CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

213135Orig1s000

PRODUCT QUALITY REVIEW(S)

RECOMMENDATION

☒ Approval
☐ Approval with Post-Marketing Commitment
☐ Complete Response

NDA 213135
Assessment 2

Drug Product Name	**SUTAB** (sodium sulfate, magnesium sulfate, and potassium chloride) tablets
Dosage Form	Tablet
Strength	1.479 g sodium sulfate, 0.225 g magnesium sulfate, and 0.188 g potassium chloride
Route of Administration	Oral
Rx/OTC Dispensed	Rx
Applicant	Braintree Laboratories, Inc.; USA
US agent, if applicable	N/A

Submission(s) Assessed	Document Date	Discipline(s) Affected
Amendment – Resubmission	May 12, 2020	OPQ
Amendment	June 11, 2020	ONDP
Amendment	June 19, 2020	ONDP
Amendment	June 25, 2020	OPMA, ONDP
Amendment – Labeling	July 1, 2020	ONDP
Amendment	July 2, 2020	OPMA, ONDP
Amendment	August 17, 2020	OPMA

QUALITY ASSESSMENT TEAM

Discipline	Primary Assessment	Secondary Assessment
Drug Substance	Sukhamaya (Sam) Bain	Donna Christner
Drug Product	Jane Chang	Moo-Jhong Rhee
Manufacturing/Microbiology/Facilities	Qin Liang	Nallaperumal Chidambaram
Regulatory Business Process Manager	Oumou Barry	
Application Technical Lead	Hitesh Shroff	

EXECUTIVE SUMMARY

IQA NDA Assessment Guide Reference

I. RECOMMENDATIONS AND CONCLUSION ON APPROVABILITY

The applicant has provided sufficient CMC information to assure the identity, strength, purity, and quality of the proposed SUTAB (sodium sulfate, magnesium sulfate, and potassium chloride) Tablets 1.479 g/0.225 g/0.188 g

The claim for the Categorical Exclusion for the Environmental Assessment is granted.

The Office of Pharmaceutical Manufacturing Assessment (OPMA) has made a final overall "**Approval**" recommendation for the facilities involved in this application.

The label/labeling issues have been satisfactorily resolved for the CMC perspective.

Therefore, from the OPQ perspective, this NDA is recommended for **"Approval"**.

II. SUMMARY OF QUALITY ASSESSMENTS

This NDA was originally submitted on May 15, 2019 and it was not recommended for approval from OPQ perspective per 21 CFR 314.125(b)(13) due to the following deficiencies (see Memo to OPQ Review #1 dated March 9, 2020). A complete response (CR) was issued on March 13, 2020.

- Braintree Laboratories, Inc. is responsible for the drug product manufacturing, packaging, release and stability testing. A pre-approval inspection was performed during October 15 - 22, 2019. A Form-483 was issued listing inspection observations. Based on the firm's inadequate response, the Office of Pharmaceutical Manufacturing Assessment recommended "**Withhold**" recommendation due to lack of readiness of Braintree Laboratories Inc. for commercial manufacturing of the drug product.

On May 12, 2020 Braintree Laboratories Inc. submitted an amendment to the complete response letter (CR) that included the following information:

- Modifications to drug product manufacturing process and in-process controls
- Revised drug product specification
- Additional drug product stability data
- Revised drug product container closure system
- Revised drug product container/carton labels

Braintree's response to deficiencies described in the complete response letter (CR) and subsequent amendments are reviewed in this OPQ quality review.

A. Product Overview

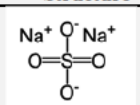
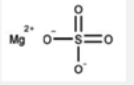
SUTAB (sodium sulfate, magnesium sulfate and potassium chloride) Tablets, for oral administration intended for gastrointestinal cleansing prior to colonoscopy in adults. Sulfates are poorly absorbed, so they stay in lumen of the gastrointestinal tract and act as osmotic laxatives. The tablet formulation is derived from the applicant's liquid based SUPREP (NDA 22372). SUTAB tablets are supplied in 2 bottles. Each bottle contains 12 tablets.

Proposed Indication(s) including Intended Patient Population	SUTAB is an osmotic laxative indicated for cleansing of the colon in preparation for colonoscopy in adults.
Duration of Treatment	Split Dose (2-day) regiment. Evening before colonoscopy and morning of the colonoscopy
Maximum Daily Dose	12 tablets per day. Each tablet contains 1.479 g sodium sulfate, 0.225 g magnesium sulfate, and 0.188 g potassium chloride
Alternative Methods of Administration	N/A

B. Quality Assessment Overview

Drug Substances: Adequate

The drug substances in SUTAB tablets are the following: sodium sulfate (anhydrous), magnesium sulfate (anhydrous) and potassium chloride. All three drug substances are USP grade. The detailed CMC information including physicochemical properties, manufacturing process, characterization, specification, Certificate of Analysis, container closure system and stability of the drug substances are provided in the DMFs from their manufacturers. The letters of authorization were provided. The DMFs were reviewed and deemed adequate.

DMF	Chemical Name	Structure	DMF Holder	Status
(b) (4)	Sodium Sulfate (anhydrous)		(b) (4)	Adequate. Reviewed by Joseph Leginus, 8/27/2019
	Magnesium Sulfate (anhydrous)			Adequate. Reviewed by Joseph Leginus, 9/23/2019
	Potassium Chloride	KCl		Adequate Reviewed by M. Akter, 7/10/2018

No additional CMC information for the drug substance was provided in this resubmission. The substance reviewer has concluded that the CMC information regarding the drug substance provided in this NDA is adequate to support the drug

product. An Approval is recommended from the drug substance CMC perspective. (see the **Drug Substance** review).

Drug Product: Adequate

Previously used desiccant, [redacted] (b) (4) s replaced with [redacted] (b) (4) . The applicant has provided sufficient CMC information regarding [redacted] (b) (4) in the NDA.

Based on satisfactory long-term and accelerated stability data of three drug product commercial scale registration batches assuring the identity, strength, purity and quality, a 24-month of expiration dating period when stored between 20ºC to 25ºC in the proposed 30cc HDPE bottle with a desiccant, [redacted] (b) (4) is granted.

The drug product CMC information including the revised drug product specification was reviewed and deemed adequate. An Approval is recommended from the drug product CMC perspective. (**see Drug Product** Review)

Manufacturing: Adequate

SUTAB tablets are manufactured by Braintree Laboratories, Inc.; MA. [redacted] (b) (4) The drug product manufacturing process was reviewed and deemed acceptable. (See the **Manufacturing Integrated Assessment**).

Labeling: Adequate

The labels and labeling issues are satisfactorily resolved from the CMC perspective. (See the **Labeling** review).

Facilities Adequate

Braintree Laboratories, Inc. is responsible for the drug product manufacturing, packaging, release and stability testing. A pre-approval inspection was performed during October 15 - 22, 2019. A Form-483 was issued listing inspection observations. Based on firm's inadequate response the Office of Pharmaceutical Manufacturing Assessment recommended "Withhold" due to lack of readiness of Braintree Laboratories Inc. for commercial manufacturing of the drug product.

On May 12, 2020 Braintree Laboratories Inc. submitted an amendment to the complete response letter (CR). A pre-approval inspection of the drug product manufacturing facility, Braintree Laboratories, was recommended. As it was not possible to perform on-site inspection due to COVID-19 imposed travel restrictions, ORA and OPMA initiated 704(a)(4) process in-lieu of the site inspection. The applicant provided documents regarding the drug product manufacturing facility, list of equipment, manufacturing process, executed batch records and stability data. These documents were reviewed and it was determined that the drug product manufacturing facility, Braintree Laboratories, is acceptable.

The Office of Pharmaceutical Manufacturing Assessment (OPMA) has made an "Adequate" recommendation for all manufacturing and testing facilities involved in this NDA. (see **Manufacturing Integrated Assessment**).

C. Risk Assessment

SUTAB (sodium sulfate, magnesium sulfate, and potassium chloride) tablets

Product Attribute / CQA	Factors that can impact the CQA	Risk Ranking	Risk Mitigation Approach	Risk Evaluation	LifeCycle consideration/ Comments
Assay and content uniformity	• Formulation • Raw materials • Process parameters • Scale/equipment	L	(b) (4)	The drug product is expected to be safe for oral administration during the entire shelf life from product quality perspective. Low to None	None
Related Substances Impurities / Degradants	•Raw materials •Process parameters	L		Low to None	None

Application Technical Lead Name and Date:

Hitesh Shroff, Ph.D.
Application Technical Lead, Branch V
Division of New Drug Products II
October 5, 2020

Hitesh N. Shroff -S

Digitally signed by Hitesh N. Shroff -S
DN: c=US, o=U.S. Government, ou=HHS, ou=FDA, ou=People, 0.9.2342.19200300.100.1.1=2000348333, cn=Hitesh N. Shroff -S
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QUALITY ASSESSMENT DATA SHEET

IQA NDA Assessment Guide Reference

1. RELATED/SUPPORTING DOCUMENTS

A. DMFs:

DMF #	Type	Holder	Item Referenced	Status	Date Assessment Completed	Comments
(b) (4)	Type II		(b) (4)	Active	Reviewed by Joseph Leginus, 9/23/2019 Adequate	LOA Aug 15, 2019
	Type II			Active	Reviewed by Joseph Leginus, 8/27/2019 Adequate	LOA Feb 21, 2019
	Type II			Active	Reviewed by M. Akter, 7/10/2018 Adequate	LOA Jun 25, 2018
	Type III			Active	N/A	LOA July 12, 2018
	Type III			Active	N/A	LOA Jun 29, 2018
	Type III			Active	N/A	LOA Jun 29, 2018
	Type III			Active	N/A	LOA Jun 28, 2018
	Type III			Active	N/A	LOA Jun 28, 2018
	Type III			Active	N/A	LOA Jun 28, 2018
	Type III			Active	N/A	LOA Jun 29, 2018
	Type III			Active	N/A	LOA Mar 4, 2020

B. OTHER DOCUMENTS: *IND, RLD, RS, Approved NDA*

Document	Application Number	Description
NDA	22372	SUPREP Bowel Prep Kit

2. CONSULTS

Discipline	Status	Recommendation	Date	Assessor
Biostatistics				
Pharmacology/Toxicology				
CDRH-ODE				
CDRH-OC				
Clinical				
Other				

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U.S. FOOD & DRUG ADMINISTRATION

MEMORANDUM

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

DATE: June 2, 2020

TO: NDA 213135 Resubmission Quality Assessment – Labeling

FROM: Jane Chang, Ph.D.
Senior Reviewer, OPQ/ONDP/DNDP II/Branch 4

THROUGH Moo-Jhong Rhee, Ph.D.
Chief, Branch 4
OPQ/ONDP/DNDP II

SUBJECT: **Labeling Assessment #2**

SUMMARY

The previous Quality Assessment – Labeling, Assessment Cycle #1 Addendum dated 03-Mar-2020 made a recommendation of approval from the CMC labeling/label perspective. In the resubmission eCTD-0034, updated carton and container labels are provided. Minor edits were made to the container and carton labels, which were evaluated and concluded to be adequate. In addition, Prescribing Information and Medication Guide labeling was submitted in eCTD-0032. eCTD-0032 contains the same quality labeling information as eCTD-0028, which has been evaluated in Quality Assessment – Labeling, Assessment Cycle #1 Addendum dated 03-Mar-2020 and remains adequate.

