CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

761127Orig1s000

OTHER REVIEW(S)

MEMORANDUM

REVIEW OF REVISED LABEL AND LABELING

Division of Medication Error Prevention and Analysis 1 (DMEPA 1)

Office of Medication Error Prevention and Risk Management (OMEPRM)

Office of Surveillance and Epidemiology (OSE)

Center for Drug Evaluation and Research (CDER)

Date of This Memorandum:	September 7, 2022
Requesting Office or Division:	Division of Dermatology and Dentistry (DDD)
Application Type and Number:	BLA 761127
Product Name and Strength:	Daxxify (daxibotulinum toxinA-lanm) for injection, 50 units/vial and 100 units/vial
Applicant/Sponsor Name:	Revance Therapeutics
OSE RCM #:	2019-2405-2
Acting DMEPA 1 Team Leader:	Madhuri R. Patel, PharmD
DMEPA 1 Associate Director for Nomenclature and Labeling:	Mishale Mistry, PharmD, MPH

1 PURPOSE OF MEMORANDUM

The Applicant submitted revised container labels on March 8, 2022 and revised carton labeling received on September 2, 2022 for Daxxify. The Division of Dermatology and Dentistry (DDD) requested that we review the revised container labels and carton labeling for Daxxify (Appendix A) to determine if they are acceptable from a medication error perspective. The revisions are to increase the prominence of the medication guide statement on the container labels and carton labeling to "ATTENTION PHARMACIST: Each patient is required to receive the enclosed Medication Guide."

2 CONCLUSION

We find the revised container labels and carton labeling acceptable from a medication error perspective and we have no additional recommendations at this time.

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MADHURI R PATEL
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MISHALE P MISTRY
09/07/2022 11:10:38 AM

MEMORANDUM

REVIEW OF REVISED LABEL AND LABELING
Division of Medication Error Prevention and Analysis (DMEPA)
Office of Medication Error Prevention and Risk Management (OMEPRM)
Office of Surveillance and Epidemiology (OSE)
Center for Drug Evaluation and Research (CDER)

Date of This Memorandum:	October 2, 2020
Requesting Office or Division:	Division of Dermatology and Dentistry (DDD)
Application Type and Number:	BLA 761127
Product Name and Strength:	Daxxify (daxibotulinumtoxinA-lanm) for injection, 50 units/vial and 100 units/vial
Applicant/Sponsor Name:	Revance Therapeutics, Inc.
OSE RCM #:	2019-2405-1
DMEPA Safety Evaluator:	Madhuri R. Patel, PharmD
DMEPA Team Leader:	Sevan Kolejian, PharmD, MBA, BCPPS

1 PURPOSE OF MEMORANDUM

The Applicant submitted revised container labels and carton labeling received on September 30, 2020 for Daxxify. Division of Dermatology and Dentistry (DDD) requested that we review the revised container labels and carton labeling for Daxxify (Appendix A) to determine if they are acceptable from a medication error perspective. The revisions are in response to recommendations that we made during a previous label and labeling review.[a]

2 CONCLUSION

The Applicant implemented all of our recommendations and we also have reviewed the provided physical samples of the container labels and found the container labels and carton labeling acceptable from a medication error perspective. We have no additional recommendations at this time.

[a] Patel M. Label and Labeling Review for daxibotulinumtoxinA-xxxx (BLA 761127). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2020 MAY 21. RCM No.: 2019-2405.

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MADHURI R PATEL
10/02/2020 08:24:18 AM

SEVAN H KOLEJIAN
10/02/2020 10:15:18 AM

Clinical Inspection Summary

Date	8//27/2020
From	Christian Shenouda, M.D., Medical Officer Good Clinical Practice Assessment Branch Division of Clinical Compliance Evaluation Office of Scientific Investigations
To	Tong Li-Masters, MD, Clinical Reviewer Snezana Trajkovic, MD, Clinical Team Leader Kimberle Searcy, Regulatory Project Manager Division of Dermatology and Dental Products (DDDP)
BLA	761127
Applicant	Revance Therapeutics, Inc.
Drug	Daxibotulinumtoxin A
NME	Yes
Proposed Indication(s)	The temporary improvement in the appearance of moderate to severe glabellar lines associated with corrugator and/or procerus muscle activity in adult patients.
Consultation Request Date	12/16/2019
Summary Goal Date	9/8/2020
Action Goal Date	10/30/2020
PDUFA Date	11/25/2020

