HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use CLENPIQ® safely and effectively. See full prescribing information for CLENPIQ.

CLENPIQ® (sodium picosulfate, magnesium oxide, and anhydrous citric acid) oral solution
Initial U.S. Approval: 2012

----------RECENT MAJOR CHANGES----------

Indications and Usage (1)	08/2019
Dosage and Administration (2.1)	10/2019
Dosage and Administration (2.2)	08/2019, 10/2019
Dosage and Administration, Day-Before Dosage Regimen (2.3) Removed	10/2019
Warnings and Precautions (5.1)	08/2019

----------INDICATIONS AND USAGE----------

CLENPIQ® 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----------

Administration:

- CLENPIQ is ready to drink. It does not need to be diluted prior to administration. One bottle of CLENPIQ is equivalent to one dose. (2.1)
- Two doses of CLENPIQ are required for a complete preparation for colonoscopy as a Split-Dose regimen. (2.1)
- Additional liquids must be consumed after every dose of CLENPIQ: five or more 8-ounce cups of clear liquids after the first dose and four or more 8-ounce cups of clear liquids after the second dose. (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 CLENPIQ. (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)

Split-Dose Dosage Regimen (2.2)

- First dose: administer during evening before the colonoscopy
- Second dose: administer the next day, during the morning prior to the colonoscopy.

----------DOSAGE FORMS AND STRENGTHS----------

CLENPIQ oral solution*:* Each bottle contains 10 mg of sodium picosulfate, 3.5 g of magnesium oxide, and 12 g of anhydrous citric acid in 160 mL of solution (3)

----------CONTRAINDICATIONS----------

- Patients with severe reduced renal impairment (creatinine clearance less than 30 mL/minute) (4, 5.3, 8.6)
- Gastrointestinal (GI) obstruction or ileus (4)
- Bowel perforation (4)
- Toxic colitis or toxic megacolon (4)
- Gastric retention (4)
- Hypersensitivity to any of the ingredients in CLENPIQ (4)

----------WARNINGS AND PRECAUTIONS----------

- Risk of fluid and electrolyte abnormalities, arrhythmia, seizures, and renal impairment: Encourage adequate hydration, assess concurrent medications, and consider laboratory assessments prior to and after use. (5.1, 5.2, 5.3, 5.4, 7.1)
- Use in patients with renal impairment or taking concomitant medications that affect renal function: Use caution, ensure adequate hydration, and consider testing. (4, 5.3, 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)

----------ADVERSE REACTIONS----------

Most common adverse reactions are:

- Adults (≥2%): nausea, headache, hypermagnesemia, abdominal pain and dehydration or dizziness. (6.1)
- Pediatrics 9 to 16 years (>5%): nausea, vomiting, and abdominal pain. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Ferring Pharmaceuticals Inc. at 1-888-FERRING (1-888-337-7464) 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 and Medication Guide.

Revised: 10/2019

FULL PRESCRIBING INFORMATION: CONTENTS*

*Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

CLENPIQ 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 Administration Instructions

- Correct fluid and electrolyte abnormalities before administration of CLENPIQ.
- CLENPIQ is ready to drink. It is a clear solution with possible presence of visible particles and it does not need to be diluted prior to administration. One bottle of CLENPIQ is equivalent to one dose.
- Two doses of CLENPIQ are required for a complete preparation for colonoscopy as a Split-Dose regimen.
- The Split-Dose method consists of two separate doses: the first dose during the evening before the colonoscopy and the second dose the next day, during the morning prior to the colonoscopy *[see Dosage and Administration (2.2)]*.
- Additional liquids must be consumed after every dose of CLENPIQ: five or more 8-ounce cups of clear liquids after the first dose and four or more 8-ounce cups of clear liquids after the second dose *[see Dosage and Administration (2.2), Warnings and Precautions (5.1)]*.
- Consume only clear liquids (no solid food) from the start of CLENPIQ 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 CLENPIQ.
- Do not take oral medications within one hour of starting CLENPIQ.
- 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 CLENPIQ.
- Stop consumption of all liquids at least 2 hours before the colonoscopy.

2.2 Split-Dose Dosage Regimen

The recommended dosage in adults and pediatric patients 9 years of age and older is shown below. Instruct patients to take two separate doses in conjunction with liquids, as follows:

<u>Dose 1 – On the day before colonoscopy:</u>

- 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 (1 bottle) of CLENPIQ during the evening before the colonoscopy (e.g., 5:00 PM to 9:00 PM).
- Follow CLENPIQ by drinking five or more 8-ounce cups (cup provided) of clear liquids 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.

