SUFLAVE- polyethylene glycol 3350, sodium sulfate, potassium chloride, magnesium sulfate, and sodium chloride for oral solution
Braintree Laboratories, Inc.

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use SUFLAVE ®safely and effectively. See full prescribing information for SUFLAVE.

SUFLAVE (polyethylene glycol 3350, sodium sulfate, potassium chloride, magnesium sulfate, and sodium chloride for oral solution)
Initial U.S. Approval: 2023

INDICATIONS AND USAGE

SUFLAVE is an osmotic laxative indicated for cleansing of the colon in preparation for colonoscopy in adults. (1)

DOSAGE AND ADMINISTRATION

Preparation and Administration (2.1)

- Administration of two doses of SUFLAVE are required for a complete preparation for colonoscopy.
- One dose of SUFLAVE is equal to one bottle plus one flavor enhancing packet.
- Each bottle must be reconstituted with water before ingestion.
- An additional 16 ounces of water must be consumed after each dose.
- Stop consumption of all fluids at least 2 hours before the colonoscopy.

Recommended Dosage and Administration (2.2)

- The recommended Split-Dose (two-day) regimen consists of two doses of SUFLAVE *:*
  o *Day 1, Dose 1: Evening before Colonoscopy:* 1 bottle with flavor enhancing packet
  o *Day 2, Dose 2: Morning of the Colonoscopy (5 to 8 hours prior to the colonoscopy and no sooner than 4 hours from starting Dose 1):*1 bottle with flavor enhancing packet
- For complete information on preparation before colonoscopy and administration of the dosage regimen, see full prescribing information. (2.1, 2.2)

DOSAGE FORMS AND STRENGTHS

For Oral Solution: Two bottles and two flavor enhancing packets.

- Each bottle contains 178.7 g polyethylene glycol 3350, 7.3 g sodium sulfate, 1.12 g potassium chloride, 0.9 g magnesium sulfate, and 0.5 g sodium chloride. The bottle also contains lemon-lime flavoring. (3)

CONTRAINDICATIONS

- Gastrointestinal obstruction or ileus (4, 5.6)
- Bowel perforation (4, 5.6)
- Toxic colitis or toxic megacolon (4)
- Gastric retention (4)
- Hypersensitivity to any ingredient in SUFLAVE (4)

WARNINGS AND PRECAUTIONS

- Risk of fluid and electrolyte abnormalities: Encourage adequate hydration, assess concurrent medications and consider laboratory assessments prior to and after each use. (5.1, 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 seizures, including medications that lower the seizure threshold. (5.3, 7.1)
- Colonic mucosal ulcerations: Consider potential for ulcerations when interpreting colonoscopy findings in patients with known or suspected inflammatory bowel disease. (5.5)
- Patients with renal impairment or taking concomitant medications that affect renal function: Use caution, ensure adequate hydration and consider laboratory testing. (5.4, 7.1)
- Suspected GI obstruction or perforation: Rule out the diagnosis before administration. (4, 5.6)
- Patients at risk for aspiration: Observe during administration (5.7)
- Hypersensitivity reactions, including anaphylaxis: Inform patients to seek immediate medical care if symptoms occur (5.8)

ADVERSE REACTIONS

Most common adverse reactions (≥2%) are: nausea, abdominal distension, vomiting, abdominal pain and headache. (6.1)

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

Drugs that increase risk of fluid and electrolyte imbalance. (7.1)

See 17 for Medication Guide.

Revised: 6/2023

FULL PRESCRIBING INFORMATION: CONTENTS*

16 HOW SUPPLIED/STORAGE AND HANDLING

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

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

SUFLAVE is indicated for the cleansing of the colon as a preparation for colonoscopy in adults.

2 DOSAGE AND ADMINISTRATION

2.1 Important Preparation and Administration Instructions

- Correct fluid and electrolyte abnormalities before treatment with SUFLAVE *[see Warnings and Precautions (5.1)]*
- Two doses of SUFLAVE are required for a complete preparation for colonoscopy. One dose of SUFLAVE is equal to one bottle plus one flavor enhancing packet.
- Reconstitue each bottle with water before ingestion. Do not reconstitute SUFLAVE with liquids other than water and/or add starch-based thickeners to the mixing bottle *[see Warnings and Precautions (5.7)]* .
- Must consume an additional 16 ounces of water after each dose of SUFLAVE.
- Consume a low residue breakfast on the day before colonoscopy. After breakfast, only consume clear liquids up to 2 hours prior to colonoscopy.
- Do not eat solid food or drink milk or eat or drink anything colored red or purple.
- Do not drink alcohol.
- Do not take other laxatives while taking SUFLAVE. *[see Drug Interactions (7.3)].*
- Do not take oral medications within 1 hour of starting each dose of SUFLAVE. *[see Drug Interactions (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 each dose of SUFLAVE *[see Drug Interactions (7.2)]* .
- Stop consumption of all fluids at least 2 hours prior to the colonoscopy.
- If nausea, bloating, or abdominal cramping occurs, pause or slow the rate of drinking the solution and additional water until symptoms diminish.

