SODIUM PICOSULFATE, MAGNESIUM OXIDE AND ANHYDROUS CITRIC ACID - sodium picosulfate, magnesium oxide and anhydrous citric acid powder, metered
Camber Pharmaceuticals, Inc.

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use SODIUM PICOSULFATE, MAGNESIUM OXIDE AND ANHYDROUS CITRIC ACID FOR ORAL SOLUTION safely and effectively. See full prescribing information for SODIUM PICOSULFATE, MAGNESIUM OXIDE AND ANHYDROUS CITRIC ACID FOR ORAL SOLUTION.

SODIUM PICOSULFATE, MAGNESIUM OXIDE AND ANHYDROUS CITRIC ACID for oral solution

Initial U.S. Approval: 2012

INDICATIONS AND USAGE

Sodium picosulfate, magnesium oxide and anhydrous citric acid for oral solution is a combination of sodium picosulfate, a stimulant laxative, and magnesium oxide and anhydrous citric acid which form magnesium citrate, an osmotic laxative, indicated for cleansing of the colon as a preparation for colonoscopy in adults and pediatric patients ages 9 years and older. (1)

DOSAGE AND ADMINISTRATION

Preparation and Administration
• Each packet of sodium picosulfate, magnesium oxide and anhydrous citric acid must be dissolved with water prior to ingestion and administered according to the dosing regimen. Direct ingestion of the undissolved powder may increase the risk of nausea, vomiting and dehydration. (2.2, 5.8)
• Two doses (one packet per dose) of sodium picosulfate, magnesium oxide and anhydrous citric acid for oral solution are required for a complete preparation for colonoscopy. The preferred method is the "Split-Dose" method. The alternative is the "Day Before" method. (2.1)
• Additional fluids must be consumed after every dose of sodium picosulfate, magnesium oxide and anhydrous citric acid for oral solution in both dosing regimens. (2.1, 5.1)
• Do not take oral medications within 1 hour of start of each dose. (2.1, 7.2)
• If taking tetracycline or fluoroquinolone antibiotics, iron, digoxin, chlorpromazine, or penicillamine, take these medications at least 2 hours before and not less than 6 hours after administration of sodium picosulfate, magnesium oxide and anhydrous citric acid for oral solution. (2.1, 7.3)
• For complete information on preparation before colonoscopy and administration of the dosage regimen, see full prescribing information. (2.1, 2.2, 2.3)
Split-Dose Dosage Regimen (Preferred Method) (2.2)
• First dose: administer during evening before the colonoscopy
• Second dose: administer the next day, during the morning prior to the colonoscopy.
Day-Before Dosage Regimen (Alternative Method), if Split-Dosing is inappropriate (2.3)
• First dose: administer during afternoon or early evening before the colonoscopy.
• Second dose: administer 6 hours later during evening before colonoscopy.

DOSAGE FORMS AND STRENGTHS

For oral solution: Each of 2 packets contains 16.1 g of powder for orange flavor: 10 mg sodium picosulfate, 3.5 g magnesium oxide and 12 g anhydrous citric acid (3)

CONTRAINDICATIONS

• Severe renal impairment (creatinine clearance less than 30 mL/minute) (4)
• Gastrointestinal (GI) obstruction or ileus (4)
• Bowel perforation (4)
• Toxic colitis or toxic megacolon (4)
• Gastric retention (4)
• Hypersensitivity to any of the ingredients (4)

WARNINGS AND PRECAUTIONS

• Risk of fluid and electrolyte abnormalities: Encourage adequate hydration, assess concurrent medications, and consider laboratory assessments prior to and after use. (5.1, 5.2, 7.1)
• Cardiac arrhythmias: Consider pre-dose and post-colonoscopy ECGs in patients at increased risk. (5.2)
• Seizures: Use caution in patients with a history of seizures and patients at increased risk of seizure, including medications that lower the seizure threshold. (5.3, 7.1)
• Patients with mild to moderate renal impairment or taking concomitant medications that affect renal function: Use caution, ensure adequate hydration and consider testing. (4, 5.4, 7.1)
• Mucosal ulcerations: Consider potential for mucosal ulcerations when interpreting colonoscopy findings in patients with known or suspected inflammatory bowel disease. (5.5)
• Suspected GI obstruction or perforation: Rule out diagnosis before administration. (4, 5.6)
• Patients at risk for aspiration: Observe during administration. (5.7)
• Risk of vomiting and other GI complications with ingestion of undissolved powder: Dissolve each packet in 5 ounces of cold water and administered at separate times according to the dosing regimen. (2.3, 2.4, 5.8)

ADVERSE REACTIONS

Most common adverse reactions are:
• Adults (>1%): nausea, headache and vomiting. (6.1)
• Pediatrics 9 to 16 years (>5%): nausea, vomiting, and abdominal pain. (6.1)
To report SUSPECTED ADVERSE REACTIONS, contact Annora Pharma Private Limited at 1-866-495-1995 or FDA at 1-800-FDA-1088 or *www.fda.gov/medwatch.*

DRUG INTERACTIONS

Drugs that increase risks due to fluid and electrolyte changes. (7.1)
See 17 for PATIENT COUNSELING INFORMATION.

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FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

Sodium picosulfate, magnesium oxide and anhydrous citric acid for oral solution is indicated for cleansing of the colon as a preparation for colonoscopy in adults and pediatric patients 9 years of age and older.

2 DOSAGE AND ADMINISTRATION

2.1 Important Preparation and Administration Instructions

• Correct fluid and electrolyte abnormalities before administration of sodium picosulfate, magnesium oxide and anhydrous citric acid for oral solution *[see Warnings and Precautions (5.1)]*.
• Two doses (one packet per dose) of sodium picosulfate, magnesium oxide and anhydrous citric acid for oral solution are required for a complete preparation for colonoscopy either as a Split-Dose (preferred) or Day-Before dosing regimen.
• The preferred method is the "Split-Dose" method and consists of two separate doses: the first dose during the evening before the colonoscopy and the second dose the next day, the morning of the day of the colonoscopy *[see Dosage and Administration (2.2)]*.
• The alternative method is the "Day Before" method and consists of two separate doses: the first dose during the afternoon or early evening before the colonoscopy and the second dose 6 hours later during the evening before the colonoscopy *[see Dosage and Administration (2.3)]*.
• Each packet of sodium picosulfate, magnesium oxide and anhydrous citric acid must be dissolved in 5 ounces of cold water prior to ingestion and administered according to the dosing regimen. Direct ingestion of the undissolved powder may increase the risk of nausea, vomiting, dehydration and electrolyte disturbances *[see Warnings and Precautions (5.8)]*.
• Additional fluids must be consumed after every dose of sodium picosulfate, magnesium oxide and anhydrous citric acid for oral solution in both dosing regimens *[see Dosage and Administration (2.2), Warnings and Precautions (5.1)]*.
• Consume only clear fluids (no solid food) from the start of sodium picosulfate, magnesium oxide and anhydrous citric acid for oral solution treatment until after the colonoscopy.
• Do not eat solid food or dairy and do not drink anything colored red or purple.
• Do not drink alcohol.
• Do not take other laxatives while taking sodium picosulfate, magnesium oxide and anhydrous citric acid for oral solution.
• Do not take oral medications within one hour before or after starting sodium picosulfate, magnesium oxide and anhydrous citric acid for oral solution.
• If taking tetracycline or fluoroquinolone antibiotics, iron, digoxin, chlorpromazine, or penicillamine, take these medications at least 2 hours before and not less than 6 hours after administration of sodium picosulfate, magnesium oxide and anhydrous citric acid for oral solution *[see Drug Interactions (7.2)]*.

• Stop consumption of all fluids at least 2 hours before the colonoscopy.

2.2 Reconstitution of Sodium Picosulfate, Magnesium Oxide and Anhydrous Citric Acid Powder

1. Reconstitute the sodium picosulfate, magnesium oxide and anhydrous citric acid powder immediately before each administration. Do not prepare the solution in advance.
2. Fill the supplied dosing cup with cold water up to the lower (5-ounce) line on the cup and pour in the contents of one packet of sodium picosulfate, magnesium oxide and anhydrous citric acid powder.
3. Stir for 2 to 3 minutes. The reconstituted sodium picosulfate, magnesium oxide and anhydrous citric acid solution may become slightly warm as the powder dissolves.