<u>Dose 2 – Next morning on the day of colonoscopy (start approximately 5 hours prior to colonoscopy):</u>

- Continue to consume only clear liquids (no solid food or dairy).
- Take the second dose (the second bottle) of CLENPIQ.
- Following the CLENPIQ dose, drink four or more 8-ounce cups (cup provided) of clear liquids up to 2 hours before the colonoscopy.

3 DOSAGE FORMS AND STRENGTHS

Oral solution: Each bottle contains 10 mg of sodium picosulfate, 3.5 grams of magnesium oxide, and 12 grams of anhydrous citric acid in 160 mL of colorless to slightly yellow, clear solution with possible presence of visible particles.

4 CONTRAINDICATIONS

CLENPIQ 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 (5.3)]*.
- 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 CLENPIQ *[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 CLENPIQ. 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 CLENPIQ, consider performing post-colonoscopy lab tests (electrolytes, creatinine, and BUN) and treat accordingly. Approximately 20% of patients in both arms (sodium picosulfate, magnesium oxide, and anhydrous citric acid, or 2 L of PEG + E plus two x 5-mg bisacodyl tablets) of clinical trials of another oral sodium picosulfate, magnesium oxide, and anhydrous citric acid product had orthostatic changes in blood pressure and/or heart rate on the day of colonoscopy and up to seven days post colonoscopy. In a single study of patients 9 to 16 years of age, approximately 20% of patients who received another oral product of sodium picosulfate, magnesium oxide, and anhydrous citric acid 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 CLENPIQ. In addition, use caution when prescribing CLENPIQ 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 seizure, arrhythmia, and renal impairment *[see Drug Interactions (7.1)]*.

5.2 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 CLENPIQ 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, patients with known or suspected hyponatremia *[see Adverse Reactions (6.2)]*.

5.3 Use in Patients with Renal Impairment

As with other magnesium containing bowel preparations, use caution when prescribing CLENPIQ for patients with impaired renal function 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 CLENPIQ. Consider performing baseline and post-colonoscopy laboratory tests (electrolytes, creatinine, and BUN) in these patients. CLENPIQ 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)]*.

5.4 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 CLENPIQ 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.

5.5 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 CLENPIQ may increase this risk. Consider the potential for mucosal ulcerations 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 CLENPIQ *[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 CLENPIQ. Observe these patients during the administration of CLENPIQ.

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)]*
- Seizures *[see Warnings and Precautions (5.2)]*
- Use in Patients with Renal Impairment *[see Warnings and Precautions (5.3)]*
- Cardiac Arrhythmias *[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)]*

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.

Adults

Clinical Study of CLENPIQ - Study 1

Table 1 displays the most common adverse reactions in a randomized, multicenter, assessor-blinded, non-inferiority trial of CLENPIQ for colon cleansing in adults (Study 1). CLENPIQ was compared to another oral sodium picosulfate, magnesium oxide, and anhydrous citric acid product, both administered according to the Split-Dose dosing regimen *[see Clinical Studies (14)]*.

Table 1: Common Adverse Reactions Observed in at Least 2% of Patients Undergoing Colon Cleansing in Study 1

Adverse Reaction	**Split-Dose Regimen**	
	CLENPIQ (N=448) %	**Sodium picosulfate, magnesium oxide, and anhydrous citric acid[1] (N=453) %**
Nausea	3	3
Headache	3	3
Hypermagnesemia[2]	2	5
Abdominal pain[3]	2	2
Dehydration or dizziness	2	2

[1] Powder for reconstitution
[2] Magnesium levels returned to normal within one week after colonoscopy in all patients in the CLENPIQ group.
[3] Abdominal pain included reports of abdominal pain, abdominal pain upper, and abdominal pain lower.

Clinical Study of Another Sodium Picosulfate, Magnesium Oxide and Anhydrous Citric Acid Product - Study 2

In a randomized, multicenter, investigator-blinded, active-controlled clinical trial for colon cleansing in adults, another oral sodium picosulfate, magnesium oxide, and anhydrous citric acid product was compared with a regimen of two liters (2 L) of polyethylene glycol plus electrolytes solution (PEG + E) and two 5-mg bisacodyl tablets (Study 2). In this study the protocol specified that abdominal bloating, distention, pain/cramping, and watery diarrhea, which are known to occur in response to bowel preparation, were documented as adverse events only if they required medical intervention (such as a change in study drug or led to discontinuation, therapeutic or diagnostic procedures, met the criteria for 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. The most common adverse reactions in Study 2 are shown in Table 2.