I. OVERALL ASSESSMENT OF FINDINGS AND RECOMMENDATIONS

The clinical investigators Drs. Joel Cohen and John Joseph were inspected in support of this BLA. Based on the results of these inspections, Study 620301 (Sakura 1) appears to have been conducted adequately, and the data generated by these clinical investigators appear reliable in support of the proposed indication. The two sites selected for Study 1620302 (Sakura 2) could not be inspected (see details below). Therefore, at this time, OSI will be unable to determine if Study 1620302 was conducted adequately and whether the study data are reliable in support of the proposed indication.

II. BACKGROUND

Daxibotulinumtoxin A is an injectable medication which contains a holotoxin of onabotulinum toxin type A and has been studied for the treatment of moderate to severe glabellar lines. Two pivotal, multi-center trials, Protocols 1620301(Sakura 1) and 1620302 (Sakura 2) were conducted and are summarized below.

Both studies (Protocols 1620301 (Sakura 1) and 1620302 (Sakura 2) were multi-center, double-blinded, placebo-controlled studies in which enrolled subjects were randomized in a 2:1 fashion to either receive 40 units of the study drug or placebo. The objective of both studies

was to determine if injection of the drug resulted in reduced appearance of forehead/glabellar lines on clinician and subject rating scales.

Injections were standardized to include 5 sites on the forehead/glabellar region. Subjects completed study visits at Weeks 1, 2, 4, 8, 12, 16, 20, 24 28, 32, and 36, with the primary outcomes collected at Week 24.

Safety assessments included clinical laboratory tests (hematology, chemistry, urinalysis, prothrombin time), serum antibody tests, injection site evaluations, cranial nerves II-VII assessment, facial muscle strength, 12-lead electrocardiogram (ECG), concomitant medications, adverse event (AE) collection, adverse events of special interest (events due to the distant spread of toxin), vital signs, and physical examinations.

Both studies used the following scales as primary endpoints, which used a 0-3 rating scale:

- Patient Frown Wrinkle Severity (PFWS)
- Investigator's Global Assessment-Frown Wrinkle Severity (IGA-FWS),

Sakura 1 (1620301)

Title: "Phase 3, Randomized, Double-blind, Placebo Controlled, Multicenter Trial to Evaluate Efficacy and Safety of DaxibotulinumtoxinA for Injection to Treat Moderate to Severe Glabellar Lines (SAKURA-1)"

Subjects: 303 subjects enrolled, 275 completed the study. All 303 subjects were included in the safety and effectiveness analysis.

Sites: 15 sites (all in the US)

Study Initiation Date: (b) (6) (First subject's informed consent date)

Study Completion Date: 14 Nov 2017 (Last subject last visit/contact)

Primary efficacy endpoint: The investigator's and patient's assessment of glabellar line severity and glabellar line improvement, IGS-FWS and PFWS, respectively. Of note, glabellar line severity was assessed at maximum frown and at rest after maximum frown.

Sakura 2 (1620302)

Title: Phase 3, Randomized Double-Blind, Placebo Controlled, Multi-Center Trial to Evaluate Efficacy and Safety of DaxibotulinumtoxinA for Injection to Treat Moderate to Severe Glabellar Lines (SAKURA-2)

Subjects: 306 subjects were enrolled and 284 completed the study. All 306 were included in the safety and effectiveness analysis.

Sites: Nine trial centers in the US and Canada

Study Initiation Date: (b) (6) (First subject's informed consent date)

Study Completion Date: 03 Nov 2017 (Last subject last visit/contact)

Primary efficacy endpoint: The investigator's and patient's assessment of glabellar line severity and glabellar line improvement, IGS-FWS and PFWS, respectively. Glabellar line severity was assessed at maximum frown and at rest after maximum frown.