2.3 Split-Dose Dosing Regimen (Preferred Method)

The Split-Dose regimen is the preferred dosing method. The recommended dosage in adults and pediatric patients 9 years of age and older is shown below. Instruct patients to take two separate doses (one packet per dose) in conjunction with fluids.
Dose 1 – On the day before colonoscopy:
• Instruct patients to consume only clear liquids (no solid food or dairy) on the day before the colonoscopy up until 2 hours before the time of the colonoscopy.
• Take the first dose of sodium picosulfate, magnesium oxide and anhydrous citric acid for oral solution during the evening before the colonoscopy (e.g., 5:00 to 9:00 PM).
• Follow sodium picosulfate, magnesium oxide and anhydrous citric acid for oral solution by drinking at least five 8-ounce cups of clear liquids (40 ounces total), using the upper line on the cup, within 5 hours and before bed.
• If severe bloating, distention, or abdominal pain occurs, following the first dose, delay the second dose until the symptoms resolve.
Dose 2 – Next morning on the day of colonoscopy (start approximately 5 hours prior to colonoscopy):
• Continue to consume only clear liquids (no solid food or dairy).
• Take the second dose of sodium picosulfate, magnesium oxide and anhydrous citric acid for oral solution.
• Following the sodium picosulfate, magnesium oxide and anhydrous citric acid for oral solution dose, drink at least three 8-ounce cups of clear liquids (24 ounces), using the upper line on the cup, at least 2 hours before the colonoscopy.

2.4 Day-Before Dosing Regimen (Alternative Method)

The Day-Before regimen is the alternative dosing method for patients for whom the Split-Dosing is inappropriate. The recommended dosage in adults and pediatric patients 9 years of age and older is shown below. Instruct patients to take two separate doses (one packet per dose) in conjunction with fluids
Dose 1 – On the day before colonoscopy:
• Instruct patients to consume only clear liquids (no solid food or dairy) on the day before the colonoscopy up until 2 hours before the time of the colonoscopy.
• Take the first dose of sodium picosulfate, magnesium oxide and anhydrous citric acid for oral solution in the afternoon or early evening before the colonoscopy (e.g., 4:00 to 6:00 PM).
• Following the sodium picosulfate, magnesium oxide and anhydrous citric acid for oral solution dose, drink at least five 8-ounce cups of clear liquids (40 ounces total), using the upper line on the cup, within 5 hours and before the next dose.
• If severe bloating, distention, or abdominal pain occurs, following the first dose, delay the second dose until the symptoms resolve.
Dose 2 – Approximately 6 hours later in the evening the night before the colonoscopy (e.g., 10:00 PM to 12:00 AM):
• Take the second dose of sodium picosulfate, magnesium oxide and anhydrous citric acid for oral solution.

• Following the sodium picosulfate, magnesium oxide and anhydrous citric acid for oral solution dose, drink at least three 8-ounce cups (24 ounces), using the upper line on the cup, of clear liquids within 5 hours and before bed.
Storage
Reconstitute immediately before use. Do not prepare the solution in advance or store the solution for later use. Do not refrigerate or add ice to the solution.

3 DOSAGE FORMS AND STRENGTHS

For oral solution: Each of the two packets contains 10 mg of sodium picosulfate, 3.5 g of magnesium oxide and 12 g of anhydrous citric acid in 16.1g of powder for orange flavor.

4 CONTRAINDICATIONS

Sodium picosulfate, magnesium oxide and anhydrous citric acid for oral solution is contraindicated in the following conditions:
• Patients with severe renal impairment (creatinine clearance less than 30 mL/minute) which may result in accumulation of magnesium *[see Warnings and Precautions (5.4)]*
• Gastrointestinal obstruction or ileus *[see Warnings and Precautions (5.6)]*
• Bowel perforation *[see Warnings and Precautions (5.6)]*
• Toxic colitis or toxic megacolon
• Gastric retention
• Hypersensitivity to any of the ingredients in sodium picosulfate, magnesium oxide and anhydrous citric acid for oral solution *[see Adverse Reactions (6.2)]*

5 WARNINGS AND PRECAUTIONS

5.1 Serious Fluid and Electrolyte Abnormalities

Advise patients to hydrate adequately before, during, and after the use of sodium picosulfate, magnesium oxide and anhydrous citric acid. Use caution in patients with congestive heart failure when replacing fluids. If a patient develops significant vomiting or signs of dehydration including signs of orthostatic hypotension after taking sodium picosulfate, magnesium oxide and anhydrous citric acid, consider performing post-colonoscopy lab tests (electrolytes, creatinine, and BUN) and treat accordingly.
Approximately 20% of adult patients in both arms (sodium picosulfate, magnesium oxide and anhydrous citric acid, 2L of PEG + E plus two x 5 mg bisacodyl tablets) of clinical trials of sodium picosulfate, magnesium oxide and anhydrous citric acid had orthostatic changes (changes in blood pressure and/or heart rate) on the day of colonoscopy. In adult clinical trials orthostatic changes were documented up to seven days post colonoscopy. In a single study of patients 9 to 16 years of age, approximately 20% of patients in sodium picosulfate, magnesium oxide and anhydrous citric acid arms had orthostatic changes (changes in blood pressure and/or heart rate) compared with approximately 7% of those who received the comparator (PEG) *[see Clinical Studies (14)]*. These changes occurred up to five days post colonoscopy.
Fluid and electrolyte disturbances can lead to serious adverse reactions including cardiac arrhythmias or seizures and renal impairment. Correct fluid and electrolyte abnormalities before treatment with sodium picosulfate, magnesium oxide and anhydrous citric acid *[see Dosage and Administration (2.1)]* . In addition, use caution when prescribing sodium picosulfate, magnesium oxide and anhydrous citric acid for patients who have conditions or who are using medications that increase the risk for fluid and electrolyte disturbances or that may increase the risk of adverse events of seizure, arrhythmia, and renal impairment *[see Drug Interactions (7.1)]*.

5.2 Cardiac Arrhythmias

There have been rare reports of serious arrhythmias associated with the use of ionic osmotic laxative products for bowel preparation. Use caution when prescribing sodium picosulfate, magnesium oxide and anhydrous citric acid for patients at increased risk of arrhythmias (e.g., patients with a history of prolonged QT, uncontrolled arrhythmias, recent myocardial infarction, unstable angina, congestive heart failure, or cardiomyopathy). Consider pre-dose and post-colonoscopy ECGs in patients at increased risk of serious cardiac arrhythmias.

5.3 Seizures

There have been reports of generalized tonic-clonic seizures with the use of bowel preparation products in patients with no prior history of seizures. The seizure cases were associated with electrolyte abnormalities (e.g., hyponatremia, hypokalemia, hypocalcemia, and hypomagnesemia) and low serum osmolality. The neurologic abnormalities resolved with correction of fluid and electrolyte abnormalities.
Use caution when prescribing sodium picosulfate, magnesium oxide and anhydrous citric acid for patients with a history of seizures and in patients at risk of seizure, such as patients taking medications that lower the seizure threshold (e.g., tricyclic antidepressants), patients withdrawing from alcohol or benzodiazepines, or patients with known or suspected hyponatremia *[see Adverse Reactions (6.2)]*.

5.4 Use in Patients with Renal Impairment

Sodium picosulfate, magnesium oxide and anhydrous citric acid is contraindicated in patients with severe renal impairment (creatinine clearance less than 30 mL/min), accumulation of magnesium in plasma may occur *[see Contraindications (4)]*. As with other magnesium containing bowel preparations, use caution when prescribing sodium picosulfate, magnesium oxide and anhydrous citric acid for patients with mild to moderate renal impairment or patients taking concomitant medications that may affect renal function (such as diuretics, angiotensin converting enzyme inhibitors, angiotensin receptor blockers, or non-steroidal anti-inflammatory drugs) *[see Drug Interactions (7.1)]*. These patients may be at increased risk for renal injury. Advise these patients of the importance of adequate hydration before, during and after the use of sodium picosulfate, magnesium oxide and anhydrous citric acid. Consider performing baseline and post-colonoscopy laboratory tests (electrolytes, creatinine, and BUN) in these patients.

5.5 Colonic Mucosal Ulceration, Ischemic Colitis and Ulcerative Colitis

Osmotic laxatives may produce colonic mucosal aphthous ulcerations and there have been reports of more serious cases of ischemic colitis requiring hospitalization. Concurrent use of additional stimulant laxatives with sodium picosulfate, magnesium oxide and anhydrous citric acid may increase this risk. The potential for mucosal ulcerations should be considered when interpreting colonoscopy findings in patients with known or suspected inflammatory bowel disease *[see Adverse Reactions (6.2)]*.

5.6 Use in Patients with Significant Gastrointestinal Disease

If gastrointestinal obstruction or perforation is suspected, perform appropriate diagnostic studies to rule out these conditions before administering sodium picosulfate, magnesium oxide and anhydrous citric acid *[see Contraindications (4)]*. Use with caution in patients with severe active ulcerative colitis.

5.7 Aspiration

Patients with impaired gag reflex are at risk for regurgitation or aspiration during the administration of sodium picosulfate, magnesium oxide and anhydrous citric acid. Observe these patients during the administration of sodium picosulfate, magnesium oxide and anhydrous citric acid. Use with caution in these patients.

5.8 Risk of Vomiting and Other Gastrointestinal Complications with Ingestion of Undissolved Powder

Each packet must be dissolved in 5 ounces of cold water and administered at separate times according to the dosing regimen *[see Dosage and Administration (2.3,2.4)]* . Ingestion of additional water is important to patient tolerance. Direct ingestion of the undissolved powder may increase the risk of nausea, vomiting, dehydration, and electrolyte disturbances.