Table 2: Common Adverse Reactions[1] Observed in at Least 1% of Patients Undergoing Colon Cleansing[2] in Study 2

Adverse Reaction	Split-Dose Regimen	
	Sodium picosulfate, magnesium oxide, and anhydrous citric acid (N=305) %	2 L PEG + E[3] with 2 x 5-mg bisacodyl tablets (N=298) %
Nausea	3	4
Headache	2	2
Vomiting	1	3

[1, 2] abdominal bloating, distention, pain/cramping, and watery diarrhea not requiring an intervention were not collected

[3] 2 L PEG + E = two liters polyethylene glycol plus electrolytes solution

Electrolyte Abnormalities

In Study 1, rates of abnormal electrolyte shifts were generally similar between CLENPIQ and another sodium picosulfate, magnesium oxide, and anhydrous citric acid product (Table 3). In general, these shifts were transient and not clinically significant.

In Study 2, sodium picosulfate, magnesium oxide, and anhydrous citric acid was in general associated with numerically higher rates of abnormal electrolyte shifts on the day of colonoscopy compared to the control regimen (Table 3). These shifts were transient in nature and numerically similar between treatment arms at the Day 28 visit.

Table 3: Shifts from Normal Baseline to Outside the Normal Range Post-Baseline

Laboratory Parameter (direction of change)	Visit	Split-Dose Regimen Study 1		Split-Dose Regimen Study 2	
		CLENPIQ	Sodium picosulfate, magnesium oxide, and anhydrous citric acid[1]	Sodium picosulfate, magnesium oxide, and anhydrous citric acid[1]	2 L PEG+E with 2 x 5 mg bisacodyl tablets
		n/N (%)		n/N (%)	
Potassium (low)	Day of Colonoscopy	34/422 (8.1)	10/423 (2.4)	19/260 (7.3)	11/268 (4.1)
	24-48 hours	13/417 (3.1)	3/423 (0.7)	3/302 (1.0)	2/294 (0.7)
	Day 7	7/420 (1.7)	6/425 (1.4)	11/285 (3.9)	8/279 (2.9)
	Day 28	3/421 (0.7)	7/423 (1.7)	11/284 (3.9)	8/278 (2.9)
Sodium (low)	Day of Colonoscopy	4/426 (0.9)	23/443 (5.2)	11/298 (3.7)	3/295 (1.0)
	24-48 hours	6/423 (1.4)	9/441 (2.0)	1/303 (0.3)	1/295 (0.3)
	Day 7	6/423 (1.4)	9/440 (2.0)	2/300 (0.7)	1/292 (0.3)
	Day 28	8/427 (1.9)	9/439 (2.1)	2/299 (0.7)	3/291 (1.0)
Chloride (low)	Day of Colonoscopy	23/437 (5.3)	16/444 (3.6)	11/301 (3.7)	1/298 (0.3)
	24-48 hours	3/434 (0.7)	3/442 (0.7)	1/303 (0.3)	0/295 (0.0)
	Day 7	3/434 (0.7)	2/441 (0.5)	1/303 (0.3)	3/295 (1.0)
	Day 28	4/438 (0.9)	1/440 (0.2)	2/302 (0.7)	3/294 (1.0)
Magnesium (high)	Day of Colonoscopy	112/431 (26.0)	143/440 (32.5)	34/294 (11.6)	0/294 (0.0)
	24-48 hours	23/427 (5.4)	21/440 (4.8)	0/303 (0.0)	0/295 (0.0)

Laboratory Parameter (direction of change)	Visit	Split-Dose Regimen Study 1		Split-Dose Regimen Study 2	
		CLENPIQ	**Sodium picosulfate, magnesium oxide, and anhydrous citric acid[1]**	**Sodium picosulfate, magnesium oxide, and anhydrous citric acid[1]**	**2 L PEG+E with 2 x 5 mg bisacodyl tablets**
	Day 7	11/428 (2.6)	9/440 (2.0)	0/297 (0.0)	1/291 (0.3)
	Day 28	10/432 (2.3)	12/438 (2.7)	1/296 (0.3)	2/290 (0.7)
Calcium (low)	Day of Colonoscopy	8/436 (1.8)	1/446 (0.2)	2/292 (0.7)	1/286 (0.3)
	24-48 hours	1/434 (0.2)	0/444 (0.0)	0/303 (0.0)	0/295 (0.0)
	Day 7	0/434 (0.0)	0/444 (0.0)	0/293 (0.0)	1/283 (0.4)
	Day 28	0/439 (0.0)	2/442 (0.5)	0/292 (0.0)	1/282 (0.4)
Bicarbonate (low)	Day of Colonoscopy	6/431 (1.4)	35/438 (8.0)	N/A[2]	N/A[2]
	24-48 hours	40/430 (9.3)	43/434 (9.9)	N/A[2]	N/A[2]
	Day 7	37/430 (8.6)	40/438 (9.1)	N/A[2]	N/A[2]
	Day 28	33/433 (7.6)	43/436 (9.9)	N/A[2]	N/A[2]
Creatinine (high)	Day of Colonoscopy	6/427 (1.4)	1/432 (0.2)	5/260 (1.9)	13/268 (4.9)
	24-48 hours	6/425 (1.4)	5/431 (1.2)	1/303 (0.3)	0/295 (0.0)
	Day 7	5/426 (1.2)	4/431 (0.9)	10/264 (0.4)	13/267 (4.8)
	Day 28	4/429 (0.9)	6/429 (1.4)	11/264 (4.2)	14/265(5.3)

