HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use HalfLytely and Bisacodyl Tablets Bowel Prep Kit safely and effectively. See full prescribing information for HalfLytely and Bisacodyl Tablets Bowel Prep Kit.

HalfLytely® and Bisacodyl Tablets Bowel Prep Kit (PEG-3350, sodium chloride, sodium bicarbonate and potassium chloride for oral solution and bisacodyl delayed release tablets)
Initial U.S. Approval: 2004

----------RECENT MAJOR CHANGES----------
Dosage and Administration x/20xx

----------INDICATIONS AND USAGE----------
HalfLytely and Bisacodyl Tablets Bowel Prep Kit is a gastrointestinal lavage indicated for cleansing of the colon as a preparation for colonoscopy in adults (1)

----------DOSAGE AND ADMINISTRATION----------
- Take two 5 mg bisacodyl delayed release tablets with water. Do NOT chew or crush the tablets. (2)
- Prepare the HalfLytely solution by filling the container to the 2 liter mark with water. Cap the container. Shake to dissolve the powder. (2)
- This preparation can be used without the addition of a Flavor Pack. Wait for a bowel movement (or maximum of 6 hours) then drink the 2 liter HalfLytely solution at a rate of 8 ounces every 10 minutes. Drink all of the solution. (2)

----------DOSAGE FORMS AND STRENGTHS----------
- Two 5 mg bisacodyl delayed release tablets (3)
- One 2 liter HalfLytely bottle with powder for reconstitution (3)

----------CONTRAINDICATIONS----------
- Patients known to be allergic to polyethylene glycol (4)
- Gastrointestinal (GI) obstruction (4)
- Bowel perforation (4)
- Toxic colitis (4)
- Toxic megacolon (4)

--------WARNINGS AND PRECAUTIONS----------
- Neurologic (5.1)
- Gastrointestinal (5.2)
- Renal Insufficiency (5.3)
- Allergic Reaction (5.4)

----------ADVERSE REACTIONS----------
Most common adverse reactions (< 3%) are abdominal pain/cramping, nausea, vomiting and headache (6)

TO REPORT SUSPECTED ADVERSE REACTIONS, CONTACT BRAINTREE LABORATORIES, INC. AT 1-800-874-6756 OR FDA AT 1-800-FDA-1088 OR *WWW.FDA.GOV/MEDWATCH*.

----------DRUG INTERACTIONS----------
- Oral medication administered within one hour of the start of administration of HalfLytely solution may be flushed from the GI tract and the medication may not be absorbed. (7)
- Do not take the bisacodyl delayed release tablets within one hour of taking an antacid. (7)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

Revised: x/20xx

FULL PRESCRIBING INFORMATION: CONTENTS*

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

FULL PRESCRIBING INFORMATION:

1 INDICATIONS AND USAGE

HalfLytely and Bisacodyl Tablets Bowel Prep Kit is indicated for cleansing of the colon as a preparation for colonoscopy in adults.

2 DOSAGE AND ADMINISTRATION

The recommended HalfLytely and Bisacodyl Tablets Bowel Prep Kit oral dosage regimen for adults on the day prior to colonoscopy is as follows:

- Take two 5 mg bisacodyl delayed release tablets with water. Do NOT chew or crush the tablets.
- Add flavor pack of choice (if applicable) to the 2 liter container. No additional ingredients (other than flavor packs provided) should be added to the solution.
- Prepare the HalfLytely solution by filling the container to the 2 liter mark with water. Cap the container. Shake to dissolve the powder.
- Wait for a bowel movement (or maximum of 6 hours) then drink the 2 liter HalfLytely solution at a rate of 8 ounces every 10 minutes. Drink all of the solution.

