Naloxegol (MOVANTIK)

Criteria for Use

March 2018

VA Pharmacy Benefits Management Services, Medical Advisory Panel, and VISN Pharmacist Executives

The following recommendations are based on medical evidence, clinician input, and expert opinion. The content of the document is dynamic and will be revised as new information becomes available. The purpose of this document is to assist practitioners in clinical decision-making, to standardize and improve the quality of patient care, and to promote cost-effective drug prescribing. **THE CLINICIAN SHOULD UTILIZE THIS GUIDANCE AND INTERPRET IT IN THE CLINICAL CONTEXT OF THE INDIVIDUAL PATIENT. INDIVIDUAL CASES THAT ARE EXCEPTIONS TO THE EXCLUSION AND INCLUSION CRITERIA SHOULD BE ADJUDICATED AT THE LOCAL FACILITY ACCORDING TO THE POLICY AND PROCEDURES OF ITS P&T COMMITTEE AND PHARMACY SERVICES.**

The Product Information should be consulted for detailed prescribing information.

See the VA National PBM-MAP-VPE Monograph on this drug at www.pbm.va.gov or http://vaww.pbm.va.gov for further information.

Exclusion Criteria *If the answer to ANY item below is met, then the patient should NOT receive naloxegol.*

☐ Age less than 18 years

☐ Known or suspected gastrointestinal obstruction or at risk of recurrent obstruction

☐ Concomitant use with strong CYP3A4 inhibitors (e.g., clarithromycin, ketoconazole)

☐ Known serious or severe hypersensitivity to naloxegol or its excipients

☐ Presence of severe or frequent diarrhea

Inclusion Criteria *The answers to ALL of the following must be fulfilled in order to meet criteria.*

☐ Patient is taking opioids for chronic, non-cancer pain (including chronic pain related to prior cancer or its treatment), does not require frequent opioid dose escalation AND is documented to have opioid induced constipation (OIC).

☐ Documentation of attempts to reduce constipation by change to less constipating analgesics or reduction of opioid dose OR medical justification why changes are unable to be made in current regimen.

☐ Documentation that benefits of opioid therapy exceed risks for this patient and all VA / DOD Directives / guidelines for prescribing and monitoring long-term opioids are being followed. See ***Provider Practice Standards*** under *Issues for Consideration*.

☐ Intolerance or inadequate response to 1-month trials of the following agents (also see Table 1), unless there is a contraindication or risk factor(s) for serious adverse event(s):

- ☐ One stimulant laxative (e.g., bisacodyl, sennosides)

AND

- ☐ MIRALAX equivalent (twice daily) or other osmotic laxative (e.g., sorbitol, lactulose, magnesium (Mg) citrate, Mg hydroxide, glycerin rectal suppositories (RS))

Maintenance laxative therapy should be discontinued before starting naloxegol. Laxatives may be resumed if opioid induced constipation symptoms persist after taking naloxegol for 3 days.

Bulk forming laxatives are relatively contraindicated in OIC. A stool softener (e.g., docusate) is considered to be of low benefit and low harm for OIC and may be used but is not required prior to use of naloxegol in OIC.

Table 1. VANF Laxative Regimens

LAXATIVE	FORMULATION	INITIAL DOSE	USUAL DOSE	MAXIMUM DOSE
		(In divided doses, titrated to individual response)		
SENNOSIDES	Oral tablet	15 mg once daily	15–50 mg once or twice daily	70–100 mg in two divided doses
BISACODYL	Oral tablet	5 mg every 2–3 days	5–15 mg every 2–3 days	30 mg every 2–3 days
	Rectal suppository	10 mg every 2–3 days	10 mg every 2–3 days	10 mg every 2–3 days
DOCUSATE	Oral Capsule or Solution	50 mg once daily	50–360 mg in 1–4 divided doses	500 mg in 1–4 divided doses
	Rectal enema	Add 50-100 mg of docusate liquid (not syrup) to enema fluid (saline or water)		
LACTULOSE	Syrup	10 g (15 ml) once daily	10–20 g / day (15–30 ml / day) in 1–2 divided doses	60 ml / day in 1–2 divided doses
PEG 3350	Powder for solution, oral	17 g (about 1 heaping Tbsp) of powder mixed in 4–8 oz of water, juice, cola, or tea once daily for not longer than 2 weeks (OTC labeling). The OTC product labeling gives no limit on how frequently a course may be repeated. Under medical supervision, if the laxative response is insufficient, the dose may be increased to twice daily (off-label). Daily use (17 g/d) for constipation has been shown to be generally safe in otherwise healthy adults for up to one year.[†]		

OTC, Over-the-counter. [†] Center for Drug Evaluation and Research. MiraLax (Polyethylene Glycol 3350) Powder FDA Medical Review, 2006.

