Clinical Policy: Naldemedine (Symproic)
Reference Number: ERX.NPA.46
Effective Date: 09.01.17
Last Review Date: 08.17
Line of Business: Commercial [Prescription Drug Plan] Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
Naldemedine (Symproic®) is an opioid antagonist. Naldemedine functions as a peripherally-acting mu-opioid receptor antagonist in tissues such as the gastrointestinal tract, thereby decreasing the constipating effects of opioids.

FDA approved indication
Symproic is indicated for the treatment of opioid-induced constipation (OIC) in adult patients with chronic non-cancer pain.

Policy/Criteria
Provider must submit documentation (which may include office chart notes and lab results) supporting that member has met all approval criteria

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that Symproic is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Opioid-Induced Constipation (must meet all)**:**

1. Diagnosis of opioid-induced constipation;
2. Member has been taking opioid(s) for ≥ 4 weeks for chronic non-cancer pain;
3. Failure of 1 agent from each of the following classes while on opioid therapy, unless all are contraindicated or clinically significant adverse effects are experienced:
   a. Stimulant laxative (e.g., bisacodyl, senna);
   b. Osmotic laxative (e.g., lactulose, polyethylene glycol);
   c. Stool softener (e.g., docusate);
4. Member has used one of the aforementioned agents in the past 30 days, unless contraindicated;
5. Dose does not exceed 0.2 mg per day (1 tablet per day).

Approval duration: 6 months

B. Other diagnoses/indications

1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized)

II. Continued Therapy

A. Opioid-Induced Constipation (must meet all)**:**

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
2. Member continues to receive opioid therapy;
3. Member is responding positively to therapy (e.g., increased number of bowel movements from baseline)
4. If request is for a dose increase, new dose does not exceed 0.2 mg per day (1 tablet per day).

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
Approval duration: Duration of request or 12 months (whichever is less); or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized)

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off-label use policy – ERX.PA.01 or evidence of coverage documents

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
FDA: Food and Drug Administration
OIC: opioid-induced constipation

Appendix B: Therapeutic Alternatives

Drug	Dosing Regimen	Dose Limit/ Maximum Dose
Colace (docusate sodium)	50-300 mg/day PO given in single or divided doses	360 mg/day
Lactulose	10 to 20 g (15 to 30 mL or 1 to 2 packets) daily; may increase to 40 g (60 mL or 2 to 4 packets) daily if necessary	60 mL or 2 to 4 packets daily
MiraLax (polyethylene glycol 3350)	17 g (approximately 1 heaping tablespoon) of powder in 120 to 240 mL of fluid given PO once daily	34 g/day
Dulcolax (bisacodyl)	Oral: 5 to 15 mg once daily Rectal: Enema, suppository: 10 mg (1 enema or suppository) once daily	15 mg/day PO; 10 mg/day rectally
Senokot (senna)	1 to 2 tablets (8.6 to 17.2 mg sennosides) PO twice daily.	4 tablets (34.4 mg sennosides) PO twice daily
Magnesium citrate	150-300 mL PO as a single or divided dose (roughly 1/2 to 1 full bottle)	300 ml/24 hours PO
Milk of Magnesia (magnesium hydroxide)	15-60 mL PO per day, preferably at bedtime or in divided doses	Maximum daily dosage is age and product specific

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Opioid-induced constipation	0.2 mg once daily with or without food	0.2 mg per day

VI. Product Availability

Tablets: 0.2 mg

VII. References

1. Symproic Prescribing Information. Florham Park, NJ: Shionogi Inc.; March 2017. Available at: http://www.shionogi.com/. Accessed March 31, 2017.
2. Kumar L, Barker C, Emmanuel A. Opioid-Induced Constipation: Pathophysiology, Clinical Consequences, and Management. Gastroenterology Research and Practice. 2014;2014:141737. doi:10.1155/2014/141737.
3. Argoff CE, Brennan MJ, Camilleri M, et al. Consensus Recommendations on Initiating Prescription Therapies for Opioid-Induced Constipation. Pain Med. 2015 Dec;16(12):2324-37.

4. Pergolizzi JV, Raffa RB, Pappagallo M, et al. Peripherally acting μ-opioid receptor antagonists as treatment options for constipation in noncancer pain patients on chronic opioid therapy. Patient preference and adherence. 2017;11:107-119. doi:10.2147/PPA.S78042.
5. Nelson AD, Camilleri M. Chronic opioid induced constipation in patients with nonmalignant pain: challenges and opportunities. Therap Adv Gastroenterol. 2015 Jul;8(4):206-20.
6. Nelson AD, Camilleri M. Opioid-induced constipation: advances and clinical guidance. Ther Adv Chronic Dis. 2016 Mar; 7(2): 121–134.
7. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2017. Available at: http://www.clinicalpharmacology-ip.com/.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	04/17	08/17

Important Reminder
This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members.