N/A: not applicable.
[1] Powder for reconstitution
[2] Bicarbonate was not analyzed in Study 2.

Pediatrics
In the pediatric patients aged 9 to 16 years who received another oral product of sodium picosulfate, magnesium oxide, and anhydrous citric acid, the most common adverse reactions (> 5%) were nausea, vomiting, and abdominal pain *[see Clinical Studies (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 oral sodium picosulfate, magnesium oxide, and anhydrous citric acid products. 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, and purpura

Gastrointestinal: abdominal pain, diarrhea, fecal incontinence, proctalgia, vomiting, reversible aphthoid ileal ulcers, and ischemic colitis *[see Warnings and Precautions (5.5)]*

Neurologic: generalized tonic-clonic seizures with and without hyponatremia in epileptic patients *[see Warnings and Precautions (5.2)]*.

7 DRUG INTERACTIONS

7.1 Drugs That May Increase Risks of Fluid and Electrolyte Abnormalities

Use caution when prescribing CLENPIQ for patients with conditions 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

CLENPIQ 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 CLENPIQ.
- 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 CLENPIQ to avoid chelation with magnesium.

7.3 Antibiotics

Prior or concomitant use of antibiotics with CLENPIQ may reduce efficacy of CLENPIQ 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 CLENPIQ use in pregnant women to determine a drug-associated risk of adverse developmental outcomes. In animal reproduction studies, 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

Reproduction studies with sodium picosulfate, magnesium oxide, and anhydrous citric acid have been performed in pregnant rats following oral administration of up to 2000 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. The 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 2000 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 CLENPIQ and any potential adverse effects on the breastfed infant from CLENPIQ or the underlying maternal condition.

8.4 Pediatric Use

The safety and effectiveness of CLENPIQ have been established for cleansing of the colon as a preparation for colonoscopy in pediatric patients 9 years of age and older. Use of CLENPIQ in this age group is supported by evidence from adequate and well-controlled trials in adults and a single, dose-ranging, controlled trial in 78 pediatric patients 9 to 16 years of age all of which evaluated

another oral product of sodium picosulfate, magnesium oxide, and anhydrous citric acid *[see Clinical Studies (14)]*. The safety profile in this pediatric population was similar to that seen in adults *[see Adverse Reactions (6.1)]*. Monitor for possible hypoglycemia in pediatric patients, as CLENPIQ has no caloric substrate.

The safety and effectiveness of CLENPIQ in pediatric patients less than 9 years of age have not been established.

8.5 Geriatric Use

Of the 448 adult patients in Study 1 who received CLENPIQ, 124 (28%) patients were 65 years of age or older. No overall differences in safety or effectiveness were observed between geriatric patients and younger patients, and other reported clinical experience has not identified differences in responses between elderly and younger patients. 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

CLENPIQ 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 less severe renal impairment or patients taking concomitant medications that may affect renal function may be at increased risk for renal injury *[see Warnings and Precautions (5.3)]*. Advise these patients of the importance of adequate hydration before, during, and after the use of CLENPIQ *[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 CLENPIQ 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

CLENPIQ (sodium picosulfate, magnesium oxide, and anhydrous citric acid) oral solution is a stimulant and osmotic laxative that is provided as a cranberry-flavored, colorless to slightly yellow, clear solution with possible presence of visible particles. CLENPIQ is supplied as two bottles in each carton.

