CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

216185Orig1s000

OTHER REVIEW(S)

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: 10/11/2022

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

FROM: Division of New Drug Study Integrity (DNDSI)
Office of Study Integrity and Surveillance (OSIS)

SUBJECT: **Decline to conduct an on-site inspection**

RE: NDA 216185

The Division of New Drug Study Integrity (DNDSI) within the Office of Study Integrity and Surveillance (OSIS) determined that inspections are not needed at this time for the sites listed below. The rationale for this decision is noted below.

Rationale

The Office of Regulatory Affairs (ORA) conducted an inspection for the clinical site in September 2021, which falls within the surveillance interval. The inspection was conducted under the following submissions: (b) (4)

ORA observed the following objectionable conditions:

- Failure to conduct foreign clinical studies in accordance with good clinical practices. Specifically:
  - The approved Informed Consent Documents (ICDs) were not written at a level subjects could comprehend, including an explanation of scientific and medical terms.
  - The approved ICDs documents translateds from English to Gujarati was not a direct translation and included explanation and terminology that was not the same for the English to Hindi translation.

After reviewing the findings and reviewing the written response from the site, OSIS determined that the objectionable conditions observed did not impact data integrity or subject safety, and recommended that all study data be accepted for Agency review (Final OSIS EIR Review – February 2021 Veeda (Vedant Complex) Inspection).

OSIS conducted a Remote Regulatory Assessment (RRA) for the analytical site in (b) (4) which falls within the surveillance interval. The RRA was conducted under the following submissions: (b) (4)

OSIS concluded that data from the reviewed studies were reliable.

Inspection Sites

Facility Type	Facility Name	Facility Address
Clinical	Veeda Clinical Research Pvt., Ltd.	1st, 2nd, 3rd, and 4th Floor, Vedant Complex, Beside YMCA Club, S.G. Highway, Vejalpur, Ahmedabad, Gujarat, India
Analytical		(b) (4)

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/s/

JOSHUA L PEREZ
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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:	April 21, 2023
To:	Stephanie Parncutt 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)** Sapna Shah, PharmD Regulatory Review Officer **Office of Prescription Drug Promotion (OPDP)**
Subject:	Review of Patient Labeling: Medication Guide (MG)
Drug Name (established name):	MOTPOLY XR (lacosamide)
Dosage Form and Route:	extended-release capsules, for oral use, CV
Application Type/Number:	NDA 216185
Applicant:	Aucta Pharmaceuticals, Inc

1 INTRODUCTION

On July 6, 2022, Aucta Pharmaceuticals submitted for the Agency's review a 505(b)(2) New Drug Application (NDA) for MOTPOLY XR (lacosamide) extended-release capsules, for oral use. MOTPOLY XR (lacosamide) extended-release capsules, (b) (4) 100 mg, 150 mg and 200 mg was developed as a change in dosage form of the Reference Listed Drug (RLD), VIMPAT® (lacosamide) tablets, 50 mg, 100 mg, 150 mg and 200 mg owned by UCB INC and approved by FDA under NDA 022253.The proposed indication for MOTPOLY XR (lacosamide) is for treatment of partial-onset seizures in patients 17 years of age and older.

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 July 19, 2022, for DMPP and OPDP to review the Applicant's proposed Medication Guide (MG) for MOTPOLY XR (lacosamide) extended-release capsules, for oral use.

2 MATERIAL REVIEWED

- Draft MOTPOLY XR (lacosamide) MG received on July 6, 2022, revised by the Review Division throughout the review cycle, and received by DMPP and OPDP on April 11, 2023.
- Draft MOTPOLY XR (lacosamide) Prescribing Information (PI) received on July 6, 2022, revised by the Review Division throughout the review cycle, and received by DMPP and OPDP on April 11, 2023.
- Approved VIMPAT (lacosamide) comparator labeling dated September 9, 2022.

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.

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.

