Pharmacy Benefit Determination Policy

Policy Subject: Opioid Induced Constipation	**Dates:**
Policy Number: SHS PBD11	**Effective Date:** August 29, 2016
Category: GI Agents	**Revision Date** November 1, 2017
Policy Type: ☐ **Medical** ☒ **Pharmacy**	**Approval Date:** February 27, 2019
Department: Pharmacy	**Next Review Date:** February 2020
Product (check all that apply):	**Clinical Approval By:**
☒ Group HMO/POS	**Medical Directors**
☒ Individual HMO/POS	PHP: Peter Graham, MD
☒ PPO	**Pharmacy and Therapeutics Committee**
☒ ASO	PHP: Peter Graham, MD

Policy Statement:

Physicians Health Plan, PHP Insurance & Service Company, and Sparrow PHP will cover Movantik, Relistor & Symproic through the Pharmacy or Medical Benefit based on approval by the Clinical Pharmacist or Medical Director using the following determination guidelines

Drugs and Applicable Coding:

J-code: Relistor - J2212

Clinical Determination Guidelines:

Document the following with chart notes

A. Opioid Induced Constipation (OIC) with non-cancer pain
   1. Age: ≥18 years
   2. Opioid Use (See Appendix I)
      a. Dose: 30-1000mg per day morphine equivalent x 4 weeks AND/OR
      b. Median stable dose: ≥50mg per day morphine equivalent x 4 weeks
   3. Diagnosis and severity
      a. <3 spontaneous bowel movements (SBMs) per week
      b. ≥25% of SBM's with ≥1 of these symptoms: Straining; hard/lumpy stool; sense of partial evacuation
   4. Other Therapies (See Appendix II): Contraindicated, failed or had significant adverse effects to all below:
      a. Dietary change: Increase water and fiber
      b. Stimulant laxative: Senna, bisacodyl
      c. Saline/osmotic laxatives: Magnesium citrate, polyethylene glycol
      d. Failure: Inadequate response to other therapies for >1-week trial
   5. Dosage regimen: Peripheral mu opioid receptor antagonist (PAMORA)
      a. Maintenance laxatives: Discontinue with PAMORA initiation, restart if needed after 3 days
      b. Movantik po (naloxegol): 25 mg 1x per day in am (empty stomach), reduce to 12.5mg if not tolerated
      c. Symporic po (naldemedine): 0.2mg 1x per day

d. Relistor SC (methylnaltrexone): 12 mg 1x/day

5. Approval
   a. Initial: 4 months
   b. Re-approval: 1 year; ≥3 spontaneous bowel movements (SBM) per week and a change from baseline of ≥1 SBM/week

B. Exclusions
1. Known or suspected GI obstruction and increased risk of recurrent obstruction
2. Concomitant use with strong CYP3A4 inhibitors
3. Known or serious hypersensitivity reactions to peripheral μ opioid receptor antagonist (PAMORA's)
4. Dual therapy with another opioid antagonist

Appendix I: Opioid Equianalgesic Doses

Opioid Analgesics: Approximate Equianalgesic Doses for Adults[a,b] 27, 28		
Opioid	Equianalgesic dose	
	Oral	Parenteral
Codeine	200 mg	NA[f]
Fentanyl[c]	NA	0.1 mg
Hydrocodone	30 to 45 mg	NA
Hydromorphone	7.5 mg	1.5 mg
Levorphanol	4 mg (acute); 1 mg (chronic)	NA
Meperidine[d]	300 mg	75 mg
Methadone	See the following table	See the following table
Morphine	30 mg	10 mg
Oxycodone	20 mg	NA
Oxymorphone[e]	10 mg	1 mg

[a]Table is to be used for estimation only; individualize treatment. Data are compiled from multiple references and may be based on single-dose studies.
[b]Recommended equianalgesic doses do not apply to adults weighing less than 50 kg or patients with renal or hepatic insufficiency or other conditions affecting drug metabolism and kinetics. Initial doses should be lower for elderly patients.
[c]Refer to Fentanyl Transdermal monograph for dosing conversion.
[d]Not recommended for routine use.
[e]Refer to the Oxymorphone oral and Oxymorphone injection monographs for dosing conversion.
[f]NA = not available commercially for this route of administration.

