CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

203595Orig1s000

Trade Name: SUCLEAR

Generic Name: sodium sulfate, potassium sulfate and magnesium sulfate oral solution; and PEG-3350, sodium chloride, sodium bicarbonate and potassium chloride for oral solution

Sponsor: Braintree Labs

Approval Date: January 18, 2013

Indications: Suclear is a combination of osmotic laxatives and indicated for cleansing of the colon in preparation for colonoscopy in adults.

CENTER FOR DRUG EVALUATION AND RESEARCH

203595Orig1s000

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APPLICATION NUMBER:

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APPROVAL LETTER

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 203595

NDA APPROVAL

Braintree Laboratories, Inc.
Attention: Vivian Caballero
Vice President, Regulatory Affairs
60 Columbian Street West
PO Box 850929
Braintree, MA 02185

Dear Ms. Caballero:

Please refer to your New Drug Application (NDA) dated December 16, 2011, received December 19, 2011, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA), for Suclear (sodium sulfate, potassium sulfate, and magnesium sulfate oral solution and PEG-3350, sodium chloride, sodium bicarbonate and potassium chloride powder for oral solution) 17.5g/3.13g/1.6g, and 210g/5.6g/2.86g/0.74g.

We acknowledge receipt of your amendments dated January 10 & 24, 2012; February 14, 2012; March 9, 20 & 23, 2012; April 13 & 25, 2012; May 31, 2012; June 11 & 21, 2012, July 2, 3, 19, 23 & 25, 2012; August 10, 2012; September 5, 7, 10 & 18, 2012; October 26, 2012; and January 4, 8, 11, 14, 16, 17, 2013.

This new drug application provides for the use of Suclear (sodium sulfate, potassium sulfate, and magnesium sulfate oral solution and PEG-3350, sodium chloride, sodium bicarbonate and potassium chloride powder for oral solution) for cleansing of the colon as a preparation for colonoscopy in adults.

We have completed our review of this application, as amended. It is approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling text and with the minor editorial revisions listed below.

For the Instructions For Use presented in the booklet and on the carton, revise as follows:

1. In the "Important Information" section:
   a. Replace the bullet that reads (b) (4) with the following:
   "Drink only clear liquids:
   - the day before your colonoscopy
   - while taking Suclear
   - after taking Suclear until 2 hours before your colonoscopy."

b. Immediately after the items listed in 1.a., add the statement, aligned to the left margin, in bold type, "Do not eat or drink anything for 2 hours before your colonoscopy."
c. Under "Important Information", delete the bullet that reads [redacted] (b) (4)
d. Under "Important Information", change [redacted] (b) (4) to "alcohol."

2. In the "Split-Dose (2-Day) Suclear bowel prep kit instructions" section:
   a. Delete [redacted] (b) (4) from the descriptions of Dose 1 - step 2 and Dose 2 - step 2.
   b. For step 3, replace [redacted] (b) (4) with "after mixing."

For the 2-Liter bottle:

3. Revise the list of ingredients in the presentation of the established name to read "(PEG-3350, sodium chloride, sodium bicarbonate and potassium chloride)."

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using the FDA automated drug registration and listing system (eLIST), as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm. Content of labeling must be identical to, except with the revisions listed, the enclosed labeling (text for package insert and Medication Guide). Information on submitting SPL files using eLIST may be found in the guidance for industry *SPL Standard for Content of Labeling Technical Qs and As*, available at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf.

The SPL will be accessible via publicly available labeling repositories.

CARTON AND IMMEDIATE-CONTAINER LABELS

Submit final printed carton and immediate-container labels that are identical to the carton and immediate-container labels submitted on October 26, 2012 (6-ounce bottle label) and January 17, 2013 (Carton, 2-Liter bottle label), except with the revisions listed above, as soon as they are available, but no more than 30 days after they are printed. Please submit these labels electronically according to the guidance for industry *Providing Regulatory Submissions in Electronic Format – Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications (June 2008)*. Alternatively, you may submit 12 paper copies, with 6 of the copies individually mounted on heavy-weight paper or similar material. For administrative purposes, designate this submission "**Final Printed Carton and Container Labels for approved NDA 203595**." Approval of this submission by FDA is not required before the labeling is used.

