CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

218879Orig1s000

OTHER REVIEWS

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

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

Memorandum

Date: September 2, 2025

To: Kelly Ross, Regulatory Project Manager, Division of Neurology Products, DN2

Tracy Peters, Associate Director for Labeling, DN

From: Lindsay McCann, Regulatory Review Officer
Office of Prescription Drug Promotion (OPDP)

CC: Taylor Burnett Mmagu, Team Leader, OPDP

Subject: OPDP Labeling Comments for SUBVENITE® (lamotrigine) oral suspension

NDA: 218879

Background: In response to DN2's consult request dated March 26, 2025, OPDP has reviewed the proposed Prescribing Information (PI) for the original NDA 218879 resubmission for SUBVENITE® (lamotrigine) oral suspension.

PI/Medication Guide

OPDP's review of the proposed PI is based on the draft labeling emailed to OPDP on August 22, 2025, and our comments are provided below.

A combined OPDP and Division of Medical Policy Programs (DMPP) was completed for the proposed Medication Guide, and comments were sent under separate cover.

Carton and Container Labeling

OPDP's review of the proposed carton and container labeling is based on the draft labeling submitted to the EDR on July 21,2025, and we do not have any comments at this time.

Thank you for your consult. If you have any questions, please contact Lindsay McCann at 301-796-3719 or Lindsay.McCann@fda.hhs.gov.

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/s/

LINDSAY M MCCANN
09/02/2025 11:07:51 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 28, 2025
To:	Kelly Ross, PharmD, BCPS Regulatory Project Manager **Division of Neurology II (DN2)**
Through:	Marcia Williams, PhD Team Leader, Patient Labeling **Division of Medical Policy Programs (DMPP)**
From:	Kelly Jackson, PharmD Patient Labeling Reviewer **Division of Medical Policy Programs (DMPP)** Lindsay McCann, PharmD, BCCCP Regulatory Review Officer **Office of Prescription Drug Promotion (OPDP)**
Subject:	Review of Patient Labeling: Medication Guide (MG)
Drug Name (established name):	SUBVENITE (lamotrigine)
Dosage Form and Route:	oral suspension
Application Type/Number:	NDA 218879
Applicant:	OWP Pharmaceuticals, Inc.

1 INTRODUCTION

On March 16, 2025, OWP Pharmaceuticals, Inc. submitted for the Agency's review a Class II resubmission to their original New Drug Application (NDA) 218879 for SUBVENITE (lamotrigine) oral suspension in response to a Complete Response (CR) letter dated January 3, 2025. The applicant is seeking approval for the same indications approved for the Reference Listed Drug (RLD), LAMICTAL (lamotrigine):

- adjunctive therapy in patients aged 2 years and older:
  - partial-onset seizures
  - primary generalized tonic-clonic seizures.
  - generalized seizures of Lennox-Gastaut syndrome
- monotherapy in patients aged 16 years and older: conversion to monotherapy in patients with partial-onset seizures who are receiving treatment with carbamazepine, phenytoin, phenobarbital, primidone, or valproate as the single anti-epileptic drug.
- maintenance treatment of Bipolar 1 Disorder to delay the time to occurrence of mood episodes in patients treated for acute mood episodes with standard therapy.

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 Neurology II (DN2) on March 26, 2025, for DMPP and OPDP to review the Applicant's proposed Medication Guide (MG) for SUBVENITE (lamotrigine) oral suspension.

2 MATERIAL REVIEWED

- Draft SUBVENITE (lamotrigine) MG received on March 16, 2025, revised by the Review Division throughout the review cycle, and received by DMPP on August 22, 2025.
- Draft SUBVENITE (lamotrigine) Prescribing Information (PI) received on March 16, 2025, revised by the Review Division throughout the review cycle, and received by DMPP and OPDP on August 22, 2025.
- LAMICTAL (lamotrigine) comparator labeling dated April 25, 2025.

3 REVIEW METHODS

To enhance patient comprehension, materials should be written at a 6th to 8th grade reading level, and have a reading ease score of at least 60%. A reading ease score of 60% corresponds to an 8th grade reading level. In our review of the MG the target reading level is at or below an 8th grade level.

Additionally, 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 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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/s/

KELLY D JACKSON
08/28/2025 10:36:24 AM

LINDSAY M MCCANN
08/28/2025 10:49:56 AM

MARCIA B WILLIAMS
08/28/2025 11:01:15 AM

MEMORANDUM
REVIEW OF REVISED LABEL AND LABELING

Division of Medication Error Prevention and Analysis 2 (DMEPA 2)
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:	August 11, 2025
Requesting Office or Division:	Division of Neurology 2 (DN 2)
Application Type and Number:	NDA 218879
Product Name, Dosage Form, and Strength:	Subvenite (lamotrigine) oral suspension, 10 mg/mL
Applicant Name:	OWP Pharmaceuticals, Inc (OWP)
FDA Received Date:	July 21, 2025
TTT ID #:	2025-13694-1
DMEPA 2 Safety Evaluator:	Beverly Weitzman, PharmD
DMEPA 2 Team Leader:	Stephanie DeGraw, PharmD

1 PURPOSE OF MEMORANDUM

OWP Pharmaceuticals, Inc (OWP) submitted revised container label and carton labeling received on July 21, 2025 for Subvenite. The Division of Neurology 2 (DN 2) requested that we review the revised container label and carton labeling for Subvenite (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

OWP Pharmaceuticals, Inc (OWP) implemented all of our recommendations. The container label and carton labeling are acceptable from a medication error perspective, and we have no additional recommendations at this time.

[a] Weitzman, B. Label and Labeling Review for Subvenite (NDA 218879). Silver Spring (MD): FDA, CDER, OSE, DMEPA 2 (US); 2025 MAY 21. TTT ID: 2025-13694.

APPENDIX A. IMAGES OF LABELS AND LABELING RECEIVED ON JULY 21, 2025

Container Label:

Carton Labeling:

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

BEVERLY WEITZMAN
08/11/2025 01:34:50 PM

STEPHANIE L DEGRAW
08/11/2025 02:16:47 PM

M E M O R A N D U M

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

DATE: 8/5/2024

TO: Division of Neurology II (DN II)
Office of Neuroscience (ON)

FROM: Office of Study Integrity and Surveillance (OSIS)

SUBJECT: **Decline to conduct on-site inspections**

RE: NDA 218879

The Office of Study Integrity and Surveillance (OSIS) determined that inspections are not needed for the sites listed below. The rationale for this decision is noted below.

Rationale

Actimus Biosciences, Pvt. Ltd., (Varun Towers) Visakhapatnam: The Office of Regulatory Affairs (ORA) conducted an inspection for the clinical site in January 2024. The inspection was conducted under the following submission: ANDAs 218783 and 077440/S-005.

The following objectionable conditions were observed:

- Biochemistry data generated in support of subject eligibility and subject safety is not reliable. Specifically, Diagnostic Unit staff have changed out of range biochemistry lab values without retention of original results or documentation of the staff making the revision. Runtime data is only stored for three days and is the only evidence of the revision.
- Failure to report changes in subject electrocardiograms from Period II Check-in Pre-Dose through Period II Post Dose 72 hours, as adverse events.
- Release of subjects from the clinical facility prior to the 72 hours of confinement specified in the study protocol.
- Additional safety assessments not included in the approved protocol were performed on all subjects during the study washout period.
- Failure to maintain the images from echocardiograms performed during Period II.

After review of the objectionable conditions and the site's response, OSIS noted several discrepancies in records and documentation but concluded that data from the reviewed study appeared reliable (Final OSIS Review - January 2024).