3 DOSAGE FORMS AND STRENGTHS

- Two pink, round, enteric coated 5 mg bisacodyl delayed release tablets, stamped "BRA"
- One 2 liter HalfLytely bottle with powder for reconstitution

4 CONTRAINDICATIONS

The HalfLytely and Bisacodyl Tablets Bowel Prep Kit is contraindicated in the following conditions:

- Known allergies to polyethylene glycol or other components of the kit
- Gastrointestinal (GI) obstruction
- Bowel perforation
- Toxic colitis
- Toxic megacolon

5 WARNINGS AND PRECAUTIONS

5.1 Neurologic

There have been reports of generalized tonic-clonic seizures in patients with use of large volume (4 liter) PEG-based colon preparation products in patients with no prior history of seizures. The seizure cases were associated with severe vomiting, excessive beverage consumption and electrolyte abnormalities (for example, hyponatemia, hypokalemia). The neurologic abnormalities resolved with correction of fluid and electrolyte abnormalities. Therefore, HalfLytely and Bisacodyl Tablets Bowel Prep Kit should be used with caution in patients using concomitant medications (such as diuretics) that increase the risk of electrolyte abnormalities or patients with known or suspected hyponatremia. Monitor baseline and post-colonoscopy laboratory tests (sodium, potassium, calcium, creatinine, and BUN) in these patients.

5.2 Gastrointestinal

Use with caution in patient with severe ulcerative colitis, ileus or gastric retention. Observe patients with impaired gag reflex and patients prone to regurgitation or aspiration during administration of HalfLytely solution. If GI obstruction or perforation is suspected, appropriate studies should be performed to rule out these conditions before administration. There have been reports of ischemic colitis in patients with use of HalfLytely and 20 mg Bisacodyl Tablets Bowel Prep Kit. If patients develop severe abdominal pain or rectal bleeding, patients should be evaluated as soon as possible.

5.3 Renal Insufficiency

Patients with impaired water handling who experience severe vomiting should be closely monitored including measurement of electrolytes (sodium, potassium, calcium, BUN and creatinine).

5.4 Allergic Reaction

Hives and skin rashes have been reported with PEG-3350 based products which are suggestive of an allergic reaction.

6 ADVERSE REACTIONS

6.1 Clinical Studies Experience

Because clinical studies are conducted under widely varying conditions, adverse reaction rates observed in the clinical studies of a drug cannot be directly compared to rates in clinical studies of another drug and may not reflect the rates observed in practice.

In a clinical study of HalfLytely and (10 mg vs. 20 mg) Bisacodyl Tablets Bowel Prep Kit multicentered, controlled clinical trials, abdominal pain/cramping, nausea, vomiting and headache were the most common adverse reactions (< 3%) after the administration of HalfLytely and (10 mg or 20 mg) Bisacodyl Tablets Bowel Prep Kit. Less than 1% of patients exposed to HalfLytely and 10 mg Bisacodyl Tablets Bowel Prep Kit reported vomiting and abdominal pain/cramping.

The data in Table 1 reflects exposure in 222 patients to HalfLytely and 10 mg bisacodyl tablets vs. 223 patients exposed to HalfLytely and 20 mg bisacodyl tablets. The HalfLytely and 10 mg Bisacodyl Tablets Bowel Prep Kit population was 20-85 years of age, 46% male, 54% female, 10% African American, 85% Caucasian, 8% Hispanic requiring a colonoscopy. The demographics of the comparator group were similar.

Table 1: Adverse Reactions Observed in at Least 1% of Patients

	HalfLytely and 10 mg Bisacodyl Tablets Bowel Prep Kit (N=222)	HalfLytely and 20 mg Bisacodyl Tablets Bowel Prep Kit (N=223)
Abdominal pain/cramping	1%	2%
Nausea	1%	2%
Vomiting	1%	2%
Headache	2%	1%

Table 2 displays patient diary ratings of their symptoms associated with HalfLytely and Bisacodyl Tablets Bowel Prep Kits (10 mg bisacodyl vs. 20 mg bisacodyl tablets) in the controlled trial.

