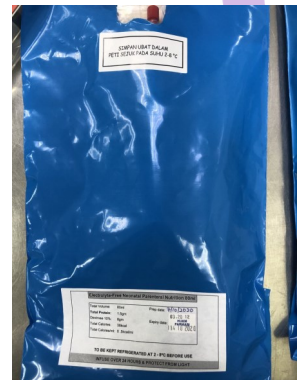
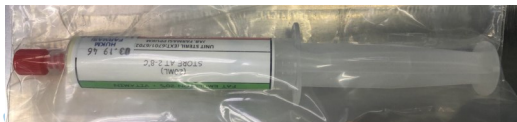
Drug (Available in HCTM)	Adult Dose	Notes	Contraindications	Caution
Metoclopramide Tab. 10mg Inj. 10mg/2mL Syr. 5mg/5mL Category B : No restrictions	PO, IM, IV, SC : 10mg 3-4 times daily prior to meals. Renal adjusted dose: CrCl >15-60mL/min : administer 50% of total daily dose CrCl <15mL/min or dialysis : administer 25% of total daily dose.	Selective D2 (dopamine) receptor antagonist. Limit use to less than 12 weeks , due to its potential in causing extrapyramidal effects (EPS) including tardive dyskinesia. IV: Infused over a period not less than 15mins.	Patient with seizure disorders (eg. epilepsy). History of dystonic reaction or tardive dyskinesia (Black Box Warning) . Patient with head injury (concerns about increased intracranial pressure). History of GI hemorrhage , mechanical obstruction perforation, pre-existing pheochromocytoma (tumor of adrenal gland)	Patient with: Hypertension Parkinson's disease History of depression Young adults (15-19 y.o.)
Erythromycin Ethyl Succinate (EES) or Erythromycin Lactobionate Tab. EES 400mg Susp. EES 400mg/5mL Inj. Lactobionate 500mg Category B : No restrictions	PO: (EES) 400mg-800mg 3-4 times daily before meals *400mg EES=250mg Erythromycin base IV: (Lactobionate) 125mg every 6 hours or 250mg every 12 hours	Motilin receptor antagonist. Should not be given for more than 3 days due to desensitization thus affecting the therapeutic effect. PO: Limit duration to 4 weeks, may induce tachyphylaxis.	Use with ergot alkaloid (eg. Ergotamine, associated with ergot toxicity- severe vascular spasm). Use with statins (eg. lovastatin, simvastatin) associated with rhabdomyolysis.	Patient with: Myasthenia gravis Porphyria (hereditary disorders of haemoglobin biosynthesis) Concurrent use with CYP4A4 substrate
Domperidone Tab. 10mg Syr. 1mg/mL (EX) Category B : No restrictions	PO: 10mg 3-4 times daily (max daily dose 40mg)	D2 receptor antagonist. Does not cross BBB minimizing CNS side effects. Risk of QT interval prolongation at dose more than 30mg/day or in patient more than 60 y.o. Withhold if the corrected QT is >470ms in male and >450ms in female. Should be taken at the lowest effective dose for the shortest duration possible.	Patient with prolactin-releasing pituitary tumor (prolactinoma). Existing prolongation of QT interval or <i>Torsade de pointes</i> Underlying cardiac diseases or significant electrolyte disturbances . Concomitant use with QT prolonging drugs (eg. Antiarrhythmic, haloperidol, erythromycin, escitalopram) Concomitant use with potent CYP3A4 inhibitor (eg azoles, macrolide antibiotic, HIV protease inhibitor)	Patient over 60 y.o.
Itopride Tab. 50mg Category A* : Gastroenterologists & Surgeons only (Upper GI)	PO: 50mg 3 times daily	D2 receptor antagonist & acetylcholine esterase inhibitor. Does not pass blood brain barrier. Not metabolized in liver- has no relevant drug interactions.	Patient in whom increase in GI motility could be harmful- GI hemorrhage, mechanical obstruction perforation.	Enhances acetylcholine and may produce cholinergic side effects

The story of Cisapride...

Cisapride is a serotonin 5-HT₄ agonist with some 5-HT₃ antagonist activity and chemically related to metoclopramide. Cisapride was known to be **more potent and has broader prokinetic activity than metoclopramide** as it increases the motility of the colon as well as esophagus, stomach and small intestine. It is unique among the prokinetic drugs that it does not have antidopaminergic effects, nor it cross the blood brain barrier. Thus, it has no antiemetic action and does not cause extra pyramidal effects.

However, **increasing reports of serious ventricular arrhythmia and sudden, unexplained death worldwide associated with cisapride** has caused cisapride to be **withdrawn from market in 2000**. The UK Committee on Safety of Medicines (CSM) reported 386 cases of serious ventricular arrhythmias with 125 fatalities and 50 cases of sudden death worldwide. Consequently, the decision was taken to withdraw the license because the **benefits of the drug did not outweigh the risks of treatment**.

TPN Starter Bag For Neonate (Electrolyte Free) 80mL



OLD Practice

Amino acid 6.5% (Vaminolact) syringe (50mL) and lipid syringe (SMOF Lipid 20%) (50mL)

Both syringes are kept in NICU.

For nutritional support in premature neonates initiated after working hours.

Consist of:

- **Vaminolact** : Amino acids: 6.5gm per 100mL
Calories: 4kcal/gm of protein
- **SMOF Lipid**: Fat: 20gm per 100mL
Calories: 9kcal/gm of fat

(SMOF consists of soybean oil, MCT, olive oil and fish oil).

NEW Practice

TPN Starter Bag For Neonate (Electrolyte Free) 80mL

2 **electrolyte free TPN bags and lipid syringes** are kept in the fridge in Sterile Unit (Basement Pharmacy). Pharmacy will supply when needed after working hour.

Content

Contains amino acids and carbohydrate

- **Protein** content: 1.5 gm in 80ml (Vaminolact)
- **Dextrose** content: 10% (8gm)
- **Calories** content: 38 kcal in 80ml (0.5kcal/ml)

Lipid syringe are provided together with the bag (Lipid needs to be infused separately)

References:

1. Camilleri, M., Parkman, H., Shafi, M., Abell, T. and Gerson, L., 2013. Clinical Guideline: Management of Gastroparesis. *American Journal of Gastroenterology*, 108(1), pp.18-37.
2. Cisapride withdrawn because of cardiac side effects. 2000. *The Pharmaceutical Journal*. 265 pp.152.
3. Camilleri, M., 2020. Treatment of Gastroparesis. *Uptodate*. [online] Uptodate.com. [Accessed 2 October 2020].
4. Medical Nutrition Therapy (MNT), Guidelines for Critically Ill Adults, 2017, Malaysian Dietitians Association, Ministry of Health Malaysia.
5. British National Formulary 79th ed. (2020). London. BMJ Group and Royal Pharmaceutical Press.

PPUKM Formulary App is now available on:



A publication of Drug Information Centre

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03-9145 5401/5415