Each bottle of CLENPIQ 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:

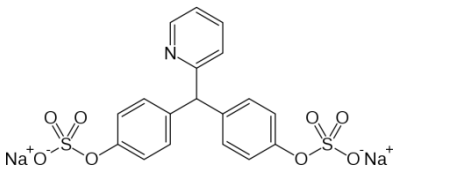
acesulfame potassium, cranberry flavor, disodium edetate, malic acid, sodium benzoate, sodium hydroxide, sodium metabisulfite, sucralose, and water. The cranberry flavor contains glyceryl triacetate (triacetin), maltodextrin, and sodium octenyl succinated starch.

The following is a description of the three active ingredients contained in CLENPIQ:

Sodium picosulfate is a stimulant laxative.

Sodium Picosulfate

- Chemical name: 4,4´-(2-pyridylmethylene) diphenyl bis(hydrogen sulfate) disodium salt, monohydrate
- Chemical formula: $C_{18}H_{13}NNa_2O_8S_2 \cdot H_2O$
- Molecular weight: 499.4
- Structural formula:



$\cdot H_2O$

Sodium picosulfate

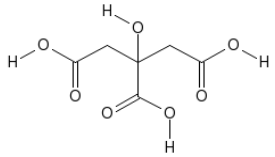
Magnesium citrate, which is formed in solution by the combination of magnesium oxide and anhydrous citric acid, is an osmotic laxative.

Magnesium Oxide

- Chemical name: Magnesium oxide
- Chemical formula: Mg O
- Molecular weight: 40.3
- Structural formula: Mg O

Anhydrous Citric Acid

- Chemical name: 2-hydroxypropane-1,2,3-tricarboxylic acid
- Chemical formula: $C_6H_8O_7$
- Molecular weight: 192.1
- 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 dose of another oral sodium picosulfate, magnesium oxide, and anhydrous citric acid product in 16 healthy subjects, the mean ± SD maximum plasma concentration (C_{max}) for picosulfate of 2.3 ± 1.4 ng/mL was reached at 2 hours. After administration of two doses separated by 6 hours, the mean ± SD plasma C_{max} for picosulfate of 3.2 ± 2.6 ng/mL was reached at approximately 7 hours after the first dose administration. In the same study, the uncorrected plasma magnesium concentration reached a C_{max} of approximately 1.9 mEq/L at 10 hours after the first dose administration, which represents an approximately 20% increase from baseline.

In patients scheduled to have an elective colonoscopy who received the Split-Dose dosing regimen of CLENPIQ, the mean ± SD plasma concentration for picosulfate was 1.05 ± 0.83 ng/mL at 15 minutes pre-second dose, 2.98 ± 1.27 ng/mL at 1-2 hours post-second dose, and 1.81 ± 0.86 ng/mL at 3-6 hours post-second dose.

Metabolism and Elimination

Metabolism and Excretion

Plasma concentrations of the free BHPM were 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 0.1%. In urine, the majority of excreted BHPM was in the glucuronide-conjugated form. The terminal half-life of sodium picosulfate was 7.4 hours.

Use in Specific Populations

Pediatric Patients

Pharmacokinetics of picosulfate was studied in pediatric patients aged from 9 to 16 years old. The half-life of picosulfate was 7 hours. The picosulfate reached the mean ± SD C_{max} of 3.5 ± 2.1 ng/mL at approximately 6 to 7 hours. 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.

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 CLENPIQ.

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 2000 mg/kg twice daily (about 1.2 times the recommended human dose based on body surface area).

14 CLINICAL STUDIES

Adults

Clinical Study with CLENPIQ – Study 1

The colon-cleansing efficacy of CLENPIQ was evaluated in a randomized, investigator-blinded, active-controlled, multicenter non-inferiority trial in the US and Canada in adult patients scheduled to have an elective colonoscopy (NCT03017235). Patients were randomized to CLENPIQ or another oral sodium picosulfate, magnesium oxide, and anhydrous citric acid product. Both products were administered by the "Split-Dose" (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 at least 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 at least four (4) 8-ounce glasses of clear liquid. Patients in both treatment groups were limited to a clear liquid diet on the day before the procedure (24 hours before).

A total of 901 adult patients were included in the primary efficacy analysis. Patients ranged in age from 20 to 80 years (mean age 57 years); 56% were female and 44% male. Self-identified race was approximately distributed as follows: 85% White, 10% Black, 2% Asian, and 3% other. Approximately 15% of patients self-identified their ethnicity as Hispanic or Latino.

The primary efficacy endpoint was the proportion of patients with successful overall colon cleansing, as assessed by blinded colonoscopists using the Modified Aronchick Scale. The Modified Aronchick Scale is a validated tool used to assess overall colon cleansing prior to suctioning or cleaning. 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 the trial, CLENPIQ was non-inferior and also met the pre-specified criteria for superiority to the comparator for overall colon cleansing. Efficacy results are provided in Table 4.