2.2 Split-Dose (2-Day) Recommended Doasge

The recommended Split-Dose (two-day) regimen consists of two doses of SUFLAVE:

- *Day 1, Dose 1: Evening before Colonoscopy*: 1 bottle with flavor enhancing packet
- *Day 2, Dose 2: Morning of the Colonoscopy (5 to 8 hours prior to the colonoscopy and no sooner than 4 hours from starting Dose 1)*: 1 bottle with flavor enhancing packet

2.3 Preparation and Administration Instructions

The Day Prior to Colonoscopy:

- A low residue breakfast may be consumed. Examples of low residue foods are white bread, biscuits, muffins (no wheat), cornflakes, eggs, cream of wheat, grits, yogurt, cottage cheese, coffee, tea, juice without pulp, fruit (no skin or seeds).
- After breakfast, only consume clear liquids until after the colonoscopy. Examples of clear liquids are water, fruit juice (without pulp), lemonade, plain coffee, tea (no cream or non-dairy creamer), chicken broth, gelatin dessert (no fruit or topping).
- No red or purple liquids, no milk or alcoholic beverages.

Day 1, Dose 1 - Early in the Evening Prior to Colonoscopy:

- Open 1 flavor enhancing packet and pour the contents into 1 bottle.
- Fill the provided bottle with lukewarm water up to the fill line. After capping the bottle, gently shake the bottle until all powder has dissolved. For best taste, refrigerate the solution for an hour before drinking. Do not freeze. Use within 24 hours.
- Drink 8 ounces of solution every 15 minutes until the bottle is empty.
- Drink an additional 16 ounces of water during the evening.

If nausea, bloating, or abdominal cramping occurs, pause or slow the rate of drinking the solution and additional water until symptoms diminish.

Day 2, Dose 2 - The Morning of the Colonoscopy (5 to 8 hours prior to the colonoscopy and no sooner than 4 hours from starting Dose 1):

Continue to consume only clear liquids until after the colonoscopy.

1. Repeat Step 1 to Step 3 from Day 1, Dose 1.
2. Drink an additional 16 ounces of water during the morning.

- Stop drinking liquids at least 2 hours prior to colonoscopy.
- If nausea, bloating, or abdominal cramping occurs, pause or slow the rate of drinking the solution and additional water until symptoms diminish.

Storage of Reconstituted Solution

After reconstitution, keep solution refrigerated 2°C to 8°C (36°F to 46°F). Do not freeze. Use within 24 hours, discard unused solution.

3 DOSAGE FORMS AND STRENGTHS

SUFLAVE is supplied as a white powder for reconstitution and is available in a carton that contains two bottles and two flavor enhancing packets.

- Each bottle contains 178.7 g polyethylene glycol 3350, 7.3 g sodium sulfate, 1.12 g potassium chloride, 0.9 g magnesium sulfate, and 0.5 g sodium chloride. The bottle contains lemon-lime flavoring.

When diluted as directed, the solution is slightly hazy to hazy.

4 CONTRAINDICATIONS

SUFLAVE is contraindicated in the following conditions:

- 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 ingredient in SUFLAVE *[see Warnings and Precautions (5.8)]*

5 WARNINGS AND PRECAUTIONS

5.1 Serious Fluid and Electrolyte Abnormalities

Advise all patients to hydrate adequately before, during, and after the use of SUFLAVE. If a patient develops significant vomiting or signs of dehydration after taking SUFLAVE, consider performing post-colonoscopy lab tests (electrolytes, creatinine, and BUN).

Bowel preparation products can cause fluid and electrolyte disturbances, which can lead to serious adverse reactions including cardiac arrhythmias, seizures, and renal impairment *[see Adverse Reactions (6.2)]* . Correct fluid and electrolyte abnormalities before treatment with SUFLAVE. Use SUFLAVE with caution in patients with conditions, or who are using medications [such as diuretics, angiotensin converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARBs)], that increase the risk for fluid and electrolyte disturbances or may increase the risk of seizure, arrhythmias, and renal impairment *[see Drug Interactions (7.1)]* .

5.2 Cardiac Arrythmias

There have been rare reports of serious arrhythmias associated with the use of ionic osmotic laxative products for bowel preparation. These occur predominantly in patients with underlying cardiac risk factors and electrolyte disturbances. Use caution when prescribing SUFLAVE for patients at increased risk of arrhythmias (e.g., patients with a history of prolonged QT interval, 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 and/or loss of consciousness associated with 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 SUFLAVE for patients with a history of seizures and in patients at increased 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 Drug Interactions (7.1)]* .

5.4 Use in Patients with Risk of Renal Injury

Use SUFLAVE with caution in 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 risk for

renal injury. Advise these patients of the importance of adequate hydration with SUFLAVE and consider performing baseline and postcolonoscopy laboratory tests (electrolytes, creatinine, and BUN) in these patients *[see Use in Specific Populations (8.6)]* .

5.5 Colonic Mucosal Ulcerations and Ischemic Colitis

Osmotic laxative products may produce colonic mucosal aphthous ulcerations, and there have been reports of more serious cases of ischemic colitis requiring hospitalization. Concurrent use of stimulant laxatives and SUFLAVE may increase these risks *[see Drug Interactions (7.3)]* . Consider the potential for mucosal ulcerations resulting from the bowel preparation when interpreting colonoscopy findings in patients with known or suspect inflammatory bowel disease.

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 SUFLAVE *[see Contraindications (4)]* .

Use with caution in patients with severe active ulcerative colitis.

5.7 Aspiration

Patients with impaired gag reflex or other swallowing abnormalities are at risk for regurgitation or aspiration of SUFLAVE. Observe these patients during administration of SUFLAVE.

Do not combine SUFLAVE with starch-based thickeners *[see Dosage and Administration (2.1)]* . Polyethylene glycol (PEG), a component of SUFLAVE, when mixed with starch-thickened liquids reduces the viscosity of the starch-thickened liquid. When a PEG-based product used for another indication was mixed in starch-based pre-thickened liquids used in patients with dysphagia, thinning of the liquid occurred and cases of choking and potential aspiration were reported.