Rationale for Site Selection

The following clinical investigator (CI) sites was chosen based on numbers of enrolled subjects, site efficacy, and protocol deviations as well as prior inspectional history.

III. INSPECTION RESULTS

1. **Joel Cohen, M.D.**
   Site #102
   AboutSkin Dermatology and DermSurgery, PC
   5340 S. Quebec St. Suite 300
   Greenwood Village, CO 80111
   Inspection Dates: 2/12/2020-2/14/2020, 2/18/2020

At this site for Protocol 1620301 (Sakura 1), 23 subjects were screened and 21 were randomized in the trial. The two subjects who were classified as screen fails were noted to violate exclusion criteria for pre-existing facial asymmetry and use of immuosuppressive medications. Twenty subjects from this site completed the protocol, and one subject was lost to follow up. The subject ((b) (6)) who was lost to follow up was noted to be assigned to the placebo group.

The FDA field investigator was able to review and verify all subject case histories including, but not limited to, informed consent, inclusion and exclusion criteria, medication usage and adverse event reporting. The subject records were noted by be organized, and data listings were matched to print-outs for corresponding assessments (ECG, laboratory results, etc.). Study documentation related to compliance, medication storage, and monitoring logs were also reviewed. There were no deficiencies identified.

The primary and secondary endpoint data were also assessed for all enrolled subjects. There were no discrepancies noted when the data line listings provided by the sponsor were compared to paper source documentation for the primary and secondary endpoints (IGS-FWS, PFWS, Global Aesthetic Improvement Scale, Frown Line Impact Scale, and Patient Global Satisfaction).

There were no serious adverse events (SAEs) reported at this site. There was no evidence of under-reporting of safety signals or adverse events.

2. **John Joseph, M.D.**
   Site #109
   Clinical Testing of Beverly Hills
   9400 Brighton Way, Suites 205 & 203
   Beverly Hills, CA 90210
   Inspection Dates: 3/9/2020 – 3/13/2020

At this site for Protocol 1620301 (Sakura 1), 37 subjects were screened, and 35 subjects were enrolled. Two subjects who were classified as screen fails were noted to violate inclusion criteria for severity of glabellar lines or ability to follow trial procedures. Thirty-two of the enrolled subjects completed the protocol. Of the three subjects who did not complete the protocol, 2 subjects (b) (6)) were in the daxibotulinum group and one subject ((b) (6)) was assigned to the placebo group. The two subjects who were in the daxibotulinum group both withdrew consent. The subject in the placebo group was lost to follow up.

The FDA field investigator was able to review and verify all subject case histories including, but not limited to, informed consent, study entry criteria, adverse event reporting, and efficacy data. Study documentation related to medication storage and accountability, study monitoring logs, and protocol compliance were reviewed. There were no deficiencies identified.

The field investigator was able to review and verify the primary endpoint data for all enrolled subjects by comparing the paper source documentation to the line listings provided by the sponsor. There were 3 SAEs reported from this site (all were deemed unrelated to the study procedures). Two of these events occurred in subjects randomized to daxibotulinum and were dysuria/sepsis (Subject (b) (6)) and bone marrow suppression (Subject (b) (6)). The other SAE was anxiety in a subject assigned to receive the placebo (Subject # (b) (6)). There was no evidence of under-reporting of adverse events.

3. **Nowell Solish, M.D.**
   Site #213 of Protocol 1620302 (Sakura 2)
   Sweat Clinics of Canada
   66 Avenue Road, Suite 1 (Concourse Level)
   Toronto, ON M5R3N8
   Canada

The COVID-19 global pandemic has significantly limited OSI's ability to conduct on-site Good Clinical Practice (GCP) inspections. As a result, and in an effort to protect the health, safety, and welfare of FDA employees and study staff, the need for planned inspections in support of BLA 761127 were reevaluated based on the completed inspections listed above. Following discussions between OSI and OND, a decision was made that assessment of the application could proceed without this GCP inspection.

