DRUG DETERMINATION POLICY

Title: DDP-01 Opioid-Induced Constipation

Effective Date: 02/23/2022

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 that require prior approval.

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 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 with non-cancer pain [must meet all listed below]
   1. Age: at least 18 years.
   2. Opioid Use (see Appendix I) [must meet one listed below]:
      a. Dose: 300 to 1000mg per day morphine equivalent for four weeks;
      b. Median stable dose: at least 50mg per day morphine milligram equivalent for four weeks.
   3. Diagnosis and severity [must meet both listed below]:
      a. Less than three spontaneous bowel movements per week.
      b. At least 25 percent of spontaneous bowel movements with at one of these symptoms: straining; hard/lumpy stool; sense of partial evacuation.
   4. Other therapies (see Appendix II and IV): contraindicated, inadequate response after one month or significant adverse effects to one of each category listed below:
      a. Dietary change: increase water and fiber.
      b. Stimulant laxative: Senna, bisacodyl.

c. Saline/osmotic laxatives: magnesium citrate, polyethylene glycol.

d. Lactulose.

5. Dosage regimen: peripheral mu opioid receptor antagonist

a. Maintenance laxatives: discontinue with peripheral mu opioid receptor initiation, restart if needed after three days.

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

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

6. Approval:

a. Initial: four months.

b. Re-approval: one year; at least three spontaneous bowel movements per week and a change from baseline of at least one spontaneous bowel movement per week.

B. Exclusions.

1. Known or suspected gastrointestinal obstruction and increased risk of recurrent obstruction.

2. Concomitant use with strong Cytochrome P450 3A4 (CYP3A4) inhibitors.

3. Known or serious hypersensitivity reactions to Peripheral μ-Opioid Receptor Antagonists (PAMORAs).

4. Dual therapy with another opioid antagonist.

4.0 Coding: NA

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, Relistor, Symproic accessed December 2020.
2. Opioid-induced constipation: advances and clinical guidance. Therapeutic Advances in Chronic Disease 2016;7(2):121-134.
3. Opioid-induced constipation. Pain Medicine 2015;16:S16-21.
4. https://www.healthnet.com/static/general/unprotected/html/national/pa_guidelines/2075.pdf accessed Nov 2017.
5. Opioid-induced constipation and bowel dysfunction: A clinical guideline. Pain Medicine 2017;18:1837-1863.
6. UpToDate. https://www.uptodate.com/contents/prevention-and-management-of-side-effects-in-patients-receiving-opioids-for-chronic-pain?search=treatment%20of%20opioid%20induced%20constipation&source=search_result&selectedTitle=1~42&usage_type=default&display_rank=1 accessed December 2020.

7.0 Appendices:

See pages 4-7.

8.0 Revision History:

Original Effective Date: August 29, 2016

Next Review Date: 01/27/2023

Revision Date	Reason for Revision
2/19	Moved to new format.
12/19	Annual review; replaced abbreviations
12/20	Annual review; added lactulose to other therapies, added new Appendix IV; replaced abbreviations, approved by P&T 2/24/21
12/21	Annual review, replaced abbreviations, removed Relistor since it is excluded

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/ Maximum Dose
Colace (docusate sodium)	50-300 mg oral per day in single or divided doses	360mg/day
Lactulose	10-20 g (15-30 mL or 1-2 packets) daily; may increase to 40 g (60 mL or 2-4 packets) daily if needed	60 mL or 2-4 packets daily
MiraLax (polyethylene glycol 350)	17 g (~1 heaping tbsp.) of powder in 120-240 mL of fluid oral daily	34 g/day
Dulcolax (bisacodyl)	Oral: 5-15 mg; rectal: enema or suppository: 10 mg (1 enema or suppository) daily	15 mg/day oral; 10 mg/day rectally
Senokot (senna)	1-2 tabs (8.6-17.2 mg sennosides) oral twice daily	4 tabs (34.4 mg sennosides) oral twice daily
Magnesium citrate	150-300 mL oral as a single or divided dose (about 1/2-1 full bottle)	300 ml per 24 hours oral
Milk of Magnesia (magnesium hydroxide)	15-60 mL oral daily, at bedtime or in divided doses	Max daily dosage is age and product specific

Appendix III: Patient Safety and Monitoring

Drug	Adverse Reactions	Monitoring	REMS
Movantik naloxegol	• Gastrointestinal (GI) abdominal pain (12-21%) • Pregnancy category: C	• Gastrointestinal: symptoms of GI obstruction (increased abdominal pain) • Central nervous system: opioid withdrawal (chills, diaphoresis, anxiety, irritability, change in blood pressure or heart rate)	None needed
Relistor Methyl-naltrexone	• Gastrointestinal: abdominal pain (21-29%), flatulence (13%), nausea (9-12%) • Pregnancy category: C	• Cardiovascular: signs and symptoms of orthostatic hypotension • Gastrointestinal: symptoms of GI obstruction (increased abdominal pain) • Central nervous system: opioid withdrawal (chills, diaphoresis, anxiety, irritability, change in blood pressure or heart rate)	None needed
Symporic naldemedine	• Gastrointestinal: abdominal pain (8%), diarrhea (7%) • Pregnancy: adverse drug reactions (ADRs) seen in animal studies; may cross placenta and cause opioid withdrawal in the fetus	• Gastrointestinal: signs and symptoms of perforation • Other: signs and symptoms of opioid withdrawal	None needed

Appendix IV: Other Therapies

Show

Common strategies for managing opioid-induced constipation

1. Nonpharmacologic approaches for all patients, unless contraindicated by medical status
Increase fluid intake
Increase dietary soluble fiber (avoid if severely debilitated or bowel obstruction is suspected)
Encourage mobility
Ensure comfort and privacy for defecation
2. Select a pharmacologic strategy*
Intermittent use of a rectal therapy, either a suppository such as bisacodyl or glycerin, or mineral oil and/or sodium phosphate enema
Intermittent use (every 2-3 days) of an osmotic laxative, such as polyethylene glycol, magnesium hydroxide, or magnesium citrate
Trial of a daily softening agent (docusate) for patients who describe hard, dry stools
Intermittent use (every 2-3 days) of a contact cathartic, such as senna or bisacodyl
Daily use of polyethylene glycol
Daily use of lactulose (unless lactose-intolerant) or sorbitol
Daily use of a contact cathartic
3. Adjust dose and dosing schedule of selected therapy to optimize effects
4. Switch or combine conventional approaches if initial therapy is inadequate
5. Consider adding a peripheral opioid antagonist (eg, methylnaltrexone, naloxegol, or an opioid-naloxone fixed combination) or lubiprostone; if constipation continues to be refractory, consider alternative drugs, eg, metoclopramide.

*Fiber supplements and/or bulk-forming laxatives (eg, psyllium) are an option for treating non-debilitated patients who maintain good oral hydration; however, efficacy is generally modest in patients with slow transit constipation, who are also more likely to experience bloating and distention. If used, patients should start with small amounts of fiber or bulking laxatives and increase gradually as tolerated.

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