Drug Monograph

Drug/Drug Class:	**Movantik™ (naloxegol) tablets/ Opioid-Induced Constipation**
Prepared for:	MO HealthNet
Prepared by:	Xerox Heritage, LLC

☒ **New Criteria** ☐ **Revision of Existing Criteria**

Executive Summary

Purpose:	The purpose of this monograph is to provide a review of new therapy to determine whether the reviewed drug should be made available on an open access basis to prescribers, require a clinical edit or require prior authorization for use.
Dosage Forms & Manufacturer:	Movantik™ is available in a tablet containing 12.5 mg or 25 mg of naloxegol. AstraZeneca Pharmaceuticals LP Wilmington, DE 19850
Summary of Findings:	The effect of Movantik for the treatment of opioid-induced constipation in patients with noncancer pain was studied in 2 replicate, randomized, double-blind, placebo-controlled clinical trials (n=1352). Compared to a response rate of 29% in patients who received placebo, 40% to 44% of patients who received Movantik 25 mg daily experienced relief of constipation.
Status Recommendation:	☒ Prior Authorization (PA) Required ☐ Open Access ☐ Clinical Edit ☐ PDL
Type of PA Criteria:	☐ Increased Risk of ADE ☐ Preferred Agent ☒ Appropriate Indications ☐ Under Solicitation

Purpose

The purpose of this monograph is to provide a review of new therapy to determine whether the reviewed drug should be considered a prior authorization drug, a clinical edit drug or an open access drug. While prescription expenditures are increasing at double-digit rates, payors are evaluating ways to control these costs by influencing prescriber behavior and guide appropriate medication usage. This review will assist in the achievement of qualitative and economic goals related to health care resource utilization. Restricting the use of certain medications can reduce costs by requiring documentation of appropriate indications for use, and where appropriate, encourage the use of less expensive agents within a drug class.

Introduction[2]

Opioids are a class of drugs that are used to treat and manage pain. A common side effect associated with the use of these drugs are that they reduce the gastrointestinal tract's motility, making bowel movements difficult and causing patients to strain, have hard or lumpy stools or experience a sensation of incomplete evacuation.

Dosage Form(s) [1]

Movantik™ is available in a tablet containing 12.5 mg or 25 mg of naloxegol.

Manufacturer [1]

AstraZeneca Pharmaceuticals LP., Wilmington, DE 19850

Indication(s) [1]

Movantik™ is indicated for the treatment of opioid-induced constipation in adults with chronic noncancer pain.

Clinical Efficacy [1] (mechanism of action/pharmacology, comparative efficacy)

Movantik™ is a mu opioid antagonist that is a derivative of naloxone. It is specific to peripheral tissues (eg. gastrointestinal tract) due to pegylation that decreases passive permeability and CNS penetration at recommended dosages.

Pharmacokinetics

	Movantik
Volume of distribution	968 to 2140 L
Metabolism	Hepatic via CYP3A to 6 minor metabolites
Excretion	Feces, 68 % (16% unchanged) Urine, 16% (< 6% unchanged)
Half-life	6 to 11 hours
Protein binding	4.2%

Movantik™ resulted in better constipation relief than placebo in patients receiving opioids for chronic noncancer pain.

STUDY DESIGN	Two randomized, double-blind, placebo-controlled, 12-week clinical trials (n=1352)

INCLUSION CRITERIA	Patients with opioid-induced constipation and noncancer pain who were receiving an opioid with an equivalent daily dosage of morphine 30 to 1000 mg for at least 4 weeks.
EXCLUSION CRITERIA	No bowel movements or an uneven distribution of bowel movements over a 2-week run-in period.
TREATMENT REGIMEN	Patients (n=1352; mean age, 52 years) were randomized to receive Movantik 12.5 mg, 25 mg, or placebo once daily for 12 weeks.
RESULTS	Patients had been receiving their current opioid therapy for an average of 3.6 and 3.7 years in the 2 studies, with a mean baseline morphine equivalent daily dosage of 140 and 136 mg/day. Significantly more patients in the Movantik 25-mg groups in both studies (44% in study 1 and 40% in study 2) responded compared with the placebo groups (29% in each study). Response was defined as > 3 spontaneous bowel movements (SBM) per week and an increase from baseline of at least 1 SBM per week for 9 of the 12 weeks and for 3 of the last 4 weeks. For the 12.5-mg groups, study 1 demonstrated statistical significance with 41% of patients responding, but study 2 did not (35%).
SAFETY	Not specified

Contraindications [(1)]

- Known or suspected gastrointestinal obstruction or at increased risk for recurrent obstruction; potential for gastrointestinal perforation
- Concomitant use with strong CYP3A4 inhibitors, such as clarithromycin and ketoconazole
- Serious or severe hypersensitivity to naloxegol or any components

Warnings and Precautions [(1)]

- Gastrointestinal perforation has been reported with other opioid antagonists in patients with peptic ulcer disease, diverticular disease, infiltrative gastrointestinal tract malignancies, and peritoneal metastases; monitoring recommended and discontinuation may be necessary.
- Avoid use in patients with severe hepatic impairment.
- Symptoms of opioid withdrawal (eg, hyperhidrosis, chills, diarrhea, abdominal pain, anxiety, irritability, yawning) have been reported, especially in patients receiving methadone or patients with disruptions to the blood-brain barrier; monitoring recommended.
- Avoid use with moderate CYP3A4 inhibitors; if coadministration is unavoidable, dosage reduction and monitoring recommended.
- Avoid use with strong CYP3A4 inducers.
- Avoid use with other opioid antagonists.
- Avoid consumption of grapefruit or grapefruit juice.

Adverse Effects [1]

Most common, ≥ 3%	Movantik™ (n=446)	Placebo (n=444)
Abdominal Pain	21%	7%
Diarrhea	9%	5%
Nausea	8%	5%
Flatulence	6%	3%
Vomiting	5%	4%
Headache	4%	3%
Hyperhidrosis	3%	< 1%

Drug Interactions [1]

- None listed

Dosage and Administration [1]

The recommended dose is 25 mg orally once daily in the morning at least 1 hour before or 2 hours after eating. If not tolerated, reduce to 12.5 mg orally once daily. The dosage should be reduced for patients with renal impairment or those taking moderate CYP3A4 inhibitors.

Cost

GENERIC NAME	BRAND NAME	MANUFACTURER	STRENGTH	DOSE	COST*/ TAB
Naloxegol	Movantik	AstraZeneca	12.5 mg tablets	1 tablet daily	$8.32
			25 mg tablets	1 tablet daily	$8.32

*WholesaleAcquisitionCost

Conclusion

Movantik™ is a peripheral opioid antagonist indicated for the treatment of opioid-induced constipation in adults with chronic noncancer pain. Significantly more patients responded to naloxegol therapy (40% to 44%) compared with placebo (29%) for the treatment of opioid-induced constipation in 2 large randomized 12-week trials. Naloxegol may be useful in select patients whose constipation cannot be adequately controlled with prophylactic use of mild laxatives and

stool softeners. The most common adverse effects are abdominal pain, diarrhea, nausea, and flatulence. Close monitoring for symptoms of opioid withdrawal is recommended. A postmarketing study is required by the US Food and Administration (FDA) to assess any potential cardiovascular risks with naloxegol.

Recommendation

The MO HealthNet Division recommends prior authorization status for this product.

References

1. Product Information: Movantik™, naloxegol tablets. AstraZeneca Pharmaceuticals LP. Wilmington, DE, 09/2014
2. FDA approves Movantik for opioid-induced constipation. Retrieved May 26, 2015 from http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm414620.htm

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