BlueCross BlueShield of Arizona
An Independent Licensee of the Blue Cross and Blue Shield Association

PHARMACY COVERAGE GUIDELINES
SECTION: DRUGS

ORIGINAL EFFECTIVE DATE: 11/16/17
LAST REVIEW DATE: 11/16/17
LAST CRITERIA REVISION DATE:
ARCHIVE DATE:

SYMPROIC® (naldemedine tosylate) oral capsule

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Pharmacy Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

This Pharmacy Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as "Description" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as "Criteria" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Pharmacy Coverage Guidelines are subject to change as new information becomes available.

For purposes of this Pharmacy Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.

This Pharmacy Coverage Guideline does not apply to FEP or other states' Blues Plans.

Information about medications that require precertification is available at www.azblue.com/pharmacy.

Some large (100+) benefit plan groups may customize certain benefits, including adding or deleting precertification requirements.

All applicable benefit plan provisions apply, e.g., waiting periods, limitations, exclusions, waivers and benefit maximums.

Precertification for medication(s) or product(s) indicated in this guideline requires completion of the request form in its entirety with the chart notes as documentation. All requested data must be provided. Once completed the form must be signed by the prescribing provider and faxed back to BCBSAZ Pharmacy Management at (602) 864-3126 or emailed to Pharmacyprecert@azblue.com. **Incomplete forms or forms without the chart notes will be returned.**

SYMPROIC® (naldemedine tosylate) oral capsule (cont.)

Description:

Symproic (naldemedine) is an opioid antagonist indicated for the treatment of opioid-induced constipation (OIC) in adult patients with chronic non-cancer pain. Naldemedine is a Schedule II controlled substance.

Naldemedine is an opioid antagonist with binding affinities for mu-, delta-, and kappa-opioid receptors. Antagonism of peripheral mu-opioid receptors the gastrointestinal tract decreases the constipating effects of opioids.

Naldemedine is a derivative of naltrexone; where a modification in the chemical structure of naltrexone side chain reduced its ability to cross the blood-brain barrier. As a result, the penetration of naldemedine into central nervous system is expected to be negligible at the recommended dose levels, limiting the potential for interference with centrally-mediated opioid analgesia.

Opioid medications are increasingly used not only for the management of acute pain but also for the long term management of cancer related and non-cancer related chronic pain syndromes. With increased use of opioids for pain there is also an increase in adverse effects from their use which includes OIC and opioid bowel dysfunction.

Constipation is a syndrome that may be defined by symptoms of difficult or infrequent passage of stool, hardness of stool, or a feeling of incomplete evacuation that may occur either alone or due to another medical disorder. The definition of constipation will differ from individual to individual, culture to culture, and even region to region.

Patients may define constipation as straining during defecation or change in stool consistency or frequency. Functional constipation may be defined by the Rome III criteria as the presence of at least two of the following: straining at stool; passage of lumpy or hard stools; sensation of incomplete evacuation or anorectal obstruction or blockage; the need to use manual maneuvers to facilitate defecation; and passing fewer than three stools per week. The criteria also include that loose stools may only rarely be present without the use of laxatives, and that there are insufficient criteria for a diagnosis of irritable bowel syndrome (IBS).

Chronic constipation can result in hemorrhoid formation, rectal pain and burning, bowel obstruction, and bowel rupture, as well as upper gut dysfunctions, including gastroesophageal reflux disease, nausea, and abdominal distention.

OIC is a result of use of opioid medications with resultant loss of gastrointestinal tone, contractility, and mobility. The cause of OIC is multifactorial and includes inhibition of gastric emptying, reduction of mucosal secretions, reduced bowel tone and contractility, decreased peristalsis with delayed transit, and increased fluid and electrolyte absorption from increased contact time. Tolerance to opioid induced gastrointestinal adverse effects does not occur.

Opioid receptors are widely distributed in the central and peripheral nervous system, intestines, and other tissues. There are three types of receptors involved in mediating the effects of opioids. These include delta, kappa, and mu receptors. They belong to the family of G-protein coupled receptors that regulate adenylate cyclase. Stimulation of the receptor results in inhibition of adenyate cyclase with a reduction of neuron excitability and neurotransmitter release. The end result is inhibition of the affected neuron.

SYMPROIC® (naldemedine tosylate) oral capsule (cont.)

Definitions:

Opioid-induce Constipation (OIC):
No more than 4 spontaneous bowel movements (SBM) total over 14 consecutive days and less than 3 SBM in a given week with at least 25% of the SBM associated with one or more of the following: straining; hard or lumpy stools; having a sensation of incomplete evacuation; and having a sensation of anorectal obstruction/blockage

Spontaneous bowel movement is a bowel movement without need of rescue laxative within 24-hours

Laxatives:
Bulk forming – calcium polycarbophil, methylcellulose, psyllium
Osmotic – glycerin, lactulose, polyethylene glycol, sorbitol
Lubricating – mineral oil
Saline – magnesium citrate, magnesium hydroxide, magnesium sulfate
Softener – dioctyl calcium sulfosuccinate, dioctyl sodium sulfosuccinate
Stimulant – bisacodyl, cascara, senna

Symproic (naldemedine tosylate)

Medication class:
Gastrointestinal Agents, Peripheral Opioid Receptor Antagonists

FDA-approved indication(s):
- Treatment of opioid-induced constipation (OIC) in adults with chronic non-cancer pain, including patients with chronic pain related to prior cancer or its treatment who do not require frequent (weekly) opioid dosage escalation

Recommended Dose:
- 0.2 mg once daily

Maximum dosage
- Not stated

Available Dosage Forms:
- 0.2 mg tablets

Warnings, Precautions, and other Clinical Information:
- Avoid use in severe hepatic impairment (Child-Pugh Class C)
- Discontinue for known, suspected, or those who develop symptoms of gastrointestinal perforation
- Discontinue use of Symproic when opioid pain medication(s) have been discontinued
- Use during pregnancy may cause opioid withdrawal symptoms in the unborn baby
- Woman who is breast feeding an infant or child should stop breast feeding
- Avoid use with strong CYP3A inducers such as carbamazepine, phenytoin, rifampin and St. John's Wort
- Avoid use with another opioid antagonist
- Symproic is not indicated for use in Chronic idiopathic constipation (CIC)

SYMPROIC® (naldemedine tosylate) oral capsule (cont.)