6 ADVERSE REACTIONS

The following serious or otherwise important adverse reactions for bowel preparations are described elsewhere in the labeling:
• Serious Fluid and Electrolyte Abnormalities *[see Warnings and Precautions (5.1)]*
• Cardiac Arrhythmias *[see Warnings and Precautions (5.2)]*
• Seizures *[see Warnings and Precautions (5.3)]*
• Use in Patients with Renal Impairment *[see Warnings and Precautions (5.4)]*
• Colonic Mucosal Ulceration, Ischemic Colitis and Ulcerative Colitis *[see Warnings and Precautions (5.5)]*
• Use in Patients with Significant Gastrointestinal Disease *[see Warnings and Precautions (5.6)]*
• Aspiration *[see Warnings and Precautions (5.7)]*
• Risk of Vomiting and Other Gastrointestinal Complications with Ingestion of Undissolved Powder *[see Warnings and Precautions (5.8)]*

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in clinical trials of another drug and may not reflect the rates observed in practice.
In randomized, multicenter, controlled clinical trials, nausea, headache, and vomiting were the most common adverse reactions (>1%) following sodium picosulfate, magnesium oxide and anhydrous citric acid administration. The patients were not blinded to the study drug. Since abdominal bloating, distension, pain/cramping, and watery diarrhea are known to occur in response to colon cleansing preparations, these effects were documented as adverse events in the clinical trials only if they required medical intervention (such as a change in study drug or led to study discontinuation, therapeutic or diagnostic procedures, met the criteria for a serious adverse event), or showed clinically significant worsening during the study that was not in the frame of the usual clinical course, as determined by the investigator.
Sodium picosulfate, magnesium oxide and anhydrous citric acid was compared for colon cleansing effectiveness with a preparation containing two liters (2L) of polyethylene glycol plus electrolytes solution (PEG + E) and two 5 mg bisacodyl tablets, all administered the day before the procedure. Table 1 displays the most common adverse reactions in Study 1 and Study 2 for the sodium picosulfate, magnesium oxide and anhydrous citric acid Split-Dose and Day-Before dosing regimens, respectively, each as compared to the comparator preparation.
Table 1: Treatment-Emergent Adverse Reactions observed in at Least (>1%) of Patients using the Split-Dose Regimen and Day-Before Regimen **

	Study 1: Split-Dose Regimen		**Study 2: Day-Before Regimen**	
Adverse Reaction	**Sodium picosulfate, magnesium oxide and anhydrous citric acid (N=305) n (% = n/N)**	**2L PEG+E* with 2 x 5-mg bisacodyl tablets (N=298) n (% = n/N)**	**Sodium picosulfate, magnesium oxide and anhydrous citric acid (N=296) n (% = n/N)**	**2L PEG+E* with 2 x 5mg bisacodyl tablets (N=302) n (% = n/N)**
Nausea	8 (2.6)	11 (3.7)	9 (3.0)	13 (4.3)
Headache	5 (1.6)	5 (1.7)	8 (2.7)	5 (1.7)
Vomiting	3 (1.0)	10 (3.4)	4 (1.4)	6 (2.0)

* 2L PEG + E = two liters polyethylene glycol plus electrolytes solution.
**abdominal bloating, distension, pain/cramping, and watery diarrhea not requiring an intervention were not collected

Electrolyte Abnormalities

In general, sodium picosulfate, magnesium oxide and anhydrous citric acid was associated with numerically higher rates of abnormal electrolyte shifts on the day of colonoscopy compared to the preparation containing 2L of PEG + E plus two x 5-mg bisacodyl tablets (Table 2). These shifts were transient in nature and numerically similar between treatment arms at the Day 30 visit.
Table 2: Shifts from Normal Baseline to Outside the Normal Range at Day 7 and Day 30

Laboratory Parameter (direction of change)	Visit	Study 1: Split-Dose Regimen		Study 2: Day-Before Regimen	
		Sodium picosulfate, magnesium oxide and anhydrous citric acid	2L PEG+E with 2x 5 mg bisacodyl tablets	Sodium picosulfate, magnesium oxide and anhydrous citric acid	2L PEG+E with 2x 5 mg bisacodyl tablets
		n/N (%)		n/N (%)	
Potassium (low)	Day of Colonoscopy	19/260 (7.3)	11/268 (4.1)	13/274 (4.7)	13/271 (4.8)
	24 to 48 hours	3/302 (1.0)	2/294 (0.7)	3/287 (1.0)	5/292 (1.7)
	Day 7	11/285 (3.9)	8/279 (2.9)	6/276 (2.2)	14/278 (5.0)
	Day 30	11/284 (3.9)	8/278 (2.9)	7/275 (2.5)	8/284 (2.8)
Sodium (low)	Day of Colonoscopy	11/298 (3.7)	3/295 (1.0)	3/286 (1.0)	3/295 (1.0)
	24 to 48 hours	1/303 (0.3)	1/295 (0.3)	1/288 (0.3)	1/293 (0.3)
	Day 7	2/300 (0.7)	1/292 (0.3)	1/285 (0.4)	1/291 (0.3)
	Day 30	2/299 (0.7)	3/291 (1.0)	1/284 (0.4)	1/296 (0.3)
Chloride (low)	Day of Colonoscopy	11/301 (3.7)	1/298 (0.3)	3/287 (1.0)	0/297 (0.0)

	24 to 48 hours	1/303 (0.3)	0/295 (0.0)	2/288 (0.7)	0/293 (0.0)
	Day 7	1/303 (0.3)	3/295 (1.0)	0/285 (0.0)	0/293 (0.0)
	Day 30	2/302 (0.7)	3/294 (1.0)	0/285 (0.0)	0/298 (0.0)
Magnesium (high)	Day of Colonoscopy	34/294 (11.6)	0/294 (0.0)	25/288 (8.7)	1/289 (0.3)
	24 to 48 hours	0/303 (0.0)	0/295 (0.0)	0/288 (0.0)	0/293 (0.0)
	Day 7	0/297 (0.0)	1/291 (0.3)	1/286 (0.3)	1/285 (0.4)
	Day 30	1/296 (0.3)	2/290 (0.7)	0/286 (0.0)	0/290 (0.0)
Calcium (low)	Day of Colonoscopy	2/292 (0.7)	1/286 (0.3)	0/276 (0.0)	2/282 (0.7)
	24 to 48 hours	0/303 (0.0)	0/295 (0.0)	0/288 (0.0)	0/293 (0.0)
	Day 7	0/293 (0.0)	1/283 (0.4)	0/274 (0.0)	0/278 (0.0)
	Day 30	0/292 (0.0)	1/282 (0.4)	0/274 (0.0)	1/283 (0.4)
Creatinine (high)	Day of Colonoscopy	5/260 (1.9)	13/268 (4.9)	12/266 (4.5)	16/270 (5.9)
	24 to 48 hours	1/303 (0.3)	0/295 (0.0)	0/288 (0.0)	0/293 (0.0)
	Day 7	10/264 (0.4)	13/267 (4.8)	10/264 (3.8)	10/265 (3.8)
	Day 30	11/264 (4.2)	14/265 (5.3)	18/264 (6.8)	10/272 (3.7)
eGFR (low)	Day of Colonoscopy	22/221 (10.0)	17/214 (7.9)	26/199 (13.1)	25/224 (11.2)
	24 to 48 hours	76/303 (25.1)	72/295 (24.4)	82/288 (28.5)	62/293 (21.2)
	Day 7	22/223 (10.0)	17/213 (8.0)	11/198 (5.6)	28/219 (12.8)
	Day 30	24/223 (10.8)	21/211 (10.0)	21/199 (10.6)	24/224 (10.7)

Pediatrics
In the pediatric patients aged 9 to 16 years who received sodium picosulfate, magnesium oxide and anhydrous citric acid, the most common adverse reactions (> 5%) were nausea, vomiting, and abdominal pain *[see Clinical Trials (14)]*. Electrolytes abnormalities were observed in pediatric patients similar to those seen in adults. Three patients had abnormally low glucose levels (40 to 47 mg/dL). Two patients received sodium picosulfate, magnesium oxide and anhydrous citric acid and one received the comparator (PEG). The abnormal values occurred at the colonoscopy visit for one patient (sodium picosulfate, magnesium oxide and anhydrous citric acid) and at the 5-day follow up visit for the other two patients (sodium picosulfate, magnesium oxide and anhydrous citric acid and PEG). All three patients were asymptomatic.

6.2 Postmarketing Experience

The following adverse reactions have been identified during post approval use of other oral formulations of sodium picosulfate, magnesium oxide and anhydrous citric acid similar to sodium picosulfate, magnesium oxide and anhydrous citric acid for oral solution. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.
Hypersensitivity: rash, urticaria, purpura, and anaphylaxis *[see Contraindications (4)]*
Gastrointestinal: abdominal pain, diarrhea, fecal incontinence, aphthoid ileal ulcers, ischemic colitis *[see Warnings and Precautions (5.5)]*
Neurologic: generalized tonic-clonic seizures with and without hyponatremia in epileptic patients *[see Warnings and Precautions (5.3)]*.