5.8 Hypersensitivity Reactions

SUFLAVE contains polyethylene glycol (PEG) and other ingredients that may cause serious hypersensitivity reactions including anaphylaxis, angioedema, rash, urticaria, and pruritus *[see Adverse Reactions (6.2)]* . Inform patients of the signs and symptoms of anaphylaxis, and instruct them to seek immediate medical care should signs and symptoms occur.

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)]*
- Patients with Risk of Renal Injury *[see Warnings and Precautions (5.4)]*
- Colonic Mucosal Ulceration and Ischemic Colitis *[see Warnings and Precautions (5.5)]*

- Patients with Significant Gastrointestinal Disease *[see Warnings and Precautions (5.6)]*
- Aspiration *[see Warnings and Precautions (5.7)]*
- Hypersensitivity Reactions *[see Warnings and Precautions (5.8)]*

6.1 Clinical Trials Experience

Because clinical studies 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.

The safety of SUFLAVE was evaluated in two randomized, parallel group, multicenter, investigator-blinded clinical trials in 929 adult patients undergoing colonoscopy. The active comparators were polyethylene glycol 3350, sodium sulfate, sodium chloride, potassium chloride, ascorbic acid and sodium ascorbate for oral solution in Study 1 and sodium sulfate, potassium sulfate, and magnesium sulfate oral solution in Study 2 *[see Clinical Studies (14)]* .

Table 1 shows the most common adverse reactions reported in at least 2% of patients in either treatment group in Study 1.

Table 1: Common Adverse Reactions [a] by Treatment Group in Adult Patients Undergoing Colonoscopy in Study 1 [b]

	SUFLAVE (%) N=233	Polyethylene glycol 3350, sodium sulfate, sodium chloride, potassium chloride, ascorbic acid and sodium ascorbate for oral solution (%) N=243
Nausea	13	9
Abdominal distension	6	3
Vomiting	6	3
Abdominal pain [c]	3	4
Headache	3	2

[a] Reported in at least 2% of patients in either treatment group.
[b] Study 1 was not designed to support comparative claims for SUFLAVE for the adverse reactions reported in this table.
[c] Abdominal pain is composed of several similar terms.

Table 2 shows the most common adverse reactions reported in at least 2% of patients in either treatment group in Study 2.

Table 2: Common Adverse Reactions [a] by Treatment Group in Adult Patients Undergoing Colonoscopy in Study 2 [b]

	SUFLAVE (%) N=227	Sodium sulfate, potassium sulfate, and magnesium sulfate oral solution (%) N=226
Nausea	7	6
Vomiting	4	7

Headache	2	2
Abdominal pain [c]	3	1
Abdominal distension	1	1

[a] Reported in at least 2% of patients in any treatment group.
[b] Study 2 was not designed to support comparative claims for SUFLAVE for the adverse reactions reported in this table.
[c] Abdominal pain is composed of several similar items.

Laboratory Changes

Electrolyte Abnormalities

In patients with normal baseline values, the most common electrolyte abnormality following study drug, on the day of colonoscopy, was increased magnesium (Study 1: 11% in SUFLAVE-treated patients and 2% in patients treated with active comparator; Study 2: 12% in SUFLAVE-treated patients and 11% in patients treated with active comparator). These changes were transient and resolved without intervention.

Renal Function Parameters

In patients with normal baseline values, at 48 to 72 hours after bowel preparation, an increase in serum creatinine of > 0.3 mg/dL and/or a decrease in eGFR of > 25% were reported in 2% of SUFLAVE-treated patients and 0 patients treated with active comparator in Study 1 and 1% of SUFLAVE-treated patients and 3% of patients treated with active comparator in Study 2. These changes were transient and resolved.

6.2 Postmarketing Experience

The following adverse reactions have been identified during post-approval use of other polyethylene glycol-based 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.

Cardiovascular: arrhythmia, atrial fibrillation, peripheral edema, asystole, acute pulmonary edema *[see Warnings and Precautions (5.2)]* .

Gastrointestinal: upper gastrointestinal bleeding from a Mallory-Weiss tear; esophageal perforation, usually with gastroesophageal reflux disease

Hypersensitivity reactions: rash, urticaria, pruritus, dermatitis, dyspnea, chest tightness and throat tightness, fever, angioedema, anaphylaxis and anaphylactic shock *[see Warnings and Precautions (5.8)]* .

Nervous system: tremor, seizure *[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 SUFLAVE to patients taking medications that increase the risk of fluid and electrolyte disturbances or may increase the risk of adverse events of seizure, arrhythmias, and prolonged QT 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

SUFLAVE can reduce the absorption of other co-administered drugs *[see Dosage and Administration (2.1)]* :

- Administer oral medications at least one hour before starting each dose of SUFLAVE.
- Administer tetracycline and fluoroquinolone antibiotics, iron, digoxin, chlorpromazine, and penicillamine at least 2 hours before and not less than 6 hours after administration of each dose of SUFLAVE to avoid chelation with magnesium.

7.3 Stimulant Laxatives

Concurrent use of stimulant laxatives and SUFLAVE may increase the risk of mucosal ulceration or ischemic colitis. Avoid use of stimulant laxatives (e.g., bisacodyl, sodium picosulfate) while taking SUFLAVE *[see Warnings and Precautions (5.5)]* .

