

PALLIATIVE CARE PHARMACY PHAST PHACT



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If you have a topic you would like the pharmacy team to answer, please send your suggestions to: pruskowskija@upmc.edu

TODAY'S TOPIC:

What's New in Palliative Care Medications Drug #1: Prucalopride (Motegrity®)

Background:

[Prucalopride \(Motegrity®\)](#) is a serotonin-4 (5-HT₄) receptor agonist indicated for the treatment of chronic idiopathic constipation (CIC) in adults

- Initial US approval: 2018
- Available as: 1mg and 2mg

Importance:

While CIC is not commonly managed by palliative care providers, prucalopride may be a valuable option for palliative care patients suffering with chronic constipation. Chronic constipation has a prevalence of 28% in the US and is often debilitating, uncomfortable and distressing for patients.

Pharmacology:

MoA:	Prucalopride, a selective serotonin type 4 (5-HT ₄) receptor agonist, is a gastrointestinal (GI) prokinetic agent that stimulates colonic peristalsis (high-amplitude propagating contractions [HAPCs]), which increases bowel motility
ADME:	<ul style="list-style-type: none">- A: Tmax: 2-3 hours, absolute bioavailability is >90% and first pass metabolism is negligible- M: CYP 3A4 substrate- E: T_{1/2}: 1 day
DIs:	<ul style="list-style-type: none">- Erythromycin: coadministration increases erythromycin mean C_{max} levels by 40%- Ketoconazole: coadministration increases the C_{max} and AUC of prucalopride by 40%

Key: MoA: Mechanism of Action; ADME: Absorption, Distribution, Metabolism, and Excretion; DI: Drug Interaction; Tmax: time until max concentration; T_{1/2}: terminal half-life; C_{max}: max concentration; AUC: area under the curve

Other Clinical Points:

CI:	<ul style="list-style-type: none"> - Hypersensitivity - Intestinal perforation or obstruction due to structural or functional disorder of GI track
Warnings and Precautions:	<ul style="list-style-type: none"> - Suicidal ideation and behavior: monitor patients for persistent worsening of depression and emergence of suicidal thoughts and behavior
Dosing:	<ul style="list-style-type: none"> - Take with or without food - Adults: 2mg PO once daily - Severe renal impairment (CrCl <30 mL/min): 1mg PO once daily
ADRs:	Most common adverse reactions (≥2%) are headache, abdominal pain, nausea, diarrhea, abdominal distension, dizziness, vomiting, flatulence, and fatigue

Key: CI: contraindications; ADRs: adverse drug reactions

The Literature:

- [Therap Adv Gastroenterol. 2012 Jan; 5\(1\): 23–30.](#)

Prucalopride: safety, efficacy and potential applications.

- Narrative review
- Table 1: Main results of the three pivotal trials of prucalopride in gastrointestinal chronic constipation

Reference	Study design (No. of patients)	Outcomes (2 mg and 4 mg prucalopride versus placebo)
[Camilleri et al. 2008b]	12 weeks (620) Prucalopride 2 mg or 4 mg daily versus placebo	No. of patients achieving: 1. ≥3 SCBM/week: 30.9% and 28.4% versus 12% 2. An increase of ≥1 SCBM/week: 47.3% and 44.6% versus 25.8%
[Quigley et al. 2009]	12 weeks (641) Prucalopride 2 mg or 4 mg daily versus placebo	No. of patients achieving: 1. ≥3 SCBM/week: 23.9% and 23.5% versus 12.1% 2. An increase of ≥1 SCBM/week: 42.6% and 44.6% versus 27.5%
[Tack et al. 2009]	12 weeks (713) Prucalopride 2 mg or 4 mg daily versus placebo	No. of patients achieving: 1. ≥3 SCBM/week: 19.5% and 23.6% versus 9.6% 2. An increase of ≥1 SCBM/week: 38.1% and 44.1% versus 20.9%

SCBM: spontaneous complete bowel movement

- “To date, high-quality evidence for prucalopride exists only in the area of CC and, then, only for women. Given the aforementioned clinical overlap between CC and IBS, studies in IBS-C are eagerly awaited, as are studies in motor disorders of the foregut and midgut. Efficacy in these latter areas would be of relevance to patients with CC given the frequency with which symptoms such as heartburn, dyspepsia and postprandial fullness occur in these patients.”

So... What does this all mean Jenn?

- Prucalopride has shown promise for CIC and there is also studies now that has shown promise in opioid induced constipation (OIC) ([Dig Dis Sci. 2010 Oct;55\(10\):2912-21.](#))
- Currently within the UPMC system: prucalopride is non-formulary (continuation from home only) and not recommended for refractory OIC – see UPMC OIC guidelines [here](#)
- Prucalopride costs \$10.68/day – this is similar to naloxegol (\$10.88/day) and linaclotide (\$10.14/day)
- Overall, prucalopride could be considered a third or fourth line for OIC

CLINICAL PEARL:

Prucalopride, approved in 2018, is a serotonin-4 receptor agonist indicated for the treatment of CIC in adults.