RECOMMENDATION:

This application is now recommended for **Approval** from the CMC labeling/label perspective.

Assessment Notes

Quality Labeling Assessment was concluded with Approval from the CMC labeling/label perspective in Assessment Cycle #1 Addendum dated 03-Mar-2020. Subsequently, the following amendments were submitted and assessed.

List Submissions being reviewed:

Document Reviewed (eCTD #)	Date Received
eCTD-0032 (SDN-32)	03/11/2020
eCTD-0034 (SDN-34)	05/12/2020

1.0 PRESCRIBING INFORMATION

See eCTD-0028 dated 02/20/2020 or eCTD-0032 dated 03/11/2020.

Conclusion: Satisfactory

Relevant product quality information in Prescribing Information submitted in eCTD-0032 dated 03/11/2020 is identical to that in eCTD-0028 dated 02/20/2020, which was evaluated in Review #1 Addendum dated 03-Mar-2020. The information remains adequate.

2.0 PATIENT LABELING

See eCTD-0030 dated 03/03/2020 or eCTD-0032 dated 3/11/2020.

Conclusion: Satisfactory

Relevant product quality information in Medication Guide submitted in eCTD-0032 dated 03/11/2020 is identical to that in eCTD-0030 dated 03/03/2020, which was evaluated in Review #1 Addendum dated 03-Mar-2020. The information remains adequate.

3.0 CARTON AND CONTAINER LABELS

3.1 CONTAINER LABEL

The information provided in eCTD-0034 dated 05/12/2020 is shown below.

Item	Information Provided in NDA	Reviewer's Comment and Recommendations
Proprietary name, established name [FD&C Act 502(e)(1)(A)(i)] [font size at least half as large as the proprietary name, and prominence per FD&C Act 502(e)(1)(B), 21 CFR 201.10(g)(2)]	SUTAB (sodium sulfate, magnesium sulfate, and potassium chloride) Tablets	**Acceptable** The font size of established name is at least half as large as the proprietary name.
Route of administration, if it is not for oral use [201.100(b)(3)]	Not provided	**Acceptable** Route of administration is not required for oral drug.
Active moiety expression of strength with equivalence statement (if applicable) [FD&C Act 502(e)(1)(A)(ii), 21 CFR 201.10(d)(1); 21 CFR 201.100(b)(4), USP <1121>]	Strength per tablet is provided: 1.479 g/0.225 g/0.188 g	**Acceptable** Active moiety expression is not applicable.
Net content [FD&C Act 502(b)(2), 21 CFR 201.51(a)]	This bottle contains 12 tablets.	**Acceptable**
Name of all inactive ingredients, in alphabetical order required for OTC drugs [FD&C Act 502(e)(1)(A)(iii), 201.10(a)] [except for oral drug per 201.100(b)(5) or limited space per 201.10(i)(2)]; [Quantitative ingredient information is required for injectables per 201.100(b)(5)(iii)]	Not provided	**Acceptable** Name of all inactive ingredients for oral drugs is optional.
"Rx only" statement [21 CFR 201.100(b)(1)]	Provided on the top left corner	**Acceptable**
NDC number [per 21 CFR 201.2, requested, but not required for all labels or	NDC 52268-200-01	**Acceptable**

labeling, also see 21 CFR 207.35(b)(3)(i)]		
Lot number (21 CFR 201.18) and expiration date (21 CFR 201.17)	The location of Lot number and expiration dating period is allocated.	**Acceptable**
Storage conditions.	Store at 25°C (77°F); excursions permitted 15°C - 30°C (59°F - 86°F)	**Acceptable**
Bar code [21CFR 201.25(c)(2)]	Provided on the right side	**Acceptable**
Adequate directions for use [FD&C Act 502(f)(1), 21 CFR 201.5] or "See package insert for dosage information" (21 CFR 201.55)	Recommended Dosage: See Prescribing Information	**Acceptable**
Name of manufacturer/distributor [502(b)(1), 21 CFR 201.1(a), 21 CFR 201.1(h)(5)]	Manufactured by Braintree Laboratories, Inc., Braintree, MA	**Acceptable**

Conclusion: **Satisfactory**

Except for the orientation of the bar code, the container label is identical to that in eCTD-0023, which was evaluated in Review #1 Addendum dated 03-Mar-2020. The information meets the regulatory requirements.

3.2 CARTON LABEL

The information provided in eCTD-0034 dated 05/12/2020 is shown below.

2 Page(s) of Draft Labeling have been Withheld in Full as B4 (CCI/TS) immediately following this page

Item	Information Provided in NDA	Reviewer's Comment and Recommendations
Proprietary name, established name [FD&C Act 502(e)(1)(A)(i)] [font size at least half as large as the proprietary name, and prominence per FD&C Act 502(e)(1)(B), 21 CFR 201.10(g)(2)]	SUTAB (sodium sulfate, magnesium sulfate, and potassium chloride) Tablets	**Acceptable** The font size of established name is at least half as large as the proprietary name.
Route of Administration [not required for oral, 21 CFR 201.100(b)(3)]	"Oral" route of administration is not explicitly included. But Panel 3 indicates that tablets are to be swallowed.	**Acceptable** Route of administration is not required for oral drug.
Active moiety expression of strength with equivalence statement (if applicable) [FD&C Act 502(e)(1)(A)(ii), 21 CFR 201.10(d)(1); 21 CFR 201.100(b)(4), USP <1121>]	Strength per tablet is provided: 1.479 g/0.225 g/0.188 g	**Acceptable** Active moiety expression is not applicable.
Net content [FD&C Act 502(b)(2), 21 CFR 201.51(a)]	On Panel 1: 2 Bottles of 12 tablets each	**Acceptable**
Name of all inactive ingredients, in alphabetical order required for OTC drugs [FD&C Act 502(e)(1)(A)(iii), 21 CFR 201.10(a)] [except for oral drug per 201.100(b)(5) or limited space per 21 CFR 201.10(i)(2)]; [Quantitative ingredient information is required for injectables per 21 CFR 201.100(b)(5)(iii)]	Not provided	**Acceptable** Name of all inactive ingredients for oral drugs is optional per 21 CFR 201.100(b)(5).
"Rx only" statement [21 CFR 201.100(b)(1)]	Provided at the bottom of Panel 1	**Acceptable**
NDC number [per 21 CFR 201.2, requested, but not required for all labels or labeling, also see 21 CFR 207.35(b)(3)(i)]	NDC 52268-201-01 provided on Panel 1	**Acceptable**
Lot number (21 CFR 201.18) and expiration date (21 CFR 201.17)	Per Principal Display Panel Kit Carton Layout, the location of Lot number and expiration dating period is allocated on the top of Panel 5 (the black ink section).	**Acceptable**
Storage conditions	Store at room temperature between 68°F to 77°F (20°C to 25°C)	**Acceptable**
Bar code [21 CFR 201.25(c)(2)]	Bar code is on Panel 4 and Panel 5.	**Acceptable**
Adequate directions for use [FD&C Act 502(f)(1), 21 CFR 201.5] or "See package insert for dosage information" (21 CFR 201.55)	Panel 5: Read the patient booklet in kit at least 2 days before your scheduled procedure.	**Acceptable**

"Keep out of reach of children" (Required for OTC. Optional for Rx drugs)	Not provided	**Acceptable** The statement is optional for Rx drugs.
Name of manufacturer/distributor [502(b)(1), 21 CFR 201.1(a), 21 CFR 201.1(h)(5)]	On Panel 1: Braintree A PART OF SEBELA PHARMACEUTICAL®	**Acceptable**
And others, if space is available	On Panel 3: Important: You must use all tablets and water at least 2 hours before your colonoscopy.	**Acceptable**

Conclusion: Satisfactory

Except for the updated US Patent number and bar code, the carton label is identical to that in eCTD-0030, which was evaluated in Review #1 Addendum dated 03-Mar-2020. The information meets the regulatory requirements.

Jane Chang

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Moo Jhong Rhee

Digitally signed by Moo Jhong Rhee
Date: 6/02/2020 03:46:38PM
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Memorandum

DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

Date: **March 9, 2020**
From: **Hitesh Shroff, Ph.D.**
Application Technical Lead, Branch V
Division of New Drug Products II
Office of New Drug Products

Through: **Moo-Jhong Rhee, Ph.D.**
Chief, Branch V
Division of New Drug Products II
Office of New Drug Products

To: **OPQ Review #1 of NDA 213135**

Subject: **Final Recommendation for NDA 213135**

At the time when the OPQ Review #1 was completed on February 16, 2020 it had noted the following pending issues:

- The label/labeling issues have ***not*** been completely resolved.

- The Office of Pharmaceutical Manufacturing Assessment (OPMA) has ***not*** made a final overall "Approval" recommendation for the facilities involved in this application.

The applicant submitted the revised immediate container labels and Prescribing Information (PI) on February 20, 2020, and the resubmitted CMC sections of the labeling/labels were reviewed and found acceptable. **(See the Attachment)**

However, the Office of Pharmaceutical Manufacturing Assessment has still ***not*** recommended final overall "Acceptable" recommendation for the facilities involved in this application due to the following issues.

- Braintree Laboratories, Inc. is responsible for the drug product manufacturing, packaging, release and stability testing. A pre-approval inspection was performed during October 15 - 22, 2019. A Form-483 was issued listing inspection observations. Based on firm's inadequate response, the Office of Pharmaceutical Manufacturing Assessment recommended "**Withhold**" recommendation due to lack of readiness of Braintree Laboratories Inc. for commercial manufacturing of the drug product.