- Symproic is not indicated for use in Irritable bowel syndrome with constipation (IBS-C)
- Symproic is not indicated for use in Irritable bowel syndrome, mixed type
- Symproic is not indicated for use in cystic fibrosis
- Symproic is not indicated for constipation other than opioid-induced constipation

Criteria:

- **Criteria for initial therapy:** Symproic (naldemedine) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

1. Individual is 18 years of age or older
2. A confirmed diagnosis of opioid-induced constipation (OIC)
3. Documentation that individual has been taking opiate medication for at least 4 week **AND** needs to continue opiate medication
4. Documentation of a trial and failure of opioid dose reduction of ≥ 15%
5. Failure, contraindication, intolerance to at least 1 agent from each of the following classes:
    - Oral senna with a stool softener used on schedule (not on an as needed basis)
        - Examples include:
            - Docusate sodium/Senna
            - Dok Plus
            - Peri-Colace
            - Senna-S
            - Senokot-S
    - Oral osmotic agent **OR** saline agent used **EITHER** routinely **OR** on an as needed basis
        - Examples include:
            - Lactulose
            - Polyethylene glycol
            - Sorbitol
    - Oral **OR** rectal stimulant used on an as needed basis
        - Such as:
            - Bisacodyl
6. There are **NO** contraindications:
    - Contraindications include:
        - Known or suspected gastrointestinal obstruction
        - Individuals at risk of recurrent obstruction
        - History of hypersensitivity reaction to naldemedine

Initial approval duration: 6 months

SYMPROIC® (naldemedine tosylate) oral capsule (cont.)

- **Criteria for continuation of coverage (renewal request):** Symproic (naldemedine) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  1. Individual's condition responded while on therapy
     - Response is defined as:
       - Increase in spontaneous bowel movements (SBM) seen as 3 SBM per week or a change from baseline of 1 SBM per week

  2. Individual has been adherent with the medication **and** continues to receive opioid therapy

  3. Individual has not developed any contraindications or other significant level 4 adverse drug effects that may exclude continued use
     - Contraindications as listed in the criteria for initial therapy section
     - Significant adverse effect such as:
       - Gastrointestinal perforation
         - Signs and symptoms may include: abdominal tenderness or severe pain in abdomen, nausea, vomiting

  4. There are no significant interacting drugs

  Renewal duration: 12 months

Resources:

Symproic. Package Insert. Revised by manufacturer 8/2017. Accessed 10/11/17.

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Fax completed prior authorization request form to 602-864-3126 or email to pharmacyprecert@azblue.com.
Call 866-325-1794 to check the status of a request.
All requested data must be provided. **Incomplete forms or forms without the chart notes will be returned.**
Pharmacy Coverage Guidelines are available at www.azblue.com/pharmacy.

Pharmacy Prior Authorization Request Form

Do not copy for future use. Forms are updated frequently.
REQUIRED: Office notes, labs, and medical testing relevant to the request that show medical justification are required.

Member Information

Member Name (first & last):	Date of Birth:	Gender:	BCBSAZ ID#:
Address:	City:	State:	Zip Code:

Prescribing Provider Information

Provider Name (first & last):	Specialty:	NPI#:	DEA#:
Office Address:	City:	State:	Zip Code:
Office Contact:	Office Phone:	Office Fax:	

Dispensing Pharmacy Information

Pharmacy Name:	Pharmacy Phone:	Pharmacy Fax:

Requested Medication Information

Medication Name:	Strength:	Dosage Form:
Directions for Use:	Quantity: / Refills:	Duration of Therapy/Use:

☐ Check if requesting **brand** only ☐ Check if requesting **generic**

☐ Check if requesting continuation of therapy (prior authorization approved by BCBSAZ expired)

Turn-Around Time For Review

☐ Standard ☐ Urgent. Sign here: _____ ☐ Exigent (requires prescriber to include a written statement)

Clinical Information

1. **What is the diagnosis? Please specify below.**

   ICD-10 Code: _____ **Diagnosis Description:** _____

2. ☐ Yes ☐ No **Was this medication started on a recent hospital discharge or emergency room visit?**

3. ☐ Yes ☐ No **There is absence of ALL contraindications.**

4. **What medication(s) has the individual tried and failed for this diagnosis? Please specify below.**
Important note: Samples provided by the provider are not accepted as continuation of therapy or as an adequate trial and failure.

Medication Name, Strength, Frequency	Dates started and stopped or Approximate Duration	Describe response, reason for failure, or allergy

5. **Are there any supporting labs or test results? Please specify below.**

Date	Test	Value

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Pharmacy Prior Authorization Request Form

6. Is there any additional information the prescribing provider feels is important to this review? Please specify below.
For example, explain the negative impact on medical condition, safety issue, reason formulary agent is not suitable to a specific medical condition, expected adverse clinical outcome from use of formulary agent, or reason different dosage form or dose is needed.

Signature affirms that information given on this form is true and accurate and reflects office notes

Prescribing Provider's Signature: Date:

Please note: Some medications may require completion of a drug-specific request form.

Incomplete forms or forms without the chart notes will be returned.

Office notes, labs, and medical testing relevant to the request that show medical justification are required.