(b) (4): OSIS conducted a Remote Regulatory Assessment (RRA) for the analytical site in (b) (4). The RRA was conducted under the following submissions: ANDAs NON-RESPONSIVE.

OSIS concluded that data from the reviewed studies were reliable.

Site

Facility Type	Facility Name	Facility Address
Clinical	Actimus Biosciences Pvt., Ltd.	3rd, 4th, and 5th Floor, Varun Towers, Kasturiba Marg, Siripuram, Visakhapatnam, Andhra Pradesh, India
Analytical		(b) (4)

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/s/

ADANMA S OJI
08/05/2024 03:12:29 PM

LABEL AND LABELING REVIEW

Division of Medication Error Prevention and Analysis 2 (DMEPA 2)
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, 2025
Requesting Office or Division:	Division of Neurology 2 (DN 2)
Application Type and Number:	NDA 218879
Product Name, Dosage Form, and Strength:	Subvenite (lamotrigine) oral suspension, 10 mg/mL
Product Type:	Single Ingredient Product
Rx or OTC:	Prescription (Rx)
Applicant Name:	OWP Pharmaceuticals, Inc (OWP)
FDA Received Date:	March 17, 2025
TTT ID #:	2025-13694 (previously reviewed under 2024-8575)
DMEPA 2 Safety Evaluator:	Beverly Weitzman, PharmD
DMEPA 2 Team Leader:	Stephanie DeGraw, PharmD

1 INTRODUCTION

On March 17, 2025, OWP Pharmaceuticals, Inc (OWP) submitted a Class 2 resubmission for NDA 218879 for Subvenite (lamotrigine) oral suspension in response to the Agency's Complete Response (CR) letter, issued January 3, 2025.[a]

The Division of Neurology 2 (DN 2) requested that we review the proposed prescribing information, medication guide, container label and carton labeling for areas of vulnerability that may lead to medication errors.

1.1 BACKGROUND

Subvenite (lamotrigine) is a proposed 505(b)(2) drug product for a new oral suspension dosage form of lamotrigine. The Listed Drug (LD) is Lamictal (lamotrigine) tablets, NDA 020241.

1.2 REGULATORY HISTORY

NDA 218879 was originally submitted on March 4, 2024. During that review cycle we completed a review of the prescribing information (PI), medication guide (MG), container label, and carton labeling on November 27, 2024.[b] However, the application received a Complete Response letter on January 3, 2025, due to issues with product quality.

As such, our recommendations for the 10 mg/mL strength container label and carton labeling were sent to OWP Pharmaceutical, Inc (OWP) as part of the CR letter. The CR letter noted that the FDA reserved comment on the proposed labeling (i.e., PI and MG) until the application is otherwise adequate. Therefore, our recommendations for the PI and MG were not communicated to OWP as part of the CR letter.

In response to the CR letter, OWP submitted a Class 2 resubmission for NDA 218879 on March 17, 2025. Under this submission, OWP submitted container label and carton labeling which were revised in response to our recommendations sent to OWP in the CR letter.[c] We note, OWP did not resubmit the prescribing information (PI) and medication guide (MG) labeling under this submission. Therefore, we refer to the PI and MG labeling submitted during the previous review cycle received on June 7, 2024 (sequence number 0008).

2 MATERIALS CONSIDERED

This section lists the materials considered for our review.

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[a] Lee, P. Complete Response Letter for NDA 218879. Issued 2025 JAN 03. Available from: https://darrts.fda.gov/darrts/ViewDocument?documentId=090140af8078f693

[b] Weitzman, B. Label and Labeling Review for Subvenite (NDA 218879). Silver Spring (MD): FDA, CDER, OSE, DMEPA 2 (US); 2024 NOV 27. TTT ID: 2024-8575.

[c] Cover Letter – NDA Resubmission for NDA 218879. Lenexa (KS). OWP Pharmaceuticals, Inc. 2025 MAR 17. Available from: \\CDSESUB1\EVSPROD\nda218879\0024\m1\us\12-cover-letters\cover-letter-03-16-2025.pdf

Table 1. Materials Considered for this Review	
Materials Considered	Appendix Section
Relevant Product Information	A
Labels and Labeling	B
Previous DMEPA Reviews	C
Previous DMEPA Review Completed November 27, 2024	D

3 CONCLUSION AND RECOMMENDATIONS

Our review of the container label and carton labeling determined OWP Pharmaceuticals, Inc implemented most of our container label and carton labeling recommendations made in our previous labeling review; however, the presentation of the established name still does not appear to be at least half the size of the proprietary name, and the lot number, expiration date, and product identifier information are missing.

As such, we reiterate our previous applicable recommendations. We provide the identified medication error issues, our rationale for concern, and our proposed recommendation to minimize the risk for medication error in Section 5 (Table 3) below for OWP Pharmaceuticals, Inc.

Our review of the proposed prescribing information (PI) and medication guide labeling determined we maintain most of our recommendations from the previous review (Appendix D). Recommendations that are still applicable are provided below in Section 4 (Table 2) for the Division of Neurology 2.

4 RECOMMENDATIONS FOR THE DIVISION OF NEUROLOGY 2 (DN 2)

Table 2. Identified Issues and Recommendations for the Division of Neurology 2 (DN 2)			
	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
Prescribing Information (PI) – General Comment			
We note the proposed Prescribing Information (PI), specifically Sections 2 and 17, for Subvenite is nearly identical to the Lamictal (RLD) PI in both content and format. As such, our recommendations are focused on improving new information that relates to the proposed product from a medication error perspective. If the RLD PI is updated prior to approval of this application, and the proposed Subvenite PI is revised to align, we can provide further recommendations as needed.			
Full Prescribing Information – Section 2 Dosage and Administration			
1.	Section 2 Dosage and Administration lacks a statement regarding the use of a calibrated measuring device, such as an oral syringe, to accurately measure and	Selecting an unacceptable measuring device may increase the risk for wrong dose medication errors.	We recommend specifying acceptable types of measuring devices. For example: "A calibrated measuring device, such as an oral dosing syringe or oral dosing cup, is recommended to measure and

Table 2. Identified Issues and Recommendations for the Division of Neurology 2 (DN 2)			
	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
	administer the prescribed dose.		deliver the prescribed dose accurately. A household teaspoon or tablespoon is not an adequate measuring device."
Full Prescribing Information – Section 16 How Supplied/Storage and Handling			
2.	The post-opening expiration date is not included in Section 16.2 Storage and Handling.	Incomplete storage information may result in improper storage of the drug product and increased risk of deteriorated drug medication errors.	We recommend including a post-opening expiration date statement, such as "Discard the unused portion 90 days after first opening." to align with the discard statement on the container label and carton labeling.
3.	The storage statement in Section 16.2 Storage and Handling does not include a "Do Not Freeze" statement that is presented on the container label and carton labeling.	Inconsistent storage information across labels and labeling may cause confusing resulting in improper storage and deteriorated drug medication errors.	OPQ confirmed that the do not freeze warning is appropriate for this product. Therefore, we recommend adding the statement "Do Not Freeze" to the PI to be consistent with the container and carton labeling.
Full Prescribing Information – Section 17 Patient Counseling			
1.	There is no statement instructing the HCP to counsel patients or caregivers to use a calibrated measuring device to measure their dose.	Selecting an unacceptable measuring device may increase the risk for wrong dose medication errors.	Add the following statements to Section 17: "Instruct patients or caregivers that a calibrated measuring device, such as an oral dosing syringe or oral dosing cup, should be obtained from the pharmacy to accurately measure and deliver the prescribed dose of medication. A household teaspoon or tablespoon is not an adequate measuring device."
Medication Guide (MG)			
1.	The medication guide (MG) does not include a "What is the most important information I should know about Subvenite" section detailing the most	To promote safe use of the product, patients and/or caregivers should be made aware of the most important information to know about of Subvenite,	We recommend revising the MG to include a "What is the most important information I should know about Subvenite" section that describes the most important information about the drug, including adverse reaction, similar