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

There are no available data on the use of SUFLAVE during pregnancy to evaluate for a drug-associated risk of major birth defects, miscarriage, or adverse maternal or fetal outcomes. Animal reproduction studies have not been conducted with polyethylene glycol 3350, sodium sulfate, potassium chloride, magnesium sulfate, and sodium chloride (SUFLAVE).

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.

8.2 Lactation

Risk Summary

There are no available data on the presence of SUFLAVE in human or animal milk, the effects of on the breastfed child, or the effects on milk production.

The developmental and health benefits of breastfeeding should be considered along with the mother’s clinical need for SUFLAVE and any potential adverse effects on the breastfed child from SUFLAVE or from the underlying maternal condition.

8.4 Pediatric Use

The safety and effectiveness of SUFLAVE in pediatric patients have not been established.

8.5 Geriatric Use

Of the 460 patients who received SUFLAVE in clinical trials, 125 (27%) were 65 years of age or older. No differences in effectiveness of SUFLAVE were observed between geriatric patients and younger adult patients. Among geriatric patients, decreases in blood pressure on the day of colonoscopy were reported more frequently with SUFLAVE than with the active comparator in Study 1 (6% in SUFLAVE-treated patients and 1% in patients treated with active comparator) in Study 2 (3% in SUFLAVE-treated patients and

0% treated with active comparator) *[see Clinical Studies (14)]* .

Geriatric 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)]* . Advise geriatric patients to hydrate adequately before, during, and after the use of SUFLAVE.

8.6 Renal Impairment

Use SUFLAVE with caution in patients with renal impairment or patients taking concomitant medications that may affect renal function. These patients may be at risk for renal injury. Advise these patients of the importance of adequate hydration before, during and after use of SUFLAVE and consider performing baseline and post-colonoscopy laboratory tests (electrolytes, creatinine, and BUN) in these patients *[see Warning and Precautions (5.4)]* .

10 OVERDOSAGE

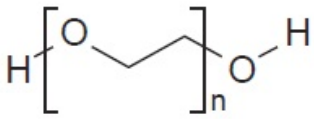
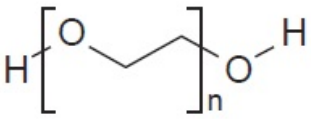
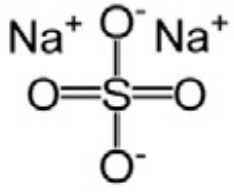
Overdosage of more than the recommended dose of SUFLAVE may lead to severe electrolyte disturbances, as well as dehydration and hypovolemia, with signs and symptoms of these disturbances *[see Warnings and Precautions (5.1, 5.2, 5.3)]* . Monitor for fluid and electrolyte disturbances and treat symptomatically.

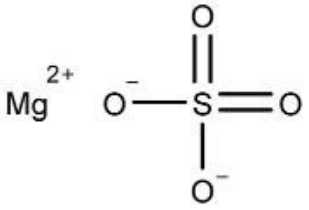
11 DESCRIPTION

SUFLAVE (polyethylene glycol 3350, sodium sulfate, potassium chloride, magnesium sulfate, and sodium chloride for oral solution) is an osmotic laxative and is provided in two bottles and two flavor enhancing packets for oral solution.

The active ingredients contained in SUFLAVE are provided in Table 3.

Table 3: Active Ingredients in SUFLAVE

Chemical Name	Chemical Formula	Average Molecular Weight (g/mol)	Chemical Structure
Polyethlyene Glycol 3350, USP		3350	
Sodium Sulfate, USP	Na_2SO_4	142.04	

Magnesium Sulfate, USP	$MgSO_4$	120.37	
Potassium Chloride, USP	KCl	74.55	
Sodium Chloride, USP	NaCl	58.44	Na^+Cl^-

Each bottle contains 178.7 g polyethylene glycol 3350, 7.3 g sodium sulfate, 1.12 g potassium chloride, 0.9 g magnesium sulfate, and 0.5 g sodium chloride, plus the following excipients: advantame, lemon-lime flavor, and neotame.

Each flavor enhancing packet contains anhydrous citric acid, colloidal silicon dioxide, malic acid, and sucralose.

Each dose of reconstituted oral solution is one liter of slightly hazy to hazy liquid that contains 178.7 g polyethylene glycol 3350, 7.3 g sodium sulfate, 1.12 g potassium chloride, 0.9 g magnesium sulfate, and 0.5 g sodium chloride and the following excipients: advantame, anhydrous citric acid, colloidal silicon dioxide, lemon-lime flavor, malic acid, neotame, and sucralose.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

The primary mode of action is the osmotic effects of polyethylene glycol 3350, sodium sulfate and magnesium sulfate, which induce a laxative effect. The physiological consequence is increased water retention in the lumen of the colon, resulting in loose stools.

12.3 Pharmacokinetics

After administration of the first dose of SUFLAVE in 18 healthy subjects, the mean ± SD maximum plasma concentration (C_{max}) for polyethylene glycol 3350 of 3.4 ± 1.4 mcg/mL was reached at 4 hours, and the mean ± SD serum C_{max} for sulfate of 27.0 ± 11.4 mcg/mL was reached at 6 hours. Following a second dose of SUFLAVE (approximately 12 hours later), the mean ± SD plasma C_{max} for polyethylene glycol 3350 of 2.9 ± 0.97 mcg/mL was reached at 4 hours, and the mean ± SD serum C_{max} for sulfate of 29.2 ± 11.0 mcg/mL was reached at 3 hours. Sulfate concentrations were below the limit of quantitation (19.2 mcg/mL) for all subjects by follow-up Day 3. Polyethylene glycol 3350 concentrations were below the limit of quantitation (LOQ 0.01 mcg/mL) for 16 of 18 subjects by follow-up Day 7.