7 DRUG INTERACTIONS

7.1 Drugs That May Increase Risks of Fluid and Electrolyte Abnormalities

Use caution when prescribing sodium picosulfate, magnesium oxide and anhydrous citric acid for patients with conditions and/or who are taking other drugs that increase the risk for fluid and electrolyte disturbances or may increase the risk of renal impairment, seizures, arrhythmias, or QT prolongation in the setting of fluid and electrolyte abnormalities *[see Warnings and Precautions (5.1, 5.2, 5.3, 5.4)]*.

7.2 Potential for Reduced Drug Absorption

Sodium picosulfate, magnesium oxide and anhydrous citric acid can reduce the absorption of other co-administered drugs *[see Dosage and Administration (2.1)]:*
• Administer oral medications at least one hour before of the start of administration of sodium picosulfate, magnesium oxide and anhydrous citric acid.
• Administer tetracycline and fluoroquinolone antibiotics *[see Drug Interactions (7.3)]*, iron, digoxin, chlorpromazine, and penicillamine at least 2 hours before and not less than 6 hours after administration of sodium picosulfate, magnesium oxide and anhydrous citric acid.

7.3 Antibiotics

Prior or concomitant use of antibiotics with sodium picosulfate, magnesium oxide and anhydrous citric acid for oral solution may reduce efficacy of sodium picosulfate, magnesium oxide and anhydrous citric acid as conversion of sodium picosulfate to its active metabolite BHPM is mediated by colonic bacteria.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary
There are no data with sodium picosulfate, magnesium oxide and anhydrous citric acid use in pregnant women to determine a drug-associated risk of major birth defects, miscarriage, or adverse maternal or fetal outcomes. In an animal reproduction study, no adverse developmental effects were observed in pregnant rats when sodium picosulfate, magnesium oxide, and anhydrous citric acid were administered orally at doses 1.2 times the recommended human dose based on body surface area during organogenesis.
The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2 to 4% and 15 to 20%, respectively.
Data

Animal Data
A reproduction study with sodium picosulfate, magnesium oxide and anhydrous citric acid has been performed in pregnant rats following oral administration of up to 2,000 mg/kg twice daily (about 1.2 times the recommended human dose based on body surface area) during the period of organogenesis. There was no evidence of harm to the fetus due to sodium picosulfate, magnesium oxide and anhydrous citric acid. A reproduction study in rabbits was not adequate, as treatment-related mortalities were observed at all doses. A pre and postnatal development study with sodium picosulfate, magnesium oxide and anhydrous citric acid in rats showed no evidence of any adverse effect on pre and postnatal development at oral doses up to 2,000 mg/kg twice daily (about 1.2 times the recommended human dose based on body surface area). Published reproduction studies with sodium picosulfate in pregnant rats and rabbits during the period of organogenesis did not show evidence of harm to the fetus at doses up to 100 mg/kg (approximately 49 and 98 times, respectively, the recommended human dose of 10 mg sodium picosulfate based on body surface area).

8.2 Lactation

Risk Summary
There are no data on the presence of magnesium oxide or anhydrous citric acid in either human or animal milk, the effects on the breastfed infant, or the effects on milk production. Published data on lactating women indicate that the active metabolite of sodium picosulfate, bis-(*p*-hydroxyphenyl)-pyridyl-2-methane (BHPM) remained below the limit of detection (1 ng/mL) in breast milk after both single and multiple doses of 10 mg/day. There are no data on the effects of sodium picosulfate on the breastfed infant or on milk production. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for sodium picosulfate, magnesium oxide and anhydrous citric acid and any potential adverse effects on the breastfed infant from sodium picosulfate, magnesium oxide and anhydrous citric acid or the underlying maternal condition.

8.4 Pediatric Use

The safety and effectiveness of sodium picosulfate, magnesium oxide and anhydrous citric acid have been established for cleansing of the colon as a preparation for colonoscopy in pediatric patients 9 years of age and older. Use of sodium picosulfate, magnesium oxide and anhydrous citric acid in this age group is supported by evidence from adequate and well-controlled trials of sodium picosulfate, magnesium oxide and anhydrous citric acid in adults and a single, dose-ranging, controlled trial in 78 pediatric patients 9 to 16 years of age *[see Clinical Studies (14)]*. The safety profile of sodium picosulfate, magnesium oxide and anhydrous citric acid in this pediatric population was similar to that seen in adults *[see Adverse Reactions (6.1)]*. Monitor for possible hypoglycemia in pediatric patients, as sodium picosulfate, magnesium oxide and anhydrous citric acid has no caloric substrate.
The safety and effectiveness of sodium picosulfate, magnesium oxide and anhydrous citric acid for oral solution in pediatric patients less than 9 years of age have not been established.

8.5 Geriatric Use

Of the 1,201 patients in clinical trials who received sodium picosulfate, magnesium oxide and anhydrous citric acid, 215 (18%) patients were 65 years of age or older. No overall differences in safety or effectiveness were observed between geriatric patients and younger patients. However, elderly patients are more likely to have decreased hepatic, renal or cardiac function and may be more susceptible to adverse reactions resulting from fluid and electrolyte abnormalities *[see Warnings and Precautions (5.1)]*.

8.6 Renal Impairment

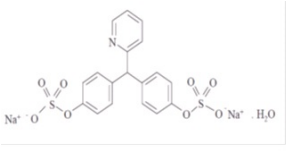
Sodium picosulfate, magnesium oxide and anhydrous citric acid is contraindicated in patients with severe renal impairment (creatinine clearance less than 30 mL/min), as accumulation of magnesium in plasma may occur *[see Contraindications (4)]*. Patients with mild to moderate renal impairment or patients taking concomitant medications that may affect renal function may be at increased risk for renal injury *[see Warnings and Precautions (5.4)]*. Advise these patients of the importance of adequate hydration before, during and after the use of sodium picosulfate, magnesium oxide and anhydrous citric acid *[see Dosage and Administration (2.1)]*. Consider performing baseline and post-colonoscopy laboratory tests (electrolytes, creatinine, and BUN) in these patients.

10 OVERDOSAGE

Overdosage of more than the recommended dose of sodium picosulfate, magnesium oxide and anhydrous citric acid may lead to severe electrolyte disturbances, as well as dehydration and hypovolemia, with signs and symptoms of these disturbances *[see Warnings and Precautions (5.1)]*. Monitor for fluid and electrolyte disturbances and treat symptomatically.

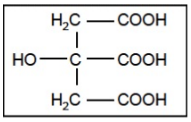
11 DESCRIPTION

Sodium picosulfate, magnesium oxide and anhydrous citric acid for oral solution is available in orange flavor, and is provided in two packets. The contents of each is to be dissolved in 5 ounces of cold water and consumed.
Each packet for orange flavor contains 10 mg sodium picosulfate, USP, 3.5 g magnesium oxide, USP and 12 g anhydrous citric acid, USP. The product also contains the following inactive ingredients: glyceryl behenate, orange flavor (contains dl-alpha-Tocopherol and Maize maltodextrin), potassium bicarbonate and saccharin sodium. The following is a description of the three active ingredients:
Sodium picosulfate is a stimulant laxative.
Sodium Picosulfate
• Chemical name: 4,4'-(2-Pyridylmethylene) diphenyl bis (hydrogen sulfate) disodium salt, monohydrate
• Chemical formula: $C_{18}H_{13}NNa_2O_8S_2.H_2O$
• Molecular weight: 499.4
• Structural formula:



• Sodium Picosulfate

Magnesium citrate, which is formed in solution by the combination of magnesium oxide and anhydrous citric acid, is an osmotic laxative.
Magnesium Oxide
• Chemical name: Magnesium oxide
• Chemical formula: Mg O
• Molecular weight: 40.3
• Structural formula: Mg O
Anhydrous Citric Acid
• Chemical name: 1,2,3-propanetricarboxylic acid, 2-hydroxy-
• Chemical formula: $C_6H_8O_7$
• Molecular weight: 192.13
• Structural formula:



Anhydrous citric acid

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Sodium picosulfate is hydrolyzed by colonic bacteria to form an active metabolite: bis-(p-hydroxy-phenyl)-pyridyl-2-methane, BHPM, which acts directly on the colonic mucosa to stimulate colonic peristalsis.
Magnesium oxide and citric acid react to create magnesium citrate in solution, which is an osmotic agent that causes water to be retained within the gastrointestinal tract.

12.2 Pharmacodynamics

The stimulant laxative activity of sodium picosulfate together with the osmotic laxative activity of magnesium citrate produces a purgative effect which, when ingested with additional fluids, produces watery diarrhea.