Table 2. Identified Issues and Recommendations for the Division of Neurology 2 (DN 2)			
	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
	important information to know about the drug product, including serious reactions. This does not align with the MG for the reference listed drug, Lamictal.	specifically serious reactions.	to the MG for the reference listed drug, Lamictal (NDA 020241) if deemed clinically relevant for this product by the clinical team.
2.	The post-opening expiration date is not included under the "How should I store Subvenite" section.	Incomplete storage information may result in improper storage of the drug product and increased risk of deteriorated drug medication errors.	We recommend including a post-opening expiration date statement in the storage section, such as "Discard (throw away) any unused medication 90 days after first opening the bottle."
3.	There is no statement instructing patients or caregivers to use a calibrated measuring device to measure their dose.	Selecting an unacceptable measuring device may increase the risk for wrong dose medication errors.	Add the following statements to the "How should I take SUBVENITE?" section of the Medication Guide: "Your pharmacist should provide you with an oral dosing syringe or dosing cup that is needed to correctly measure the dose. Do not use a household teaspoon or tablespoon."

5 RECOMMENDATIONS FOR OWP PHARMACEUTICALS, INC

Table 3. Identified Issues and Recommendations for OWP Pharmaceuticals, Inc (entire table to be conveyed to Applicant)			
	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
Container Label and Carton Labeling			
1.	The established name still does not appear to be at least half the size of the proprietary name and is difficult to read as previously noted.	We refer you to 21 CFR 201.10(g)(2) which states that the established name shall be printed in letters that are at least half as large as the letters comprising the proprietary name, and the established name shall have a	Revise the established name so that the established name is presented in accordance with 21 CFR 201.10(g)(2).

Table 3. Identified Issues and Recommendations for OWP Pharmaceuticals, Inc (entire table to be conveyed to Applicant)			
	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
		prominence commensurate with the prominence with which such proprietary name appears, taking into account all pertinent factors, including typography, layout, contrast, and other printing features.	
2.	There is no placeholder for the expiration date, and the format is not defined.	The label of an official drug product shall bear an expiration date per USP General Chapter <7>. Further, we are unable to assess the proposed expiration date format from a medication safety perspective.	Add the placeholder for the expiration date to the container label and carton labeling in accordance with USP General Chapter <7>. To minimize confusion and reduce the risk for deteriorated drug medication errors, we recommend identifying the expiration date 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

Table 3. Identified Issues and Recommendations for OWP Pharmaceuticals, Inc (entire table to be conveyed to Applicant)			
	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
			represent the month. FDA recommends that a hyphen or forward slash to separate the portions of the expiration date. See *Guidance for Industry: Product Identifiers under the Drug Supply Chain Security Act - Questions and Answers (June 2021).*
3.	There is no placeholder for the lot number.	The lot number statement is required on the immediate container and carton labeling when there is sufficient space per 21 CFR 201.10(i)(1).	Add the placeholder for the lot number to the container label and the carton labeling in accordance 21 CFR 201.10(i)(1).
Carton Labeling			
1.	The product identifier is missing.	In June 2021, FDA finalized the Guidance for Industry on product identifiers required under the Drug Supply Chain Security Act (DSCSA). The Act requires manufacturers and re-packagers to affix or imprint a product identifier to each package and homogenous case of a product intended to be introduced in a transaction in(to) commerce. The product identifier includes the NDC, serial number, lot number, and expiration date in both a human-readable form and machine-readable (2D data matrix barcode) format.	Add the product identifier placeholder, including NDC, serial number, lot number, and expiration date in both a human-readable form and machine-readable (2D data matrix barcode) format, in accordance with DSCSA. See *Guidance for Industry: Product Identifiers under the Drug Supply Chain Security Act - Questions and Answers (June 2021).*

APPENDICES: MATERIALS CONSIDERED FOR THIS REVIEW

APPENDIX A. RELEVANT PRODUCT INFORMATION

Table 4 presents relevant product information for Subvenite received on March 17, 2025, from OWP Pharmaceuticals, Inc and the Listed Drug (LD).

Table 4 Relevant Product Information for Subvenite and the Listed Drug (LD).		
Product Name	Subvenite[d]	Lamictal[e] (NDA 020241)
Initial Approval Date	NA	December 27, 1994
Active Ingredient	lamotrigine	
Indication	Epilepsy – adjunctive therapy For the following seizure types in patients aged 2 years and older: • partial-onset seizures. • primary generalized tonic-clonic (PGTC) seizures. • generalized seizures of Lennox-Gastaut syndrome. Epilepsy – monotherapy Conversion to monotherapy in adults (aged 16 years and older) with partial-onset seizures who are receiving treatment with carbamazepine, phenytoin, phenobarbital, primidone, or valproate as the single antiepileptic drug (AED). Bipolar Disorder Maintenance treatment of bipolar I disorder to delay the time to occurrence of mood episodes (depression, mania, hypomania, mixed episodes) in patients treated for acute mood episodes with standard therapy.	
Dosage Form	Oral suspension	Tablets
Strength	10 mg/mL	25 mg, 100 mg, 150 mg, and 200 mg
Route of Administration	Oral	
Dose and Frequency	*For complete dosing information see Section 2 Dosage and Administration of the proposed PI for Subvenite and the PI for Lamictal.* *Note: The proposed Subvenite PI dosing information aligns with the dosing information in the Lamictal PI.* • Refer to Tables 1 through 6 of the PI for specific dosing. • Dosing is based on concomitant medications, indication, and patient age.	

[d] Subvenite [Proposed Prescribing Information and Medication Guide] available from \\CDSESUB1\EVSPROD\nda218879\0008\m1\us\114-labeling\draft\labeling\prescribing-information.pdf

[e] Lamictal [Prescribing Information]. Drugs@FDA. U.S. Food and Drug Administration. MAR 2021. [cited 2024 MAR 27]. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/020241s064,020764s057,022251s028lbl.pdf .

Table 4 Relevant Product Information for Subvenite and the Listed Drug (LD).		
Product Name	Subvenite[d]	Lamictal[e] (NDA 020241)
	• To avoid an increased risk of rash, the recommended initial dose and subsequent dose escalations should not be exceeded. • Do not restart LAMICTAL in patients who discontinued due to rash unless the potential benefits clearly outweigh the risks. • Adjustments to maintenance doses will be necessary in most patients starting or stopping estrogen-containing oral contraceptives. • Discontinuation: Taper over a period of at least 2 weeks (approximately 50% dose reduction per week).	
How Supplied	SUBVENITE (lamotrigine) Oral Suspension contains 10 mg per mL (10 mg/mL) lamotrigine. It is a pink, cherry-flavored suspension and is supplied in high-density polyethylene (HDPE) bottles with white, polypropylene, child-resistant closures with a foam liner and heat induction layered inner seal. Available in 8 oz (240 mL).	• 25-mg, white, scored, shield-shaped tablets debossed with "LAMICTAL" and bottles of 100 and Starter Kit for Patients Taking Valproate (Blue Kit of 35 tablets). • 100-mg, peach, scored, shield-shaped tablets debossed with "LAMICTAL" and bottles of 100. • 150-mg, cream, scored, shield-shaped tablets debossed with "LAMICTAL" and bottles of 60. • 200-mg, blue, scored, shield-shaped tablets debossed with "LAMICTAL" and bottles of 60.
Storage	Store at 20°C to 25°C (68°F to 77°F); excursions permitted to 15°C to 30°C (59°F to 86°F) [See USP Controlled Room Temperature].	Store at 25°C (77°F); excursions permitted to 15°C to 30°C (59°F to 86°F) [see USP Controlled Room Temperature] in a dry place and protect from light.
Container Closure	8 oz oblong HDPE white bottle	Lamictal Tablets: Bottles: HDPE bottles with (b) (4) coiler and closed with child resistant closures. Blister packs: Polyvinyl Chloride (PVC) blister with lidding materials (pouch paper, (b) (4) aluminum foil/heat seal (b) (4)

APPENDIX B. LABEL AND LABELING

B.1 List of Label and Labeling Reviewed

Using the principles of human factors and Failure Mode and Effects Analysis,[f] along with postmarket medication error data, we reviewed the following Subvenite label and labeling submitted by OWP Pharmaceuticals, Inc.