Therefore, this NDA is ***not*** recommended for approval from the Office of Pharmaceutical Manufacturing Assessment perspective.

Recommendation:
This NDA is ***not*** recommended for Approval from the OPQ perspective.

Application Technical Lead's Assessment and Signature

The NDA is ***not*** recommended for Approval from the OPQ perspective.

Hitesh Shroff, Ph.D.
Application Technical Lead,
Branch V Division of New Drug Products II
Office of New Drug Products
March 9, 2020

U.S. FOOD & DRUG ADMINISTRATION

MEMORANDUM

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

DATE: March 3, 2020

TO: Review #1 of NDA 213135 Quality Assessment - Labeling

FROM: Jane Chang, Ph.D.
Senior Reviewer, ONDP/DNDP II/OPQ

THROUGH Moo-Jhong Rhee, Ph.D.
Chief, Branch 4
DNDP II/ONDP/OPQ

SUBJECT: **Final Recommendation on Labeling/Labels**

SUMMARY

The previous Quality Assessment – Labeling, Assessment Cycle #1 dated 17-Oct-2019, made a recommendation of not ready for approval of this NDA because of labeling deficiencies (see N213135 Labeling R1, Section 4.0). These labeling issues have been satisfactorily resolved based on the revisions made in eCTD-0020, eCTD-0023, eCTD-0028, and eCTD-0030.

RECOMMENDATION:

This application is now recommended for **Approval** from the CMC labeling/label perspective.

Assessment Notes

Labeling deficiencies from Quality Assessment were identified in Assessment Cycle #1 dated 17-Oct-2019 (see N213135 Labeling R1, Section 4.0). Subsequently, the following amendments were submitted and assessed.

List Submissions being reviewed:

Document Reviewed (eCTD #)	Date Received
eCTD-0020 (SDN-20)	11/08/2019
eCTD-0023 (SDN-23)	01/06/2020
eCTD-0028 (SDN-28)	02/20/2020
eCTD-0030 (SDN-30)	03/03/2020

1.0 PRESCRIBING INFORMATION

The information provided in eCTD-0028 dated 02/20/2020 is summarized below.

1.1 HIGHLIGHTS OF PRESCRIBING INFORMATION

1) TITLE

SUTAB (sodium sulfate, magnesium sulfate, and potassium chloride) tablets, for oral use

Initial U.S. Approval: 2020

2) DOSAGE FORMS AND STRENGTHS

Tablets: 1.479 g sodium sulfate, 0.225 g magnesium sulfate, and 0.188 g potassium chloride.

Item	Information Provided in NDA	Assessor's Comment and Recommendations
Drug name [201.57(a)(2)]		
Proprietary name and established name	SUTAB (sodium sulfate, magnesium sulfate, and potassium chloride) tablets	**Acceptable**
Dosage form, route of administration	Tablets as dosage form; oral as route of administration	**Acceptable** Oral as the route of administration for oral tablets does not need to be included in the proprietary name or established name.
Controlled drug substance symbol	N/A	N/A
Initial U.S. Approval	2020	**Acceptable** The year that this fixed-combination drug product is approved is used.
Dosage Forms and Strengths [201.57(a)(8)]		
Dosage Forms and Strengths in metric system	Tablets as dosage form. Strength is provided: 1.479 g for sodium sulfate, 0.225 g for magnesium sulfate, and 0.188 g for potassium chloride	**Acceptable**.
Whether the drug product is scored	N/A	N/A

Conclusion: Satisfactory

Regarding the Initial U.S. Approval, there are approved drug products containing single API, e.g. Zinc Sulfate Injection and Selenious Acid Injection. However, this NDA is the first drug product with the combination of these three APIs. Therefore, year 2020 is listed as Initial U.S. Approval.

The proposed proprietary name "Sutab" was determined to be acceptable per DMEPA's assessment by Teresa McMillan dated 08/09/2019. The Highlighs section pertaining to CMC meets the regulatory requirements.

1.2 FULL PRESCRIBING INFORMATION

1.2.1 Section 2: DOSAGE AND ADMINISTRATION

Item	Information Provided in NDA	Assessor's Comment and Recommendations
Special instructions for product preparation (e.g., reconstitution and resulting concentration, dilution, compatible diluents, storage conditions needed to maintain the stability of the reconstituted or diluted product)	N/A	N/A

1.2.2 Section 3: DOSAGE FORMS AND STRENGTHS

Tablets: 1.479 g sodium sulfate, 0.225 g magnesium sulfate, and 0.188 g potassium

chloride. The tablets are white to off-white, film coated, oblong, and biconvex with flat sides, debossed with *S24* on one side.

Item	Information Provided in NDA	Reviewer's Comment and Recommendations
Available dosage forms	tablets	**Acceptable**
Strengths: in metric system	1.479 g sodium sulfate, 0.225 g magnesium sulfate, 0.188 g potassium chloride	**Acceptable** Strength is expressed as per tablet
A description of the identifying characteristics of the dosage forms, including shape, color, coating, scoring, and imprinting, when applicable.	white to off-white, film coated, oblong, and biconvex with flat sides, debossed with *S24* on one side	**Acceptable** Tablets are not scored.

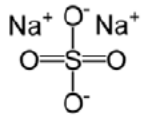
Conclusion: **Satisfactory**

Information in DOSAGE FORMS AND STRENGTHS meets the regulatory requirements.

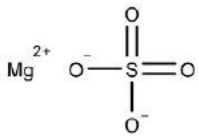
1.2.3 Section 11: DESCRIPTION

SUTAB (sodium sulfate, magnesium sulfate, and potassium chloride) tablets is an orally administered osmotic laxative and is provided as two bottles, each containing 12 tablets. Each tablet contains: 1.479 g sodium sulfate, 0.225 g magnesium sulfate, and 0.188 g potassium chloride. Inactive ingredients include: polyethylene glycol 8000, sodium caprylate, and ethylene glycol and vinyl alcohol graft copolymer.

Sodium Sulfate, USP
The molecular formula is Na_2SO_4. The average molecular weight is 142.04. The structural formula is:



Magnesium Sulfate, USP
The molecular formula is $MgSO_4$. The average molecular weight is 120.37. The structural formula is:



Potassium Chloride, USP
The molecular formula is KCl. The average molecular weight is 74.55. The structural formula is:

Cl- ---------- K+

Item	Information Provided in NDA	Reviewer's Comment and Recommendations
Proprietary name and established name [21 CFR 201.57(c)(12)(i)(A)]	SUTAB (sodium sulfate, magnesium sulfate, and potassium chloride) tablets	**Acceptable**
Dosage form and route of administration [21 CFR 201.57(c)(12)(i)(B)]	Tablets as dosage form. Oral as route of administration.	**Acceptable**
Active moiety expression of strength with equivalence statement (if applicable) [FD&C Act 502(e)(1)(A)(ii), 21 CFR 201.10(d)(1); 21 CFR 201.100(b)(4), USP <1121>]	1.479 g sodium sulfate, 0.225 g magnesium sulfate, and 0.188 g potassium chloride	**Acceptable** Active moiety expression is not applicable.
Inactive ingredient information [21 CFR 201.57(c)(12)(i)(C)] [quantitative, if injectables 21CFR201.100(b)(5)(iii), listed by USP/NF names (if any)]. For ingredients added to adjust the pH or make isotonic, include the name and statement of effect. If alcohol is present, must provide the amount of alcohol in terms of percent volume of absolute alcohol	polyethylene glycol 8000, sodium caprylate, and ethylene glycol and vinyl alcohol graft copolymer	**Acceptable** Even though inactive ingredients are not required for drugs of oral use per 21CFR201.100(b)(5), it is acceptable to include them in Section 11. (b) (4)
Pharmacological/ therapeutic class [21 CFR 201.57(c)(12)(i)(E)]	osmotic laxative	**Acceptable**
Chemical name, structural formula [21 CFR 201.57(c)(12)(i)(F)]	Molecular formula, structural formula and molecular weight for each active ingredient are provided.	**Acceptable**
Other important chemical or physical properties (such as pKa or pH) [21 CFR 201.57(c)(12)(ii)]	N/A	N/A
For oral prescription drug products, include gluten statement if applicable	N/A	N/A

Conclusion: **Satisfactory**

Information in DESCRIPTION meets the regulatory requirements.

1.2.4 Section 16: HOW SUPPLIED/STORAGE AND HANDLING

16.1 How Supplied

Each tablet of SUTAB contains 1.479 g sodium sulfate, 0.225 g magnesium sulfate, and 0.188 g potassium chloride. The tablets are white to off-white, film coated, oblong, and biconvex with flat sides, debossed with *S24* on one side.

Each carton of SUTAB (NDC 52268-201-01) contains:

- Two bottles, each bottle (NDC 52268-200-01) contains 12 tablets.
- One container with a 16-ounce fill line.

Storage

Store at 20° to 25°C (68° to 77°F). Excursions permitted between 15° to 30°C (59° to 86°F). See USP controlled room temperature.

Item	Information Provided in NDA	Reviewer's Comment and Recommendations
Dosage form	tablets	**Acceptable**
Strength of dosage form in metric system	1.479 g sodium sulfate, 0.225 g magnesium sulfate, 0.188 g potassium chloride	**Acceptable** Strength per tablet is provided.
Available units (e.g., bottles of 100 tablets)	Two bottles: Each bottle contains 12 tablets.	**Acceptable**
Identification of dosage forms, e.g., shape, color, coating, scoring, imprinting, NDC number.	white to off-white, film coated, oblong, and biconvex with flat sides, debossed with *S24* on one side Bottle: NDC 52268-200-01 Carton: NDC 52268-201-01	**Acceptable**
Special handling (e.g., protect from light, refrigerate).	N/A	N/A
Storage conditions.	Store at 20° to 25°C (68° to 77°F). Excursions permitted between 15° to 30°C (59° to 86°F). See USP controlled room temperature.	**Acceptable**
Child-resistant packaging	Not provided	**Acceptable** Statement regarding child-resistant packaging is optional. (b) (4) [redacted]

Conclusion: Satisfactory

Information in HOW SUPPLIED/STORAGE AND HANDLING meets the regulatory requirements.