12.3 Pharmacokinetics

Absorption
After administration of the first packet of sodium picosulfate, magnesium oxide and anhydrous citric acid in 16 healthy subjects, mean maximum concentration (C_{max}) for picosulfate of 2.3 ± 1.4 ng/mL was reached at 2 hours. After administration of 2 packets of sodium picosulfate, magnesium oxide and anhydrous citric acid separated by 6 hours, picosulfate reached the mean C_{max} of 3.2 ± 2.6 ng/mL at approximately 7 hours (T_{max}). In the same study, baseline uncorrected magnesium reached a C_{max} of approximately 1.9 mEq/L, which occurred at 10 hours post first packet administration (T_{max}). This represents an approximately 20% increase from the baseline.
Distribution
The apparent volume of distribution (V/F) for picosulfate was 4,199 liters in healthy adults.
Metabolism and Elimination
Sodium picosulfate, which is a prodrug, is converted to its active metabolite, BHPM, by colonic bacteria. Plasma concentration of the free BHPM were low, and below the lower limit of quantification (0.1 ng/mL) in 13 out of 16 subjects studied. The fraction of the sodium picosulfate dose excreted unchanged in urine was 0.2%. In urine, the majority of excreted BHPM was in the glucuronide- conjugated form. The terminal half-life of sodium picosulfate was 7.4 hours. The apparent clearance (CL/F) of picosulfate was 629 L/h.
Use in Specific Populations
Pediatric Patients
Pharmacokinetics of picosulfate was studied in pediatric patients aged from 9 to 16 years old.
For picosulfate, the apparent clearance is from 316 to 409 L/h. The corresponding estimates for apparent volume of distribution are from 2457 to 3935 liters. The derived half-life using these model estimates would be 7 hours. The picosulfate reached the mean C_{max} of 3.5 ± 2.1 ng/mL at approximately 6 to 7 hours (T_{max})
The baseline uncorrected mean serum magnesium concentration was 2.02 mEq/L at 10 hours after the first dose of sodium picosulfate, magnesium oxide and anhydrous citric acid and ranged from 1.7 to 2.46 mEq/L in pediatric patients from 9 to 16 years of age.
Drug Interaction Studies
In an *in vitro* study using human liver microsomes, sodium picosulfate did not inhibit the major CYP enzymes (CYP 1A2, 2B6, 2C8, 2C9, 2C19, 2D6 and 3A4/5) evaluated. Based on an *in vitro* study using freshly isolated hepatocyte culture, sodium picosulfate is not an inducer of CYP1A2, CYP2B6 or CYP3A4/5.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Long-term studies in animals to evaluate carcinogenic potential or studies to evaluate mutagenic potential have not been performed with sodium picosulfate, magnesium oxide and anhydrous citric acid. Sodium picosulfate was not mutagenic in the Ames test, the mouse lymphoma assay and the mouse bone marrow micronucleus test.
In an oral fertility study in rats, sodium picosulfate, magnesium oxide and anhydrous citric acid did not cause any significant adverse effect on male or female fertility parameters up to a maximum dose of 2,000 mg/kg twice daily (about 1.2 times the recommended human dose based on the body surface area).

14 CLINICAL STUDIES

Adults
The colon cleansing efficacy of sodium picosulfate, magnesium oxide and anhydrous citric acid was evaluated for non-inferiority against a comparator in two randomized, investigator-blinded, active-controlled, multicenter US trials in adult patients scheduled to have an elective colonoscopy. In all, 1,195 adult patients were included in the primary efficacy analysis: 601 from Study 1, and 594 from Study 2. Patients ranged in age from 18 to 80 years (mean age 56 years); 61% were female and 39% male. Self-identified race was distributed as follows: 90% White, 10% Black, and less than 1% other. Of these, 3% self-identified their ethnicity as Hispanic or Latino.
Patients randomized to sodium picosulfate, magnesium oxide and anhydrous citric acid in the two studies were treated with one of two dosing regimens:
• In Study 1, sodium picosulfate, magnesium oxide and anhydrous citric acid was given by “Split-Dose” (evening before and day of) dosing, where the first packet was taken the evening before the colonoscopy (between 5:00 and 9:00 PM), followed by five (5) 8-ounce glasses of clear liquid, and the second packet was taken the morning of the

colonoscopy (at least 5 hours prior to but no more than 9 hours prior to colonoscopy), followed by three (3) 8-ounce glasses of clear liquid.
• In Study 2, sodium picosulfate, magnesium oxide and anhydrous citric acid was given by "Day-Before" (afternoon/evening before only) dosing, where both packets were taken separately on the day before the colonoscopy, with the first packet taken in the afternoon (between 4:00 and 6:00 PM), followed by five (5) 8-ounce glasses of clear liquid, and the second packet taken in the late evening (approximately 6 hours later, between 10:00 PM and 12:00 AM), followed by three (3) 8-ounce glasses of clear liquid. The comparator was a preparation containing two liters of polyethylene glycol plus electrolytes solution (PEG + E) and two 5-mg bisacodyl tablets, administered the day before the procedure. All patients in both the sodium picosulfate, magnesium oxide and anhydrous citric acid and comparator groups were limited to a clear liquid diet on the day before the procedure (24 hours before).
The primary efficacy endpoint was the proportion of patients with successful colon cleansing, as assessed by blinded colonoscopists using the Aronchick Scale. The Aronchick scale is a tool used to assess overall colon cleansing. Successful colon cleansing was defined as bowel preparations with >90% of the mucosa seen 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.
In both studies, sodium picosulfate, magnesium oxide and anhydrous citric acid was non-inferior to the comparator. In addition, sodium picosulfate, magnesium oxide and anhydrous citric acid provided by Split-Dose dosing met the pre-specified criteria for superiority to the comparator for colon cleansing in Study 1. The comparator in that study was administered entirely on the day prior to colonoscopy. See Tables 3 and 4 below.

Table 3: Proportion of Patients with Successful Colon Cleansing in Study 1 Split-Dose Regimen

Sodium picosulfate, magnesium oxide and anhydrous citric acid Split-Dose Regimen	**2L PEG+E* with 2 x 5-mg bisacodyl tablets**	**Difference between treatment groups**	
% (n/N)	**% (n/N)**	**Difference**	**95% CI**
84 % (256/304)	74.4 % (221/297)	10%	(3.4%, 16.2%) †

* 2L PEG + E = two liters polyethylene glycol plus electrolytes solution.
† Non-inferior and superior 2L PEG+E with 2 x 5 mg bisacodyl tablets

Table 4: Proportion of Patients with Successful Colon Cleansing in Study 2 Day-Before Regimen

Sodium picosulfate, magnesium oxide and anhydrous citric acid Day-Before Regimen	**2L PEG+E* with 2 x 5mg bisacodyl tablets**	**Difference between treatment groups**	
% (n/N)	**% (n/N)**	**Difference**	**95% CI**
83% (244/294)	80% (239/300)	3 %	(-2.9%, 9.6%) ‡

* 2L PEG + E = two liters polyethylene glycol plus electrolytes solution.
‡ Non-inferior

Pediatric Patients 9 Years of Age and Older
Sodium picosulfate, magnesium oxide and anhydrous citric acid was evaluated for colon cleansing in a randomized, assessor-blind, multicenter, dose-ranging, active-controlled study in 78 pediatric patients 9 years to 16 years of age. The majority of patients were female (68%), white (91%), and of non-Hispanic or non-Latino ethnicity (95%). The mean age was 12 years of age. All 78 patients were included in the primary efficacy analysis.
Patients aged 9 years to 12 years were randomized into 3 arms (1:1:1):
• Sodium picosulfate, magnesium oxide and anhydrous citric acid one-half packet administered as two doses
• Sodium picosulfate, magnesium oxide and anhydrous citric acid one-packet administered as two doses
• comparator (oral PEG-based solution per local standard of care).
Patients aged 13 years to 16 years were randomized into 2 arms (1:1):
• Sodium picosulfate, magnesium oxide and anhydrous citric acid one-packet administered as two doses
• comparator (oral PEG-based solution per local standard of care)
Patients randomized to sodium picosulfate, magnesium oxide and anhydrous citric acid had two options for dosing, as determined by the investigator. The "Split Dose" regimen was the preferred method and the "Day Before" regimen was the alternative method if the "Split Dose" was not appropriate.
"Split-Dose" Regimen: (evening before and day of) dosing, where the first dose was taken the evening before the colonoscopy (between 5:00 and 9:00 PM), followed by five (5) 8-ounce glasses of clear liquid, and the second dose was taken the morning of the colonoscopy (at least 5 hours prior to but no more than 9 hours prior to colonoscopy), followed by three (3) 8-ounce glasses of clear liquid.
"Day-Before" Regimen: (afternoon/evening before only) dosing, where both doses were taken separately on the day before the colonoscopy, with the first dose taken in the afternoon (between 4:00 and 6:00 PM), followed by five (5) 8-ounce glasses of clear liquid, and the second dose taken in the late evening (approximately 6 hours later, between 10:00 PM and 12:00 AM), followed by three (3) 8-ounce glasses of clear liquid.
All patients randomized to sodium picosulfate, magnesium oxide and anhydrous citric acid were limited to a clear liquid diet on the day before the procedure. Those who received the comparator were given dietary instructions per the trial site's standard of care.
The primary efficacy endpoint was the proportion of patients with successful colon cleansing as defined as a rating of either "Excellent" (> 90% of mucosa seen, mostly liquid stool, minimal suctioning needed for adequate visualization) or "Good" (> 90% of mucosa seen, mostly liquid stool, significant suctioning needed for adequate visualization) using the Aronchick scale, as assessed by blinded colonoscopists.
The sodium picosulfate, magnesium oxide and anhydrous citric acid regimen of one-half packet administered as two doses did not demonstrate comparable efficacy to the comparator, PEG, in patients 9 to 12 years of age and is not a recommended dosage regimen *[see Dosage and Administration (2)]*.
The sodium picosulfate, magnesium oxide and anhydrous citric acid regimen of one packet administered as two doses demonstrated successful colon cleansing in both the 9 to 12 year age group and the 13 to 16 year age group. The efficacy rates were similar to those observed in the PEG groups, as shown in Table 5.

