

NDA 21-551/S-005

Page 2

BRAINTREE LABORATORIES, INC.

HalfLyte[®] and Bisacodyl Tablets

Bowel Prep Kit

Rx Only

PEG-3350, sodium chloride, sodium bicarbonate and potassium chloride for oral solution and bisacodyl delayed release tablets

DESCRIPTION

Each **HalfLyte[®] and Bisacodyl Tablets Bowel Prep Kit** (Polyethylene glycol 3350, sodium chloride, sodium bicarbonate and potassium chloride for oral solution and bisacodyl delayed release tablets) consists of:

One pack of 4 bisacodyl delayed release tablets: Each pink, round, enteric coated delayed release tablet (stamped “BRA”) contains 5 mg bisacodyl, USP ($C_{22}H_{19}NO_4$); MW=361.40. **Inactive ingredients:** 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, confections sugar, kaolin USP, sucrose NF, opalux pink, beeswax, carnuba wax.

The bisacodyl delayed release tablets are administered orally prior to drinking the solution.

One 2 liter bottle of HalfLyte[®] (PEG-3350, sodium chloride, sodium bicarbonate and potassium chloride for oral solution): A white powder for reconstitution containing 210 g polyethylene glycol 3350, 2.86 g sodium bicarbonate, 5.6 g sodium chloride, 0.74 g potassium chloride and 1.0 g flavoring ingredient (if applicable). When dissolved in water to a volume of 2 liters, the solution is isosmotic. The solution is administered orally as a gastrointestinal lavage in combination with four bisacodyl delayed release tablets. All solutions are clear and colorless.

CLINICAL PHARMACOLOGY

HalfLyte and Bisacodyl Tablets Bowel Prep Kit induces a diarrhea which cleanses the bowel. Bisacodyl is a contact stimulant laxative. After being hydrolyzed by intestinal brush border enzymes and colonic bacteria, its active metabolite, bis-(p-hydroxyphenyl)-pyridyl-2 methane (BHPM) acts directly on the colonic mucosa to produce peristalsis throughout the large intestine.

The osmotic activity of polyethylene glycol 3350 and electrolytes result in virtually no net absorption or excretion of ions or water.

INDICATIONS AND USAGE: HalfLyte and Bisacodyl Tablets Bowel Prep Kit is indicated for bowel cleansing prior to colonoscopy.

CONTRAINDICATIONS: HalfLyte and Bisacodyl Tablets Bowel Prep Kit is contraindicated in patients known to be hypersensitive to any of the components.

HalfLyte and Bisacodyl Tablets Bowel Prep Kit is contraindicated in patients with ileus, gastrointestinal obstruction, gastric retention, bowel perforation, toxic colitis or toxic megacolon.

NDA 21-551/S-005

Page 3

WARNINGS: No additional ingredients, e.g. flavorings, should be added to the solution. HalfLyately and Bisacodyl Tablets Bowel Prep Kit should be used with caution in patients with severe ulcerative colitis. Do NOT chew or crush the bisacodyl delayed release tablets.

PRECAUTIONS

General: Patients with impaired gag reflex and patients prone to regurgitation or aspiration should be observed during the administration of the solution. If a patient experiences severe bloating, distention or abdominal pain, administration of the solution should be slowed or temporarily discontinued until the symptoms abate. If gastrointestinal obstruction or perforation is suspected, appropriate studies should be performed to rule out these conditions before administration of HalfLyately and Bisacodyl Tablets Bowel Prep Kit.

Patients should avoid consumption of large quantities of water during or after preparation or colonoscopy. Patients with impaired water handling (renal insufficiency or patients taking diuretics) that experience severe vomiting or nausea should be closely monitored including measurement of electrolytes.

Information for patients: HalfLyately and Bisacodyl Tablets Bowel Prep Kit produces a watery stool which cleanses the bowel before examination. Prepare the solution according to the instructions on the kit. For best results, no solid food or milk (clear liquids only) should be consumed on the day of the preparation. No antacids should be taken within one hour of taking the bisacodyl delayed release tablets.

Adults swallow all four bisacodyl delayed release tablets with water (do NOT chew or crush). The first bowel movement should occur in approximately 1-6 hours after taking the bisacodyl delayed release tablets. Wait for a bowel movement (or maximum of 6 hours) then drink the solution, 1 (8 oz) glass every 10 minutes (approximately 8 glasses). Drink ALL of the solution. Rapid drinking of each portion is better than drinking small amounts continuously. A watery bowel movement should occur in approximately 1 hour after drinking the solution. You may experience some abdominal bloating and distention before the bowels start to move. If severe discomfort or distention occurs, stop drinking the solution temporarily or drink each portion at longer intervals until these symptoms disappear.

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

Carcinogenesis, Mutagenesis, Impairment of Fertility:

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

NDA 21-551/S-005

Page 4

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

Nursing Mothers: It is not known whether HalfLyte and Bisacodyl Tablets Bowel Prep Kit is excreted in human milk, caution should be exercised when HalfLyte and Bisacodyl Tablets Bowel Prep Kit is administered to a nursing woman.

Pediatric Use: Safety and effectiveness in pediatric patients has not been established.

Geriatric Use: There is no evidence for special consideration when administered to elderly patients. Of the total number of subjects in clinical studies (n=186), 28 percent were aged 65 or older, while 9.1 percent were over 75. No overall differences in safety or effectiveness were observed.