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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/s/

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

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

Memorandum

Date: April 20, 2023

To: Stephanie Parncutt, Regulatory Project Manager, Division of Neurology 2 (DN2)

Amy Kao, Clinical Reviewer, DN2

Tracy Peters, Associate Director for Labeling, DN2

From: Sapna Shah, Regulatory Review Officer
Office of Prescription Drug Promotion (OPDP)

CC: Aline Moukhtara, Team Leader, OPDP

Subject: OPDP Labeling Comments for MOTPOLY XR™ (lacosamide) extended-release capsules, for oral use, CV

NDA: 216185

Background:
In response to DN2's consult request dated July 19, 2022, OPDP has reviewed the proposed Prescribing Information (PI), Medication Guide, and carton and container labeling for the original NDA submission for MOTPOLY XR™ (lacosamide) extended-release capsules, for oral use, CV (Motpoly).

PI/Medication Guide:
OPDP's review of the proposed PI is based on the draft labeling emailed to OPDP from DN2 (Stephanie Parncutt) on April 11, 2023, and our comments are provided below.

A combined OPDP and Division of Medical Policy Programs (DMPP) review will be completed for the proposed Medication Guide, and comments will be 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 by the sponsor to the electronic document room on March 10, 2023, and we do not have any comments at this time.

Thank you for your consult. If you have any questions, please contact Sapna Shah at 240-402-6068 or Sapna.Shah@fda.hhs.gov.

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SAPNA SHAH
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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)

Date of This Memorandum:	March 15, 2023
Requesting Office or Division:	Division of Neurology 2 (DN 2)
Application Type and Number:	NDA 216185
Product Name and Strength:	Motpoly XR (lacosamide) extended-release capsules, 100 mg, 150 mg and 200 mg
Applicant/Sponsor Name:	Aucta Pharmaceuticals, Inc. (Aucta)
TTT ID #:	2022-241-2
DMEPA 2 Safety Evaluator:	Beverly Weitzman, PharmD
DMEPA 2 Acting Team Leader:	Stephanie DeGraw, PharmD

1 PURPOSE OF MEMORANDUM

Aucta submitted revised container labels for Motpoly XR extended-release capsules for the 100 mg, 150 mg and 200 mg strength extended-release capsules, and revised professional sample carton labeling for the 100 mg strength extended-release capsule received on March 10, 2023, for Motpoly XR.

The Division of Neurology 2 (DN 2) requested that we review the revised container labels and carton labeling for Motpoly XR (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 our recommendations, and we have no additional comments at this time.

[a] Weitzman B. Label and Labeling Review for Motpoly XR (NDA 216185). Silver Spring (MD): FDA, CDER, OSE, DMEPA 2 (US); 2023 MAR 06. TTT ID No.: 2022-241-1.

APPENDIX A. LABEL AND LABELING AND COVER LETTER

A.1. List of Labels and Labeling and Response to Agency's Recommendations dated March 6, 2023.

Using the principles of human factors and Failure Mode and Effects Analysis, along with postmarket medication error data, we reviewed the following Motpoly XR labels and labeling, and cover letter submitted by Aucta Pharmaceuticals, Inc. received on March 10, 2023.

- Response to the Agency's recommendations available from docuBridge via: \\CDSESUB1\EVSPROD\nda216185\0013\m1\us\aucta-response-labeling-ir.pdf
- Container labels (100 mg, 150 mg, 200 mg)[b]
- Professional sample carton labeling (100 mg)

Excerpt from Applicant's response to our recommendations:

1. Increased the font size of the dosage form "extended-release capsules" relative to the size of the established name to increase prominence. Presentation now is similar to the dosage form on the proposed container labels submitted on September 28, 2022.
2. Increased the prominence with bold font and enlarged font size. The revised "CV" symbol has been relocated underneath the established name due to insufficient space for the container labels with presentation similar to the dosage form on the proposed container labels submitted on September 28, 2022. The location of the revised "CV" symbol for Professional Sample Carton Label remains the same.
3. Strength statement has been revised from (b) (4) to "100 mg per capsule" to avoid wrong dose errors.