Marketing the product with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

MARKET PACKAGE

Please submit one market package of the drug product when it is available to the following address:

Matthew Scherer
Food and Drug Administration
Center for Drug Evaluation and Research
White Oak Building 22, Room: 5139
10903 New Hampshire Avenue
Silver Spring, Maryland
Use zip code **20903** *if shipping via United States Postal Service (USPS).*
Use zip code **20993** *if sending via any carrier other than USPS (e.g., UPS, DHL, FedEx).*

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We are waiving the pediatric study requirement for ages birth to less than 1 year because the product does not represent a meaningful therapeutic benefit over existing therapies for pediatric patients in this age group **and** is not likely to be used in a substantial number of pediatric patients in this group. In this age group, bowel cleansing can be achieved with administration of clear liquids only for 24 hours with or without suppositories or enemas. Additionally, there are an insubstantial number of colonoscopies performed in pediatric patients under age 1 year.

We are deferring submission of your pediatric studies for patients 1 to 16 years of age for this application because this product is ready for approval for use in adults and the pediatric studies have not been completed.

Your deferred pediatric studies required by section 505B(a) of the FDCA are required postmarketing studies. The status of this postmarketing study must be reported annually according to 21 CFR 314.81 and section 505B(a)(3)(B) of the FDCA. The required studies are listed below.

1998-1 An open-label pilot study assessing the efficacy and tolerability of Suclear in pediatric patients 12-16 years of age, inclusive. This study will include PK assessments.

Final Protocol Submission: 06/14
Study Completion: 03/15
Final Report Submission: 06/15

1998-2 A randomized, single-blind, multicenter, dose-ranging study comparing the safety and efficacy of Suclear (up to 3 doses) versus community standard of care in pediatric patients 12-16 years of age, inclusive.

Final Protocol Submission: 09/15
Study Completion: 09/16
Final Report Submission: 12/16

1998-3 A randomized, single-blind, multicenter, dose-ranging study comparing the safety and efficacy of Suclear (up to 3 doses) versus community standard of care in pediatric patients 3-11 years of age, inclusive.

Final Protocol Submission: 03/17
Study Completion: 03/18
Final Report Submission: 06/18

1998-4 A randomized, single-blind, multicenter, dose-ranging study comparing the safety and efficacy of Suclear (up to 3 doses) versus community standard of care in pediatric patients 1-2 years of age, inclusive.

Final Protocol Submission: 09/18
Study Completion: 09/19
Final Report Submission: 12/19

1998-5 Assess the systemic exposure and pharmacokinetics of PEG 3350, (b) (4) ollowing oral administration of Suclear in an adequate number of pediatric patients, encompassing all relevant age groups. These assessments may be conducted as part of the PREA required studies listed above.

Final Protocol Submission: 09/18
Study Completion: 09/19
Final Report Submission: 12/19

Submit the protocols to your IND 102894 with a cross-reference letter to this NDA.

Reports of these required pediatric postmarketing studies must be submitted as a new drug application (NDA) or as a supplement to your approved NDA with the proposed labeling changes you believe are warranted based on the data derived from these studies. When submitting the reports, please clearly mark your submission "**SUBMISSION OF REQUIRED PEDIATRIC ASSESSMENTS**" in large font, bolded type at the beginning of the cover letter of the submission.

POSTMARKETING REQUIREMENTS UNDER 505(o)

Section 505(o)(3) of the FDCA authorizes FDA to require holders of approved drug and biological product applications to conduct postmarketing studies and clinical trials for certain purposes, if FDA makes certain findings required by the statute.