Table 5. Proportion of Patients 9 to 16 Years of Age with Successful Colon Cleansing [1]

	Sodium picosulfate, magnesium oxide and anhydrous citric acid One Packet Administered as Two Doses either as Split Dose or Day Before Regimen [2]		**PEG Comparator [3]**	
	% (n/N)	**95% CI**	**% (n/N)**	**95%**

				CI
Age 9-12	88% (14/16)	(62, 98)	81% (13/16)	(54, 96)
Age 13-16	81% (13/16)	(54, 96)	86% (12/14)	(57, 98)

[1]Successful colon cleansing as defined by “Excellent” or “Good” on the Aronchick scale
[2]Of the 32 patients, 9 received the Split Dose Regimen and 23 the Day Before Regimen
[3]Oral PEG-based preparation was used in the study as per standard of care

16 HOW SUPPLIED/STORAGE AND HANDLING

How Supplied
Sodium Picosulfate, Magnesium Oxide and Anhydrous Citric Acid for Oral Solution is supplied in a carton containing 2 packets, each holding 16.1 grams of powder in orange flavor, along with a pre-marked dosing cup. Each packet for orange flavor contains 10 mg of sodium picosulfate, 3.5 g of magnesium oxide and 12 g anhydrous citric acid. The excipients for orange flavor contains glyceryl behenate, orange flavor, potassium bicarbonate and saccharin sodium. The orange flavor contains dl-alpha-Tocopherol and maize maltodextrin.
Orange flavor:
Kit, 2 packets and cup NDC 31722-874-16
Storage
Store at 20º to 25ºC (68º to 77ºF) [see USP Controlled Room Temperature].

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Medication Guide and Instructions for Use).
Instruct patients:
• Each packet must be dissolved in 5 ounces of cold water and administered according to the dosing regimen. Direct ingestion of the undissolved powder may increase the risk of nausea, vomiting, dehydration, and electrolyte disturbances *[see Warnings and Precautions (5.8)]*.
• Two doses (one packet per dose) of sodium picosulfate, magnesium oxide and anhydrous citric acid for oral solution are required for a complete preparation for colonoscopy either as a Split-Dose (preferred) or Day-Before dosing regimen.
• Not to take other laxatives while they are taking sodium picosulfate, magnesium oxide and anhydrous citric acid for oral solution.
• Do not eat solid food or dairy and do not drink anything colored red or purple.
• Do not drink alcohol.
• Do not take oral medications within one hour of starting sodium picosulfate, magnesium oxide and anhydrous citric acid for oral solution.
• If taking tetracycline or fluoroquinolone antibiotics, iron, digoxin, chlorpromazine, or penicillamine, take these medications at least 2 hours before and not less than 6 hours after administration of sodium picosulfate, magnesium oxide and anhydrous citric acid for oral solution.
• To follow the directions in the *Instructions for Use,* for either the Split-Dose or the Day-Before regimen, as prescribed.
• To consume additional fluids after each dose of sodium picosulfate, magnesium oxide and anhydrous citric acid for oral solution.
• To delay the second dose of sodium picosulfate, magnesium oxide and anhydrous citric acid for oral solution, if severe bloating, distention, or abdominal pain occurs following the first dose until the symptoms resolve.
• To contact their healthcare provider if they develop significant vomiting or signs of dehydration after taking sodium picosulfate, magnesium oxide and anhydrous citric acid for oral solution or if they experience altered consciousness (e.g. confusion, delirium, loss of consciousness) or seizures *[see Warnings and Precautions (5.1, 5.3, 5.4)]*.

Manufactured for:
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Piscataway, NJ 08854

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MEDICATION GUIDE

Sodium Picosulfate, Magnesium Oxide and Anhydrous Citric Acid for Oral Solution
(SOW dee um pye ko SUL fate, mag NEE zhum OKS ide & SI trik AS id)

Read and understand this Medication Guide and the Instructions for Use that come with sodium picosulfate, magnesium oxide and anhydrous citric acid for oral solution **at least 2 days before** your colonoscopy and again before you start taking sodium picosulfate, magnesium oxide and anhydrous citric acid for oral solution.
What is the most important information I should know about sodium picosulfate, magnesium oxide and anhydrous citric acid for oral solution?
Sodium picosulfate, magnesium oxide and anhydrous citric acid for oral

solution and other bowel preparations can cause serious side effects, including:
Serious loss of body fluid (dehydration) and changes in blood salts (electrolytes) in your blood. These changes can cause:
• abnormal heartbeats that can cause death.
• seizures . This can happen even if you have never had a seizure.
• kidney problems.
Your chance of having fluid loss and changes in blood salts with sodium picosulfate, magnesium oxide and anhydrous citric acid for oral solution is higher if you:
• have heart problems
• have kidney problems
• take water pills or non-steroidal anti-inflammatory drugs (NSAIDS)
Tell your healthcare provider right away if you have any of these symptoms of a loss of too much body fluid (dehydration) while taking sodium picosulfate, magnesium oxide and anhydrous citric acid for oral solution:
• vomiting • dizziness
• urinating less often than normal • headache

See "What are the possible side effects of sodium picosulfate, magnesium oxide and anhydrous citric acid for oral solution?" for more information about side effects.
What is sodium picosulfate, magnesium oxide and anhydrous citric acid for oral solution?
Sodium picosulfate, magnesium oxide and anhydrous citric acid for oral solution is a prescription medicine used by adults and children 9 years of age and older, to clean the colon before a colonoscopy. Sodium picosulfate, magnesium oxide and anhydrous citric acid for oral solution cleans your colon by causing you to have diarrhea. Cleaning your colon helps your healthcare provider see the inside of your colon more clearly during your colonoscopy.
It is not known if sodium picosulfate, magnesium oxide and anhydrous citric acid for oral solution is safe and effective in children under 9 years of age.
Do not take sodium picosulfate, magnesium oxide and anhydrous citric acid for oral solution if your healthcare provider has told you that you have:
• serious kidney problems.
• a blockage in your intestine (bowel obstruction).
• an opening in the wall of your stomach or intestines (bowel perforation).
• a very dilated intestine (toxic megacolon).
• problems with the emptying of food and fluid from your stomach (gastric retention).
• an allergy to any of the ingredients in sodium picosulfate, magnesium oxide and anhydrous citric acid for oral solution. See the end of this Medication Guide for a complete list of ingredients in sodium picosulfate, magnesium oxide and anhydrous citric acid for oral solution.
Before taking sodium picosulfate, magnesium oxide and anhydrous citric acid for oral solution, tell your healthcare provider about all of your medical conditions, including if you:
• have problems with serious loss of body fluid (dehydration) and changes in blood salts (electrolytes).
• have a history of seizures or take medicines for seizures.
• are withdrawing from drinking alcohol or from taking benzodiazepines.
• have low blood salt (sodium) level.
• have kidney problems or take medicines for kidney problems.
• have heart problems.
• have stomach or bowel problems including ulcerative colitis.
• have problems with swallowing or gastric reflux.
• are pregnant. It is not known if sodium picosulfate, magnesium oxide and anhydrous citric acid for oral solution will harm your unborn baby. Talk to your healthcare provider if you are pregnant.
• are breastfeeding or plan to breastfeed. It is not known if sodium picosulfate, magnesium oxide and anhydrous citric acid passes into your breast milk. You and your healthcare provider should decide if you will take sodium picosulfate, magnesium oxide and anhydrous citric acid for oral solution while breastfeeding.
Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. Sodium picosulfate, magnesium oxide and anhydrous citric acid for oral solution may affect how other medicines work, and other medicines may affect how sodium picosulfate, magnesium oxide and anhydrous citric acid for oral solution works. Medicines taken by mouth may not be absorbed properly when taken within 1 hour before the start of sodium picosulfate, magnesium oxide and anhydrous citric acid for oral solution.
Especially tell your healthcare provider if you take:
• medicines for blood pressure or heart problems.
• medicines for kidney problems.
• medicines for seizures.
• water pills (diuretics).
• nonsteroidal anti-inflammatory medicines (pain medicines).
• medicines for depression or mental health problems.
• laxatives. **Do not** take other laxatives while taking sodium picosulfate, magnesium oxide and anhydrous citric acid for oral solution.
The following medicines should be taken at least 2 hours before starting sodium picosulfate, magnesium oxide and anhydrous citric acid for oral solution and not less than 6 hours after taking sodium picosulfate, magnesium oxide and anhydrous citric acid for oral solution:
• tetracycline • digoxin (Lanoxin)
• fluoroquinolone antibiotics • chlorpromazine
• iron • penicillamine (Cuprimine, Depen)
Ask your healthcare provider or pharmacist for a list of these medicines if you are not sure if you are taking the medicines listed above.
Know the medicines you take. Keep a list of them to show your healthcare provider and pharmacist when you get a new medicine.
How should I take sodium picosulfate, magnesium oxide and anhydrous citric acid for oral solution?
See the Instructions for Use for dosing instructions. You must read, understand, and follow these instructions to take sodium picosulfate, magnesium oxide and anhydrous citric acid for oral solution the right way .
• Take sodium picosulfate, magnesium oxide and anhydrous citric acid for oral solution exactly as your healthcare provider tells you to take it.
• **Do not take sodium picosulfate, magnesium oxide and anhydrous citric acid powder that has not been mixed with water. It may increase your risk of nausea, vomiting, and fluid loss (dehydration).**
• Each packet of sodium picosulfate, magnesium oxide and anhydrous citric acid powder must be mixed with 5 ounces of **cold water** before drinking.
• It is important for you to drink the additional prescribed amount of clear liquids listed in the Instructions for Use to prevent fluid loss (dehydration).
• Two doses of sodium picosulfate, magnesium oxide and anhydrous citric acid for oral solution are required for a complete colonoscopy preparation. 1 packet of sodium picosulfate, magnesium oxide and anhydrous citric acid for oral solution equals 1 dose.
• There are 2 different methods for taking sodium picosulfate, magnesium oxide and anhydrous citric acid for oral solution. **It is better** (preferred) to use the **Split-Dose** method. If you cannot do the Split-Dose method, you can take sodium picosulfate, magnesium oxide and anhydrous citric acid for oral solution using the **Day-Before** method. See the Instructions for Use for more information.
• All people taking sodium picosulfate, magnesium oxide and anhydrous citric acid for oral solution should follow these general instructions starting 1 day **before** your colonoscopy:
o only drink clear liquids all day and the next day until 2 hours before your colonoscopy.