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(b) (4)

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/s/

BEVERLY WEITZMAN
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STEPHANIE L DEGRAW
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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)

Date of This Memorandum:	March 6, 2023
Requesting Office or Division:	Division of Neurology 2 (DN 2)
Application Type and Number:	NDA 216185
Product Name and Strength:	Motpoly XR (lacosamide) extended-release capsules, 100 mg, 150 mg and 200 mg
Applicant/Sponsor Name:	Aucta Pharmaceuticals, Inc (Aucta)
TTT ID #:	2022-241-1
DMEPA 2 Safety Evaluator:	Beverly Weitzman, PharmD
DMEPA 2 Acting Team Leader:	Stephanie DeGraw, PharmD

1 PURPOSE OF MEMORANDUM

Aucta submitted revised container labels for Motpoly XR extended-release capsules for the 100 mg, 150 mg and 200 mg strength extended-release capsules as well as the newly proposed professional sample blister label pack container label and carton labeling for the 100 mg strength extended-release capsule received on February 13, 2023, for Motpoly XR.

The Division of Neurology 2 (DN 2) requested that we review the revised trade container labels as well as the proposed professional blister label pack and carton labeling for Motpoly XR (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]

[a] Weitzman B. Label and Labeling Review for Motpoly XR (NDA 216185). Silver Spring (MD): FDA, CDER, OSE, DMEPA 2 (US); 2023 FEB 02. TTT ID No.: 2022-241.

2 ASSESSMENT AND CONCLUSION

Of note, Aucta states [redacted] (b) (4)

The Applicant implemented all our initial recommendations for the other strength container labels. However, we note the Applicant has decreased the prominence (i.e., font size) of the dosage form and controlled substance symbol on the container labels (i.e., the font size is smaller compared to presentation from the previous container labels submission). Thus, the revised container labels are unacceptable from a medication error perspective.

Additionally, the newly proposed professional sample carton labeling may be improved to promote the safe use of this product from a medication error perspective. We have no recommendations for the professional sample container (blister pack) label at this time.

We provide the identified medication error issues, our rationale for concern, and our proposed recommendations to minimize the risk for medication error in Section 3 (Table 1) for the Aucta Pharmaceuticals, Inc.

3 RECOMMENDATIONS FOR AUCTA PHARMACEUTICALS, INC

Table 1. Identified Issues and Recommendations for Aucta Pharmaceuticals, Inc. (entire table to be conveyed to Applicant)

	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
Container Labels and Professional Sample Carton Labeling			
1.	The dosage form (i.e., extended-release capsules) lacks sufficient prominence and is difficult to read.	The dosage form is critical information that should appear prominently. We are concern that users may have difficulty reading and identifying the dosage form.	To increase readability, we recommend increasing the prominence/font size of the dosage form "extended-release capsules" relative to the size of the established name. If more space is needed, you may consider placing the dosage form underneath the established name. Consider the presentation of the dosage form on the proposed container labels submitted on September 28, 2022.

[redacted] (b) (4)

Table 1. Identified Issues and Recommendations for Aucta Pharmaceuticals, Inc. (entire table to be conveyed to Applicant)			
	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
2.	The controlled substance lacks sufficient prominence.	Per 21 CFR 1302.04, the controlled substance "symbol on labels and labeling should be clear and large enough to afford easy identification of the schedule of the controlled substance upon inspection without removal from the dispenser's shelf".	Increase the prominence of the controlled substance symbol. To increase its prominence, you may consider the use of a bold font, enlarging the font size and relocating it to a different location. When considering how to increase the prominence of the controlled substance symbol, ensure the symbol does not interfere with the readability of the proprietary name, established name, or strength. Consider the presentation of the controlled substance symbol on the proposed container labels submitted on September 28, 2022.
Professional Sample Carton Labeling			
1.	It is not immediately clear that the product strength (i.e., 100 mg) is per single unit (i.e., per capsule).	Failure to express the product strength as "mg per single unit" may lead to wrong dose errors.	We recommend revising the strength statement so there is no confusion as to how much product is contained in each capsule as compared to the total contents of the blister pack. Revise to read: "XXX mg per capsule"

APPENDIX A. LABEL AND LABELING AND COVER LETTER

A.1. List of Labels and Labeling and Response to Agency's Recommendations dated February 2, 2023.