14 CLINICAL STUDIES

The colon cleansing efficacy of SUFLAVE was evaluated in two randomized, single-blind, active-controlled, multicenter trials (Study 1 and Study 2). These trials included adult

patients undergoing colonoscopy for colorectal cancer screening and surveillance, or diagnostic colonoscopy, including patients with abdominal pain, diarrhea, constipation and non-severe inflammatory bowel disease.

In Study 1 (NCT04446299), 471 adult patients were included in the efficacy analysis. Patients ranged in age from 20 to 84 years (median age 58 years) and 54% were female. The racial distribution was 70% White, 27% African-American, 2% Asian, and 1% American Indian or Alaska Native. The population was 8% Hispanic or Latino. Patients were randomized to one of the following two colon preparation regimens: SUFLAVE or polyethylene glycol 3350, sodium sulfate, sodium chloride, potassium chloride, ascorbic acid and sodium ascorbate for oral solution. Both preparations were administered according to a split-dose regimen *[see Dosage and Administration (2.2)]* . Patients receiving SUFLAVE were limited to a low residue breakfast followed by clear liquids on the day prior to the colonoscopy; patients receiving the comparator bowel prep were allowed to have a normal breakfast and a light lunch, followed by clear liquids and/or yogurt for dinner on the day prior to the colonoscopy.

In Study 2 (NCT04446312), 450 adult patients were included in the efficacy analysis. Patients ranged in age from 18 to 80 years (median age 57 years) and 58% were female. The racial distribution was 85% White, 10% African-American, 3% Asian, and < 1% American Indian or Alaska Native. The population was 21% Hispanic or Latino. Patients were randomized to one of the following two colon preparation regimens: SUFLAVE or sodium sulfate, potassium sulfate, and magnesium sulfate oral solution. Both preparations were administered according to a split-dose regimen *[see Dosage and Administration (2.2)]* . Patients receiving SUFLAVE were limited to a low residue breakfast followed by clear liquids on the day prior to the colonoscopy; patients receiving the comparator bowel prep were allowed a light breakfast followed by clear liquids on the day prior to the colonoscopy.

The primary efficacy endpoint in each trial was the proportion of patients with successful colon cleansing, as assessed by the blinded colonoscopist utilizing the four-point scale described in Table 4. Success was defined as an overall cleansing assessment of 3 (Good) or 4 (Excellent).

Table 4: Description of Colonoscopy Scoring

Score	Grade	Description
1	Poor	Large amount of fecal residue, additional bowel preparation required.
2	Fair	Enough feces even after washing and suctioning to prevent clear visualization of the entire colonic mucosa.
3	Good	Feces and fluid requiring washing and suctioning, but still achieves clear visualization of the entire colonic mucosa.
4	Excellent	No more than small bits of feces/fluid which can be suctioned easily; achieves clear visualization of the entire colonic mucosa.

Results for the primary endpoint in Studies 1 and 2 are shown in Table 5. In both trials, SUFLAVE was non-inferior to the active comparator.

Table 5: Proportion of Adult Patients with Overall Cleansing Success [a] in Two Controlled Trials with a Split-Dose Regimen

	SUFLAVE % (n/N)	Active Comparator % (n/N)	SUFLAVE-Active Comparator	
			Difference [b](%)	99% Confidence Interval [b]
Study 1	93% (215/232)	89% [c] (212/239)	3.4%	(-1.7%, 8.5%) [e]
Study 2	94% (212/226)	94% [d] (211/224)	0.2%	(-4.0%, 4.3%) [e]

[a] success was defined as an overall cleaning assessment of 3 (Good) or 4 (Excellent) by the blinded endoscopist, with scores assigned on withdrawal of colonoscope.

[b] common risk differences and confidence intervals were based on Mantel-Haenszel method adjusting for study site

[c] active comparator in Study 1 was polyethylene glycol 3350, sodium sulfate, sodium chloride, potassium chloride, sodium ascorbate and ascorbic acid for oral solution

[d] active comparator in Study 2 was sodium sulfate, potassium sulfate, and magnesium sulfate oral solution

[e] non-inferiority was demonstrated

16 HOW SUPPLIED/STORAGE AND HANDLING

SUFLAVE (polyethylene glycol 3350, sodium sulfate, potassium chloride, magnesium sulfate, and sodium chloride for oral solution) is supplied as a white powder for reconstitution and is lemon-lime flavored.

Each carton of SUFLAVE (NDC 52268-550-01) contains:

- Two bottles, each bottle (NDC 52268-551-01), closed with child resistant closure, contains a white powder of 178.7 g polyethylene glycol 3350, 7.3 g sodium sulfate, 1.12 g potassium chloride, 0.9 g magnesium sulfate, and 0.5 g sodium chloride for reconstitution. The bottle contains lemon-lime flavor.
- Two flavor enhancing packets (NDC 52268-552-01).