1.2.5 Other Sections of Labeling

N/A

1.2.6 Section 17: PATIENT COUNSELING INFORMATION

Manufactured by:

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

Item	Information Provided in NDA	Reviewer's Comment and Recommendations
Manufacturer/distributor name [21 CFR 201.1(h)(5)]	Braintree Laboratories, Inc. 270 Centre Street Holbrook, MA 02343	**Acceptable**

Conclusion: Satisfactory

2.0 PATIENT LABELING

For convenience, the labeling deficiencies from Assessment Cycle #1 dated 17-Oct-2019 are repeated in this assessment in **bold**, followed by the applicant's response.

Medication Guide

1. **Delete (b) (4) from the established name. That is,**
   SUTAB™ (Soo'tab)
   (sodium sulfate, magnesium sulfate, and potassium chloride) Tablets
2. **Include "ethylene glycol and vinyl alcohol graft copolymer" in "Inactive ingredients". That is,**
   Inactive ingredients: polyethylene glycol 8000, sodium caprylate, and ethylene glycol and vinyl alcohol graft copolymer

Relevant product quality information in Medication Guide submitted in eCTD-0030 dated 03/03/2020 is shown below.

SUTAB™ (Sootab)
(sodium sulfate, magnesium sulfate, and potassium chloride)
tablets, for oral use

How should I store SUTAB?
Store SUTAB at room temperature, between 68° to 77°F (20° to 25°C).

Active ingredients: sodium sulfate, magnesium sulfate, and potassium chloride
Inactive ingredients: polyethylene glycol 8000, sodium caprylate, and ethylene glycol and vinyl alcohol graft copolymer

Manufactured by:

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

Conclusion: Satisfactory

The deficiencies identified in Assessment Cycle #1 dated 17-Oct-2019 have been addressed. Additional edits, e.g., expression of temperature in Fahrenheit (with Celsius in parenthesis), were recommended by Division of Medical Policy Programs (DMPP), the Office of Prescription Drug Promotion (OPDP), and Division of Medication Error Prevention and Analysis (DMEPA).

3.0 CARTON AND CONTAINER LABELS

The following issues were identified in Assessment Cycle #1 dated 17-Oct-2019.

1. Address the following for both container and carton labels:
   a) Add "and" between magnesium sulfate and potassium chloride in the established name.
   b) Replace "Tablet" with "Tablets" for the proprietary name and established name.
   c) Add strength "1.479 g/0.225 g/0.188 g" underneath the established name. That is, the proprietary name, established name and strength should be:

      SUTAB
      (sodium sulfate, magnesium sulfate, and potassium chloride) Tablets
      1.479 g/0.225 g/0.188 g

   d) Allocate the location of Lot number and expiration dating period.

2. Address the following for container label:
   a) Add the statement "Recommended Dosage: See Prescribing Information".
   b) Correct the typographical error "Manufactored" with "Manufactured".

3. Address the following for carton label:
   a) Add "Rx only" statement.
   b) Regarding Panel 1, add a space between "Booklet" and "includes" as well as between "Patient" and "Instructions".
   c) Regarding Panel 3, Day 1, Step 1, insert a space between the words [redacted] (b) (4)
   d) Regarding Panel 3, Day 2, insert a space between the words "[redacted] (b) (4)

3.1 CONTAINER LABEL

The information provided in eCTD-0023 dated 01/06/2020 is shown below.

Item	Information Provided in NDA	Reviewer's Comment and Recommendations
Proprietary name, established name [FD&C Act 502(e)(1)(A)(i)] [font size at least half as large as the proprietary name, and prominence per FD&C Act 502(e)(1)(B), 21 CFR 201.10(g)(2)]	SUTAB (sodium sulfate, magnesium sulfate, and potassium chloride) Tablets	**Acceptable** The font size of established name is at least half as large as the proprietary name.
Route of administration, if it is not for oral use [201.100(b)(3)]	Not provided	**Acceptable** Route of administration is not required for oral drug.
Active moiety expression of strength with equivalence statement (if applicable) [FD&C Act 502(e)(1)(A)(ii), 21 CFR 201.10(d)(1); 21 CFR 201.100(b)(4), USP <1121>]	Strength per tablet is provided: 1.479 g/0.225 g/0.188 g	**Acceptable** Active moiety expression is not applicable.
Net content [FD&C Act 502(b)(2), 21 CFR 201.51(a)]	This bottle contains 12 tablets.	**Acceptable**
Name of all inactive ingredients, in alphabetical order required for OTC drugs [FD&C Act 502(e)(1)(A)(iii), 201.10(a)] [except for oral drug per 201.100(b)(5) or limited space per 201.10(i)(2)]; [Quantitative ingredient information is required for injectables per 201.100(b)(5)(iii)]	Not provided	**Acceptable** Name of all inactive ingredients for oral drugs is optional.
"Rx only" statement [21 CFR 201.100(b)(1)]	Provided on the top left corner	**Acceptable**
NDC number [per 21 CFR 201.2, requested, but not required for all labels or	NDC 52268-200-01	**Acceptable**

labeling, also see 21 CFR 207.35(b)(3)(i)]		
Lot number (21 CFR 201.18) and expiration date (21 CFR 201.17)	The location of Lot number and expiration dating period is allocated.	**Acceptable**
Storage conditions.	Store at 25°C (77°F); excursions permitted 15°C - 30°C (59°F - 86°F)	**Acceptable**
Bar code [21CFR 201.25(c)(2)]	Provided on the right side	**Acceptable**
Adequate directions for use [FD&C Act 502(f)(1), 21 CFR 201.5] or "See package insert for dosage information" (21 CFR 201.55)	Recommended Dosage: See Prescribing Information	**Acceptable**
Name of manufacturer/distributor [502(b)(1), 21 CFR 201.1(a), 21 CFR 201.1(h)(5)]	Manufactured by Braintree Laboratories, Inc., Braintree, MA	**Acceptable**

Conclusion: **Satisfactory**

The issues identified for container label in Assessment Cycle #1 dated 17-Oct-2019 have been addressed.

3.2 CARTON LABEL

The information provided in eCTD-0030 dated 03/03/2020 is shown below.

2 Page(s) of Draft Labeling have been Withheld in Full as B4 (CCI/TS) immediately following this page

Item	Information Provided in NDA	Reviewer's Comment and Recommendations
Proprietary name, established name [FD&C Act 502(e)(1)(A)(i)] [font size at least half as large as the proprietary name, and prominence per FD&C Act 502(e)(1)(B), 21 CFR 201.10(g)(2)]	SUTAB (sodium sulfate, magnesium sulfate, and potassium chloride) Tablets	**Acceptable** The font size of established name is at least half as large as the proprietary name.
Route of Administration [not required for oral, 21 CFR 201.100(b)(3)]	"Oral" route of administration is not explicitly included. But Panel 3 indicates that tablets are to be swallowed.	**Acceptable** Route of administration is not required for oral drug.
Active moiety expression of strength with equivalence statement (if applicable) [FD&C Act 502(e)(1)(A)(ii), 21 CFR 201.10(d)(1); 21 CFR 201.100(b)(4), USP <1121>]	Strength per tablet is provided: 1.479 g/0.225 g/0.188 g	**Acceptable** Active moiety expression is not applicable.
Net content [FD&C Act 502(b)(2), 21 CFR 201.51(a)]	On Panel 1: 2 Bottles of 12 tablets each	**Acceptable**
Name of all inactive ingredients, in alphabetical order required for OTC drugs [FD&C Act 502(e)(1)(A)(iii), 21 CFR 201.10(a)] [except for oral drug per 201.100(b)(5) or limited space per 21 CFR 201.10(i)(2)]; [Quantitative ingredient information is required for injectables per 21 CFR 201.100(b)(5)(iii)]	Not provided	**Acceptable** Name of all inactive ingredients for oral drugs is optional per 21 CFR 201.100(b)(5).
"Rx only" statement [21 CFR 201.100(b)(1)]	Provided at the bottom of Panel 1	**Acceptable**
NDC number [per 21 CFR 201.2, requested, but not required for all labels or labeling, also see 21 CFR 207.35(b)(3)(i)]	NDC 52268-201-01 provided on Panel 1	**Acceptable**
Lot number (21 CFR 201.18) and expiration date (21 CFR 201.17)	Per Principal Display Panel Kit Carton Layout, the location of Lot number and expiration dating period is allocated on the top of Panel 5 (the black ink section).	**Acceptable**
Storage conditions	Store at room temperature between 68°F to 77°F(20°C to 25°C)	**Acceptable**
Bar code [21 CFR 201.25(c)(2)]	Bar code are on Panel 4 and Panel 5.	**Acceptable**
Adequate directions for use [FD&C Act 502(f)(1), 21 CFR 201.5] or "See package insert for dosage information" (21 CFR 201.55)	Panel 5: Read the patient booklet in kit at least 2 days before your scheduled procedure.	**Acceptable**

"Keep out of reach of children" (Required for OTC. Optional for Rx drugs)	Not provided	**Acceptable** The statement is optional for Rx drugs.
Name of manufacturer/distributor [502(b)(1), 21 CFR 201.1(a), 21 CFR 201.1(h)(5)]	On Panel 1: Braintree A PART OF SEBELA PHARMACEUTICAL®	**Acceptable**
And others, if space is available	On Panel 3: Important: You must use all tablets and water at least 2 hours before your colonoscopy.	**Acceptable**

Conclusion: Satisfactory

The issues identified for the container label in Assessment Cycle #1 dated 17-Oct-2019 have been addressed. Of note, the information on Panel 3 Preparation Procedure has been revised to be consistent with the prescribing information. As such, the statements "(b) (4) " and "(b) (4)" have been deleted. Therefore, Deficiencies 3c) and 3d) identified in Assessment Cycle #1 dated 17-Oct-2019 are no longer applicable. In the amendment dated 11/08/2019, a NDC number (b) (4) was assigned to the booklet. This NDC number has been deleted in the amendment dated 01/06/2020 per the Agency's request since NDC assignment is limited to drugs and the contents of the booklet are considered part of labeling.

The revised storage condition, i.e., "Store at room temperature between 68°F to 77°F (20°C to 25°C)", was based on the recommendation by DMPP and OPDP (see their Patient Labeling Review dated 2/6/2020). This temperature statement, which is not typically used in carton labels (e.g., the use of "room temperature" and with Celsius in parenthesis), is recommended for patient labeling to reduce patient confusion. For this product, the patient labeling is also the carton labeling.