Using the principles of human factors and Failure Mode and Effects Analysis, along with postmarket medication error data, we reviewed the following Motpoly XR labels and labeling, and cover letter submitted by Aucta Pharmaceuticals, Inc. on February 13, 2023.

- Response to the Agency's recommendations available from docuBridge via: \\CDSESUB1\EVSPROD\nda216185\0010\m1\us\aucta-response-labeling-ir.pdf
- Container labels (100 mg, 150 mg, 200 mg)
- Professional sample Blister label pack (100 mg)
- Professional sample carton labeling (100 mg)

Excerpt from Applicant's response to our recommendations:

2. The placeholder, "PROPRIETARY" has been revised to conditionally acceptable proprietary name "Motpoly XR" and use the intend- to market font, color, etc.
3. The presentation of the established name has been revised to be at least half the size of the proprietary name in accordance with 21 CFR 201.10(g)(2).
4. Lot number and expiration date have been added to the container label to clearly differentiated from each other.
5. The human-readable expiration dating format of YYYY-MMM has been added.
6. A human-readable and machine-readable (2D data matrix barcode) product identifier which includes NDC, SERIAL, LOT AND EXP. have been added to compliance with FDA guidance finalized in June 2021.
7. The Warning Statement "Swallow capsule whole with liquid. Do not open, chew or crush" has been added.
8. The Medication Guide statement has been relocated from bottom of the principal display panel (PDP) to appear under the strength statement. "Rx Only" and net quantity statement have been relocated to appear on the bottom of PDP on proposed container.
9. [redacted] (b) (4) has been revised to "Recommended Dosage: See prescribing information.".

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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:	February 2, 2023
Requesting Office or Division:	Division of Neurology 2 (DN 2)
Application Type and Number:	NDA 216185
Product Name and Strength:	Motpoly XR (lacosamide) extended-release capsules, (b) (4) 100 mg, 150 mg and 200 mg
Product Type:	Single Ingredient Product
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	Aucta Pharmaceuticals, Inc (Aucta)
FDA Received Date:	July 7, 2022, September 28, 2022, October 4, 2022, and December 20, 2022
TTT ID #:	2022-241
DMEPA 2 Safety Evaluator:	Beverly Weitzman, PharmD
DMEPA 2 Acting Team Leader:	Stephanie DeGraw, PharmD

1 REASON FOR REVIEW

As part of the approval process for Motpoly XR (lacosamide) extended-release capsule, the Division of Neurology 2 (DN 2) requested that we review the proposed Motpoly XR prescribing information (PI), medication guide (MG) and container labels for areas of vulnerability that may lead to medication errors.

1.1 REGULATORY HISTORY

NDA 216185 is a 505(b)(2) NDA and the listed drug product is Vimpat, NDA 022253.

2 MATERIALS REVIEWED

Table 1. Materials Considered for this Label and Labeling Review

Material Reviewed	Appendix Section (for Methods and Results)
Product Information/Prescribing Information	A
Previous DMEPA Reviews	B (N/A)
ISMP Newsletters*	C (N/A)
FDA Adverse Event Reporting System (FAERS)*	D (N/A)
Information request	E
Labels and Labeling	F

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 ASSESSMENT AND CONCLUSION

Discussion with the Office of Pharmaceutical Quality (OPQ):

During our initial review, we identified a discrepancy in the proposed administration instructions in Section 2 and information provided in Section 12 of the prescribing information (PI). (b) (4) . We further note, that Aucta indicated in their CMC drug-product-quality summary document that (b) (4)

We consulted with the Office of Pharmaceutical Quality (OPQ) via email communication on November 29, 2022, to determine the appropriate administration instructions for lacosamide

extended-release capsules [redacted] (b) (4)

[redacted] (b) (4)

We confirmed with OPQ via email correspondence on January 26, 2023, that Acuta's response is acceptable, and that the labels and labeling should include the administration instruction "do not open capsules" to reflect this change for this drug product.