Storage
Store SUFLAVE at room temperature between 20º to 25°C (68º to 77°F), excursions permitted from 15º to 30°C (59º to 86°F). 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:

- Administration of two doses of SUFLAVE are required for a complete preparation for colonoscopy.
- Must reconstitute each bottle with water before ingestion.
- Must consume an additional 16 ounces of water after each dose of SUFLAVE.
- To hydrate adequately with clear liquids before, during, and after the use of SUFLAVE to prevent dehydration *[see Warnings and Precautions (5.1)]* . Examples of clear liquids can be found in the *Instructions for Use*.
- If nausea, bloating, or abdominal cramping occurs, pause or slow the rate of drinking

the solution and additional water until symptoms diminish.
- Do not take other laxatives while taking SUFLAVE.
- Do not drink milk or eat or drink anything colored red or purple.
- Do not drink alcohol.
- Do not take oral medications within one hour of starting each dose of SUFLAVE *[see Drug Interactions (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 each dose of SUFLAVE *[see Drug Interactions (7.2)]* .
- Complete all SUFLAVE and required water at least two hours prior to colonoscopy.
- Contact their healthcare provider if they develop significant vomiting or signs of dehydration after taking SUFLAVE or if they experience cardiac arrhythmias or seizures *[see Warnings and Precautions (5.1, 5.2, 5.3)]* .
- Seek immediate medical care if signs and symptoms of a hypersensitivity reaction occur *[see Warnings and Precautions (5.8)]* .

Manufactured by:

Braintree Laboratories, Inc.
270 Centre Street
Holbrook, MA 02343

Please see www.sebelapharma.com for patent information.

MEDICATION GUIDE
SUFLAVE ®(Soo-FLAVE)
(polyethylene glycol 3350, sodium sulfate, potassium chloride, magnesium sulfate, and sodium chloride for oral solution)

Read and understand this Medication Guide and the Instructions for Use **at least 2 days before**your colonoscopy and again before you start taking SUFLAVE.

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

SUFLAVE 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 body salts with SUFLAVE is higher if you:
- have heart problems.
- have kidney problems.
- take water pills (diuretics), high blood pressure medication, 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 SUFLAVE:

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

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

What is SUFLAVE?

SUFLAVE is a prescription medicine used by adults to clean the colon before a colonoscopy. SUFLAVE cleans your colon by causing you to have diarrhea (loose stools). Cleaning your colon helps your healthcare provider see the inside of your colon more clearly during your colonoscopy.

It is not known if SUFLAVE is safe and effective in children.

Do not take SUFLAVE if your healthcare provider has told you that you have:

- a blockage in your bowel (obstruction) or a problem with food moving too slowly through your intestines (ileus).
- an opening in the wall of your stomach or intestine (bowel perforation).
- a very dilated intestine (toxic colitis or toxic megacolon).
- problems with food and fluid emptying from your stomach (gastric retention).
- an allergy to any ingredient in SUFLAVE. See the end of this Medication Guide for a complete list of the ingredients in SUFLAVE.

Before taking SUFLAVE, 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 heart problems.
- have stomach or bowel problems including ulcerative colitis.
- have problems with swallowing, gastric reflux, or if you inhale food or fluid into your lungs when eating or drinking (aspirate).
- have a history of seizures.
- are withdrawing from drinking alcohol or from taking benzodiazepines.
- have a low blood salt (sodium) level.
- have kidney problems.
- are pregnant. It is not known if SUFLAVE 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 SUFLAVE passes into your breast milk. You and your healthcare provider should decide if you will take SUFLAVE while breastfeeding.

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

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

Especially tell your healthcare provider if you take:

- medicines to treat a blood salt (electrolyte) imbalance.
- medicines for blood pressure or heart problems.
- medicines for kidney problems.
- medicines for seizures.
- water pills (diuretics).
- non-steroidal anti-inflammatory drugs (NSAIDs).
- medicines for depression or other mental health problems.
- laxatives. **Do not**take other laxatives while taking SUFLAVE.
- starch-based thickeners. For patients who have trouble swallowing, **do not**mix SUFLAVE with starch-based thickeners.

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

• tetracycline	• iron	• chlorpromazine
• fluoroquinolone antibiotics	• digoxin	• penicillamine

Ask your healthcare provider or pharmacist for a list of these medicines if you are not sure if you are taking any of 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 SUFLAVE?

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

- Take SUFLAVE exactly as your healthcare provider tells you to take it.
- Two doses of SUFLAVE are required for a complete colonoscopy preparation. One dose of SUFLAVE is equal to one bottle plus one flavor enhancing packet.
- It is important for you to drink the additional prescribed amount of water listed in the Instructions for Use to prevent fluid loss (dehydration).
- SUFLAVE is taken using the **Split-Dose**method. See the Instructions for Use for more information.
- All people taking SUFLAVE should follow these general instructions starting 1 day before your colonoscopy:
  o you can eat a low-residue breakfast. Low-residue foods include white bread, biscuits, muffins (no wheat), cornflakes, eggs, cream of wheat, grits, yogurt, cottage cheese, coffee, tea, juice without pulp, and fruit (no skin or seeds).
  o after breakfast 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. Examples of clear liquids include water, fruit juices (without pulp), lemonade, coffee, tea (no cream or non-dairy creamer), chicken broth, and gelatin desserts (no fruit or topping).
  o after taking the first dose of SUFLAVE if you have any nausea, bloating or feeling like your stomach is upset, wait to take your second dose of SUFLAVE until your stomach feels better. Start taking your second dose 5 to 8 hours before the colonoscopy, but no sooner than 4 hours from taking your first dose.
- While taking SUFLAVE, **do not**:
  o take any other laxatives

o take oral medicines within 1 hour of starting each dose of SUFLAVE
o eat solid foods, dairy such as milk, or drink alcohol
o eat or drink anything colored red or purple

Contact your healthcare provider right away if after taking SUFLAVE you have severe vomiting, signs of too much fluid loss (dehydration), abnormal heartbeats or seizures.