Table 4: Proportion of Patients with Successful Colon Cleansing According to the Modified Aronchick Scale in Study 1 Using the Split-Dose Regimen

CLENPIQ	**Sodium picosulfate, magnesium oxide, and anhydrous citric acid[1]**	**Difference between treatment groups[2]**	
% (n/N)	**% (n/N)**	**Difference**	**95% CI**
87.7% (393/448)	81.5% (369/453)	6.3%	(1.8%, 10.9%)[3]

[1] Powder for reconstitution
[2] Difference and 95% CI are based on stratified difference in proportions, where the stratification weight is based on Cochran-Mantel-Haenszel weight.
[3] Non-inferior and superior to sodium picosulfate, magnesium oxide, and anhydrous citric acid

Clinical Study of Another Oral Sodium Picosulfate, Magnesium Oxide and Anhydrous Citric Acid Product – Study 2

The colon cleansing efficacy of another oral sodium picosulfate, magnesium oxide, and anhydrous citric acid product was evaluated in a randomized, investigator-blinded, active-controlled, multicenter US non-inferiority trial in adult patients scheduled to have an elective colonoscopy (NCT01073930).

Patients were randomized to sodium picosulfate, magnesium oxide, and anhydrous citric acid group or polyethylene glycol plus electrolytes (PEG + E) and bisacodyl.

- Sodium picosulfate, magnesium oxide, and anhydrous citric acid was given by "Split-Dose" (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.

- The comparator was given as 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 treatment groups were limited to a clear liquid diet on the day before the procedure (24 hours before).

A total of 601 adult patients were included in the primary efficacy analysis. Patients ranged in age from 18 to 80 years (mean age 55 years); 59% were female and 41% male. Self-identified race was distributed as follows: 88% White, 10% Black, and less than 2% other. Of these, 2% self-identified their ethnicity as Hispanic or Latino.

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.

Sodium picosulfate, magnesium oxide, and anhydrous citric acid was non-inferior to the comparator. In addition, sodium picosulfate, magnesium oxide, and anhydrous citric acid met the pre-specified criteria for superiority to the comparator for colon cleansing. Efficacy results are provided in Table 5.

Table 5: Proportion of Patients with Successful Colon Cleansing in Study 2

Sodium picosulfate, magnesium oxide, and anhydrous citric acid	**2 L PEG+E[1] with 2 x 5-mg bisacodyl tablets**	**Difference between treatment groups**	
% (n/N)	**% (n/N)**	**Difference**	**95% CI**
84% (256/304)	74% (221/297)	10%	(3.4%, 16.2%)[2]

[1] 2 L PEG + E = two liters polyethylene glycol plus electrolytes solution.
[2] Non-inferior and superior to 2 L PEG+E with 2 x 5-mg bisacodyl tablets

Pediatric Patients 9 Years of Age and Older

The safety and efficacy of CLENPIQ in pediatric patients 9 years of age and older has been established based on another oral product of sodium picosulfate, magnesium oxide and anhydrous citric acid provided in powder packets for reconstitution (NCT01928862).

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 per dose administered as two doses
- Sodium picosulfate, magnesium oxide, and anhydrous citric acid one packet per dose 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 per dose 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 was 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 per dose 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 CLENPIQ recommended dosage regimen *[see Dosage and Administration (2)]*.

The sodium picosulfate, magnesium oxide, and anhydrous citric acid regimen of one packet per dose 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 6.

Table 6. 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

CLENPIQ is supplied in a carton containing two bottles, each holding 160 mL of cranberry-flavored, colorless to slightly yellow, clear oral solution with possible presence of visible particles. Each bottle contains 10 mg sodium picosulfate, 3.5 g magnesium oxide, and 12 g anhydrous citric acid. An eight-ounce cup for measuring fluids for hydration is also supplied.

CLENPIQ Cranberry flavor: NDC# 55566-6700-1.

Storage

Store CLENPIQ at 25°C (77°F). Excursions permitted at 15°C to 30°C (59°F to 86°F). [See USP Controlled Room Temperature]. Do not refrigerate or freeze.

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Medication Guide and Instructions for Use).