Jane Chang

Digitally signed by Jane Chang
Date: 3/03/2020 02:23:58PM
GUID: 5034f819000053b21e2574590781f330

Moo Jhong Rhee

Digitally signed by Moo Jhong Rhee
Date: 3/03/2020 02:27:04PM
GUID: 502d0913000029f9798ca689a802fa55

Hitesh Shroff

Digitally signed by Hitesh Shroff
Date: 3/09/2020 10:38:18AM
GUID: 502d1ab500002afd219fd67e3b9c99c8

RECOMMENDATION

☐ Approval
☐ Approval with Post-Marketing Commitment
☒ Complete Response

NDA 213135
Assessment 1

Drug Product Name	**SUTAB** (sodium sulfate, magnesium sulfate, and potassium chloride) tablets
Dosage Form	Tablet
Strength	1.479 g sodium sulfate, 0.225 g magnesium sulfate, and 0.188 g potassium chloride
Route of Administration	Oral
Rx/OTC Dispensed	Rx
Applicant	Braintree Laboratories, Inc.; USA
US agent, if applicable	N/A

Submission(s) Assessed	Document Date	Discipline(s) Affected
Original	May 15, 2019	OPQ
Amendment	Jun 26, 2019	ONDP
Amendment	Jul 5, 2019	ONDP
Amendment	July 19, 2019	ONDP
Amendment	Aug 6, 2019	ONDP, OPMA
Amendment	Aug 9, 2019	ONDP
Amendment	Aug 9, 2019	ONDP, OPMA
Amendment	Aug 23, 2019	ONDP, OPMA
Amendment	Sep 27, 2019	ONDP
Amendment	Oct 28, 2019	OPF
Amendment	Dec 20, 2019	ONDP, OPMA

QUALITY ASSESSMENT TEAM

Discipline	Primary Assessment	Secondary Assessment
Drug Substance	Joseph Leginus	Donna Christner
Drug Product	Jane Chang	Moo-Jhong Rhee
Manufacturing/Microbiology/ Facilities	Qin Liang	Nallaperumal Chidambaram
Biopharmaceutics	Vincent Li	Tapash Ghosh
Regulatory Business Process Manager	Oumou Barry	
Application Technical Lead	Hitesh Shroff	
Laboratory (OTR)	N/A	N/A
Environmental	Jane Chang	Moo-Jhong Rhee

EXECUTIVE SUMMARY

IQA NDA Assessment Guide Reference

I. RECOMMENDATIONS AND CONCLUSION ON APPROVABILITY

The applicant has provided sufficient CMC information to assure the identity, strength, purity, and quality of the proposed SUTAB (sodium sulfate, magnesium sulfate, and potassium chloride) Tablets 1.479 g/0.225 g/0.188 g

The claim for the Categorical Exclusion for the Environmental Assessment is granted.

The Office of Pharmaceutical Manufacturing Assessment (OPMA) has ***not*** made a final overall "Approval" recommendation for the facilities involved in this application as of this review.

The label/labeling issues have ***not*** been satisfactorily resolved.

Therefore, from the OPQ perspective, this NDA is ***not*** deemed ready for approval in its present form per 21 CFR 314.125(b)(13) and 21 CFR 314.125(b)(6), until above mentioned issues are satisfactorily resolved. **(see the List of Deficiencies)**

II. SUMMARY OF QUALITY ASSESSMENTS

A. Product Overview

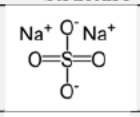
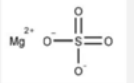
SUTAB (sodium sulfate, magnesium sulfate and potassium chloride) Tablets, for oral administration intended for gastrointestinal cleansing prior to colonoscopy in adults. Sulfates are poorly absorbed, so they stay in lumen of the gastrointestinal tract and act as osmotic laxatives. The tablet formulation is derived from the applicant's liquid based SUPREP (NDA 22372). SUTAB tablets are supplied in 2 bottles. Each bottle contains 12 tablets.

Proposed Indication(s) including Intended Patient Population	SUTAB is an osmotic laxative indicated for cleansing of the colon in preparation for colonoscopy in adults.
Duration of Treatment	Split Dose (2-day) regiment. Evening before colonoscopy and morning of the colonoscopy
Maximum Daily Dose	12 tablets per day. Each tablet contains 1.479 g sodium sulfate, 0.225 g magnesium sulfate, and 0.188 g potassium chloride
Alternative Methods of Administration	N/A

B. Quality Assessment Overview

Drug Substances: Adequate

The drug substances in SUTAB tablets are the following: sodium sulfate (anhydrous), magnesium sulfate (anhydrous) and potassium chloride. All three drug substances are USP grade. The detailed CMC information including physicochemical properties, manufacturing process, characterization, specification, Certificate of Analysis, container closure system and stability of the drug substances are provided in the DMFs from their manufacturers. The letters of authorization were provided. The DMFs were reviewed and deemed adequate.

DMF	Chemical Name	Structure	DMF Holder	Status
(b) (4)	Sodium Sulfate (anhydrous)		(b) (4)	Adequate. Reviewed by Joseph Leginus, 8/27/2019
	Magnesium Sulfate (anhydrous)			Adequate. Reviewed by Joseph Leginus, 9/23/2019
	Potassium Chloride	KCl		Adequate Reviewed by M. Akter, 7/10/2018

The CMC information was reviewed by the drug substance reviewer, Dr. Joseph Leginus, and concluded that the submitted information is adequate to support the drug product (see the **Drug Substance** review).

Drug Product: Adequate

SUTAB tablets are white to off-white, film coated, oblong and biconvex with flat sides immediate release tablets. Each tablet is debossed with *S24* on one side. Each SUTAB contains 1.479 g of sodium sulfate, 0.225 g of magnesium sulfate and 0.188 g of potassium chloride as active pharmaceutical ingredients and the following inactive ingredients: polyethylene glycol 8000 (b) (4) and sodium caprylate (b) (4) ethylene glycol and vinyl alcohol graft copolymer.

The tablets are supplied in 30cc white, round high-density polyethylene bottles with a canister containing silica gel. The bottles are sealed with induction seal and (b) (4) cap. Each bottle contains 12 tablets.

The overall control strategy for the drug product is deemed adequate based on raw material controls, drug product specification including appearance, identification, assay, uniformity of dosage units per USP <905>, dissolution per USP <711>, nephelometric turbidity and microbial limits. For identification tests,

assay and nephelometric turbidity test the applicant developed and used non-compendial, validated in-house methods.

Based on satisfactory long-term and accelerated stability data of three drug product commercial scale registration batches assuring the identity, strength, purity and quality, a 24-month of expiration dating period when stored between 20ºC to 25ºC in the proposed 30cc HDPE bottle is granted (See the **Drug Product** review by Dr. Jane Chang).

Manufacturing: Adequate

SUTAB tablets are manufactured by Braintree Laboratories, Inc.; MA. (b) (4) The drug product manufacturing process was reviewed by Dr. Liang Qin and was found to be acceptable. (See the **Manufacturing Integrated Assessment**).

Biopharmaceutics: Adequate

Biopharmaceutics: All active ingredients in the tablet formulation are highly water soluble. The drug product dissolution method for rapidly dissolving oral dosage forms was adopted from FDA guidance. (b) (4)

The drug product dissolution method, dissolution data and dissolution specification were reviewed by Dr. Vincent Li and deemed acceptable from Biopharmaceutics perspective. (See the **Biopharmaceutics** review)

Microbiology (if applicable): Adequate

In the amendment dated the applicant submitted a revised drug product specification. It includes microbial testing and limits per USP <61> and USP <62>. (see **Attachment 1**) The drug product microbiology related sections were reviewed by Dr. Liang Qin and deemed acceptable. (See the **Manufacturing Integrated Assessment**).

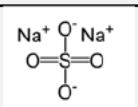
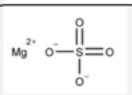
Labeling: Inadequate

The labels and labeling issues are ***not*** satisfactorily resolved from the CMC

perspective according to the labeling reviewer, Dr. Jane Chang. Therefore, this application is not deemed ready for approval in its present form per 21CFR 314.125(b)(6) from the OPQ perspective until the deficiencies listed below are satisfactorily resolved. (See the **Labeling** review).

Facilities Inadequate

The following manufacturing and testing facilities for all three drug substances are acceptable.

Chemical Name	Structure	Manufacturing Facility	Status
Sodium Sulfate (anhydrous)		(b) (4)	Approve
Magnesium Sulfate (anhydrous)			Approve
Potassium Chloride	KCl		Approve

The following raw materials, drug substances and drug product testing facilities are acceptable.

Facility Name/FEI	Testing Responsibilities	Status
(b) (4)		Approve
		Approve
		Approve
		Approve

Braintree Laboratories, Inc. is responsible for the drug product manufacturing, packaging, release and stability testing. A pre-approval inspection was performed during October 15 - 22, 2019. A Form-483 was issued listing inspection observations. Based on firm's inadequate response the Office of Pharmaceutical Manufacturing Assessment recommended "Withhold" due to lack of readiness of Braintree Laboratories Inc. for commercial manufacturing of the drug product.

Drug Product	Manufacturing Facility	Status

SUTAB Tablets	Braintree Laboratories, Inc.; MA FEI: 1000513636	**Withhold**

The Office of Pharmaceutical Manufacturing Assessment reviewer, Dr. Liang Qin has made an "Adequate" recommendation for the manufacturing and testing facilities of all three drug substances. However, for the drug product manufacturing facility, Braintree Laboratories, Inc.; MA, a "Withhold" recommendation has been made. (see **Manufacturing Integrated Assessment**).

Environmental Assessment Adequate

Per 21 CFR § 25.15(d) and 25.31(c), Braintree claimed a categorical exclusion from the requirements to submit an Environmental Assessment for SUTAB tablets. Under 21 CFR 25.31(c), a categorical exclusion exists for action on an NDA, an abbreviated application or a supplement to such applications for substances that occur naturally in the environment when the action does not alter significantly the concentration or distribution of the substance, its metabolites, or degradation products in the environment.