What are the possible side effects of SUFLAVE?

SUFLAVE can cause serious side effects, including:

- **See "What is the most important information I should know about SUFLAVE?"**
- **Changes in certain blood tests.** Your healthcare provider may do blood tests after you take SUFLAVE 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 (abdominal) cramping o headache
  o urine less than usual
  o trouble drinking clear liquid
- **Heart problems. SUFLAVE may cause abnormal heartbeats.**
- **Seizures.**
- **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.
- **Serious allergic reactions.** Get medical help right away if you have any signs and symptoms of a serious allergic reaction while taking SUFLAVE including:
  o difficulty breathing o itching
  o swelling of the face, lips, taongue and throat o raised red patches on your skin (hives)
  o skin rash

The most common side effects of SUFLAVE include:

- nausea
- stomach (abdominal) pain
- stomach bloating (abdominal distention)
- headache
- vomiting

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

- Store SUFLAVE at room temperature between 68°F to 77°F (20°C to 25°C).
- Store mixed (reconstituted) SUFLAVE solution in the refrigerator at 36°F to 46°F (2°C to 8°C). Do not freeze.
- Used mixed (reconstituted) SUFLAVE solution within 24 hours.
- After 24 hours, throw away (discard) any mixed (reconstituted) SUFLAVE solution that is not used.

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

General information about the safe and effective use of SUFLAVE.

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use SUFLAVE for a condition for which it was not prescribed. Do not give SUFLAVE 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 that is written for health professionals.

What are the ingredients in SUFLAVE?
Active ingredients: polyethylene glycol 3350, sodium sulfate, potassium chloride, magnesium sulfate, and sodium chloride.
Inactive ingredients: advantame, anhydrous citric acid, colloidal silicon dioxide, lemon-lime flavor, malic acid, neotame, and sucralose.

Manufactured by:
Braintree Laboratories, Inc.
270 Centre Street
Holbrook, MA 02343
For more information, go to www.braintreelabs.comor call 1-800-874-6756.

This Medication Guide has been approved by the U.S. Food and Drug Administration.
Issued 06/2023

Principal Display Panel - Carton Label

NDC 52268-550-01

Dispense the enclosed Medication Guide to each patient.

SUFLAVE
(polyethylene glycol 3350, sodium sulfate, potassium chloride, magnesium sulfate, and sodium chloride for oral solution)
178.7g/7.3g/1.12 g/0.9g/0.5g

2 Doses of SUFLAVE are required for a complete preparation.

This carton contains:
2 Flavor Enhancing Packets
2 Bottles
1 Patient booklet, which includes:
1. Instructions for Use
2. Full Prescribing Information
3. Medication Guide

Rx only

Braintree
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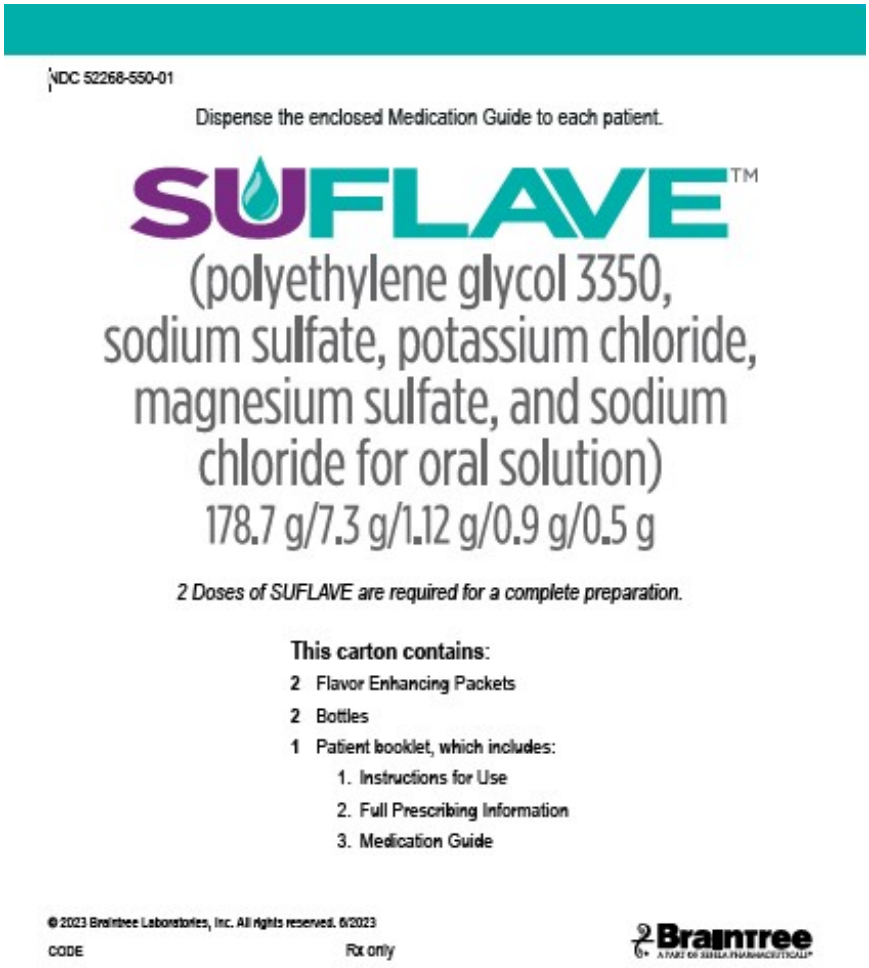


Principal Display Panel - Bottle Label

NDC 52268-551-01

SUFLAVE(polyethylene glycol 3350, sodium sulfate, potassium chloride, magnesium sulfate, and sodium chloride for oral solution)

178.7g/7.3g/1.12 g/0.9g/0.5g

Dispense the enclosed Medication Guide to each patient.