Instruct patients:

- CLENPIQ is ready to drink. It is a clear solution with possible presence of visible particles and it does not need to be diluted prior to administration. One bottle of CLENPIQ is equivalent to one dose.
- Two doses of CLENPIQ are required for a complete preparation for colonoscopy as a Split-Dose regimen. See *Instructions for Use.*
- Not to take other laxatives while they are taking CLENPIQ.
- 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 CLENPIQ.
- 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 CLENPIQ.
- To follow the directions in the Instructions for Use, for the Split-Dose regimen, as prescribed.
- To consume additional liquids after each dose of CLENPIQ: five or more 8-ounce cups of clear liquids after the first dose and four or more 8-ounce cups of clear liquids after the second dose.
- To delay the second dose of CLENPIQ, 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 CLENPIQ or if they experience altered consciousness (e.g. confusion, delirium, loss of consciousness) or seizures *[see Warnings and Precautions (5.1, 5.2, 5.4)]*.

Manufactured by:

ASM Aerosol-Service AG
Industriestrasse 11, CH - 4313 Möhlin
Switzerland

Manufactured for:

Ferring Pharmaceuticals Inc.
Parsippany, N.J. 07054

MEDICATION GUIDE
CLENPIQ® (CLEN-pik)
(sodium picosulfate, magnesium oxide, and anhydrous citric acid)
oral solution

Read and understand these Medication Guide instructions **at least 2 days before** your colonoscopy and again before you start taking CLENPIQ.

What is the most important information I should know about CLENPIQ?

CLENPIQ 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 CLENPIQ 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 CLENPIQ:

- vomiting
- urinating less often than normal
- dizziness
- headache

See "What are the possible side effects of CLENPIQ?" for more information about side effects.

What is CLENPIQ?

CLENPIQ is a prescription medicine used by adults and children 9 years of age and older, to clean the colon before a colonoscopy. CLENPIQ 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 CLENPIQ is safe and effective in children under 9 years of age.

Do not take CLENPIQ 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 CLENPIQ. See the end of this leaflet for a complete list of ingredients in CLENPIQ.

Before taking CLENPIQ, 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 CLENPIQ will harm your unborn baby. Talk to your provider if you are pregnant.
- are breastfeeding or plan to breastfeed. It is not known if CLENPIQ passes into your breast milk. You and your healthcare provider should decide if you will take CLENPIQ while breastfeeding.

Tell your healthcare provider about all the medicines you take, including prescription and non-prescription medicines, vitamins, and herbal supplements.

CLENPIQ may affect how other medicines work. Medicines taken by mouth may not be absorbed properly when taken within 1 hour before the start of CLENPIQ.

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 CLENPIQ.

The following medicines should be taken at least 2 hours before starting CLENPIQ and not less than 6 hours after taking CLENPIQ:

- tetracycline
- fluoroquinolone antibiotics
- iron
- digoxin (Lanoxin)
- chlorpromazine
- 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 CLENPIQ?

See the Instructions for Use for dosing instructions. You must read, understand, and follow these instructions to take CLENPIQ the right way.

- Take CLENPIQ exactly as your healthcare provider tells you to take it.
- CLENPIQ comes ready to drink and does not need to be mixed with anything else before you take your dose of medicine.
- CLENPIQ is a clear liquid that may have particles.
- 1 bottle of CLENPIQ equals 1 dose. Two separate doses of CLENPIQ are required for complete colonoscopy preparation.
- CLENPIQ is taken using the **Split-Dose** method. See the instructions for use for more information.
- All people taking CLENPIQ should follow these general instructions starting 1 day **before** your colonoscopy:
  - 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.
  - after taking CLENPIQ 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 CLENPIQ, do not:**
  - take any other laxatives.
  - take any medicines by mouth (oral) within 1 hour of starting CLENPIQ.
  - eat solid foods, dairy such as milk, or alcohol while taking CLENPIQ and until after your colonoscopy.
  - eat or drink anything colored red or purple.

Contact your healthcare provider right away if after taking CLENPIQ you have severe vomiting, signs of dehydration, changes in consciousness such as feeling confused, delirious or fainting (loss of consciousness) or seizures after taking CLENPIQ.

What are the possible side effects of CLENPIQ?
CLENPIQ can cause serious side effects, including:
See "**What is the most important information I should know about CLENPIQ"?**

- **Changes in certain blood tests**. Your healthcare provider may do blood tests after you take CLENPIQ to check your blood for changes.
- Tell your healthcare provider if you have any symptoms of too much fluid loss, including:
  - vomiting
  - nausea
  - bloating
  - dizziness
  - stomach area (abdominal) cramping
  - urinate less than usual
  - trouble drinking clear liquids
  - troubles swallowing
  - seizures
  - heart problems
- **Ulcers of the bowel or bowel problems (ischemic colitis)**. Tell your healthcare provider right away if you have severe stomach-area (abdominal) pain or rectal bleeding.