Overall, the proposed prescribing information (PI), medication guide (MG), and container labels may be improved to promote the 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 in Section 4 (Table 2) for the Division and in Section 5 (Table 3) for Aucta Pharmaceuticals, Inc.

4 RECOMMEDATIONS FOR DIVISION OF NEUROLOGY 2 (DN 2)

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

	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
Prescribing Information (PI) and Medication Guide (MG) – General Issues			
1.	The placeholder, "PROPRIETARY NAME" may be updated with the conditionally acceptable name, Motpoly XR.	The proposed proprietary name, Motpoly XR was found conditionally acceptable on May 13, 2022.[a]	Replace the placeholder "PROPRIETAY NAME" with the conditionally acceptable proprietary name, Motpoly XR throughout the PI and MG labeling.
Highlights of Prescribing Information (HPI)			
1.	In the Dosage Forms and strengths section of the HPI the dosage form is presented as "capsules."	"Capsules" is not the appropriate dosage form for this product. The appropriate dosage form for this product is	We recommend revising the dosage form "capsules" to the appropriate dosage form "extended-release capsules."

[a] Weitzman, B. Proprietary Name Review for Motpoly XR (NDA 216185). Silver Spring (MD): FDA, CDER, OSE, DMEPA 2 (US); 2022 DEC 12. PNR ID No. 2022-1044724778

Table 2. Identified Issues and Recommendations for Division of Neurology 2 (DN 2)			
	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
		"extended-release capsules." See USP General Chapter <1121> Nomenclature. Available from https://www.uspnf.com/sites/default/files/usp_pdf/EN/USPNF/1121Nomenclature.pdf.	
Full Prescribing Information – Section 2 Dosage and Administration			
1.	Section 2.5 "Administration Instructions" does not include a warning statement to advise the user that the capsules should not be opened.	The lack of the warning statement "do not open capsules" may increase the risk for wrong technique administration errors.	We recommend revising the warning statement "PROPRIETARY NAME capsules should be swallowed whole with liquid. Do not chew or crush capsules." to "Motpoly XR should be swallowed whole with liquid. Do not open, chew, or crush capsules."
Full Prescribing Information – Section 3 Dosage Forms and Strengths			
1.	The dosage form is presented as "capsules."	"Capsules" is not the appropriate dosage form for this product. The appropriate dosage form for this product is "extended-release capsules."	We recommend revising the dosage form "capsules" to the appropriate dosage form "extended-release capsules."
Full Prescribing Information – Section 16 How Supplied/Storage and Handling			
1.	The dosage form is presented as "capsules."	"Capsules" is not the appropriate dosage form for this product. The appropriate dosage form for this product is "extended-release capsules."	We recommend revising the dosage form "capsules" to the appropriate dosage form "extended-release capsules."
Full Prescribing Information – Section 17 Patient Counseling			
1.	Administration instructions advising	Omission of administration instructions necessary for	We recommend including the administration instructions to

Table 2. Identified Issues and Recommendations for Division of Neurology 2 (DN 2)			
	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
	users on proper administration technique is missing.	users to use the drug safety and to ensure proper administration may increase the risk of wrong technique administration errors.	advise users on proper administration of Motpoly XR capsules as follows: "Motpoly XR should be swallowed whole with liquid. Do not open, chew, or crush capsules."
Medication Guide (MG)			
1.	The instructions under the heading "How should I take PROPRIETARY NAME?" does not include a warning statement to advise the user that the capsules should not be opened.	The lack of the warning statement "do not open capsules" may increase the risk for wrong technique administration errors.	We recommend revising the warning statement "Swallow PROPRIETARY NAME whole with liquid. Do not chew or crush capsules." to "Swallow Motpoly XR whole with liquid. Do not open, chew, or crush capsules."