2 Doses of SUFLAVE are required for a complete preparation.

Rx only

Net Weight 188.73 g

NDC 52268-551-01

(polyethylene glycol 3350, sodium sulfate, potassium chloride, magnesium sulfate, and sodium chloride for oral solution)
178.7 g/7.3 g/1.12 g/0.9 g/0.5 g

Dispense the enclosed Medication Guide to each patient.

2 Doses of SUFLAVE are required for a complete preparation.

Rx only

Net Weight 188.73 g

Principal Display Panel - Flavor Enhancing Packet

NDC 52268-552-01

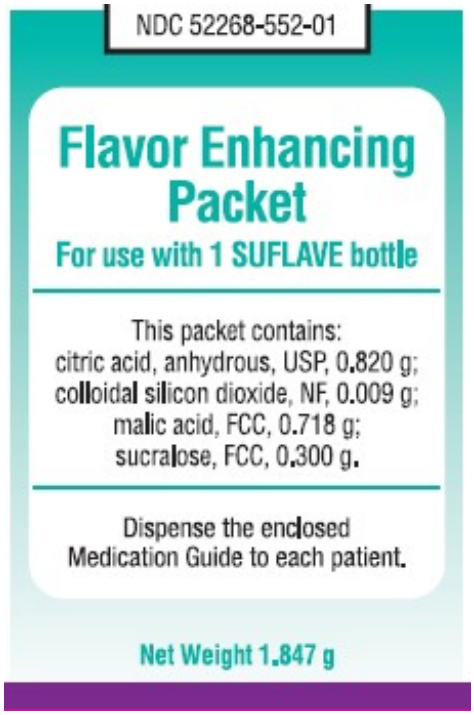
SUFLAVE

For use with 1 SUFLAVE Bottle

This packet contains:
citric acid, anhydrous, USP, 0.820 g;
colloidal silicon dioxide, NF, 0.009 g;
malic acid, FCC, 0.718 g;
sucralose, FCC, 0.300 g.

Dispense the enclosed Medication Guide to each patient.

Net Weight 1.847 g



SUFLAVE

polyethylene glycol 3350, sodium sulfate, potassium chloride, magnesium sulfate, and sodium chloride for oral solution kit

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:52268-550

Packaging				
#	**Item Code**	**Package Description**	**Marketing Start Date**	**Marketing End Date**
1	NDC:52268-550-01	1 in 1 KIT	06/15/2023	

Quantity of Parts		
Part #	**Package Quantity**	**Total Product Quantity**
Part 1		2
Part 2		2

Part 1 of 2

SUFLAVE

polyethylene glycol 3350, sodium sulfate, potassium chloride, magnesium sulfate, and sodium chloride for oral solution powder, for solution

Product Information

Item Code (Source)	NDC:52268-551
Route of Administration	ORAL

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
POLYETHYLENE GLYCOL 3350 (UNII: G2M7P15E5P) (POLYETHYLENE GLYCOL 3350 - UNII:G2M7P15E5P)	POLYETHYLENE GLYCOL 3350	178.7 g
SODIUM SULFATE (UNII: 0YPR65R21J) (SODIUM SULFATE ANHYDROUS - UNII:36KCS0R750)	SODIUM SULFATE	7.3 g
POTASSIUM CHLORIDE (UNII: 660YQ98I10) (POTASSIUM CATION - UNII:295O53K152)	POTASSIUM CATION	1.12 g
MAGNESIUM SULFATE ANHYDROUS (UNII: ML30MJ2U7I) (MAGNESIUM CATION - UNII:T6V3LHY838)	MAGNESIUM SULFATE ANHYDROUS	0.9 g
SODIUM CHLORIDE (UNII: 451W47IQ8X) (CHLORIDE ION - UNII:Q32ZN48698)	SODIUM CHLORIDE	0.5 g

Inactive Ingredients	
Ingredient Name	**Strength**
ADVANTAME (UNII: 3ZA6810AWX)	
NEOTAME (UNII: VJ597D52EX)	

Product Characteristics			
Color	white	**Score**	
Shape		**Size**	
Flavor	LEMON (Lemon-Lime)	**Imprint Code**	
Contains			

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA	NDA215344	06/15/2023	

Part 2 of 2

FLAVOR ENHANCING PACKET

flavor enhancing packet powder, for solution

Product Information	
Item Code (Source)	NDC:52268-552
Route of Administration	ORAL

Inactive Ingredients

Ingredient Name	Strength
MALIC ACID (UNII: 817L1N4CKP)	0.718 g
ANHYDROUS CITRIC ACID (UNII: XF417D3PSL)	0.82 g
SUCRALOSE (UNII: 96K6UQ3ZD4)	0.3 g
SILICON DIOXIDE (UNII: ETJ7Z6XBU4)	0.009 g

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA	NDA215344	06/15/2023	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA	NDA215344	06/15/2023	

Labeler - Braintree Laboratories, Inc. (107904591)

Establishment

Name	Address	ID/FEI	Business Operations
Braintree Laboratories, Inc.		617357954	manufacture(52268-550) , analysis(52268-550)

Revised: 6/2023 Braintree Laboratories, Inc.