Sodium sulfate, magnesium sulfate and potassium chloride are naturally occurring substances in very large quantities. The claim for categorical exclusion is deemed acceptable. (See the **Drug Product** review by Dr. Jane Chang)

C. Risk Assessment

SUTAB (sodium sulfate, magnesium sulfate, and potassium chloride) tablets

Product Attribute / CQA	Factors that can impact the CQA	Risk Ranking	Risk Mitigation Approach	Risk Evaluation	LifeCycle consideration/ Comments
Assay and content uniformity	• Formulation • Raw materials • Process parameters • Scale/equipment	L	(b) (4)	The drug product is expected to be safe for oral administration during the entire shelf life from product quality perspective. Low to None	None
Related Substances Impurities / Degradants	•Raw materials •Process parameters	L		Low to None	None

D. List of Deficiencies for Complete Response

1. Labeling Deficiencies

A. Medication Guide

1. Delete "(b) (4)" from the established name.

   That is, SUTAB™ (Soo'tab)
   (sodium sulfate, magnesium sulfate, and potassium chloride) Tablets

2. Include "ethylene glycol and vinyl alcohol graft copolymer" in "Inactive ingredients". That is,

   Inactive ingredients: polyethylene glycol 8000, sodium caprylate, and ethylene glycol and vinyl alcohol graft copolymer

B. Regarding the Container/Carton Labels

3. Address the following for both container and carton labels:
   a) Add "and" between magnesium sulfate and potassium chloride in the established name.
   b) Replace "Tablet" with "Tablets" for the proprietary name and established name.
   c) Add strength "1.479 g/0.225 g/0.188 g" underneath the established name. That is, the proprietary name, established name and strength should be:

      SUTAB
      (sodium sulfate, magnesium sulfate, and potassium chloride) Tablets
      1.479 g/0.225 g/0.188 g

   d) Allocate the location of Lot number and expiration dating period.

4. Address the following for container label:
   a) Add the statement "Recommended Dosage: See Prescribing Information".
   b) Correct the typographical error "Manufactored" with "Manufactured".

5. Address the following for carton label:
   a) Add "Rx only" statement.
   b) Regarding Panel 1, add a space between "Booklet" and "includes" as well as between "Patient" and "Instructions".
   c) Regarding Panel 3, Day 1, Step 1, insert a space between the words "(b) (4)".
   d) Regarding Panel 3, Day 2, insert a space between the words "(b) (4)".

2. Manufacturing Deficiencies

Braintree Laboratories, Inc. is responsible for the drug product manufacturing, packaging, release and stability testing. A pre-approval inspection was performed during October 15 - 22, 2019. A Form-483 was issued listing inspection observations. Based on firm's inadequate response the Office of Pharmaceutical Manufacturing Assessment recommended "Withhold" recommendation due to lack of readiness of Braintree Laboratories Inc. for commercial manufacturing of the drug product.

Application Technical Lead Name and Date:

Hitesh Shroff, Ph.D.
Application Technical Lead, Branch V
Division of New Drug Products II
February 16, 2020

QUALITY ASSESSMENT DATA SHEET

IQA NDA Assessment Guide Reference

1. RELATED/SUPPORTING DOCUMENTS

A. DMFs:

DMF #	Type	Holder	Item Referenced	Status	Date Assessment Completed	Comments
(b) (4)	Type II		(b) (4)	Active	Reviewed by Joseph Leginus, 9/23/2019 Adequate	LOA Aug 15, 2019
	Type II			Active	Reviewed by Joseph Leginus, 8/27/2019 Adequate	LOA Feb 21, 2019
	Type II			Active	Reviewed by M. Akter, 7/10/2018 Adequate	LOA Jun 25, 2018
	Type III			Active	N/A	LOA July 12, 2018
	Type III			Active	N/A	LOA Jun 29, 2018
	Type III			Active	N/A	LOA Jun 29, 2018
	Type III			Active	N/A	LOA Jun 28, 2018
	Type III			Active	N/A	LOA Jun 28, 2018
	Type III			Active	N/A	LOA Jun 28, 2018
	Type III			Active	N/A	LOA Jun 29, 2018

B. OTHER DOCUMENTS: *IND, RLD, RS, Approved NDA*

Document	Application Number	Description
NDA	22372	SUPREP Bowel Prep Kit

2. CONSULTS

Discipline	Status	Recommendation	Date	Assessor
Biostatistics				
Pharmacology/Toxicology				
CDRH-ODE				
CDRH-OC				
Clinical				
Other				

Attachment 1

SUTAB Tablets Specification

Test	Method	Specification
Description	Visual	(b) (4)
Identification for: a) Sulfate b) Sodium c) Potassium d) Magnesium e) Chloride	STM0050	
Uniformity of Dosage Unit (Weight Variation) for Sodium	STM0050 and Current USP <905>	
Uniformity of Dosage Unit (Content Uniformity) for Potassium	STM0050 and Current USP <905>	
Uniformity of Dosage Unit (Content Uniformity) for Magnesium	STM0050 and Current USP <905>	
Assay for Sulfate	STM0050	
Assay for Sodium	STM0050	
Assay for Potassium	STM0050	
Assay for Magnesium	STM0050	
Assay for Chloride	STM0050	
Dissolution ((b) (4)	STM0050 and Current USP <711>	
Nephelometric Turbidity	STM0050	
Microbial Limits	USP <61> a) TAMC b) TYMC	
Microbial Examination	USP<62> *E.coli* only	

U.S. FOOD & DRUG ADMINISTRATION

CHAPTER VI: BIOPHARMACEUTICS

IQA NDA Assessment Guide Reference

Product Information	SUTAB (Sodium Sulfate, Magnesium Sulfate, Potassium Chloride Oral Sulfate Tablets)
NDA Number	213135
Assessment Cycle Number	#1a
Drug Product Name/ Strength	SUTAB (Sodium Sulfate, Magnesium Sulfate, Potassium Chloride Oral Sulfate Tablets)/35.5 g, 5.4 g, 4.5 g
Route of Administration	Oral
Applicant Name	BRAINTREE LABORATORIES, INC.
Therapeutic Classification/ OND Division	OND/ODEIII/DGIEP
RLD Number	NDA 22372
Proposed Indication	Bowel cleansing prior to colonoscopy in adults

Assessment Recommendation: **Adequate**

Assessment Summary:

The applicant developed an immediate release oral tablet containing 35.5 g of Sodium Sulfate, 5.4 g of Magnesium Sulfate, and 4.5 g of Potassium Chloride as a compact dosage form for bowel cleansing prior to colonoscopy in adults. The Reference List Product is the liquid version of approved NDA 22372.

All active ingredients are highly water soluble. Hence, the applicant adopted one of the recommended dissolution methods per the FDA guidance "Dissolution Testing and Acceptance Criteria for Immediate-Re/ease Solid Oral Dosage Form Drug Products Containing High Solubility Drug Substances" for rapidly dissolving oral dosage forms. (b) (4) The method is adequate. The proposed dissolution specification of Q = % of labeled amount of sulfate in 15 minutes is acceptable.

For Biopharmaceutics perspective, this NDA is adequate.

CQAs	Initial Risk Ranking	Comments	Updated Risk Ranking after Assessment Cycle #	Comments
Dissolution	Low	All active ingredients are highly water soluble	Low	(b) (4)

List Submissions being assessed (table):

Document(s) Assessed	Date Received
Application 213135 - Sequence 0001 - 0001 (1) 05/15/2019 ORIG-1 /Multiple Categories/Subcategories	**5/15/2019**
Application 213135 - Sequence 0007 - 0007 (7) 07/19/2019 ORIG-1 /Quality/Response To Information Request	**7/19/2019**

Highlight Key Issues from Last Cycle and Their Resolution:

- Missing dissolution method report
  Resolution: The applicant provided the missing information on July 19, 2019. The information provided is adequate.
- Missing individual dissolution data of clinical batch and exhibit batches
  Resolution: The applicant provided the missing information on July 19, 2019. The information provided is adequate.
- Revised dissolution acceptance criterion
  Resolution: The applicant revised the dissolution specifications for product release and stability to our recommended acceptance criterion of Q (b) (4)% in 15 minutes.
- Justification for omission of dissolution testing of potassium chloride.
  Resolution: The applicant justified the omission (b) (4) The justification is acceptable.

Concise Description of Outstanding Issues (List bullet points with key information and update as needed):

- None

B.2 DISSOLUTION METHOD AND ACCEPTANCE CRITERIA

Dissolution Method

All active ingredients are highly water soluble. The applicant monitored sulfate ion only during dissolution. As KCl is even more soluble than sulfates, its dissolution was not deemed necessary to be monitored. The applicant adopted one of the recommended dissolution methods per the FDA guidance "Dissolution Testing and Acceptance Criteria for Immediate-Re/ease Solid Oral Dosage Form Drug Products Containing High Solubility Drug Substances."

(b) (4)

A 100 rpm is chosen because the tablet has a mass of around 1.99 g per tablet.

Dissolution apparatus	Rotational speed	Dissolution media	Volume	Acceptance criterion
II (paddle)	100 rpm	water	900 mL	Q= (b) (4) % of labeled amount of sulfate in 15 minutes

Dissolution Acceptance Criterion

All the exhibit batches reached close to 100% in 15 minutes at product release as well for 6 months stored at room temperature. The following table summarize the product release data.

The applicant proposed the following acceptance criterion for dissolution of sulfate:

Q = (b) (4)% of the labeled amount of sulfate in 15 minutes

The cumulative % (Q) of sulfate is based on the total sulfate from label amount of sodium sulfate and magnesium sulfate in each tablet.

The dissolution of the product did not change with time on stability and close to 100% dissolved at 15 minutes.

Cumulative % Release at 15 min at time zero		
RD1348	RD1349	RD1350
		(b) (4)

Assessment: *Adequate*

The dissolution method is adequate for its intended use to monitor dissolution of total sulfates. Both sulfates and KCl are highly soluble. As KCl is even more soluble than sulfates, it's dissolution was not deemed necessary to be monitored. The proposed dissolution acceptance criterion of Q (b) (4)% in 15 minutes for product release and stability is acceptable. All exhibit batches comply with the proposed acceptance criterion.

B.12 BRIDGING OF FORMULATIONS

Assessment: *Adequate*
There is no change of formulation from Phase III pivotal clinical study to commercial launch. No bridging is needed.

B. 13 BIOWAIVER REQUEST

Assessment: *Adequate*
There is only one strength. There is no biowavier request.

R. REGIONAL INFORMATION

Comparability Protocols

Assessment: *N/A*
There is no Comparability Protocols submitted by the applicant.

Post-Approval Commitments

Assessment: *N/A*

Lifecycle Management Considerations

None

BIOPHARMACEUTICS LIST OF DEFICIENCIES

None

Primary Biopharmaceutics Assessor's Name and Date:
Vincent Li, Ph.D.