Table 2: Percentage of Patients Reporting in their Diaries "bothersome" to "severely distressing" Symptoms in Controlled Clinical HalfLytely and Bisacodyl Tablets Bowel Prep Kit Trial[1]

	HalfLytely and 10 mg Bisacodyl Tablets Bowel Prep Kit (N=222)	HalfLytely and 20 mg Bisacodyl Tablets Bowel Prep Kit (N=223)
Nausea	13%	21%
Abdominal cramping	7%	14%
Abdominal fullness	11%	13%
Vomiting	5%	8%
Overall Discomfort	14%	20%

[1] Patients were specifically asked about the occurrence of the following symptoms: nausea, abdominal cramping, fullness, vomiting and overall discomfort.

6.2 Postmarketing Experience

The following adverse reactions have been identified during postapproval use of HalfLytely and Bisacodyl Tablets Bowel Prep Kit. 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.

Allergic Reactions: Cases of urticaria, rhinorrhea, dermatitis and anaphylactic reactions have been reported with PEG-based products which may represent allergic reactions.

Gastrointestinal: There are isolated reports of serious post-marketing events following the administration of PEG-based products in patients over 60 years of age. These adverse reactions include upper GI bleeding from a Mallory-Weiss tear, esophageal perforation, asystole, and acute pulmonary edema after vomiting and aspirating the PEG-based solution. In addition, during administration of 4 liters of PEG-3350 colon cleansing preparation the following serious adverse reactions were seen: two deaths in end stage renal failure patients who developed diarrhea, vomiting and dysnatremia.

Ischemic colitis has been reported with use of HalfLytely and 20 mg Bisacodyl Tablets Bowel Prep Kit for colon preparation prior to colonoscopy. However, a causal relationship between these ischemic colitis cases and the use of HalfLytely and Bisacodyl Tablets Bowel Prep Kit has not been established.

Neurologic: There have been reports of generalized tonic-clonic seizures associated with use of large volume (4 liter) PEG-based colon preparation products in patients with no prior history of seizures. Cases of dizziness and syncope have been reported [see *Warnings and Precautions (5.1)*].

7 DRUG INTERACTIONS

- Oral medication administered within one hour of the start of administration of HalfLytely solution may be flushed from the GI tract and the medication may not be absorbed.
- Do not take the bisacodyl delayed release tablets within one hour of taking an antacid.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Category C. Animal reproduction studies have not been conducted. It is not known whether HalfLytely and Bisacodyl Tablets Bowel Prep Kit can cause fetal harm when administered to a pregnant woman or can affect reproductive capacity. HalfLytely and Bisacodyl Tablets Bowel Prep Kit should be given to a pregnant or nursing woman only if clearly needed.

8.3 Nursing Mothers

It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when HalfLytely and Bisacodyl Tablets Bowel Prep Kit is administered to a nursing woman.

8.4 Pediatric Use

Safety and effectiveness in pediatric patients has not been established.

8.5 Geriatric Use

Of the 222 patients who received HalfLytely and 10 mg Bisacodyl Tablets Bowel Prep Kit in clinical trials, 73 (33%) were 65 years of age or older, while 18 (8%) were 75 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 geriatric patients and younger patients but greater sensitivity of some older individuals cannot be ruled out.

11 DESCRIPTION

Each **HalfLytely and Bisacodyl Tablets Bowel Prep Kit** [Polyethylene glycol (PEG) 3350, sodium chloride, sodium bicarbonate and potassium chloride for oral solution and bisacodyl delayed release tablets] consists of one 2 liter bottle of HalfLytely (PEG-3350, sodium chloride, sodium bicarbonate and potassium chloride for oral solution) powder for reconstitution and two 5 mg bisacodyl, delayed release tablets.