5 RECOMMENDATIONS FOR AUCTA PHARMACEUTICALS, INC

Table 3. Identified Issues and Recommendations for Aucta Pharmaceuticals, Inc (entire table to be conveyed to Applicant)			
	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
Container Labels			
1.	We note you submitted sample labels and labeling in your original submission received on July 7, 2022. We also note that you submitted revised container labels received on September 28, 2022, to include the proprietary name placeholder. However, you did not submit revised professional sample labels and labeling with that submission. If you intend to distribute sample packaging, consider applying all relevant recommendations to the sample labels and labeling, and consider submitting the revised sample labels and labeling for our review.		
2.	The placeholder, "PROPRIETARY" may be updated with the conditionally acceptable name, Motpoly XR.	We reference our December 13, 2022, Proprietary Name Conditionally Acceptable Letter informing you that	Revise the container labels to include the conditionally acceptable proprietary name, Motpoly XR, and use the intend-to market font, color, etc.

Table 3. Identified Issues and Recommendations for Aucta Pharmaceuticals, Inc (entire table to be conveyed to Applicant)			
	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
		the proprietary name, Motpoly XR, was found conditionally acceptable.	
3.	The established name lacks prominence commensurate with the proprietary name placeholder.	It is unclear if the established name is at least half the size of the proprietary name placeholder.	Ensure the presentation of the established name is at least half the size of the proprietary name taking into account all pertinent factors, including typography, layout, contrast, and other printing features in accordance with 21 CFR 201.10(g)(2).
4.	The containers labels do not contain a lot number and expiration date.	The lot number and expiration date are required on the container label per 21 CFR 201.10(i)(1) and 21 CFR 211.137, respectively	Ensure the lot number and expiration date appear on the container labels. In addition, ensure the lot number is clearly differentiated from the expiration date.
5.	The format for expiration date is not defined.	We are unable to assess the proposed expiration date format from a medication safety perspective (e.g., risk for deteriorated drug medication errors).	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

Table 3. Identified Issues and Recommendations for Aucta Pharmaceuticals, Inc (entire table to be conveyed to Applicant)			
	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
			used to separate the portions of the expiration date.
6.	As currently presented, the human-readable and machine-readable (2D data matrix barcode) product identifier is missing on the container labels.	In June 2021, FDA finalized guidance on product identifiers required under the Drug Supply Chain Security Act.* The Act requires manufacturers and repackagers, respectively, 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 beginning November 27, 2017, and November 27, 2018, respectively. *The final guidance is available from: https://www.fda.gov/ucm/groups/fdagov-public/@fdagov-drugs-gen/documents/document/ucm621044.pdf	We recommend that you review the final guidance. If you determine that the product identifier requirements apply to your product's labeling, we request you add a placeholder for the machine readable (2-D data matric barcode) and human-readable product identifier to the container labels. The DSCSA guidance on product identifiers recommends that the human-readable portion be located near the 2D data matrix barcode and recommends the following format: NDC: [insert product's NDC] SERIAL: [insert product's serial number] LOT: [insert product's lot number] EXP: [insert product's expiration date]
7.	The container labels are missing the warning statements "Swallow capsules whole with liquid. Do not open, chew or crush."	Incomplete administration instructions may lead to wrong administration technique errors.	We recommend including the warning statements "Swallow capsules whole with liquid. Do not open, chew or crush" If additional space is needed, consider reducing the size of the Aucta logo.
8.	The location of the Medication Guide statement, the net quantity statement, and	Per 21 CFR 208.24(d), the Medication Guide statement shall appear on the label in a prominent	To ensure the medication guide is prominently displayed and to avoid numerical confusion, we recommend relocating the