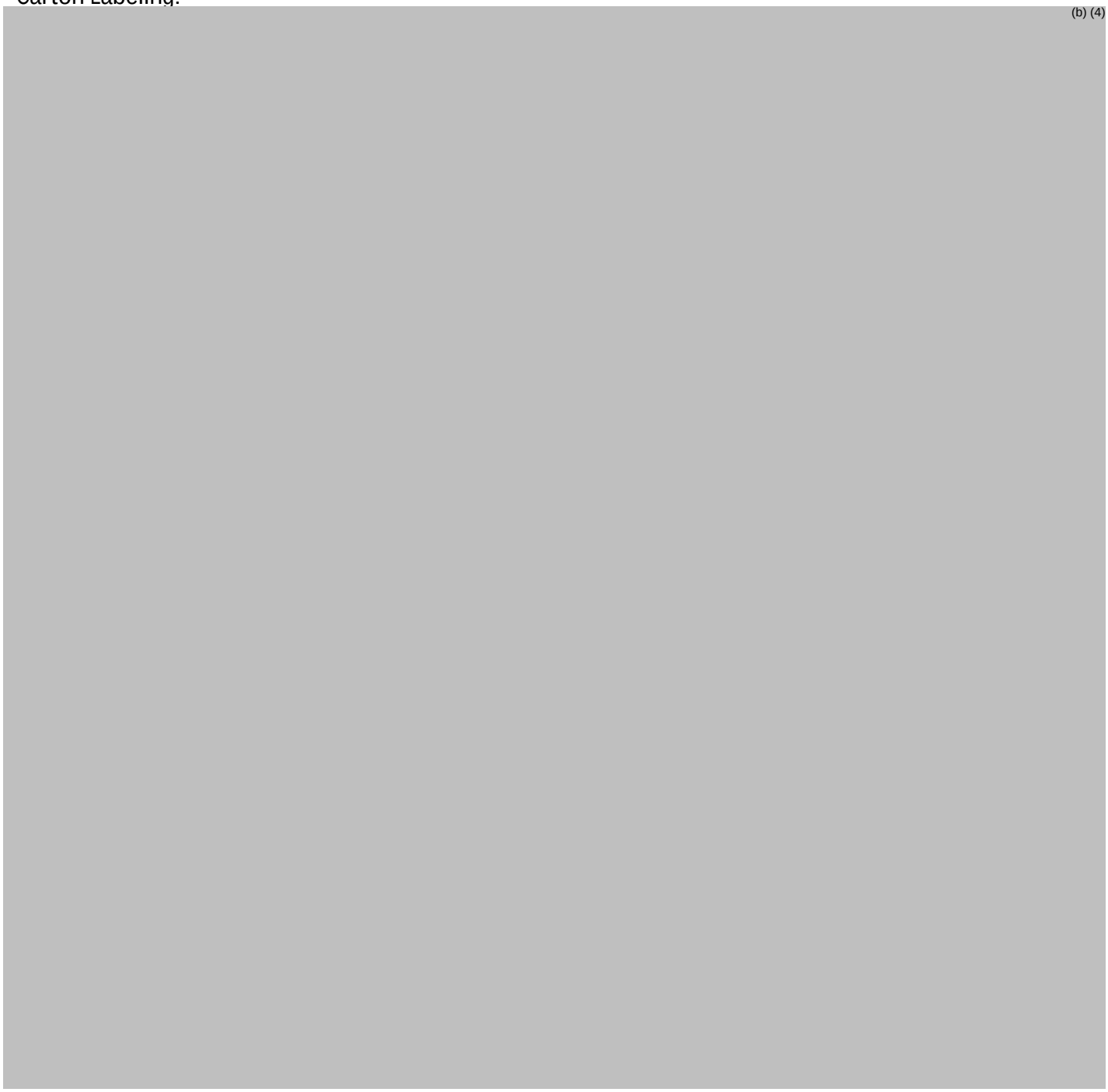
- Container label received on March 17, 2025
- Carton labeling received on March 17, 2025
- Prescribing Information and medication guide (image not shown) received on June 7, 2024, available from \\CDSESUB1\EVSPROD\nda218879\0008\m1\us\114-labeling\draft\labeling\prescribing-information.pdf

B.2 Container Label and Carton Labeling Images

Container Label:

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

Carton Labeling:



APPENDIX C. PREVIOUS DMEPA REVIEWS

On March 27, 2025, we searched for previous DMEPA reviews relevant to this current review using the terms, Subvenite and NDA 218879. Our search identified one previous review[g], and we considered our previous recommendations to see if they are applicable for this current review.

[g] Weitzman, B. Label and Labeling Review for Subvenite (NDA 218879). Silver Spring (MD): FDA, CDER, OSE, DMEPA 2 (US); 2024 NOV 27. TTT ID: 2024-8575.

APPENDIX D. Previous DMEPA Review Completed November 27, 2024

Available from: https://darrts.fda.gov/darrts/ViewDocument?documentId=090140af807849a5

Excerpted Recommendations for the PI and MG

4 RECOMMENDATIONS FOR THE DIVISION OF NEUROLOGY 2 (DN 2)

Table 2. Identified Issues and Recommendations for the Division of Neurology 2 (DN 2)

	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
Prescribing Information – General Comment			
We note the proposed Prescribing Information (PI), specifically Sections 2 and 17, for Subvenite is nearly identical to the Lamictal (RLD) PI in both content and format. As such, our recommendations are focused on improving new information that relates to the proposed product from a medication error perspective.			
Full Prescribing Information – Section 2 Dosage and Administration			
1.	Section 2 Dosage and Administration lacks a statement regarding the use of a calibrated measuring device, such as an oral syringe, to accurately measure and administer the prescribed dose.	Selecting an unacceptable measuring device may increase the risk for wrong dose medication errors.	We recommend specifying acceptable types of measuring devices. For example: "A calibrated measuring device, such as an oral dosing syringe or oral dosing cup, is recommended to measure and deliver the prescribed dose accurately. A household teaspoon or tablespoon is not an adequate measuring device."
Full Prescribing Information – Section 16 How Supplied/Storage and Handling			
1.	The net quantity statement (i.e., 8 oz (240 mL)) stated in Section 16.1 How Supplied is inconsistent with the net quantity statement (i.e., (b) (4) presented on the container label and carton labeling.	Inconsistent net quantity information can lead to confusion during ordering and distribution of the drug product.	Revise the net quantity statement to accurately reflect the total volume per bottle consistently across all labels and labeling. Note: this also impacts container label and carton labeling recommendations in the table below.
2.	The post-opening expiration date is not included in Section 16.2 Storage and Handling.	Incomplete storage information may result in improper storage of the drug product and increased risk of deteriorated drug medication errors.	We recommend including a post-opening expiration date statement, such as "Discard the unused portion 90 days after first opening." to align with the discard statement on the container label and carton labeling.
3.	The storage statement in Section 16.2 Storage and Handling does not include a "Do Not Freeze" statement that is presented on the container label and carton labeling.	Inconsistent storage information across labels and labeling may cause confusing resulting in improper storage and deteriorated drug medication errors.	OPQ confirmed that the do not freeze warning is appropriate for this product. Therefore, we recommend adding the statement "Do Not Freeze" to the PI to be consistent with the container and carton labeling.

