



## 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

By age 50 most adults should have a colonoscopy and complete visualization of the bowel is needed to conduct a thorough colonoscopy and to identify precancerous lesions and other gastrointestinal disorders. Aversion to bowel prep solutions, including the substantial liquid volume, is a key barrier to completion of essential colonoscopy prep regimens.

## Dosage Form(s)<sup>1</sup>

Prepopik™ contains 2 packets of powder for reconstitution and each of the two packets contains 10 mg of sodium picosulfate, 3.5 grams of magnesium oxide, and 12.0 grams of anhydrous citric acid in 16.1 grams of powder.

## Manufacturer

Manufactured by: Ferring Pharmaceuticals (China) Co., Ltd. No. 6 HuiLing Lu (Ferring Road)  
National Health Technology Park Zhongshan City, Guangdong Province, CHINA  
Manufactured for: Ferring Pharmaceuticals Inc. Parsippany, N.J. 07054

## Indication(s)<sup>1</sup>

Prepopik™ is FDA approved for cleansing of the colon as a preparation for colonoscopy in adults.

## Clinical Efficacy<sup>1-2</sup> (mechanism of action/pharmacology, comparative efficacy)

Prepopik™ contains sodium picosulfate, magnesium oxide, and anhydrous citric acid. Citric acid and magnesium oxide react in solution to create magnesium citrate, which acts as an osmotic laxative that retains water in the gastrointestinal tract. Sodium picosulfate is hydrolyzed by colonic bacteria to bis-(p-hydroxy-phenyl)-pyridyl-2-methane (BHPM), which stimulates colonic peristalsis by direct action on colonic mucosa. When administered together as a precolonoscopy preparation with additional fluids, the stimulant and osmotic laxatives produce a purgative effect.

## PHARMACOKINETICS (1)

Pharmacokinetic data for Prepopik are limited. Sodium picosulfate is a prodrug that is metabolized by colonic bacteria to its active form, BHPM. The terminal half-life of sodium picosulfate is 7.4 hours in healthy adults and approximately 0.19% is excreted unchanged in the urine.

## EFFICACY (1,2) SUMMARY

The approval of Prepopik was primarily based upon 2 randomized, investigator-blind, active-controlled clinical trials involving 1195 adult patients scheduled to have a colonoscopy. Patients were randomly assigned to the Prepopik Split-Dose regimen, the Prepopik Day-Before regimen, or a control preparation of polyethylene glycol plus electrolytes (PEG-E) solution together with oral bisacodyl 10 mg. The studies were designed to measure the number of patients whose colons were successfully cleansed. In both studies, Prepopik was as effective as the control preparation in cleansing the colon. In the study where Prepopik was administered in the Split-Dose regimen (the day before colonoscopy and the morning of colonoscopy), it was superior to the control preparation in cleansing the colon. The control preparation was administered on the day before colonoscopy.

### PRECOLONOSCOPY PREPARATION

<b>STUDY DESIGN</b>	Two multicenter, randomized, investigator-blind, active-controlled clinical trials (n=1195).
<b>INCLUSION CRITERIA</b>	Adult patients scheduled to have an elective colonoscopy: Study 1, n=601; Study 2, n=594. Patients ranged in age from 18 to 80 years (mean age, 56 years); 61% were female and 39% were male.
<b>EXCLUSION CRITERIA</b>	Not specified.
<b>TREATMENT REGIMEN</b>	Patients randomized to Prepopik in the 2 studies were treated with one of 2 dosing regimens. In Study 1, Prepopik was given by Split-Dose dosing, where the first packet was taken the evening before the colonoscopy (between 5 and 9 PM) and followed by five 8-ounce glasses of clear liquid, and the second packet was taken the morning of the colonoscopy, at least 5 hours prior but no more than 9 hours prior to the procedure, and followed by three 8-ounce glasses of clear liquid. In Study 2, Prepopik was given by Day-Before dosing, where both packets were taken separately on the day before the colonoscopy in the afternoon (between 4 and 6 PM) with five 8-ounce glasses of clear liquid and in the late evening (approximately 6 hours later, between 10 PM and 12 AM) with three 8-ounce glasses of clear liquid. The comparator was a preparation containing 2 L of polyethylene glycol plus electrolytes solution (PEG-E) together with 2 tablets of bisacodyl 5 mg administered the day before the procedure. All patients were limited to a clear liquid diet for 24 hours before the procedure. The primary efficacy endpoint was the proportion of patients with successful colon cleansing as assessed by a blinded colonoscopist using the Aronchick Scale. Successful colon cleansing was defined as bowel preparations with > 90% of the mucosa visible and mostly liquid stool that were graded excellent (minimal suctioning needed for adequate visualization) or good (significant suctioning needed for adequate visualization) by the colonoscopist.

<b>RESULTS</b>	In both studies, treatment with Prepopik was noninferior to PEG-E solution and bisacodyl. The proportion of subjects with successful colon cleansing in Study 1 was 84.2% for patients receiving Prepopik compared with 74.4% for the comparator (95% CI, 3.4% to 16.2%). In Study 2, the proportion of subjects with successful colon cleansing was 83% for patients receiving Prepopik compared with 79.7% for the comparator (95% CI, -2.9% to 9.6%).
<b>SAFETY</b>	The most common adverse reactions for Prepopik were nausea, headache, and vomiting.