Stop drinking all fluids at least 2 hours before the colonoscopy.
o after taking sodium picosulfate, magnesium oxide and anhydrous citric acid for oral solution if you have any bloating or feeling like your stomach is upset, wait to take your second dose until your stomach feels better.
• While taking sodium picosulfate, magnesium oxide and anhydrous citric acid for oral solution, do not:
o take any other laxatives.
o take any medicines by mouth (oral) within 1 hour of starting sodium picosulfate, magnesium oxide and anhydrous citric acid for oral solution.
o eat solid foods, dairy such as milk, or alcohol while taking sodium picosulfate, magnesium oxide and anhydrous citric acid for oral solution and until after your colonoscopy.
o eat or drink anything colored red or purple.
Contact your healthcare provider right away if after taking sodium picosulfate, magnesium oxide and anhydrous citric acid for oral solution you have severe vomiting, signs of dehydration, changes in consciousness such as feeling confused, delirious or fainting (loss of consciousness) or seizures after taking sodium picosulfate, magnesium oxide and anhydrous citric acid for oral solution.
What are the possible side effects of sodium picosulfate, magnesium oxide and anhydrous citric acid for oral solution?
Sodium picosulfate, magnesium oxide and anhydrous citric acid for oral solution can cause serious side effects, including:
• See **"What is the most important information I should know about sodium picosulfate, magnesium oxide and anhydrous citric acid for oral solution?"**
• **Changes in certain blood tests.** Your healthcare provider may do blood tests after you take sodium picosulfate, magnesium oxide and anhydrous citric acid for oral solution to check your blood for changes. Tell your healthcare provider if you have any symptoms of too much fluid loss, including:

o vomiting

o nausea

o bloating

o dizziness
o stomach-area (abdomen) cramping

o urinate less than usual

o trouble drinking clear liquids

o trouble swallowing
o seizures

o heart problems
• Ulcers of the bowel or bowel problems (ischemic colitis). Tell your healthcare provider right away if you have severe stomach-area (abdomen) pain or rectal bleeding.
The most common side effects of sodium picosulfate, magnesium oxide and anhydrous citric acid for oral solution in adults include:
• nausea • headache • vomiting
The most common side effects of sodium picosulfate, magnesium oxide and anhydrous citric acid for oral solution in children 9 to 16 years of age include:
• nausea • vomiting • stomach area (abdominal) pain
These are not all the possible side effects of sodium picosulfate, magnesium oxide and anhydrous citric acid for oral solution.
Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.
How should I store sodium picosulfate, magnesium oxide and anhydrous citric acid for oral solution?
• Store sodium picosulfate, magnesium oxide and anhydrous citric acid for oral solution at room temperature between 68ºF to 77ºF (20ºC to 25ºC).
Keep sodium picosulfate, magnesium oxide and anhydrous citric acid for oral solution and all medicines out of the reach of children.
General information about the safe and effective use of sodium picosulfate, magnesium oxide and anhydrous citric acid for oral solution.
Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use sodium picosulfate, magnesium oxide and anhydrous citric acid for oral solution for a condition for which it was not prescribed. Do not give sodium picosulfate, magnesium oxide and anhydrous citric acid for oral solution to other people, even if they are going to have the same procedure you are. It may harm them. You can ask your pharmacist or healthcare provider for information about sodium picosulfate, magnesium oxide and anhydrous citric acid for oral solution that is written for health professionals.
What are the ingredients in sodium picosulfate, magnesium oxide and anhydrous citric acid for oral solution?
Sodium picosulfate, magnesium oxide and anhydrous citric acid for oral solution comes in a carton containing 2 packets, each containing 16.1 grams of powder in orange flavor, along with a pre-marked dosing cup.
Active ingredients: sodium picosulfate, magnesium oxide and anhydrous citric acid
Inactive ingredients: glyceryl behenate, orange flavor (contains dl-alpha-Tocopherol and Maize maltodextrin), potassium bicarbonate and saccharin sodium.
For more information, call Annora Pharma Private Limited at 1-866-495-1995.
This Medication Guide has been approved by the U.S. Food and Drug Administration

Medication guide available at http://camberpharma.com/medication-guides

CAMBER®
PHARMACEUTICALS, INC.

Manufactured for:
Camber Pharmaceuticals, Inc.,
Piscataway, NJ 08854

By: Annora Pharma Pvt. Ltd.

Sangareddy - 502313, Telangana, India.

Revised: 08/2022

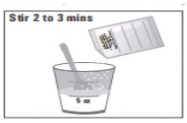
INSTRUCTIONS FOR USE
Sodium Picosulfate, Magnesium Oxide and Anhydrous Citric Acid for Oral Solution
(SOW dee um pye ko SUL fate, mag NEE zhum OKS ide & SI trik AS id)
Before Taking sodium picosulfate, magnesium oxide and anhydrous citric acid for oral solution
There are 2 different methods for taking sodium picosulfate, magnesium oxide and anhydrous citric acid for oral solution. It is better (preferred) to use the **Split-Dose** method. If you cannot use the Split-Dose method, you can take sodium picosulfate, magnesium oxide and anhydrous citric acid for oral solution using the **Day-Before** method. Talk with your healthcare provider before you start if you have any questions.
• Start a clear-liquid diet **theday before** your colonoscopy. Only drink clear liquids all day the day before your colonoscopy, and the next day until 2 hours before your colonoscopy. Stop drinking all fluids at least 2 hours before the colonoscopy.
• You **must** drink enough clear liquids to keep your body hydrated for the entire day before your colonoscopy.
Important:
See **Table 1** for a list of liquids you can drink for your clear liquid diet.

Table 1: List of liquids for the clear-liquid diet
- Water (plain or flavored)
- Black coffee or tea (**no** milk, cream, soy, or nondairy creamer)
- Clear broth or bouillon
- Sports drinks (**not red or purple**)
- Clear juices without pulp (such as apple juice or **white** grape juice)
- Ginger ale and other sodas (**not red or purple**)
- Plain jello (**not red or purple**)
- Frozen juice bars (**not red or purple**)

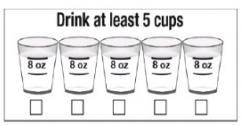
Important:
See **Table 2** for the items you **cannot** eat or drink before your colonoscopy.