Full Prescribing Information – Section 17 Patient Counseling			
1.	There is no statement instructing the HCP to counsel patients or caregivers to use a calibrated measuring device to measure their dose.	Selecting an unacceptable measuring device may increase the risk for wrong dose medication errors.	Add the following statements to Section 17: "Instruct patients or caregivers that a calibrated measuring device, such as an oral dosing syringe or oral dosing cup, should be obtained from the pharmacy to accurately measure and deliver the prescribed dose of

Table 2. Identified Issues and Recommendations for the Division of Neurology 2 (DN 2)

	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
			medication. A household teaspoon or tablespoon is not an adequate measuring device."
Medication Guide (MG)			
1.	The medication guide (MG) does not include a "What is the most important information I should know about Subvenite" section detailing the most important information to know about the drug product, including serious reactions. This does not align with the MG for the reference listed drug, Lamictal.	To promote safe use of the product, patients and/or caregivers should be made aware of the most important information to know about of Subvenite, specifically serious reactions.	We recommend revising the MG to include a "What is the most important information I should know about Subvenite" section that describes the most important information about the drug, including adverse reaction, similar to the MG for the reference listed drug, Lamictal (NDA 020241) if deemed clinically relevant for this product by the clinical team.
2.	The post-opening expiration date is not included under the "How should I store Subvenite" section.	Incomplete storage information may result in improper storage of the drug product and increased risk of deteriorated drug medication errors.	We recommend including a post-opening expiration date statement in the storage section, such as "Discard (throw away) any unused medication 90 days after first opening the bottle."
3.	There is no statement instructing patients or caregivers to use a calibrated measuring device to measure their dose.	Selecting an unacceptable measuring device may increase the risk for wrong dose medication errors.	Add the following statements to the "How should I take SUBVENITE?" section of the Medication Guide: "Your pharmacist should provide you with an oral dosing syringe or dosing cup that is needed to correctly measure the dose. **Do not** use a household teaspoon or tablespoon."

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05/21/2025 08:38:07 AM

STEPHANIE L DEGRAW
05/21/2025 01:05:18 PM

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

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

Memorandum

Date: December 4, 2024

To: Kell Ross, Regulatory Project Manager, Division of Neurology 2 (DN 2)

Tracy Peters, Associate Director for Labeling, Division of Neurology

From: Lindsay McCann, Regulatory Review Officer
Office of Prescription Drug Promotion (OPDP)

CC: Taylor Burnett Mmagu, Team Leader, OPDP

Subject: OPDP Labeling Comments for SUBVENITE® (lamotrigine) oral suspension

NDA: 218879

This memo is in response to the DN 2 labeling consult request dated March 22, 2024. OPDP defers comment on the proposed labeling at this time, and requests that DN 2 submit a new consult request during the subsequent review cycle. If you have any questions, please contact Lindsay McCann at 301-796-3719 or Lindsay.McCann@fda.hhs.gov.

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/s/

LINDSAY M MCCANN
12/04/2024 02:29:12 PM

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

REVIEW DEFERRAL MEMORANDUM

Date:	December 3, 2024
To:	Stephanie Parncutt, MHA Senior Regulatory Project Manager **Division of Neurology II (DN2)**
Through:	LaShawn Griffiths, MSHS-PH, BSN, RN Associate Director for Patient Labeling **Division of Medical Policy Programs (DMPP)** Marcia Williams, PhD Team Leader, Patient Labeling **Division of Medical Policy Programs (DMPP)**
From:	Kelly Jackson, PharmD Patient Labeling Reviewer **Division of Medical Policy Programs (DMPP)**
Subject:	Review Deferred: Medication Guide (MG)
Drug Name (established name):	SUBVENITE (lamotrigine)
Dosage Form and Route:	oral suspension
Application Type/Number:	NDA 218879
Applicant:	OWP Pharmaceuticals, Inc.

1 INTRODUCTION

On March 1, 2024, OWP Pharmaceuticals, Inc. submitted for the Agency's review a New Drug Application (NDA) 218879 for SUBVENITE (lamotrigine) oral suspension with the proposed indication for treatment for bipolar disorder and epilepsy. On March 22, 2024, the Division of Neurology II (DN2) requested that the Division of Medical Policy Programs (DMPP) review the Applicant's proposed Medication Guide (MG) for SUBVENITE (lamotrigine).

This memorandum documents the DMPP review deferral of the Applicant's proposed Medication Guide (MG) for SUBVENITE (lamotrigine) oral suspension.

2 CONCLUSIONS

Due to outstanding Chemistry, Manufacturing and Controls (CMC) deficiencies, DN2 plans to issue a Complete Response (CR) letter.

Therefore, DMPP defers comment on the Applicant's patient labeling at this time. A final review will be performed after the Applicant submits a complete response to the Complete Response (CR) letter. Please send us a new consult request at such time.

Please notify us if you have any questions.

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/s/

KELLY D JACKSON
12/03/2024 01:06:55 PM

MARCIA B WILLIAMS
12/03/2024 01:23:23 PM

LABEL AND LABELING REVIEW

Division of Medication Error Prevention and Analysis 2 (DMEPA 2)
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:	November 27, 2024
Requesting Office or Division:	Division of Neurology 2 (DN 2)
Application Type and Number:	NDA 218879
Product Name, Dosage Form, and Strength:	Subvenite[a] (lamotrigine) oral suspension (b) (4) (10 mg/mL)
Product Type:	Single Ingredient Product
Rx or OTC:	Prescription (Rx)
Applicant Name:	OWP Pharmaceuticals, Inc
FDA Received Date:	March 4, 2024 and June 7, 2024
TTT ID #:	2024-8575
DMEPA 2 Safety Evaluator:	Beverly Weitzman, PharmD
DMEPA 2 Team Leader:	Stephanie DeGraw, PharmD

[a] The proposed proprietary name Subvenite was found conditionally acceptable for NDA 218879 on June 03, 2024.

1 INTRODUCTION

As part of the approval process for Subvenite (lamotrigine) oral suspension, the Division of Neurology 2 (DN 2) requested that we review the proposed Subvenite prescribing information (PI), medication guide (MG), container label, and carton labeling for areas of vulnerability that may lead to medication errors.

1.1 BACKGROUND

Subvenite (lamotrigine) is a proposed 505(b)(2) drug product for a new oral suspension dosage form of lamotrigine. The Listed Drug (LD) is Lamictal (lamotrigine) tablets, NDA 020241.

2 MATERIALS REVIEWED

This section lists the materials considered for our review of NDA 218879.