We have determined that an analysis of spontaneous postmarketing adverse events reported under subsection 505(k)(1) of the FDCA will not be sufficient to assess a known serious risk of fluid and serum chemistry abnormalities, and the signal of a serious risk related to exposure to toxic impurities (b) (4) associated with the use of Suclear (sodium sulfate, potassium sulfate, and magnesium sulfate oral solution and PEG-3350, sodium chloride, sodium bicarbonate and potassium chloride powder for oral solution).

Furthermore, the new pharmacovigilance system that FDA is required to establish under section 505(k)(3) of the FDCA will not be sufficient to assess these serious risks.

Finally, we have determined that only clinical trials (rather than a nonclinical or observational study) will be sufficient to assess a known serious risk of fluid and serum chemistry abnormalities and the signal of a serious risk related to exposure to toxic impurities.

Therefore, based on appropriate scientific data, FDA has determined that you are required to conduct the following:

1998-6 An adequate randomized, active control, single-blind trial to evaluate renal dysfunction and laboratory abnormalities in adult patients, including elderly patients, patients with renal impairment, and patients with hepatic impairment taking Suclear prior to colonoscopy. Serial laboratory and clinical assessments will be performed at regular pre-specified intervals for at least 30 days post-treatment.

The timetable you submitted on January 8, 2013, states that you will conduct this trial according to the following schedule:

Final Protocol Submission:	06/14
Trial Completion:	06/16
Final Report Submission:	12/16

1998-7 Assess the systemic exposure and pharmacokinetics of PEG3350, (b) (4) [redacted] ollowing oral administration of Suclear to adult patients. These assessments may be conducted as part of 1998-6 (above).

The timetable you submitted on January 8, 2013, states that you will conduct this trial according to the following schedule:

Final Protocol Submission:	06/14
Trial Completion:	06/16
Final Report Submission:	12/16

Submit the protocols to your IND 102894 with a cross-reference letter to this NDA. Submit all final report(s) to your NDA. Prominently identify the submission with the following wording in bold capital letters at the top of the first page of the submission, as appropriate: **"Required Postmarketing Protocol Under 505(o)", "Required Postmarketing Final Report Under 505(o)", "Required Postmarketing Correspondence Under 505(o)"**.

Section 505(o)(3)(E)(ii) of the FDCA requires you to report periodically on the status of any study or clinical trial required under this section. This section also requires you to periodically report to FDA on the status of any study or clinical trial otherwise undertaken to investigate a safety issue. Section 506B of the FDCA, as well as 21 CFR 314.81(b)(2)(vii) requires you to report annually on the status of any postmarketing commitments or required studies or clinical trials.

FDA will consider the submission of your annual report under section 506B and 21 CFR 314.81(b)(2)(vii) to satisfy the periodic reporting requirement under section 505(o)(3)(E)(ii) provided that you include the elements listed in 505(o) and 21 CFR 314.81(b)(2)(vii). We remind you that to comply with 505(o), your annual report must also include a report on the status of any study or clinical trial otherwise undertaken to investigate a safety issue. Failure to submit an annual report for studies or clinical trials required under 505(o) on the date required will be considered a violation of FDCA section 505(o)(3)(E)(ii) and could result in enforcement action.

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit, in triplicate, a cover letter requesting advisory comments, the proposed materials in draft or mock-up form with annotated references, and the package insert to:

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion
5901-B Ammendale Road
Beltsville, MD 20705-1266

As required under 21 CFR 314.81(b)(3)(i), you must submit final promotional materials, and the package insert, at the time of initial dissemination or publication, accompanied by a Form FDA 2253. For instruction on completing the Form FDA 2253, see page 2 of the Form. For more information about submission of promotional materials to the Office of Prescription Drug Promotion (OPDP), see http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm.

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, call Matthew Scherer, Regulatory Project Manager, at (301)796-2307.

Sincerely,

{See appended electronic signature page}

Donna Griebel, MD
Director
Division of Gastroenterology and Inborn Errors Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

Enclosure:
Content of Labeling

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

DONNA J GRIEBEL
01/18/2013