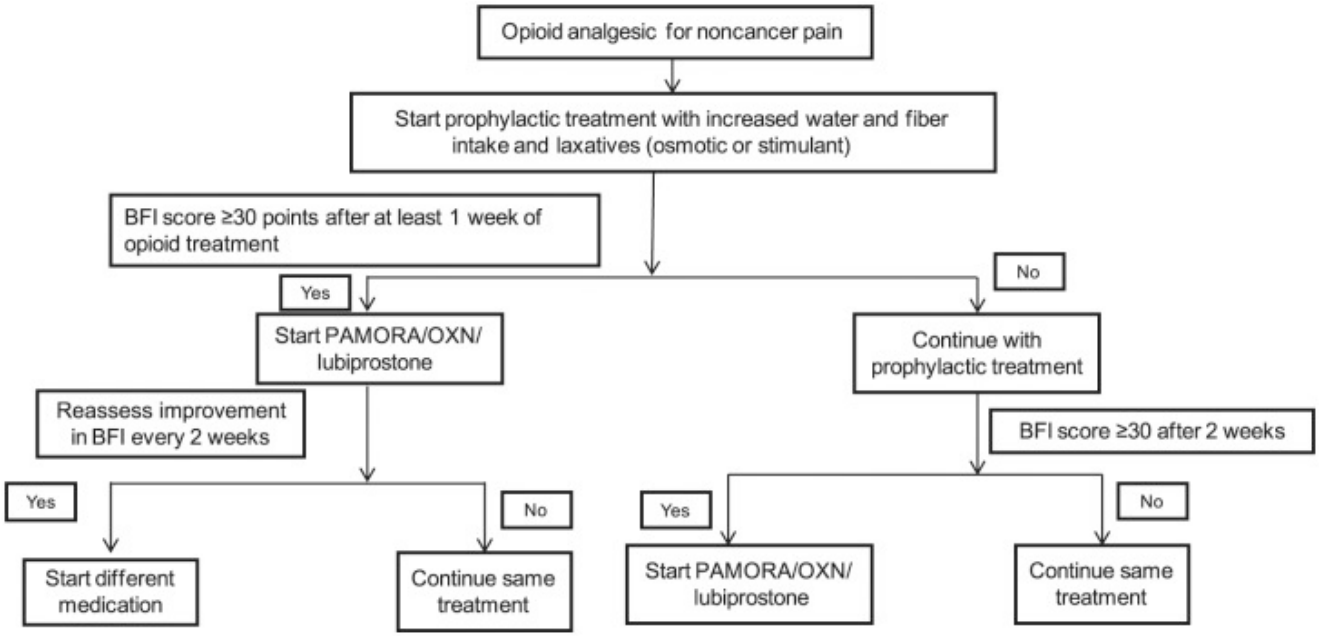
Appendix II: Therapeutic Alternatives

Drug	Dosing Regimen	Dose Limit/ Max. Dose
Colace (docusate sodium)	50-300 mg/day PO in single or divided doses	360mg/day
Lactulose	10-20 g (15-30 mL or 1-2 packets) QD; may ↑ to 40 g (60 mL or 2-4 packets) QD if needed	60 mL or 2-4 packets daily
MiraLax (polyethylene glycol	17 g (~1 heaping tbsp) of powder in 120-240 mL of fluid PO QD	34 g/day
Dulcolax (bisacodyl)	Oral: 5-15 mg QD; Rectal: Enema/supp: 10 mg (1 enema or supp) QD	15 mg/day PO; 10 mg/day rectally
Senokot (senna)	1-2 tabs (8.6-17.2 mg sennosides) PO BID	4 tabs (34.4 mg sennosides) PO BID
Magnesium citrate	150-300 mL PO as a single or divided dose (~1/2-1 full bottle)	300 ml/24 hrs PO
Milk of Magnesia (magnesium	15-60 mL PO/day, at bedtime or in divided doses	Max daily dosage is age & product specific

Appendix III: Patient Safety and Monitoring

Drug	Adverse Reactions	Monitoring	REMS
Movantik naloxegol	• GI: Abdominal pain (12-21%) • Pregnancy category: C	• GI: sx of GI obstruction (↑ abdominal pain) • CNS: Opioid withdrawal (chills, diaphoresis, anxiety, irritability, change in BP or HR)	None needed
Relistor Methyl-naltrexone	• GI: abdominal pain (21-29%), flatulence (13%), nausea (9-12%) • Pregnancy category: C	• CV: s &sx of orthostatic hypotension • GI: sx of GI obstruction (↑ abdominal pain) • CNS: Opioid withdrawal (chills, diaphoresis, anxiety, irritability, change in BP or HR)	None needed
Symporic naldemedine	• GI: Abdominal pain (8%), diarrhea (7%) • Preg: ADR's seen in animal studies; may cross placenta & cause opioid withdrawal in the fetus	• GI: S & Sx of perforation • Other: S & Sx of opioid withdrawal	None needed

Appendix IV: Clinical guidance for treatment of OIC in patients with non-cancer pain



Abbreviations: BFI - Bowel Function Index; OXN - oxycodone & naloxone; PAMORA - peripheral μ opioid receptor antagonist.

Therapeutic Advances in Chronic Disease.2016;7(2):121-134.

References and Resources:

1. Lexicomp Online®, Lexi-Drugs®, Hudson, Ohio: Lexi-Comp, Inc.; Movantik accessed December 2018
2. Lexicomp Online®, Lexi-Drugs®, Hudson, Ohio: Lexi-Comp, Inc.; Relistor accessed December 2018
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5. Opioid-induced constipation. Pain Medicine 2015;16:S16-21.
6. https://www.caremark.com/portal/asset/FEP_Criteria_Opioid_Antagonists.pdf accessed Nov 2017
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8. Opioid-induced constipation and bowel dysfunction: A clinical guideline. Pain Medicine 2017;18:1837-1863

Approved By:

2/27/19

Peter Graham, MD – PHP Executive Medical Director — Date

2/27/19

Kurt Batteen - Human Resources — Date