Secondary Assessor Name and Date (and Secondary Summary, as needed):
Tapash Ghosh, Ph.D.

Vincent Li

Digitally signed by Vincent Li
Date: 10/09/2019 01:48:08PM
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Tapash Ghosh

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CHAPTER IV: LABELING

IQA NDA Assessment Guide Reference

List Submissions being reviewed:

Document Reviewed (eCTD #)	Date Received
eCTD-0001 (SDN-1)	05/15/2019
eCTD-0002 (SDN-2)	06/12/2019
eCTD-0015 (SDN-15)	09/06/2019

1.0 PRESCRIBING INFORMATION

The information provided in eCTD-0015 dated 09/06/2019 is summarized below.

1.1 HIGHLIGHTS OF PRESCRIBING INFORMATION

1) TITLE

SUTAB (sodium sulfate, magnesium sulfate, and potassium chloride) tablets, for oral use

Initial U.S. Approval: YYYY

2) DOSAGE FORMS AND STRENGTHS

Tablets: 1.479 g sodium sulfate, 0.225 g magnesium sulfate, and 0.188 g potassium chloride.

Item	Information Provided in NDA	Assessor's Comment and Recommendations
Drug name [201.57(a)(2)]		
Proprietary name and established name	SUTAB (sodium sulfate, magnesium sulfate, and potassium chloride) tablets	**Acceptable**
Dosage form, route of administration	Tablets as dosage form; oral as route of administration	**Acceptable** Oral as the route of administration for oral tablets does not need to be included in the proprietary name or established name.
Controlled drug substance symbol	N/A	N/A
Initial U.S. Approval	YYYY	**Acceptable** The year that this drug product is approved will be used.
Dosage Forms and Strengths [201.57(a)(8)]		
Dosage Forms and Strengths in metric system	Tablets as dosage form. Strength is provided: 1.479 g for sodium sulfate, 0.225 g for magnesium sulfate, and 0.188 g for potassium chloride	**Acceptable**.
Whether the drug product is scored	N/A	N/A

Conclusion: Satisfactory

The proposed proprietary name "Sutab" was determined to be acceptable per DMEPA's assessment by Teresa McMillan dated 08/09/2019. The Highlighs section pertaining to CMC meets the regulatory requirements.

1.2 FULL PRESCRIBING INFORMATION

1.2.1 Section 2: DOSAGE AND ADMINISTRATION

Item	Information Provided in NDA	Assessor's Comment and Recommendations
Special instructions for product preparation (e.g., reconstitution and resulting concentration, dilution, compatible diluents, storage conditions needed to maintain the stability of the reconstituted or diluted product)	N/A	N/A

1.2.2 Section 3: DOSAGE FORMS AND STRENGTHS

Tablets: 1.479 g sodium sulfate, 0.225 g magnesium sulfate, and 0.188 g potassium chloride. The tablets are white to off-white, film coated, oblong, and biconvex with flat sides, debossed with *S24* on one side.

Item	Information Provided in NDA	Reviewer's Comment and Recommendations
Available dosage forms	tablets	**Acceptable**
Strengths: in metric system	1.479 g sodium sulfate, 0.225 g magnesium sulfate, 0.188 g potassium chloride	**Acceptable** Strength is expressed as per tablet
A description of the identifying characteristics of the dosage forms, including shape, color, coating, scoring, and imprinting, when applicable.	white to off-white, film coated, oblong, and biconvex with flat sides, debossed with *S24* on one side	**Acceptable** Tablets are not scored.

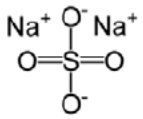
Conclusion: **Satisfactory**

Information in DOSAGE FORMS AND STRENGTHS meets the regulatory requirements.

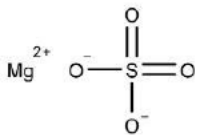
1.2.3 Section 11: DESCRIPTION

SUTAB (sodium sulfate, magnesium sulfate, and potassium chloride) tablets is an orally administered osmotic laxative and is provided as two bottles, each containing 12 tablets. Each tablet contains: 1.479 g sodium sulfate, 0.225 g magnesium sulfate, and 0.188 g potassium chloride. Inactive ingredients include: polyethylene glycol 8000, sodium caprylate, and ethylene glycol and vinyl alcohol graft copolymer.

Sodium Sulfate, USP
The molecular formula is Na_2SO_4. The average Molecular Weight is 142.04. The structural formula is:



Magnesium Sulfate, USP
The molecular formula is $MgSO_4$. The average Molecular Weight: 120.37. The structural formula is:



Potassium Chloride, USP
The chemical name is KCl. The average Molecular Weight is 74.55. The structural formula is:

Cl- ---------- K+

Item	Information Provided in NDA	Reviewer's Comment and Recommendations
Proprietary name and established name [21 CFR 201.57(c)(12)(i)(A)]	SUTAB (sodium sulfate, magnesium sulfate, and potassium chloride) tablets	**Acceptable**
Dosage form and route of administration [21 CFR 201.57(c)(12)(i)(B)]	Tablets as dosage form. Oral as route of administration.	**Acceptable**
Active moiety expression of strength with equivalence statement (if applicable) [FD&C Act 502(e)(1)(A)(ii), 21 CFR 201.10(d)(1); 21 CFR 201.100(b)(4), USP <1121>]	1.479 g sodium sulfate, 0.225 g magnesium sulfate, and 0.188 g potassium chloride	**Acceptable** Active moiety expression is not applicable.
Inactive ingredient information [21 CFR 201.57(c)(12)(i)(C)] [quantitative, if injectables 21CFR201.100(b)(5)(iii), listed by USP/NF names (if any)]. For ingredients added to adjust the pH or make isotonic, include the name and statement of effect. If alcohol is present, must provide the amount of alcohol in terms of percent volume of absolute alcohol	polyethylene glycol 8000, sodium caprylate, and ethylene glycol and vinyl alcohol graft copolymer	**Acceptable** Even though inactive ingredients are not required for drugs of oral use per 21CFR201.100(b)(5), it is acceptable to include them in Section 11. (b) (4)
Pharmacological/ therapeutic class [21 CFR 201.57(c)(12)(i)(E)]	osmotic laxative	**Acceptable**
Chemical name, structural formula [21 CFR 201.57(c)(12)(i)(F)]	Molecular formula, structural formula and molecular weight for each active ingredient are provided.	**Acceptable**
Other important chemical or physical properties (such as pKa or pH) [21 CFR 201.57(c)(12)(ii)]	N/A	N/A
For oral prescription drug products, include gluten statement if applicable	N/A	N/A

Conclusion: **Satisfactory**

Information in DESCRIPTION meets the regulatory requirements.

1.2.4 Section 16: HOW SUPPLIED/STORAGE AND HANDLING

16.1 How Supplied

Each SUTAB (sodium sulfate, magnesium sulfate, and potassium chloride) tablet contains 1.479 g sodium sulfate, 0.225 g magnesium sulfate, and 0.188 g potassium chloride. The tablets are white to off-white, film coated, oblong, and biconvex with flat sides, debossed with *S24* on one side.

- SUTAB (NDC 52268-201-01) is supplied as two bottles containing 12 tablets each.
- One container with a 16-ounce fill line.

Storage
Store at 20° to 25°C (68° to 77°F). Excursions permitted between 15° to 30°C (59° to 86°F). See USP controlled room temperature.

Item	Information Provided in NDA	Reviewer's Comment and Recommendations
Dosage form	tablets	**Acceptable**
Strength of dosage form in metric system	1.479 g sodium sulfate, 0.225 g magnesium sulfate, 0.188 g potassium chloride	**Acceptable** Strength per tablet is provided.
Available units (e.g., bottles of 100 tablets)	Two bottles containing 12 tablets each.	**Acceptable**
Identification of dosage forms, e.g., shape, color, coating, scoring, imprinting, NDC number.	white to off-white, film coated, oblong, and biconvex with flat sides, debossed with *S24* on one side NDC 52268-201-01	**Acceptable**
Special handling (e.g., protect from light, refrigerate).	N/A	N/A
Storage conditions.	Store at 20° to 25°C (68° to 77°F). Excursions permitted between 15° to 30°C (59° to 86°F). See USP controlled room temperature.	**Acceptable**
Child-resistant packaging	Not provided	**Acceptable** Statement regarding child-resistant packaging is optional. (b) (4) [redacted]

Conclusion: Satisfactory

Information in HOW SUPPLIED/STORAGE AND HANDLING meets the regulatory requirements.

1.2.5 Other Sections of Labeling

N/A

1.2.6 Section 17: PATIENT COUNSELING INFORMATION

Manufactured by:

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

Item	Information Provided in NDA	Reviewer's Comment and Recommendations
Manufacturer/distributor name [21 CFR 201.1(h)(5)]	Braintree Laboratories, Inc. 270 Centre Street Holbrook, MA 02343	**Acceptable**

Conclusion: Satisfactory

2.0 PATIENT LABELING

Relevant product quality information in Medication Guide submitted in eCTD-0001 dated 05/15/2019 is shown below.

SUTAB™ (Soo'tab)
(b) (4) sodium sulfate, magnesium sulfate and potassium chloride) Tablets

How should I store SUTAB?
Store SUTAB at room temperature, between 20° to 25°C (68° to 77°F). Excursions permitted between 15° to 30°C (59° to 86°F).

Active ingredients: sodium sulfate, magnesium sulfate, potassium chloride
Inactive ingredients: polyethylene glycol 8000, sodium caprylate,

Manufactured by:

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

Conclusion: Unsatisfactory

The recommended revisions are shown below:

SUTAB™ (Soo'tab)
(b) (4) sodium sulfate, magnesium sulfate, and potassium chloride) Tablets

Active ingredients: sodium sulfate, magnesium sulfate, potassium chloride

Inactive ingredients: polyethylene glycol 8000, sodium caprylate, and ethylene glycol and vinyl alcohol graft copolymer

3.0 CARTON AND CONTAINER LABELS

The information provided in eCTD-0002 dated 06/12/2019 is shown below.