Table 1. Materials Considered for this Label and Labeling Review

Material(s) Reviewed	Appendix Section
Relevant Product Information	A
Labels and Labeling	B

3 CONCLUSION

The proposed Subvenite Prescribing Information (PI), Medication Guide (MG), container label, and carton labeling may be improved to promote safe use of this product from a medication error perspective. We provide the identified medication error issues, our rationale for concern, and our proposed recommendations to minimize the risk for medication error for the Division of Neurology 2 (DN 2) in **Section 4** (Table 2) and for OWP Pharmaceuticals, Inc in **Section 5** (Table 3).

4 RECOMMENDATIONS FOR THE DIVISION OF NEUROLOGY 2 (DN 2)

Table 2. Identified Issues and Recommendations for the Division of Neurology 2 (DN 2)

	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
Prescribing Information – General Comment			
We note the proposed Prescribing Information (PI), specifically Sections 2 and 17, for Subvenite is nearly identical to the Lamictal (RLD) PI in both content and format. As such, our recommendations are focused on improving new information that relates to the proposed product from a medication error perspective.			
Full Prescribing Information – Section 2 Dosage and Administration			
1.	Section 2 Dosage and Administration lacks a statement regarding the use of a calibrated measuring device, such	Selecting an unacceptable measuring device may increase the risk for wrong dose medication errors.	We recommend specifying acceptable types of measuring devices. For example: "A calibrated measuring device, such as an oral

Table 2. Identified Issues and Recommendations for the Division of Neurology 2 (DN 2)			
	IDENTIFIED ISSUE	**RATIONALE FOR CONCERN**	**RECOMMENDATION**
	as an oral syringe, to accurately measure and administer the prescribed dose.		dosing syringe or oral dosing cup, is recommended to measure and deliver the prescribed dose accurately. A household teaspoon or tablespoon is not an adequate measuring device."
Full Prescribing Information – Section 16 How Supplied/Storage and Handling			
1.	The net quantity statement (i.e., 8 oz (240 mL)) stated in Section 16.1 How Supplied is inconsistent with the net quantity statement (i.e., (b) (4)) presented on the container label and carton labeling.	Inconsistent net quantity information can lead to confusion during ordering and distribution of the drug product.	Revise the net quantity statement to accurately reflect the total volume per bottle consistently across all labels and labeling. Note: this also impacts container label and carton labeling recommendations in the table below.
2.	The post-opening expiration date is not included in Section 16.2 Storage and Handling.	Incomplete storage information may result in improper storage of the drug product and increased risk of deteriorated drug medication errors.	We recommend including a post-opening expiration date statement, such as "Discard the unused portion 90 days after first opening." to align with the discard statement on the container label and carton labeling.
3.	The storage statement in Section 16.2 Storage and Handling does not include a "Do Not Freeze" statement that is presented on the container label and carton labeling.	Inconsistent storage information across labels and labeling may cause confusing resulting in improper storage and deteriorated drug medication errors.	OPQ confirmed that the do not freeze warning is appropriate for this product. Therefore, we recommend adding the statement "Do Not Freeze" to the PI to be consistent with the container and carton labeling.
Full Prescribing Information – Section 17 Patient Counseling			
1.	There is no statement instructing the HCP to counsel patients or caregivers to use a calibrated measuring device to measure their dose.	Selecting an unacceptable measuring device may increase the risk for wrong dose medication errors.	Add the following statements to Section 17: "Instruct patients or caregivers that a calibrated measuring device, such as an oral dosing syringe or oral dosing cup, should be obtained from the pharmacy to accurately measure and deliver the prescribed dose of

Table 2. Identified Issues and Recommendations for the Division of Neurology 2 (DN 2)			
	IDENTIFIED ISSUE	**RATIONALE FOR CONCERN**	**RECOMMENDATION**
			medication. A household teaspoon or tablespoon is not an adequate measuring device."
Medication Guide (MG)			
1.	The medication guide (MG) does not include a "What is the most important information I should know about Subvenite" section detailing the most important information to know about the drug product, including serious reactions. This does not align with the MG for the reference listed drug, Lamictal.	To promote safe use of the product, patients and/or caregivers should be made aware of the most important information to know about of Subvenite, specifically serious reactions.	We recommend revising the MG to include a "What is the most important information I should know about Subvenite" section that describes the most important information about the drug, including adverse reaction, similar to the MG for the reference listed drug, Lamictal (NDA 020241) if deemed clinically relevant for this product by the clinical team.
2.	The post-opening expiration date is not included under the "How should I store Subvenite" section.	Incomplete storage information may result in improper storage of the drug product and increased risk of deteriorated drug medication errors.	We recommend including a post-opening expiration date statement in the storage section, such as "Discard (throw away) any unused medication 90 days after first opening the bottle."
3.	There is no statement instructing patients or caregivers to use a calibrated measuring device to measure their dose.	Selecting an unacceptable measuring device may increase the risk for wrong dose medication errors.	Add the following statements to the "How should I take SUBVENITE?" section of the Medication Guide: "Your pharmacist should provide you with an oral dosing syringe or dosing cup that is needed to correctly measure the dose. **Do not** use a household teaspoon or tablespoon."

5 RECOMMENDATIONS FOR OWP PHARMACEUTICALS, INC

Table 3. Identified Issues and Recommendations for OWP Pharmaceuticals, Inc (entire table to be conveyed to Applicant)			
	IDENTIFIED ISSUE	**RATIONALE FOR CONCERN**	**RECOMMENDATION**
Container Label and Carton Labeling			
1.	As currently presented, the format for the expiration date is not defined.	We are unable to assess the proposed expiration date format from a medication safety perspective.	To minimize confusion and reduce the risk for deteriorated drug medication errors, we recommend identifying the expiration date 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 forward slash to separate the portions of the expiration date. See *Guidance for Industry: Product Identifiers under the Drug Supply Chain Security Act - Questions and Answers (June 2021).*
2.	The placeholder for the lot number is missing.	Lot number statement is required on the immediate container AND carton labeling when there is sufficient space per 21 CFR 201.10(i)(1).	Add the placeholder for the lot number to the container label and the carton labeling in accordance 21 CFR 201.10(i)(1).

Table 3. Identified Issues and Recommendations for OWP Pharmaceuticals, Inc (entire table to be conveyed to Applicant)			
	IDENTIFIED ISSUE	**RATIONALE FOR CONCERN**	**RECOMMENDATION**
			See also recommendation below regarding the product identifier for the carton labeling.
3.	The recommended dosage statement can be improved.	This may be revised to ensure consistency with the terminology in the prescribing information.	Revise the dosage statement [redacted (b) (4)] to read "Recommended Dosage: See prescribing information."
4.	The discard statement "Discard any unused product remaining after ninety (90) days of first opening the bottle" lacks prominence.	Lack of prominence may result in overlooked information which may lead to risk of administration of degraded drug product.	Consider increasing the prominence of the discard statement by using bold font or by other means. Also refer to comment number five directly below.
5.	As currently presented, [redacted (b) (4)] "Discard After", for the beyond use date . [redacted (b) (4)] Discard After: ____/____/____	[redacted (b) (4)]. This may lead to risk of administration of deteriorated drug product or usable unused product being discarded before 90 days.	We recommend allocating only one space to write the beyond use date (i.e., "Discard After" date). Also, consider relocating the statement "Discard any unused product remaining after ninety (90) days of first opening" to appear directly above the "Discard After" date (see comment number 4 directly above). For example: **Discard any unused product remaining after ninety (90) days of first opening.** Discard After __/__/__
6.	The overall font type, style, and kerning for the strength statement "10 mg/mL" is difficult to read as shown below:	Narrow, light typeface font with tight kerning, or spacing between characters, may impact the readability of the strength statement.	To improve readability, we recommend adjusting the font type/style (e.g., consider a less narrow and/or more bold option) and improving the kerning in the