4. Arthur Swift, M.D.
Site #214 of Protocol 1620302 (Sakura 2)
4141 suite 230 rue Sherbrooke St. West
Montreal, QC, H3Z 1B7
Canada

After selection of this site, OSI was notified by BIMO International that the site was closed and was unable to be inspected. Site enrollment numbers and site level data from this site were examined and the review division was contacted regarding the inability to inspect this site. At that time, we discussed alternate selections for inspection from the Sakura 2 study, but ultimately deemed that the review could proceed with the remaining inspections.

{See appended electronic signature page}

Christian N. Shenouda, M.D.
Good Clinical Practice Assessment Branch
Division of Clinical Compliance Evaluation
Office of Scientific Investigations

CONCURRENCE:

{See appended electronic signature page}

Phillip Kronstein, M.D.
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CONCURRENCE: *{See appended electronic signature page}*

Kassa Ayalew, M.D., M.P.H
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CC:

Central Doc. Rm. BLA 761127
DAAP Review Division /Medical Team Leader/ Snezana Trajkovic
DAAP Review Division /Project Manager/ Kimberle Searcy
DAAP Review Division/MO/ Tong Li-Masters
OSI/Office Director/ Ni Khin

OSI/DCCE/ Division Director/ David Burrow
OSI/DCCE/Branch Chief/ Kassa Ayalew
OSI/DCCE/Team Leader/ Phillip Kronstein
OSI/DCCE/GCP Reviewer/ Christian Shenouda
OSI/ GCP Program Analysts/ Yolanda Patague
OSI/Database PM/Dana Walters

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08/28/2020 08:24:48 AM

Department of Health and Human Services
Public Health Service
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Medical Policy

PATIENT LABELING REVIEW

Date:	August 5, 2020
To:	Kimberle Searcy Regulatory Project Manager **Division of Dermatology and Dentistry (DDD)**
Through:	LaShawn Griffiths, MSHS-PH, BSN, RN Associate Director for Patient Labeling **Division of Medical Policy Programs (DMPP)**
From:	Shawna Hutchins, MPH, BSN, RN Senior Patient Labeling Reviewer **Division of Medical Policy Programs (DMPP)** Laurie Buonaccorsi, PharmD Regulatory Review Officer **Office of Prescription Drug Promotion (OPDP)**
Subject:	Review of Patient Labeling: Medication Guide (MG)
Drug Name (established name):	TRADENAME (daxibotulinumtoxinA)
Dosage Form and Route:	For injection, for intramuscular use
Application Type/Number:	BLA 761127
Applicant:	Revance Therapeutics, Inc.

1 INTRODUCTION

On November 24, 2019, Revance Therapeutics, Inc., submitted for the Agency's review an original Biologic License Application (BLA) for TRADENAME (daxibotulinumtoxinA) injection, for intramuscular use, for the proposed indication of the (b) (4) temporary improvement in the appearance of moderate to severe glabellar lines associated with corrugator and procerus muscle activity in adult patients.

This collaborative review is written by the Division of Medical Policy Programs (DMPP) and the Office of Prescription Drug Promotion (OPDP) in response to a request by the Division of Dermatology and Dentistry (DDD) on December 4, 2019 for DMPP and OPDP to review the Applicant's proposed Medication Guide (MG) for TRADENAME (daxibotulinumtoxinA) injection, for intramuscular use.

2 MATERIAL REVIEWED

- Draft TRADENAME (daxibotulinumtoxinA) MG received on November 25, 2019 and received by DMPP and OPDP on July 30, 2020.
- Draft TRADENAME (daxibotulinumtoxinA) Prescribing Information (PI) received on November 25, 2019, revised by the Review Division throughout the review cycle, and received by DMPP and OPDP on July 30, 2020.
- Approved JEUVEAU (prabotulinumtoxinA) comparator labeling dated February 1, 2020.

3 REVIEW METHODS

In 2008 the American Society of Consultant Pharmacists Foundation (ASCP) in collaboration with the American Foundation for the Blind (AFB) published *Guidelines for Prescription Labeling and Consumer Medication Information for People with Vision Loss*. The ASCP and AFB recommended using fonts such as Verdana, Arial or APHont to make medical information more accessible for patients with vision loss. We reformatted the MG document using the Arial font, size 10.