Table 2: Do not eat or drink these items during the clear-liquid diet
- **no** solid foods
- **no** alcohol
- **no** dairy or non-dairy types of milk or cream
- **no** soy milk or drinks
- **no** juices with pulp
- **no** red or purple drinks
- **no** other liquids that you cannot see through

Important:
• Sodium picosulfate, magnesium oxide and anhydrous citric acid is a powder that must be added to **cold water** right before use.
• **Do not** prepare the solution ahead of time. Take sodium picosulfate, magnesium oxide and anhydrous citric acid for oral solution right after it is prepared.
• **Do not** swallow the powder without adding it to **cold water** first.
Split-Dose Instructions
Dose 1 – In the evening the day before your colonoscopy (sometime between 5:00 PM to 9:00 PM)
• **Fill** the dosing cup with **cold water** up to the lower line (5 ounces).
Note: Do not use any other clear liquid to mix sodium picosulfate, magnesium oxide and anhydrous citric acid for oral solution.



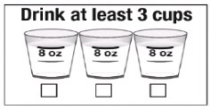
• **Open 1 packet of sodium picosulfate, magnesium oxide and anhydrous citric acid** and add all of the powder to the cold water in the dosing cup. To open the sodium picosulfate, magnesium oxide and anhydrous citric acid packet cut along the dotted line at the top of the packet using scissors.
• **Stir for 2 to 3 minutes** to dissolve the powder. Use a clock or timer The dosing cup may feel slightly warm as the powder dissolves. This is normal.
• **Drink all** the solution right away.
Note: Sodium picosulfate, magnesium oxide and anhydrous citric acid powder should be mixed in cold water immediately before use. Do not prepare the solution ahead of time or store the solution for later use. Do not refrigerate or add ice to the solution.
• Follow this sodium picosulfate, magnesium oxide and anhydrous citric acid for oral solution dose by drinking **at least five 8 ounce cups of clear liquid** (using the upper line on the dosing cup provided- **see figure below**) over the next 5 hours.



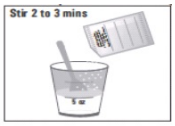
• After taking sodium picosulfate, magnesium oxide and anhydrous citric acid for oral

solution if you have any bloating or feeling like your stomach is upset, wait to take your second dose until your stomach feels better.
Important: See **Table 1** for a list of acceptable clear liquids.
Dose 2 - In the morning of colonoscopy (approximately 5 hours prior to colonoscopy)
Note: Do not eat solid food. Drink only clear liquids.
• **Fill** the dosing cup with **cold water** up to the lower line (5 ounces).
Note: Do not use any other clear liquid to mix sodium picosulfate, magnesium oxide and anhydrous citric acid for oral solution.

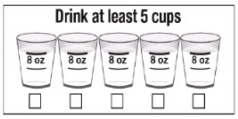
• **Open the second packet of sodium picosulfate, magnesium oxide and anhydrous citric acid** and add all the powder to the cold water in the dosing cup.
• **Stir for 2 to 3 minutes** to dissolve the powder. Use a clock or timer.
• **Drink all** the solution right away.
Note: Sodium picosulfate, magnesium oxide and anhydrous citric acid powder should be mixed in cold water immediately before use. Do not prepare the solution ahead of time or store the solution for later use. Do not refrigerate or add ice to the solution.
• Follow this sodium picosulfate, magnesium oxide and anhydrous citric acid for oral solution dose by drinking **at least three 8 ounce cups of clear liquids** (using the upper line on the dosing cup **-see figure below**). You can continue to drink clear liquids up to 2 hours before the colonoscopy.



Important: See **Table 1** for a list of acceptable clear liquids.
Stop drinking clear liquids 2 hours before your colonoscopy, or as advised by your healthcare provider.
Day-Before
Instructions
Dose 1 – In the afternoon or early evening the day before your colonoscopy (sometime between 4:00 PM to 6:00 PM)
• **Fill** the dosing cup with **cold water** up to the lower line (5 ounces).
Note: Do not use any other clear liquid to mix sodium picosulfate, magnesium oxide and anhydrous citric acid for oral solution.

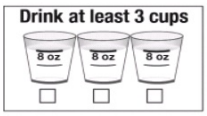


• **Open 1 packet of sodium picosulfate, magnesium oxide and anhydrous citric acid** and add all the powder to the cold water in the dosing cup. To open the sodium picosulfate, magnesium oxide and anhydrous citric acid packet cut along the dotted line at the top of the packet using scissors.
• **Stir for 2 to 3 minutes** to dissolve the powder. Use a clock or timer. The dosing cup may feel slightly warm as the powder dissolves. This is normal.
• **Drink all** the solution right away.
Note: Sodium picosulfate, magnesium oxide and anhydrous citric acid powder should be mixed in cold water immediately before use. Do not prepare the solution ahead of time or store the solution for later use. Do not refrigerate or add ice to the solution.
• Follow this sodium picosulfate, magnesium oxide and anhydrous citric acid for oral solution dose by drinking **at least five 8 ounce cups of clear liquids** (using the upper line on the dosing cup **-see figure below**) over the next 5 hours.



After taking sodium picosulfate, magnesium oxide and anhydrous citric acid for oral solution if you have any bloating or feeling like your stomach is upset, wait to take your second dose until your stomach feels better.
Important: See **Table 1** for a list of acceptable clear liquids.
Dose 2 – In the evening before your colonoscopy (sometime between 10:00 PM to 12:00 AM):
Note: Do not eat solid food. Drink only clear liquids.

• **Fill** the dosing cup with **cold water** up to the lower line (5 ounces).
Note: Do not use any other clear liquid to mix sodium picosulfate, magnesium oxide and anhydrous citric acid for oral solution.
• **Open the second packet of sodium picosulfate, magnesium oxide and anhydrous citric acid** and add all of the powder to the cold water in the dosing cup.
Stir for 2 to 3 minutes to dissolve the powder. Use a clock or timer.
• **Drink all** of this solution right away.
Note: Sodium picosulfate, magnesium oxide and anhydrous citric acid powder should be mixed in cold water immediately before use. Do not prepare the solution ahead of time or store the solution for later use. Do not refrigerate or add ice to the solution.
• Follow this sodium picosulfate, magnesium oxide and anhydrous citric acid for oral solution dose by drinking **at least three 8 ounce cups of clear liquids** (using the upper line on the dosing cup **-see figure below**) over the next 5 hours.

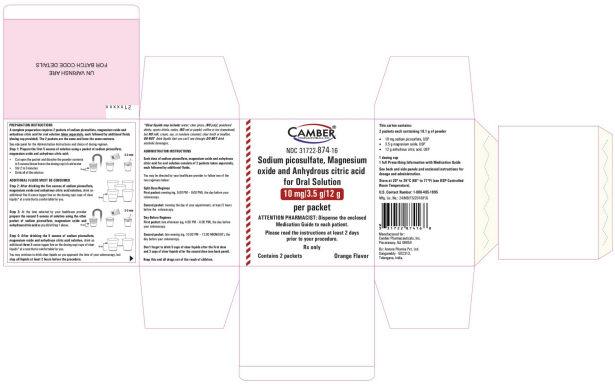


Important: See **Table 1** for a list of acceptable clear liquids.
Stop drinking clear liquids 2 hours before your colonoscopy, or as advised by your healthcare provider.
This Instructions for Use has been approved by the U.S. Food and Drug Administration.

Revised: 08/2022

PACKAGE LABEL.PRINCIPAL DISPLAY PANEL

Sodium Picosulfate, Mgo and Anhydrous Citric Acid Container Carton Label



Sodium Picosulfate, Mgo and Anhydrous Citric Acid Sachet Label

SODIUM PICOSULFATE, MAGNESIUM OXIDE AND ANHYDROUS CITRIC ACID

sodium picosulfate, magnesium oxide and anhydrous citric acid powder, metered

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:31722-874
Route of Administration	ORAL		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
SODIUM PICOSULFATE (UNII: LR57574HN8) (DEACETYLBISACODYL - UNII:R09078E41Y)	SODIUM PICOSULFATE	10 mg in 16.1 g
MAGNESIUM OXIDE (UNII: 3A3U0GI71G) (MAGNESIUM CATION - UNII:T6V3LHY838)	MAGNESIUM CATION	3.5 g in 16.1 g
ANHYDROUS CITRIC ACID (UNII: XF417D3PSL) (ANHYDROUS CITRIC ACID - UNII:XF417D3PSL)	ANHYDROUS CITRIC ACID	12 g in 16.1 g

Inactive Ingredients

Ingredient Name	Strength
GLYCERYL DIBEHENATE (UNII: R8WTH25YS2)	
POTASSIUM BICARBONATE (UNII: HM5Z15LEBN)	
SACCHARIN SODIUM (UNII: SB8ZUX40TY)	
MALTODEXTRIN (UNII: 7CVR7L4A2D)	
.ALPHA.-TOCOPHEROL, DL- (UNII: 7QWA1RIO01)	

Product Characteristics

Color		**Score**	
Shape		**Size**	
Flavor	ORANGE	**Imprint Code**	
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:31722-874-16	2 in 1 CARTON	07/18/2022	
1		16.1 g in 1 PACKET; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA212789	07/18/2022	

Labeler - Camber Pharmaceuticals, Inc. (826774775)

Establishment

Name	Address	ID/FEI	Business Operations
Annora Pharma Private Limited		650980746	manufacture(31722-874)

Revised: 8/2022 Camber Pharmaceuticals, Inc.