Table 3. Identified Issues and Recommendations for OWP Pharmaceuticals, Inc (entire table to be conveyed to Applicant)			
	IDENTIFIED ISSUE	**RATIONALE FOR CONCERN**	**RECOMMENDATION**
	10 mg/mL		strength statement so that the strength fills up more of the (b) (4) box. For example: 10 mg/mL
7.	The established name "lamotrigine USP" is not at least half the size of the proprietary name. Overall, the entire established name and dosage form statement "(lamotrigine USP) Oral Suspension" lacks sufficient prominence.	We refer you to 21 CFR 201.10(g)(2) which states that the established name shall be printed in letters that are at least half as large as the letters comprising the proprietary name, and the established name shall have a prominence commensurate with the prominence with which such proprietary name appears, taking into account all pertinent factors, including typography, layout, contrast, and other printing features.	Increase the prominence (i.e., increase the font size, use bold font) of the established name and dosage form to improve readability and to be in accordance with 21 CFR 201.10(g)(2).
8.	As currently presented, the finished dosage form statement (b) (4) directly underneath the strength statement is not in alignment with USP requirements [General chapter <1121> nomenclature] for this type of pharmaceutical dosage form.	The dosage form for this product is "oral suspension". Additionally, the correct dosage form statement "Oral Suspension" is already present on the PDP of the container label and carton labeling.	We recommend removing the incorrect duplicate dosage form statement (b) (4)
9.	The net quantity statement (b) (4) on the container and	Inconsistent net quantity information can lead to confusion during ordering	Clarify which net quantity statement (b) (4) 8 oz (240 mL)) is correct for your proposed

Table 3. Identified Issues and Recommendations for OWP Pharmaceuticals, Inc (entire table to be conveyed to Applicant)			
	IDENTIFIED ISSUE	**RATIONALE FOR CONCERN**	**RECOMMENDATION**
	carton labeling is inconsistent with the quantity statement (i.e., 8 oz (240 mL) in Section 16 of the prescribing information (PI).	and distribution of the drug product.	product. Revise the net quantity statement to accurately reflect the total volume per bottle consistently across all labels and labeling.
10.	The first temperature numerical of each temperature range is missing the Celsius or Fahrenheit symbol.	The storage statement should be clearly stated to prevent incorrect storage which may lead to deteriorated drug medication errors.	Revise the storage statement to read "Store at 20°C to 25°C (68°F to 77°F); excursions permitted to 15°C to 30°C (59°F to 86°F) [see USP Controlled Room Temperature]."
11.	The storage statement "DO NOT FREEZE" is presented in all capital letters in bold font.	This competes in prominence with other important information on the side panel.	We recommend de-bolding the "DO NOT FREEZE" statement and presenting the text in mixed-case lettering. For example, "Do Not Freeze".
12.	The discard statement "Discard any unused product remaining after ninety (90) days of first opening the bottle" lacks prominence.	Lack of prominence may result in overlooked information which may lead to risk of administration of degraded drug product.	Consider increasing the prominence of the discard statement by using bold font or by other means.
13.	As currently presented, the (b) (4)-colored graphics, OWP logos, and (b) (4) images compete in prominence with critical and/or important information on the container label and carton labeling.	Per 21 CFR 201.15, critical product information such as the proprietary, established name, strength, and dosage form should appear as the most prominent information on the principal display panel. Specifically, we have the following concerns: The (b) (4)-colored graphic in front of the proprietary may detract from the readability of the proprietary name and established name.	Therefore, we recommend the following: • Consider relocating and/or decreasing the prominence of the graphic in front of the proprietary name on the container label and carton labeling. • Consider decreasing the prominence of the graphic on the side panel of the carton labeling such that it does not compete in prominence with important information. • Consider decreasing the prominence of the OWP name

Table 3. Identified Issues and Recommendations for OWP Pharmaceuticals, Inc (entire table to be conveyed to Applicant)			
	IDENTIFIED ISSUE	**RATIONALE FOR CONCERN**	**RECOMMENDATION**
		Additionally, the large (b) (4) -colored graphic on the side panel of the carton labeling, the OWP logos, and the (b) (4) images may distract the reader from critical information and other important information, such as the storage information and discard statements.	and logo on the container label and carton labeling such that it does not compete in prominence with important information. • Consider decreasing the size of the (b) (4) graphic on the carton labeling such that it does not compete in prominence with critical information and other important information.
Container Label			
1.	The (b) (4) statement on the container label is not necessary and is promotional in tone.	Per 21 CFR 201.56(a)(2), the labeling must be informative and accurate and not promotional in tone.	We recommend removing (b) (4) .
Carton Labeling			
1.	The product identifier is missing.	In June 2021, FDA finalized the Guidance for Industry on product identifiers required under the Drug Supply Chain Security Act (DSCSA). The Act requires manufacturers and re-packagers to affix or imprint a product identifier to each package and homogenous case of a product intended to be introduced in a transaction in(to) commerce. The product identifier includes the NDC, serial number, lot number, and expiration date in both a human-readable form and machine-readable	We recommend that you review the guidance to determine if the product identifier requirements apply to your product's labeling. See Guidance for Industry: Product Identifiers under the Drug Supply Chain Security Act - Questions and Answers (June 2021). If you determine that the product identifier requirements apply to your product's labeling, we request you add a place holder to the carton labeling.

Table 3. Identified Issues and Recommendations for OWP Pharmaceuticals, Inc (entire table to be conveyed to Applicant)			
	IDENTIFIED ISSUE	**RATIONALE FOR CONCERN**	**RECOMMENDATION**
		(2D data matrix barcode) format.	
2.	As currently presented, the statement (b) (4) is inconsistent with the statement on the container label (i.e., "SHAKE WELL BEFORE EACH USE").	Inconsistent preparation instructions may lead to confusion.	If a specific time requirement for shaking has not been established, we recommend revising the "shake" statement to read "Shake Well Before Each Use" to be consistent with the container label.
3.	The same background color (b) (4) is used to highlight the net quantity statement and the strength statement (i.e., 10 mg/mL).	Using the same color to highlight the strength statement and net quantity statement minimizes the difference between them and may lead to confusion.	We recommend removing the (b) (4)-colored box highlighting the net quantity statement on the carton labeling.

APPENDICES: METHODS & RESULTS FOR EACH MATERIALS REVIEWED

APPENDIX A. RELEVANT PRODUCT INFORMATION

Table 4 presents relevant product information for Subvenite received on March 4, 2024 from OWP Pharmaceuticals, Inc, and the Listed Drug (LD).

Table 4 Relevant Product Information for Subvenite and the Listed Drug (LD).

Product Name	**Subvenite**[b]	**Lamictal**[c] (NDA 020241)
Initial Approval Date	NA	December 27, 1994
Active Ingredient	lamotrigine	
Indication	**Epilepsy – adjunctive therapy** For the following seizure types in patients aged 2 years and older: • partial-onset seizures. • primary generalized tonic-clonic (PGTC) seizures. • generalized seizures of Lennox-Gastaut syndrome. **Epilepsy – monotherapy** Conversion to monotherapy in adults (aged 16 years and older) with partial-onset seizures who are receiving treatment with carbamazepine, phenytoin, phenobarbital, primidone, or valproate as the single antiepileptic drug (AED). **Bipolar Disorder** Maintenance treatment of bipolar I disorder to delay the time to occurrence of mood episodes (depression, mania, hypomania, mixed episodes) in patients treated for acute mood episodes with standard therapy.	
Dosage Form	oral suspension	Tablets
Strength	50 mg/5mL (10 mg/mL)	25 mg, 100 mg, 150 mg, and 200 mg
Route of Administration	Oral	
Dose and Frequency	*For complete dosing information see Section 2 Dosage and Administration of the proposed PI for Subvenite and the PI for Lamictal.* *Note: The proposed Subvenite PI dosing information aligns with the dosing information in the Lamictal PI.* • Refer to Tables 1 through 6 of the PI for specific dosing. • Dosing is based on concomitant medications, indication, and patient age.	