Dosage and Administration

The RECOMMENDED dose of naloxegol is 25 mg once daily in the morning.

If patient is unable to tolerate 25 mg, consider 12.5 mg daily.

If creatinine clearance is < 60 ml/min, 12.5 mg once daily is recommended with option to titrate to 25 mg daily if naloxegol is tolerated at the 12.5-mg dose.

Instruct patient to take naloxegol on an empty stomach one hour prior to the first meal of the day or two hours after the meal.

Consumption of grapefruit or grapefruit juice should be avoided.

Issues for Consideration

- In clinical trials, **opioid-induced constipation** was defined as < 3 spontaneous bowel movements (SBMs) per week on average with at least 25% of the SBMs associated with one or more of the following: straining; hard or lumpy stools; and sensation of incomplete evacuation. SBMs were defined as bowel movements without rescue laxatives taken within the past 24 hours.
    - Response was defined as ≥ 3 SBMs per week and a change from baseline of ≥ 1 SBM per week for at least 9 of the 12 study weeks and 3 of the last 4 weeks.
- Although naloxegol is reported not to cross the blood-brain barrier, patients have reported symptoms consistent with **opioid withdrawal** (e.g., hyperhidrosis, chills, diarrhea, abdominal pain, anxiety, irritability and yawning). The frequency of gastrointestinal adverse reactions that may have been related to opioid withdrawal was higher in patients taking methadone than in those taking other opioids. Disruptions in the blood-brain barrier may increase the risk of opioid withdrawal or reduced analgesia. It is recommended that the prescriber monitor for opioid withdrawal symptoms.
- No **gastrointestinal perforations** were reported in clinical trials studying naloxegol, however agents in this class carry a warning for gastrointestinal perforation. Use with caution in patients at risk for gastrointestinal perforation, such as those with peptic ulcer disease, diverticular disease, infiltrative gastrointestinal malignancy, peritoneal metastases or Crohn's disease.
- **Pregnancy Category C**. Naloxegol may cross the fetus's immature blood-brain barrier and precipitate opioid withdrawal in the fetus. Use naloxegol during pregnancy only if the potential benefit justifies the potential risk to the fetus.
- **Nursing Mothers.** There is a potential for opioid withdrawal and other serious adverse reactions in nursing infants. Discontinue nursing or using naloxegol, taking into consideration the risks and benefits of the drug to the mother.
- **Practice Standards for Provision of Opioid Therapy.** General principles, defined by CDC and VA/DoD Clinical Practice Guidelines for prescribing of opioids for chronic pain, should be utilized to guide management of long-term opioid therapy. Practitioners should obtain informed consent from each patient after explaining the risks, benefits, and obligatory terms of long term treatment with opioids. All federal and state guidelines on prescribing and dispensing opioids should be strictly followed. There should be an initial and periodic checking of the respective SPDMP (if available), consideration of provision of naloxone rescue, and exercise of other strategies to mitigate risk of chronic opioid therapy. Providers should ensure risk mitigation strategies are in place when starting opioids per the VA / DOD Clinical Practice Guideline on the Management of Opioid Therapy (OT) for Chronic Pain (2017) https://www.healthquality.va.gov/. These strategies include an informed consent conversation covering the risks and benefits of opioid therapy as well as alternative therapies. Other strategies and their frequency should be commensurate with risk factors and include: ongoing, random urine drug testing (including appropriate confirmatory testing); checking state prescription drug monitoring programs; monitoring for overdose potential and suicidality; providing overdose education; and prescribing of naloxone rescue and accompanying education.

Initial Prescription Supply

- Up to 2 weeks

Renewal Criteria

- Patient experiences clinically important benefit (i.e., improved constipation and abdominal pain) after an adequate therapeutic trial and tolerates treatment.
- An adequate therapeutic trial is 1 week.

Revised: March 2018 (Added to Inclusion Criteria to reflect new indication labeling and to add elements of practice standards for opioid therapy.)
Originally Prepared: June 2015. David Andrew Jacob, PharmD,[1] April Casselman, PharmD,[1] Michelle Shank, RPh, VPE[1]
Contact: Francine Goodman, PharmD, BCPS, National Clinical Pharmacy Program Manager – Formulary (10P4P)[2]
[1]VISN-17 Pharmacy Benefits Management, Temple, TX, [2]VA Pharmacy Benefits Management Services, Hines, Il