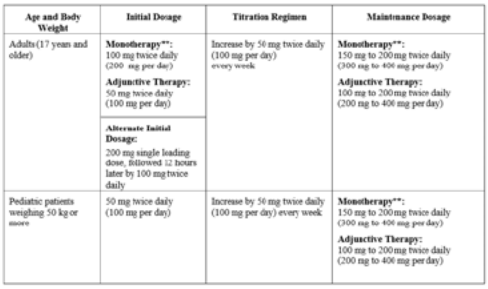
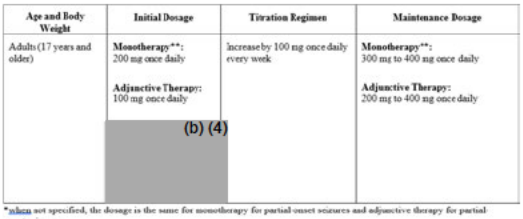
Table 3. Identified Issues and Recommendations for Aucta Pharmaceuticals, Inc (entire table to be conveyed to Applicant)			
	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
	the "Rx Only" statement can be improved.	and conspicuous manner. Additionally, the current location of the "Rx Only" and net quantity statements detract from the medication guide statement. Further, the net quantity statement appears in close proximity to the strength statement which may increase the risk of numerical confusion.	medication guide statement from the bottom of the principal display panel (PDP) to appear under the strength statement, and relocating the "Rx Only" and net quantity statements to appear on the bottom of the PDP.
9.	The recommended dosage statement can be improved.	This may be revised to ensure consistency with the prescribing information.	Revise the statement, (b) (4) to read "Recommended Dosage: See prescribing information."

APPENDICES: METHODS & RESULTS FOR EACH MATERIAL REVIEWED

APPENDIX A. PRODUCT INFORMATION/PRESCRIBING INFORMATION

Table presents relevant product information for Motpoly XR that Aucta Pharmaceuticals, Inc submitted on July 7, 2022, and the listed drug (LD), Vimpat tablets (NDA 022253).

Table 4. Relevant Product Information for Listed Drug and Motpoly XR

Product Name	Vimpat	Motpoly XR
Initial Approval Date	October 28, 2008	N/A
Active Ingredient	lacosamide	
Indication	• Treatment of partial-onset seizures in patients 1 month of age and older • Adjunctive therapy in the treatment of primary generalized tonic-clonic seizures in patients 4 years of age and older	Treatment of partial-onset seizures in patients 17 years of age and older.
Route of Administration	oral	
Dosage Form	Tablets	Extended-release capsules
Strength	50 mg, 100 mg, 150 mg and 200 mg	(b) (4) 100 mg, 150 mg and 200 mg
Dose and Frequency	Table 1: Recommended Dosages for Partial-Onset Seizures (Monotherapy or Adjunctive Therapy) in Patients 1 Month and Older, and for Primary Generalized Tonic-Clonic Seizures (Adjunctive Therapy) in Patients 4 Years of Age and Older* 	The recommended dosage for monotherapy and adjunctive therapy for partial-onset seizures in patients 17 years of age and older is included in Table 1.  (b) (4)

Age and Body Weight	Initial Dosage	Titration Regimen	Maintenance Dosage
Adults (17 years and older)	**Monotherapy**:** 100 mg twice daily (200 mg per day) **Adjunctive Therapy:** 50 mg twice daily (100 mg per day) **Alternate Initial Dosage:** 200 mg single loading dose, followed 12 hours later by 100 mg twice daily	Increase by 50 mg twice daily (100 mg per day) every week	**Monotherapy**:** 150 mg to 200 mg twice daily (300 mg to 400 mg per day) **Adjunctive Therapy:** 100 mg to 200 mg twice daily (200 mg to 400 mg per day)
Pediatric patients weighing 50 kg or more	50 mg twice daily (100 mg per day)	Increase by 50 mg twice daily (100 mg per day) every week	**Monotherapy**:** 150 mg to 200 mg twice daily (300 mg to 400 mg per day) **Adjunctive Therapy:** 100 mg to 200 mg twice daily (200 mg to 400 mg per day)

Age and Body Weight	Initial Dosage	Titration Regimen	Maintenance Dosage
Adults (17 years and older)	**Monotherapy**:** 200 mg once daily **Adjunctive Therapy:** 100 mg once daily	Increase by 100 mg once daily every week	**Monotherapy**:** 300 mg to 400 mg once daily **Adjunctive Therapy:** 200 mg to 400 mg once daily

(b) (4)

*when not specified, the dosage is the same for monotherapy for partial-onset seizures and adjunctive therapy for partial onset seizures.
**Monotherapy for partial-onset seizures only

(b) (4)