ADVERSE REACTIONS: Nausea, cramping and abdominal fullness are the most common adverse reactions (occurring in up to 50% of patients) to administration of HalfLyte and Bisacodyl Tablets Bowel Prep Kit. Vomiting occurs less frequently (approximately 2.7% of patients versus 6.7% of patients taking large volume PEG solutions). In clinical studies, most of these complaints were significantly reduced when compared to the 4 liter preparation. Table 1 shows patient rating of symptoms associated with the preparation from 2 clinical studies (n= 400). These adverse reactions are transient and subside rapidly. Isolated cases of urticaria, rhinorrhea, dermatitis and (rarely) anaphylactic reaction have been reported with PEG based products which may represent allergic reactions.

	HalfLyte and Bisacodyl Tablets Bowel Prep Kit	4 liters of PEG electrolyte solution
Nausea	17.1%	31.8%
Cramping	9.1%	17.4%
Fullness	22.3%	44.1%
Vomiting	5.9%	13.7%
Overall Discomfort	19.1%	37.3%

Published literature contains isolated reports of serious adverse reactions following the administration of (4L) PEG-ELS products in patients over 60 years of age. These adverse events include upper GI bleeding from Mallory-Weiss syndrome, esophageal perforation, asystole, sudden dyspnea with pulmonary edema, and “butterfly-like” infiltrate on chest X-ray after vomiting and aspirating PEG.

In addition, during administration of 4L PEG-3350 bowel cleansing preparations the following serious adverse events were seen: two deaths in end-stage renal failure patients who developed diarrhea, vomiting, dysnatremia; tonic-clonic seizures in patients with and without prior history of seizures. These adverse events have not been reported in HalfLyte and Bisacodyl Tablets Bowel Prep Kit clinical trials.

NDA 21-551/S-005

Page 5

Post-marketing cases of ischemic colitis have been associated with the use of HalfLyte[®] and Bisacodyl Tablets Bowel Prep Kit for colon preparation prior to colonoscopy. However, a causal relationship between these ischemic colitis cases and the use of HalfLyte[®] and Bisacodyl Tablets Bowel Prep Kit has not been established.

DOSAGE AND ADMINISTRATION:

HalfLyte[®] and Bisacodyl Tablets Bowel Prep Kit is administered orally. Ideally, the patient should only consume clear liquids (no solid food, no milk) prior to HalfLyte[®] and Bisacodyl Tablets Bowel Prep Kit administration. No antacids should be given for at least one hour before beginning the regimen.

Oral administration: Swallow all four bisacodyl delayed release tablets with water (do **NOT** chew or crush). The first bowel movement should occur in approximately 1-6 hours after taking the bisacodyl delayed release tablets. Wait for a bowel movement (or maximum of 6 hours) then drink the solution at a rate of 1 (8 oz) glass every 10 minutes (approximately 8 glasses). **Drink ALL of the solution.** Rapid drinking of each portion is preferred to drinking small amounts continuously. A watery bowel movement should occur in approximately 1 hour after drinking the solution.

The recommended regimen is to consume clear liquids only (no solid food, no milk) the day of the preparation, take all four bisacodyl delayed release tablets at noon, following the first bowel movement or a maximum of 6 hours, begin drinking the solution.

Preparation of the solution: The solution is prepared by filling the container to the 2 liter mark with water, cap the bottle and shake to dissolve ingredients. Dissolution is facilitated by using lukewarm water. The reconstituted solution may be refrigerated and should be used within 48 hours. All reconstituted solutions are clear and colorless.

HOW SUPPLIED: HalfLyte[®] and Bisacodyl Tablets Bowel Prep Kit is available in Lemon-Lime flavor. Each foil lined blister pack contains 4 (5 mg each) bisacodyl delayed release tablets for ingestion prior to drinking of the solution. Each disposable bottle contains powder for oral administration as a solution following reconstitution.

Each HalfLyte[®] and Bisacodyl Tablets Bowel Prep Kit contains:

One pack bisacodyl delayed release tablets: Four (5 mg each) bisacodyl delayed release tablets.

One 2 liter bottle of HalfLyte[®] (PEG-3350, sodium chloride, sodium bicarbonate and potassium chloride for oral solution): polyethylene glycol 3350 210 g, sodium bicarbonate 2.86 g, sodium chloride 5.60 g, potassium chloride 0.74 g, and 1.0 g flavoring ingredient (if applicable). When made up to 2 liters volume with water, the solution contains PEG-3350 31.3 mmol/L, sodium 65 mmol/L, chloride 53 mmol/L, bicarbonate 17 mmol/L and potassium 5 mmol/L.

All reconstituted solutions are clear and colorless.

NDA 21-551/S-005

Page 6

STORAGE: Store at 20-25°C (68-77°F). Excursions permitted between 15-30°C (59-86°F). When reconstituted, you may keep solution refrigerated. Use within 48 hours.

Lemon-Lime HalfLytely and Bisacodyl Tablets
Bowel Prep Kit
HalfLytely and Bisacodyl Tablets
Bowel Prep Kit with Flavor Packs

NDC 52268-502-01

NDC 52268-520-01

**Distributed by Braintree Laboratories, Inc.
Braintree, MA 02185**