3.1 CONTAINER LABEL

Item	Information Provided in NDA	Reviewer's Comment and Recommendations
Proprietary name, established name [FD&C Act 502(e)(1)(A)(i)] [font size at least half as large as the proprietary name, and prominence per FD&C Act 502(e)(1)(B), 21 CFR 201.10(g)(2)]	SUTAB (sodium sulfate, magnesium sulfate, potassium chloride) Tablet	**Unacceptable** Add "and" between magnesium sulfate and potassium chloride in the established name. Replace "Tablet" with "Tablets". The font size of established name is at least half as large as the proprietary name.
Route of administration, if it is not for oral use [201.100(b)(3)]	Not provided	**Acceptable** Route of administration is not required for oral drug.
Active moiety expression of strength with equivalence statement (if applicable) [FD&C Act 502(e)(1)(A)(ii), 21 CFR 201.10(d)(1); 21 CFR 201.100(b)(4), USP <1121>]	Not provided	**Unacceptable** Active moiety expression is not applicable. Strength (per tablet) "1.479 g/0.225 g/0.188 g" should be provided underneath the established name.
Net content [FD&C Act 502(b)(2), 21 CFR 201.51(a)]	This bottle contains 12 tablets.	**Acceptable**
Name of all inactive ingredients, in alphabetical order required for OTC drugs [FD&C Act 502(e)(1)(A)(iii), 201.10(a)] [except for oral drug per 201.100(b)(5) or limited space per 201.10(i)(2)]; [Quantitative ingredient information is required for	Not provided	**Acceptable** Name of all inactive ingredients for oral drugs is optional.

injectables per 201.100(b)(5)(iii)]		
"Rx only" statement [21 CFR 201.100(b)(1)]	Provided on the top left corner	**Acceptable**
NDC number [per 21 CFR 201.2, requested, but not required for all labels or labeling, also see 21 CFR 207.35(b)(3)(i)]	NDC 52268-200-01	**Acceptable**
Lot number (21 CFR 201.18) and expiration date (21 CFR 201.17)	Not provided	**Unacceptable** The location of Lot number and expiration dating period should be allocated.
Storage conditions.	Store at 25°C (77°F); excursions permitted 15ºC - 30°C (59ºF - 86°F)	**Acceptable**
Bar code [21CFR 201.25(c)(2)]	Provided on the right side	**Acceptable**
Adequate directions for use [FD&C Act 502(f)(1), 21 CFR 201.5] or "See package insert for dosage information" (21 CFR 201.55)	Not provided	**Unacceptable** Add the statement "Recommended Dosage: See Prescribing Information".
Name of manufacturer/distributor [502(b)(1), 21 CFR 201.1(a), 21 CFR 201.1(h)(5)]	Manufactored by Braintree Laboratories, Inc., Braintree, MA	**Unacceptable** The name of the manufacturer provided is acceptable. However, the typographical error "Manufactored" should be corrected with "Manufactured".

Conclusion: **Unsatisfactory**

In an email communication dated 8/9/2019 with DMEPA assessor for labeling of another NDA, the assessor stated that based on DMEPA management's involvement with the Labeling Workgroup, it was recently determined that the usual dosage statement be changed from "See package insert for dosage information" to "Recommended Dosage: See Prescribing Information".

The recommended revisions are shown below:

1. Add "and" between magnesium sulfate and potassium chloride in the established name.
2. Replace "Tablet" with "Tablets" for the proprietary name and established name.
3. Add strength "1.479 g/0.225 g/0.188 g" underneath the established name. That is, the proprietary name, established name and strength should be:

   SUTAB
   (sodium sulfate, magnesium sulfate, and potassium chloride) Tablets
   1.479 g/0.225 g/0.188 g

4. Allocate the location of Lot number and expiration dating period.
5. Add the statement "Recommended Dosage: See Prescribing Information".
6. Correct the typographical error "Manufactored" with "Manufactured".

2 Page(s) of Draft Labeling have been Withheld in Full as B4 (CCI/TS) immediately following this page

Item	Information Provided in NDA	Reviewer's Comment and Recommendations
Proprietary name, established name [FD&C Act 502(e)(1)(A)(i)] [font size at least half as large as the proprietary name, and prominence per FD&C Act 502(e)(1)(B), 21 CFR 201.10(g)(2)]	SUTAB (sodium sulfate, magnesium sulfate, potassium chloride) Tablet	**Unacceptable** Add "and" between magnesium sulfate and potassium chloride in the established name. Replace "Tablet" with "Tablets". The font size of established name is at least half as large as the proprietary name.
Route of Administration [not required for oral, 21 CFR 201.100(b)(3)]	Not provided	**Acceptable** Route of administration is not required for oral drug.
Active moiety expression of strength with equivalence statement (if applicable) [FD&C Act 502(e)(1)(A)(ii), 21 CFR 201.10(d)(1); 21 CFR 201.100(b)(4), USP <1121>]	Strengths are not provided	**Unacceptable** Active moiety expression is not applicable. Strength (per tablet) "1.479 g/0.225 g/ 0.188 g" should be provided underneath the established name.
Net content [FD&C Act 502(b)(2), 21 CFR 201.51(a)]	2 Bottles of 12 tablets each	**Acceptable**
Name of all inactive ingredients, in alphabetical order required for OTC drugs [FD&C Act 502(e)(1)(A)(iii), 21 CFR 201.10(a)] [except for oral drug per 201.100(b)(5) or limited space per 21 CFR 201.10(i)(2)]; [Quantitative ingredient information is required for injectables per 21 CFR 201.100(b)(5)(iii)]	Not provided	**Acceptable** Name of all inactive ingredients for oral drugs is optional per 21 CFR 201.100(b)(5).
"Rx only" statement [21 CFR 201.100(b)(1)]	Not provided	**Unacceptable** "Rx only" statement should be added.
NDC number [per 21 CFR 201.2, requested, but not required for all labels or labeling, also see 21 CFR 207.35(b)(3)(i)]	NDC 52268-201-01 provided on Panel 1 and Patient Instructions Panel	**Acceptable**
Lot number (21 CFR 201.18) and expiration date (21 CFR 201.17)	Not provided	**Unacceptable** The location of Lot number and expiration dating period should be allocated.
Storage conditions	Store at 25°C (77°F); excursions permitted to 15°C - 30°C (59° F - 86°F)	**Acceptable**
Bar code [21 CFR 201.25(c)(2)]	The locations of Bar code are allocated on Panel 4 and Panel 5.	**Acceptable**
Adequate directions for use [FD&C Act 502(f)(1), 21 CFR 201.5] or "See package insert for dosage information" (21 CFR 201.55)	"Read patient booklet contained in kit at least 2 days before scheduled procedure	**Acceptable**

"Keep out of reach of children" (Required for OTC. Optional for Rx drugs)	Not provided	**Acceptable** The statement is optional for Rx drugs.
Name of manufacturer/distributor [502(b)(1), 21 CFR 201.1(a), 21 CFR 201.1(h)(5)]	Braintree A PART OF SEBELA PHARMACEUTICAL	**Acceptable**
And others, if space is available	Both 12-tablet bottles are required for a complete preparation.	**Acceptable**

Conclusion: Unsatisfactory

The recommended revisions are shown below:

1. Add "and" between magnesium sulfate and potassium chloride in the established name.
2. Replace "Tablet" with "Tablets" for the proprietary name and established name.
3. Add strength "1.479 g/0.225 g/0.188 g" underneath the established name. That is, the proprietary name, established name and strength should be:

   SUTAB
   (sodium sulfate, magnesium sulfate, and potassium chloride) Tablets
   1.479 g/0.225 g/0.188 g

4. Allocate the location of Lot number and expiration dating period.
5. Add "Rx only" statement.
6. Regarding Panel 1, add a space between "Booklet" and "includes" as well as between "Patient" and "Instructions".
7. Regarding Panel 3, Day 1, Step 1, insert a space between the words (b) (4)
8. Regarding Panel 3, Day 2, insert a space between the words (b) (4)

4.0 LIST OF DEFICIENCIES:

A. Medication Guide

1. Delete (b) (4) from the established name. That is,

   SUTAB™ (Soo'tab)
   (sodium sulfate, magnesium sulfate, and potassium chloride) Tablets

2. Include "ethylene glycol and vinyl alcohol graft copolymer" in "Inactive ingredients". That is,

   Inactive ingredients: polyethylene glycol 8000, sodium caprylate, and ethylene glycol and vinyl alcohol graft copolymer

B. Regarding the Container/Carton Labels

3. Address the following for both container and carton labels:

a) Add "and" between magnesium sulfate and potassium chloride in the established name.
b) Replace "Tablet" with "Tablets" for the proprietary name and established name.
c) Add strength "1.479 g/0.225 g/0.188 g" underneath the established name. That is, the proprietary name, established name and strength should be:

SUTAB
(sodium sulfate, magnesium sulfate, and potassium chloride) Tablets
1.479 g/0.225 g/0.188 g

d) Allocate the location of Lot number and expiration dating period.

4. Address the following for container label:
   a) Add the statement "Recommended Dosage: See Prescribing Information".
   b) Correct the typographical error "Manufactored" with "Manufactured".

5. Address the following for carton label:
   a) Add "Rx only" statement.
   b) Regarding Panel 1, add a space between "Booklet" and "includes" as well as between "Patient" and "Instructions".
   c) Regarding Panel 3, Day 1, Step 1, insert a space between the words "[redacted (b) (4)]".
   d) Regarding Panel 3, Day 2, insert a space between the words [redacted (b) (4)]

OVERALL ASSESSMENT:
Issues on established name, strength, Lot number, expiration date, and lack of "Rx only" and "Recommended Dosage: See Prescribing Information" statements as well as incomplete inactive ingredients are identified for the container and carton labels and Medication Guide.

Recommendation:

From the ONDP perspective, this application is ***not*** ready for approval in its present form per 21 CFR 314.125(b)(6) until the deficiencies delineated above are satisfactorily resolved.

Primary Labeling Assessor Name and Date:

Jane Chang, Ph.D.
Senior reviewer
DNDP II/ONDP
09/10/2019

*Secondary **Assessor** Name and Date (and Secondary Summary, as needed):*

I agree with Dr. Chang's assessment on the labeling and labels and concur with her recommendation that this application is not ready for approval as of this review until the issues delineated in the List of deficiencies are satisfactorily resolved.

Moo-Jhong Rhee, Ph.D.
Chief, Branch V
DNDP II/ONDP
09/10/2019

Jane Chang

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Moo Jhong Rhee

Digitally signed by Moo Jhong Rhee
Date: 10/17/2019 12:39:55PM
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Hitesh
Shroff

Digitally signed by Hitesh Shroff
Date: 3/09/2020 10:37:12AM
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