In our collaborative review of the MG we:

- simplified wording and clarified concepts where possible
- ensured that the MG is consistent with the Prescribing Information (PI)
- removed unnecessary or redundant information
- ensured that the MG is free of promotional language or suggested revisions to ensure that it is free of promotional language
- ensured that the MG meets the Regulations as specified in 21 CFR 208.20
- ensured that the MG meets the criteria as specified in FDA's Guidance for Useful Written Consumer Medication Information (published July 2006)

- ensured that the MG is consistent with the approved comparator labeling where applicable

4 CONCLUSIONS

The MG is acceptable with our recommended changes.

5 RECOMMENDATIONS

- Please send these comments to the Applicant and copy DMPP and OPDP on the correspondence.
- Our collaborative review of the MG is appended to this memorandum. Consult DMPP and OPDP regarding any additional revisions made to the PI to determine if corresponding revisions need to be made to the MG.

Please let us know if you have any questions.

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LAURIE J BUONACCORSI
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LASHAWN M GRIFFITHS
08/05/2020 03:26:32 PM

BFOOD AND DRUG ADMINISTRATION
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion

****Pre-decisional Agency Information****

Memorandum

Date: August 4, 2020

To: Tong Li-Masters, Medical Officer, Clinical Reviewer,
Division of Dermatology and Dentistry (DDD)
Kimberle Searcy, Regulatory Project Manager, DDD

From: Laurie Buonaccorsi, Regulatory Review Officer
Office of Prescription Drug Promotion (OPDP)

CC: Matthew Falter, Team Leader, OPDP

Subject: OPDP Labeling Comments for daxibotulinumoxinA-lanm for injection, for intramuscular use

BLA: 761127

In response to DDD's consult request dated December 4, 2019, OPDP has reviewed the proposed product labeling (PI), Medication Guide, and carton and container labeling for the original BLA submission for daxibotulinumoxinA-lanm for injection, for intramuscular use.

PI and Medication Guide: OPDP's comments on the proposed labeling are based on the draft PI received by electronic mail from DDD on July 30, 2020 and are provided below.

A combined OPDP and Division of Medical Policy Programs (DMPP) review will be completed, and comments on the proposed Medication Guide will be sent under separate cover.

Carton and Container Labeling: OPDP has reviewed the attached proposed carton and container labeling submitted by the Sponsor to the electronic document room on November 25, 2019, and we do not have any comments.

Thank you for your consult. If you have any questions, please contact Laurie Buonaccorsi at (240) 402-6297 or laurie.buonaccorsi@fda.hhs.gov.

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LAURIE J BUONACCORSI
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LABEL AND LABELING REVIEW
Division of Medication Error Prevention and Analysis (DMEPA)
Office of Medication Error Prevention and Risk Management (OMEPRM)
Office of Surveillance and Epidemiology (OSE)
Center for Drug Evaluation and Research (CDER)

*** This document contains proprietary information that cannot be released to the public***

Date of This Review:	May 21, 2020
Requesting Office or Division:	Division of Dermatology and Dentistry (DDD)
Application Type and Number:	BLA 761127
Product Name, Dosage Form, and Strength:	(daxibotulinumtoxinA-xxxx)[a] for Injection, 50 units/vial and 100 units/vial
Product Type:	Single Ingredient Product
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	Revance Therapeutics, Inc.
FDA Received Date:	November 25, 2019
OSE RCM #:	2019-2405
DMEPA Safety Evaluator:	Madhuri R. Patel, PharmD
DMEPA Team Leader:	Sevan Kolejian, PharmD, MBA

[a] The proposed nonproprietary name has not yet been conditionally accepted. We therefore refer to the proposed product as "daxibotulinumtoxinA-xxxx" throughout this review in place of the nonproprietary name for this product.

1 REASON FOR REVIEW

As part of the approval process for daxibotulinumtoxinA-xxxx for injection, the Division of Dermatology and Dentistry (DDD) requested that we review the proposed labels and labeling for areas that may lead to medication errors.

2 MATERIALS REVIEWED

We considered the materials listed in Table 1 for this review. The Appendices provide the methods and results for each material reviewed.