- **Bisacodyl delayed release tablets:** Each pink, round, enteric coated bisacodyl delayed release tablet (stamped "BRA") contains 5 mg of bisacodyl, USP ($C_{22}H_{19}NO_4$) with a molecular weight of 361.40. Inactive ingredients include lactose (anhydrous) NF, microcrystalline cellulose NF, croscarmellose sodium NF, magnesium stearate NF, Eudragit L 30-55, polyethylene glycol 400, talc USP, gelatin, calcium sulfate (anhydrous) NF, confectioners sugar, kaolin USP, sucrose NF, Opalux pink, beeswax, and carnauba wax. The bisacodyl delayed release tablets are administered orally prior to drinking the HalfLytely solution [see *Dosage and Administration (2)*].
- **HalfLytely (PEG-3350, sodium chloride, sodium bicarbonate and potassium chloride for oral solution):** A white powder for reconstitution containing 210 grams of PEG-3350, 2.86 grams of sodium bicarbonate, 5.6 grams of sodium chloride, 0.74 grams of potassium chloride and 1 gram of flavoring ingredient (if applicable). Flavor Packs are available in Cherry, Lemon-Lime and Orange. This preparation can be used without the addition of a Flavor Pack. When dissolved in water to a volume of 2 liters, the HalfLytely solution is isosmotic, clear, and colorless. The HalfLytely solution is administered orally after taking the two bisacodyl delayed release tablets [see *Dosage and Administration (2)*].

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

HalfLytely and Bisacodyl Tablets Bowel Prep Kit induces diarrhea which cleanses the colon.

12.2 Pharmacodynamics

Bisacodyl, a stimulant laxative, is hydrolyzed by intestinal brush border enzymes and colonic bacteria to form an active metabolite [bis-(p-hydroxyphenyl) pyridyl-2 methane; (BHPM)] that acts directly on the colonic mucosa to produce colonic peristalsis.

12.3 Pharmacokinetics

The osmotic activity of HalfLytely solution results in no net absorption or excretion of ions or water.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Long-term studies in animals have not been performed to evaluate the carcinogenic potential of HalfLytely and Bisacodyl Tablets Bowel Prep Kit. Studies to evaluate its potential for impairment of fertility or its mutagenic potential have not been performed.

14 CLINICAL STUDIES

The colon cleansing efficacy of HalfLytely and Bisacodyl Tablets Bowel Prep Kit (with 10 mg of bisacodyl) was evaluated in a randomized, single blind, active-controlled, multicenter study. In this study, 444 adult patients were included in the efficacy analysis. Patients ranged in age from 19 to 86 years old (mean age 57 years old) with 53% female and 47% male patients. Race was distributed as follows: 86% Caucasian, 9% African American, 7% Hispanic or Latino, and 3% other.

Patients were randomized to one of the following two colon preparations: **1)** HalfLytely and Bisacodyl Tablets Bowel Prep Kit [20 mg of bisacodyl tablets were given at noon on the day before colonoscopy followed by 2 liters of HalfLytely (after the first bowel movement or maximum of 6 hours)] at a rate of 8 ounces every 10 minutes and **2)** a modified HalfLytely and Bisacodyl Tablets Bowel Prep Kit [containing 10 mg of bisacodyl tablets given at noon on the day before colonoscopy followed by 2 liters of HalfLytely (after the first bowel movement or maximum of 6 hours)] at a rate of 8 ounces every 10 minutes.

Patients were instructed to refrain from solid food and to have clear liquids on the day before colonoscopy. In addition, patients were instructed to consume nothing by mouth, except clear liquids, from the time the preparation was completed until midnight. Patients were instructed not to eat or drink anything from midnight until after the colonoscopy was completed.

The primary efficacy endpoint was the proportion of patients with successful colon cleansing (assessed by the colonoscopists), see Table 3 below.

Table 3: Colon Cleansing Efficacy*

Treatment Group	Responders[1] n/N (%)	Non-responders[2] n/N (%)
HalfLytely and 20 mg Bisacodyl Tablets Bowel Prep Kit (N=223)	196/223 (88)	27/223 (12)
HalfLytely and 10 mg Bisacodyl Tablets Bowel Prep Kit (N=221)	192/221 (87)	29/221 (13)

[1] Responders were patients whose colon preparations were graded excellent (no more than small bits of adherent feces/fluid) or good (small amounts of feces or fluid not interfering with the exam) by the colonoscopist;

[2] Non-responders were patients whose colon preparations were graded fair (enough feces or fluid to prevent a completely reliable exam) or poor (large amounts of fecal residue requiring additional cleansing) by the colonoscopists or patients who were unable to tolerate their colon preparation.