### Contraindications<sup>1</sup>

- Patients with severely reduced renal function (CrCl < 30 mL/min); possible risk for magnesium accumulation
- Gastrointestinal obstruction or ileus
- Bowel perforation
- Toxic colitis or megacolon
- Gastric retention

### Warnings and Precautions<sup>1</sup>

- Fluid and electrolyte abnormalities, arrhythmias, seizures, and renal impairment are possible; encourage adequate hydration, assess concurrent medications, and consider laboratory assessments prior to and after use.
- Preexisting renal insufficiency or concomitant medications that affect renal function may predispose to renal injury; ensure adequate hydration and consider laboratory assessments prior to and after use.
- Colonic mucosal ulceration and ischemic colitis may occur; risk is increased with concomitant use of stimulant laxatives.
- Suspected gastrointestinal obstruction or perforation; evaluate patient prior to use.
- Patients at risk for aspiration; observe closely during administration.
- Powder is not for direct ingestion; dissolve and take with additional water.

### Adverse Effects<sup>1</sup>

#### STUDY 1 : SPLIT DOSE REGIMEN

Most Common ≥ 1%	PREPOPIK (n=305)	PEG-E & BISACODYL (n=298)
Nausea	2.6%	3.7%
Headache	1.6%	1.7%
Vomiting	1.0%	3.4%

#### STUDY 2 : DAY BEFORE REGIMEN

Most Common ≥ 1%	PREPOPIK (n=296)	PEG-E & BISACODYL (n=302)
Nausea	3.0%	4.3%
Headache	2.7%	1.7%
Vomiting	1.4%	2.0%

## Drug Interactions<sup>1</sup>

- Antibiotics (prevent colonic conversion)
- Chlorpromazine
- Digoxin
- Fluoroquinolones: ciprofloxacin, gemifloxacin, levofloxacin, moxifloxacin, norfloxacin, ofloxacin
- Iron
- Penicillamine
- Tetracycline

## Dosage and Administration<sup>1</sup>

Prepopik™, supplied as a powder, must be reconstituted with cold water right before its use. There are two dosing regimens, each requires two separate dosing times:

Split-Dose Dosing Regimen (Preferred Method):

- Take the first dose during the evening before the colonoscopy (e.g., 5:00 to 9:00 PM) followed by five 8-ounce drinks (upper line on the dosing cup) of clear liquids before bed. Consume clear liquids within 5 hours.
- Take second dose, the next day approximately 5 hours before the colonoscopy followed by at least three 8-ounce drinks of clear liquids before the colonoscopy. Consume clear liquids within 5 hours up until 2 hour before the time of the colonoscopy.

Day-Before Dosing Regimen (Alternative Method):

- Take the first dose in the afternoon or early evening (e.g., 4:00 to 6:00 PM) before the colonoscopy followed by five 8-ounce drinks (upper line on the dosing cup) of clear liquids before the next dose. Consume clear liquids within 5 hours.
- Take the second dose approximately 6 hours later in the late evening (e.g., 10:00 PM to 12:00 AM), the night before the colonoscopy followed by three 8-ounce drinks of clear liquids before bed. Consume clear liquids within 5 hours.

## Cost Comparisons (at commonly used dosages)

**COST (WAC)\***

GENERIC NAME	BRAND NAME	MANUFACTURER	STRENGTH	COST/PACKAGE
Sodium picosulfate/magnesium/citric acid solution	Prepopik	Ferring	10 mg/3.5 g/12 g/packet, 2 packets/carton	\$74.96 (WAC)*

\*Wholesale Acquisition Cost (WAC)

## Conclusion

Prepopik™ is a combination of sodium picosulfate, magnesium oxide, and citric acid, which provides both stimulant and osmotic laxatives. This combination has demonstrated efficacy for cleansing of the colon as a preparation for colonoscopy in adults. Complete visualization of the bowel is needed to conduct a thorough colonoscopy and to identify precancerous lesions and

other gastrointestinal disorders. Aversion to bowel prep solutions, including the substantial liquid volume, is a key barrier to completion of essential colonoscopy prep regimens. Prepopik is the lowest volume colon preparation available for oral solution and provides a new option for adults undergoing a colonoscopy exam. However, its comparative cost to other colonoscopy preparations may be an important consideration in product selection.

## Recommendation

MO HealthNet Division recommends Open Access status for this product.

## References

1. Product Information: Prepopik™, sodium picosulfate, magnesium oxide, and anhydrous citric acid for oral solution. Ferring Pharmaceuticals, Inc., Parsippany, NJ, 07/2012.
2. Flemming JA, Vanner SJ & Hookey LC: Split-dose picosulfate, magnesium oxide, and citric acid solution markedly enhances colon cleansing before colonoscopy: a randomized, controlled trial. *Gastrointest Endosc* 2012; 75(3):537-544.

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