Table 1. Materials Considered for this Review	
Material Reviewed	Appendix Section (for Methods and Results)
Product Information/Prescribing Information	A
Previous DMEPA Reviews	B – N/A
Human Factors Study	C – N/A
ISMP Newsletters*	D – N/A
FDA Adverse Event Reporting System (FAERS)*	E – N/A
Other	F – N/A
Labels and Labeling	G

N/A=not applicable for this review
*We do not typically search FAERS or ISMP Newsletters for our label and labeling reviews unless we are aware of medication errors through our routine postmarket safety surveillance

3 OVERALL ASSESSMENT OF THE MATERIALS REVIEWED

We reviewed the Prescribing Information (PI), Medication Guide (MG), container labels and carton labeling for (daxibotulinumtoxinA-xxxx) for injection. We note that the labels and labeling can be improved to facilitate product identification, to prevent deteriorated drug errors, and to increase the prominence of important information (e.g. nonproprietary name). We note the use of the placeholder "TRADENAME" in place of the proposed proprietary name.

4 CONCLUSION & RECOMMENDATIONS

We conclude that the proposed label and labeling can be improved to facilitate product identification, to prevent deteriorated drug errors, and to increase the prominence of important information. We provide recommendations below in Section 4.1 for the Division and Section 4.2 for the Applicant to address our concerns.

4.1 RECOMMENDATIONS FOR DIVISION OF DERMATOLOGY AND DENTISTRY (DDD)

A. General Comments

1. We recommend the placeholder, "TRADENAME" be removed throughout the labels and labeling and replaced by approved proprietary name once a new name is found conditionally acceptable.
2. We note the use of the term "single-patient-use" to describe the product in the Prescribing Information and carton labeling. We defer to the Office of Pharmaceutical Quality (OPQ) to determine the package type term for this product. Ensure that the OPQ determined package type term is used throughout the labels and labeling.
3. The Applicant is proposing to market 50 mg/vial and 100 mg/ vial strength presentations. We note that the proposed dosing is 40 Units per treatment session (8 units into each of the 5 sites). We defer to DDD to determine the need for 100 mg per vial strength presentation.

B. Prescribing Information

1. How Supplied/Storage and Handling Section
    a. As currently presented the National Drug Code (NDC) is denoted by a placeholder (NDC ####-####-01). Replace this NDC placeholder with the actual NDC when it is determined.

4.2 RECOMMENDATIONS FOR REVANCE THERAPEUTICS, INC.

We recommend the following be implemented prior to approval of this BLA:

A. General Comments (Container labels & Carton Labeling)

1. Once a proprietary name is found conditionally acceptable, the placeholder "TRADENAME" must be replaced with the proprietary name on the container labels and carton labeling and the revised labels and labeling must be submitted to the Agency for review.
2. Revise the presentation of the names on the container labels and carton labeling as follows in accordance with *21 CFR 610.62(a)* and Draft Guidance: Safety Considerations for Container Labels:

    daxibotulinumtoxinA-xxxx

    TRADENAME

    for Injection

    for intramuscular use

3. As currently presented the National Drug Code (NDC) is denoted by a placeholder (NDC: XXXX-XXXX-XXX or NDC-XXXXX-XXX-XX). Replace these NDC

placeholders with the actual NDC when it is determined and submit the revised labels and labeling to the Agency for review.

4. As currently presented, the format for the expiration date is not defined. To minimize confusion and reduce the risk for deteriorated drug medication errors, identify the format you intend to use. FDA recommends that the human-readable expiration date on the drug package label include a year, month, and non-zero day. FDA recommends that the expiration date appear in YYYY-MM-DD format if only numerical characters are used or in YYYY-MMM-DD if alphabetical characters are used to represent the month. If there are space limitations on the drug package, the human-readable text may include only a year and month, to be expressed as: YYYY-MM if only numerical characters are used or YYYY-MMM if alphabetical characters are used to represent the month. FDA recommends that a hyphen or a space be used to separate the portions of the expiration date.