*The HalfLytely and 20 mg Bisacodyl Tablet Bowel Prep Kit does not provide any additional efficacy benefits over the HalfLytely and 10 mg Bisacodyl Tablets Bowel Prep Kit.

16 HOW SUPPLIED/STORAGE AND HANDLING

Each HalfLytely and Bisacodyl Tablets Bowel Prep Kit contains:

One pack of bisacodyl delayed release tablets containing two pink, round, enteric coated 5 mg bisacodyl delayed release tablets, stamped "BRA"

One 2 liter bottle of HalfLytely (PEG-3350, sodium chloride, sodium bicarbonate and potassium chloride for oral solution) powder for reconstitution containing 210 grams of polyethylene glycol (PEG) 3350, 2.86 grams of sodium bicarbonate, 5.6 grams of sodium chloride, 0.74 grams of potassium chloride, and 1 gram of flavoring ingredient (if applicable). After adding 2 liters of water, the reconstituted HalfLytely solution (clear and colorless) contains 31.3 mmol/L of PEG-3350, 65 mmol/L of sodium, 53 mmol/L of chloride, 17 mmol/L of bicarbonate and 5 mmol/L of potassium.

Lemon-Lime HalfLytely and Bisacodyl Tablets Bowel Prep Kit contains 1 gram lemon-lime flavoring ingredient. HalfLytely and Bisacodyl Tablets Bowel Prep Kit with Flavor Packs contains 3 packs (1gram each Cherry, Lemon-Lime and Orange flavors).

Storage:

Store at 20-25°C (68-77°F). Excursions permitted between 15-30°C (59-86°F). The reconstituted HalfLytely solution, which may be refrigerated, should be used within 48 hours.

Lemon-Lime HalfLytely and Bisacodyl Tablets Bowel Prep Kit	**NDC 52268-502-02**
HalfLytely and Bisacodyl Tablets Bowel Prep Kit with Flavor Packs	**NDC 52268-520-05**

17 PATIENT COUNSELING INFORMATION

See FDA-Approved Patient Labeling

- If a patient experiences severe bloating, distention or abdominal pain, administration of the solution should be slowed or temporarily discontinued until the symptoms abate. Patients should be advised to report these events to their physician.
- Hives and skin rashes have been reported that are suggestive of an allergic reaction. Patients should be advised to report to their physician any allergic reaction. Medication should be discontinued.
- Instruct patients NOT to drink large quantities of clear liquids [see *Warnings and Precautions (5.1)*].
- Consider performing baseline and post-colonoscopy laboratory tests (sodium, potassium, calcium, creatinine, and BUN) in patients with impaired water handling (renal insufficiency, taking diuretics) [see *Warnings and Precautions (5.1) and (5.3)*].
- Inform patients that oral medication administered within one hour of the start of administration of HalfLytely solution may be flushed from the GI tract and the medication may not be absorbed.

17.4 FDA-Approved Patient Labeling

- HalfLytely and Bisacodyl Tablets Bowel Prep Kit produces a watery stool which cleanses the colon.
- No solid food or milk (clear liquids only) should be consumed on the day of the preparation.
- Take two 5 mg bisacodyl delayed release tablets with water (do NOT chew or crush tablets).
- Prepare the HalfLytely solution according to the instructions on the kit.
- No additional ingredients (other than flavor packs provided) should be added to the solution.
- After you have a bowel movement, or waiting a maximum of six hours, drink ALL of the HalfLytely solution.
- Drink the 2 liter HalfLytely solution at a rate of 8 ounces every 10 minutes. Rapid drinking of each portion is better than drinking small amounts continuously.
- No antacids should be taken within one hour of taking the bisacodyl delayed release tablets.
- Do not drink large quantities of clear liquids after taking the HalfLytely solution until your colonoscopy.
- The first bowel movement should occur approximately 1-6 hours after taking the two bisacodyl delayed release tablets.
- Abdominal bloating or distention may occur before the first bowel movement. If your abdominal distention or discomfort continues stop drinking the HalfLytely solution temporarily or drink each portion at longer intervals until your symptoms disappear.

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