The most common side effects of CLENPIQ in adults include:

- nausea
- high magnesium levels in your blood
- dehydration or dizziness
- headache
- stomach area (abdominal) pain

The most common side effects of CLENPIQ in children 9 to 16 years of age include:

- nausea
- vomiting
- stomach area (abdominal) pain

These are not all the possible side effects of CLENPIQ.
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 CLENPIQ?

- Store CLENPIQ at room temperature, between 68 to 77°F (20° to 25°C).
- **Do not** put CLENPIQ in the refrigerator or freezer.

Keep CLENPIQ and all medicines out of the reach of children.

General information about the safe and effective use of CLENPIQ.

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use CLENPIQ for a condition for which it was not prescribed. Do not give CLENPIQ to other people, even if they have the same symptoms that you have. It may harm them. You can ask your pharmacist or healthcare provider for information about CLENPIQ that is written for health professionals.

What are the ingredients in CLENPIQ?

CLENPIQ comes in a carton containing 2 bottles, along with an 8-ounce cup for measuring fluids for hydration.
Each bottle contains:
Active ingredients: sodium picosulfate, magnesium oxide, and anhydrous citric acid
Inactive ingredients:
acesulfame potassium, cranberry flavor, disodium edetate, malic acid, sodium benzoate, sodium hydroxide, , sodium metabisulfite, sucralose, and water. The cranberry flavor contains glyceryl triacetate (triacetin), maltodextrin, and sodium octenyl succinated starch.

Manufactured for: Ferring Pharmaceuticals Inc.
Parsippany, NJ 07054, USA

For more information, go to www.CLENPIQ.com or call 1-888-337-7464.

This Medication Guide has been approved by the U.S. Food and Drug Administration Issued: October 2019

Instructions for Use
CLENPIQ® (CLEN-pik)
(sodium picosulfate, magnesium oxide, and anhydrous citric acid)
oral solution

Before Taking CLENPIQ

Take CLENPIQ using the **Split-Dose** method. Split-Dose means you will take 2 separate doses. You will take dose 1 the evening before your colonoscopy and dose 2 the morning of your colonoscopy. Talk with your healthcare provider before you start if you have any questions.

- Start a clear-liquid diet **the day 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 liquids 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. Drink **FIVE or more** 8-ounce cups of clear liquids after the first dose and **FOUR or more** 8-ounce cups of clear liquids after the second dose.

Note: Do not refrigerate or freeze CLENPIQ. CLENPIQ is ready to drink and does not need to be mixed with anything else before you take your dose of medicine. CLENPIQ is a clear liquid that may have particles.

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

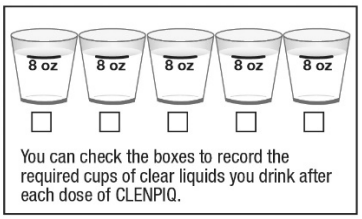
- **no** solid foods
- **no** alcohol
- **no** dairy or non-dairy types of milk or cream
- **no** soy milk or drinks
- **no** juices with pulp
- **no** red or purple drinks
- **no** other liquids that you cannot see through

Split-Dose Instructions

Dose 1 – In the evening the day before your colonoscopy (sometime between 5:00 PM to 9:00 PM)

- Drink the entire first bottle of CLENPIQ. Drink CLENPIQ right from the bottle.

- Follow this dose by drinking **five or more** 8 ounce (oz) cups of clear liquids using the cups provided over the next 5 hours.



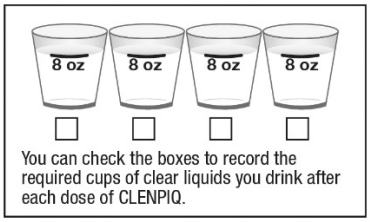
- After taking CLENPIQ if you have any bloating or feeling like your stomach is upset, wait to take your second dose until your stomach feels better.

Important: See **Table 1** for a list of clear liquids you can drink.

Dose 2 – In the morning of colonoscopy (about 5 hours before your colonoscopy):

- **Do not** eat solid food. **Drink only clear liquids**.
- Drink the entire second bottle of CLENPIQ. Drink CLENPIQ right from the bottle.

- Follow this dose by drinking **four or more 8** ounce (oz) cups of clear liquids using the cup provided. You can continue to drink clear liquids up to 2 hours before the colonoscopy.



Important: See **Table 1** for a list of clear liquids you can drink.

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.

Ferring Pharmaceuticals Inc.
Parsippany, NJ 07054, USA

10/2019