B. Container Labels

1. Remove the (b) (4) "REVANCE" words in the background as it takes away prominence from important information (e.g. proprietary name, established name, product strength).

2. As currently presented, the nonproprietary name lacks prominence commensurate with the U.S. License number, NDC, and the package type term. Decrease the prominence of U.S. License number, NDC, and the package type term as it competes in prominence with the nonproprietary name as per Draft Guidance: Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors, April 2013.

3. As currently presented the storage information is incomplete and this could lead to incorrect storage medication errors. If space permits, add complete storage information. Otherwise, remove all storage information.

C. Carton Labeling

1. Consider revising the net quantity statement "1 vial" on the Principal Display Panel (PDP) of the carton labeling to read "1 Single-Dose Vial – Discard Unused Portion" to minimize risk of the entire contents of the vial being given as a single dose.

2. Add or relocate the route of administration to the PDP of the carton labeling per Draft Guidance: Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors, April 2013.

3. For prominence, relocate the Medication Guide (MG) statement from the side panel to the PDP of the carton labeling per 21 CFR 208.24(d).

4. Decrease the prominence of "revance" on the PDP as it competes in prominence with the nonproprietary name as per Draft Guidance: Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors, April 2013.

5. To ensure consistency with the Prescribing Information, revise the statement, "Recommended Dosage: See package insert" to read "Dosage: See prescribing information."

6. Revise and bold the statement "Unused reconstituted TRADENAME vials must be refrigerated at 2°C to 8°C (36°F to 46°F). Must be used within 72 hours. Do not freeze reconstituted TRADENAME. Protect from light.". We recommend this to increase the prominence of this important information and minimize the risk of the storage information being overlooked.

APPENDICES: METHODS & RESULTS FOR EACH MATERIALS REVIEWED

APPENDIX A. PRODUCT INFORMATION/PRESCRIBING INFORMATION

Table 2 presents relevant product information for (daxibotulinumtoxinA-xxxx) received on November 25, 2019 from Revance Therapeutics, Inc..

Table 2. Relevant Product Information for (daxibotulinumtoxinA-xxxx)	
Initial Approval Date	N/A
Nonproprietary Name	(daxibotulinumtoxinA-xxxx)
Indication	the (b) (4) temporary improvement in the appearance of moderate to severe glabellar lines associated with corrugator and procerus muscle activity in adult patients
Route of Administration	intramuscular
Dosage Form	for Injection
Strength	50 units/vial and 100 units/vial
Dose and Frequency	total recommended dose is 40 Units per treatment session divided into five equal intramuscular injections of 8 Units each (two injections in each corrugator muscle and one injection in the procerus muscle). (b) (4) no more frequently than every three months.
How Supplied	powder, sterile lyophilized, is supplied in single-patient-use vials: 50 units/vial and 100 units/vial
Storage	stored at room temperature 20°C to 25°C (68 to 77 °F) or can be stored in the refrigerator at 2°C to 8° C (36°F to 46°F) and protected from light. Reconstituted vials be stored refrigerated at 2°C to 8° C (36°F to 46°F), protected from light and used within 72 hours.
Container Closure	vials with latex-free rubber closures and tamper-proof aluminum seals

APPENDIX G. LABELS AND LABELING

G.1 List of Labels and Labeling Reviewed

Using the principles of human factors and Failure Mode and Effects Analysis,[b] along with postmarket medication error data, we reviewed the following (daxibotulinumtoxinA-xxxx) labels and labeling submitted by Revance Therapeutics, Inc..

- Container labels received on November 25, 2019
- Carton labeling received on November 25, 2019
- Prescribing Information (Image not shown) received on November 25, 2019, available from \\cdsesub1\evsprod\bla761127\0001\m1\us\114-labeling\draft\labeling\draft-labeling-text.pdf
- Medication Guide (Image not shown) received on November 25, 2019, available from \\cdsesub1\evsprod\bla761127\0001\m1\us\114-labeling\draft\labeling\medication-guide.pdf

G.2 Label and Labeling Images

Container Labels

(b) (4)

[b] Institute for Healthcare Improvement (IHI). Failure Modes and Effects Analysis. Boston. IHI:2004.

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