[b] Subvenite [Proposed Prescribing Information] available from \\CDSESUB1\EVSPROD\nda218879\0008\m1\us\114-labeling\draft\labeling\prescribing-information.pdf

[c] Lamictal [Prescribing Information]. Drugs@FDA. U.S. Food and Drug Administration. MAR 2021. [cited 2024 SEP 10]. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/020241s064,020764s057,022251s028lbl.pdf .

Table 4 Relevant Product Information for Subvenite and the Listed Drug (LD).		
Product Name	**Subvenite**[b]	**Lamictal**[c] (NDA 020241)
	• To avoid an increased risk of rash, the recommended initial dose and subsequent dose escalations should not be exceeded. • Do not restart LAMICTAL in patients who discontinued due to rash unless the potential benefits clearly outweigh the risks. • Adjustments to maintenance doses will be necessary in most patients starting or stopping estrogen-containing oral contraceptives. • Discontinuation: Taper over a period of at least 2 weeks (approximately 50% dose reduction per week).	
How Supplied	SUBVENITE (lamotrigine) Oral Suspension contains 10 mg per mL (10 mg/mL) lamotrigine. It is a pink, cherry-flavored suspension and is supplied in high-density polyethylene (HDPE) bottles with white, polypropylene, child-resistant closures with a foam liner and heat induction layered inner seal. Available in 8 oz (240 mL).	• 25-mg, white, scored, shield-shaped tablets debossed with "LAMICTAL" and bottles of 100 and Starter Kit for Patients Taking Valproate (Blue Kit of 35 tablets). • 100-mg, peach, scored, shield-shaped tablets debossed with "LAMICTAL" and bottles of 100. • 150-mg, cream, scored, shield-shaped tablets debossed with "LAMICTAL" and bottles of 60. • 200-mg, blue, scored, shield-shaped tablets debossed with "LAMICTAL" and bottles of 60.
Storage	Store at 20°C to 25°C (68°F to 77°F); excursions permitted to 15°C to 30°C (59°F to 86°F) [See USP Controlled Room Temperature].	Store at 25°C (77°F); excursions permitted to 15°C to 30°C (59°F to 86°F) [see USP Controlled Room Temperature] in a dry place and protect from light.
Container Closure	8 oz oblong HDPE white bottle	Lamictal Tablets: Bottles: HDPE bottles with (b) (4) coiler and closed with child resistant closures. Blister packs: Polyvinyl Chloride (PVC) blister with lidding materials (pouch paper, (b) (4), aluminum foil/heat seal (b) (4)

APPENDIX B. LABELS AND LABELING

B.1 List of Label and Labeling Reviewed

Using the principles of human factors and Failure Mode and Effects Analysis,[d] along with postmarket medication error data, we reviewed the following Subvenite label and labeling submitted by OWP Pharmaceuticals, Inc.

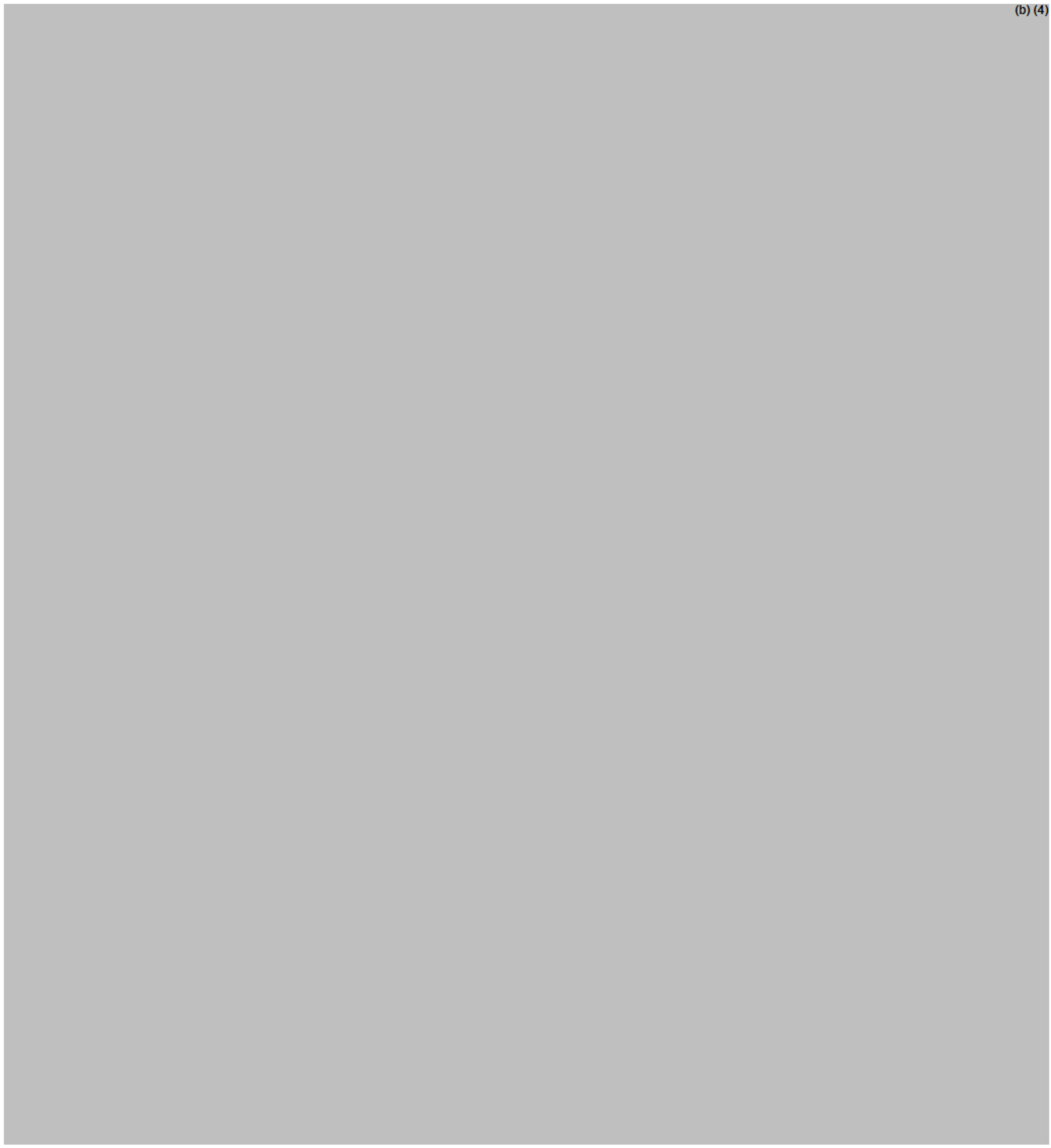
- Prescribing Information and Medication Guide (image not shown) received June 7, 2024 available from \\CDSESUB1\EVSPROD\nda218879\0008\m1\us\114-labeling\draft\labeling\prescribing-information.pdf
- Container label received on March 4, 2024
- Carton labeling received on March 4, 2024

B.2 Container Label and Carton Labeling Images

Container label

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

Carton labeling



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/s/

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11/27/2024 10:21:22 AM

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