DRUG DETERMINATION POLICY

Title: DDP-01 Opioid-Induced Constipation

Effective Date: 06/04/2019

Physicians Health Plan
PHP Insurance Company
PHP Service Company

Important Information - Please Read Before Using This Policy

The following policy applies to health benefit plans administered by PHP and may not be covered by all PHP plans. Please refer to the member's benefit document for specific coverage information. If there is a difference between this general information and the member's benefit document, the member's benefit document will be used to determine coverage. For example, a member's benefit document may contain a specific exclusion related to a topic addressed in a coverage policy.

Benefit determinations for individual requests require consideration of:

1. The terms of the applicable benefit document in effect on the date of service.
2. Any applicable laws and regulations.
3. Any relevant collateral source materials including coverage policies.
4. The specific facts of the particular situation.

Contact PHP Customer Service to discuss plan benefits more specifically.

1.0 Policy:

This policy describes the determination process for coverage of specific drugs.

This policy does not guarantee or approve benefits. Coverage depends on the specific benefit plan. Drug Determination Policies are not recommendations for treatment and should not be used as treatment guidelines.

2.0 Background or Purpose:

Movantic, Relistor and Symproic are drugs indicated for opioid-induced constipation, which can be treated with a number of over-the-counter (OTC) and prescription agents. These criteria were developed and implemented to ensure use of appropriate OTC and generic products prior to the use of these agents.

3.0 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 for four weeks; AND/OR
      b. Median stable dose: At least 50mg per day morphine milligram equivalent for four weeks.
   3. Diagnosis and severity.
      a. Less than three spontaneous bowel movements (SBMs)/week.
      b. Greater than or equal to 25% of spontaneous bowel movements (SBMs) with at least one 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 greater than1-week trial.

5. Dosage regimen: peripheral mu opioid receptor antagonist (PAMORA).

a. Maintenance laxatives: discontinue with PAMORA initiation, restart if needed after three days.

b. Movantik po (naloxegol): 25 mg one time per day in am (empty stomach), reduce to 12.5mg if not tolerated.

c. Symporic po (naldemedine): 0.2mg one time per day.

d. Relistor SC (methylnaltrexone): 12 mg one time per day.

6. Approval

a. Initial: four months.

b. Re-approval: one year; at least three SBMs per week and a change from baseline of at least one SBM per 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 PAMORAs.

4. Dual therapy with another opioid antagonist.

4.0 Coding:

AFFECTED CODES			
Code	**Brand name**	**Generic name**	**Billing unit (1u)**
J2212	Relistor IV	Methylnaltrexone	0.1mg

5.0 Unique Configuration/Prior Approval/Coverage Details:

None.

6.0 References, Citations & 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.

3. Lexicomp Online®, Lexi-Drugs®, Hudson, Ohio: Lexi-Comp, Inc.; Symproic accessed December 2018.

4. Opioid-induced constipation: advances and clinical guidance. Therapeutic Advances in Chronic Disease 2016;7(2):121-134.
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.
7. https://www.healthnet.com/static/general/unprotected/html/national/pa_guidelines/2075.pdf accessed Nov 2017.
8. Opioid-induced constipation and bowel dysfunction: A clinical guideline. Pain Medicine 2017;18:1837-1863.

7.0 Appendices:

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

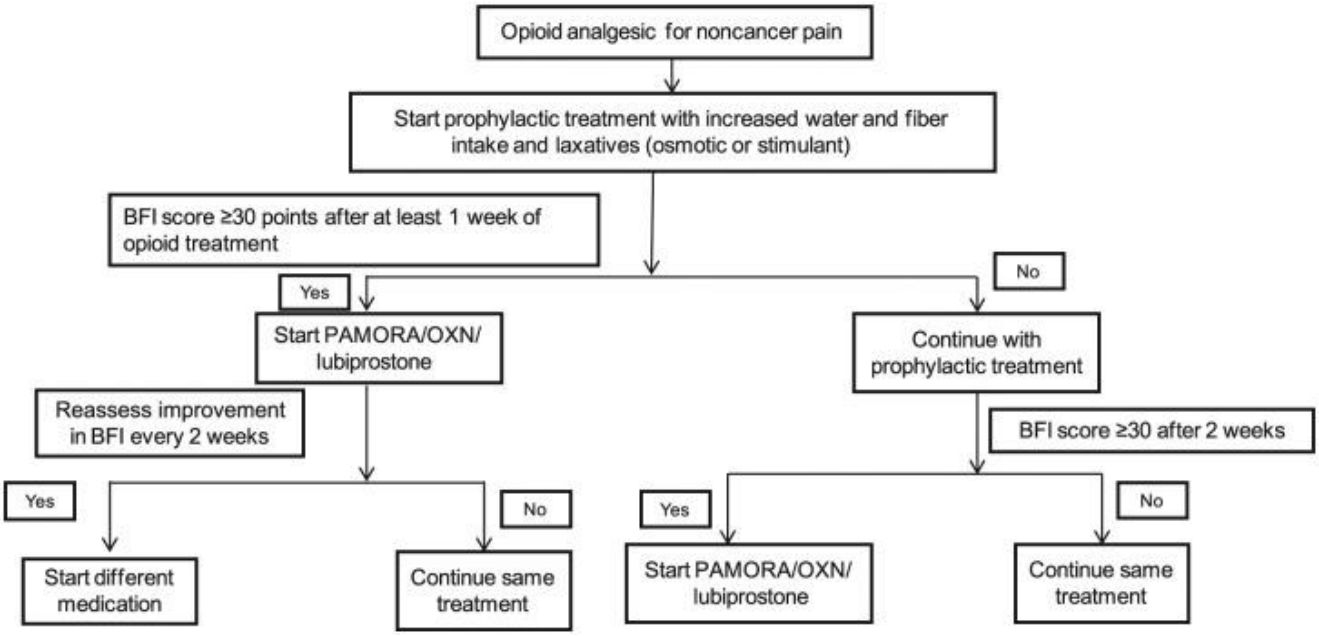
Drug	Dosing Regimen	Dose Limit/ Max. Dose
Colace (docusate sodium)	50-300 mg/day PO in single or divided doses	360mg/day
Lactulose	10-20 g (15-30 mL or 1-2 packets) QD; may ↑ to 40 g (60 mL or 2-4 packets) QD if needed	60 mL or 2-4 packets daily
MiraLax (polyethylene glycol 3350)	17 g (~1 heaping tbsp) of powder in 120-240 mL of fluid PO QD	34 g/day

Drug	Dosing Regimen	Dose Limit/ Max. Dose
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 hydroxide)	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: symptoms 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: signs and symptoms of orthostatic hypotension • GI: symptoms 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: ADRs seen in animal studies; may cross placenta and cause opioid withdrawal in the fetus	• GI: signs and symptoms of perforation • Other: signs and symptoms 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.

8.0 Revision History:

Original Effective Date: August 29, 2016

Last Approval Date: 06/04/2019

Next Review Date: 06/04/2020

Revision Date	Reason for Revision
2/19	Moved to new format.