	<table><tr><th>Age and Body Weight</th><th>Initial Dosage</th><th>Titration Regimen</th><th>Maintenance Dosage</th></tr><tr><td>Pediatric patients weighing 30 kg to less than 50 kg</td><td>1 mg/kg twice daily (2 mg/kg/day)</td><td>Increase by 1 mg/kg twice daily (2 mg/kg/day) every week</td><td>2 mg/kg to 4 mg/kg twice daily (4 mg/kg/day to 8 mg/kg/day)</td></tr><tr><td>Pediatric patients weighing 11 kg to less than 30 kg Pediatric patients weighing 6 kg to less than 11 kg *</td><td>1 mg/kg twice daily (2 mg/kg/day)</td><td>Increase by 1 mg/kg twice daily (2 mg/kg/day) every week</td><td>3 mg/kg to 6 mg/kg twice daily (6 mg/kg/day to 12 mg/kg/day)</td></tr><tr><td rowspan="2">Pediatric patients weighing less than 6 kg *</td><td>Intravenous: 0.66 mg/kg three times daily (2 mg/kg/day)</td><td>Intravenous: Increase by 0.66 mg/kg three times daily (2 mg/kg/day) every week</td><td>Intravenous: 2.5 mg/kg to 5 mg/kg three times daily (7.5 mg/kg/day to 15 mg/kg/day)</td></tr><tr><td>Oral: 1 mg/kg twice daily (2 mg/kg/day)</td><td>Oral: Increase by 1 mg/kg twice daily (2 mg/kg/day) every week</td><td>Oral: 3.75 mg/kg to 7.5 mg/kg twice daily (7.5 mg/kg/day to 15 mg/kg/day)</td></tr></table> *when not specified, the dosage is the same for monotherapy for partial-onset seizures and adjunctive therapy for partial-onset seizures or primary generalized tonic-clonic seizures. Oral and intravenous dosages are the same unless specified. **Monotherapy for partial-onset seizures only ± indicated only for partial-onset seizures VIMPAT Injection Dosage: VIMPAT injection may be used when oral administration is temporarily not feasible VIMPAT injection can be administered intravenously to adult and pediatric patients weighing 6 kg or more with the same dosing regimens described for oral dosing. For pediatric patients weighing less than 6 kg, VIMPAT injection may be initiated with a dose of 0.66 mg/kg three times daily (see Table 1). The clinical study experience of intravenous VIMPAT is limited to 5 days of consecutive treatment. Loading Dose in Adult Patients (17 Years and Older): VIMPAT and VIMPAT injection may be initiated in adult patients with a single loading dose of 200 mg,	(b) (4) 2.2 Converting From a Single Antiepileptic (AED) to Lacosamide Extended-Release Capsules Monotherapy for the Treatment of Partial-Onset Seizures: For patients who are already on a single AED and will convert to Lacosamide Extended-Release Capsules monotherapy, withdrawal of the concomitant AED should not occur until the therapeutic dosage of Lacosamide Extended-Release Capsules is achieved and has been administered for at least (b) (4) days. A gradual withdrawal of the concomitant AED over at least 6 weeks is recommended. 2.3 Dosage Information for Patients with Renal Impairment For patients with mild to moderate renal impairment, no dosage adjustment is necessary. For patients with severe renal impairment [creatinine clearance (CLCR) less than 30 mL/min as estimated by the Cockcroft-Gault equation for adults; CLCR less than 30 mL/min/1.73m2 as estimated by the Schwartz equation for pediatric patients] or end-stage renal disease, (b) (4) (b) (4)

	followed approximately 12 hours later by 100 mg twice daily (200 mg per day). The maintenance dose regimen should be continued for one week. VIMPAT can then be titrated as recommended in Table 1. The adult loading dose should be administered with medical supervision because of the increased incidence of CNS adverse reactions. The use of a loading dose in pediatric patients has not been studied. 2.2 Converting From a Single Antiepileptic (AED) to VIMPAT Monotherapy for the Treatment of Partial-Onset Seizures: For patients who are already on a single AED and will convert to VIMPAT monotherapy, withdrawal of the concomitant AED should not occur until the therapeutic dosage of VIMPAT is achieved and has been administered for at least 3 days. A gradual withdrawal of the concomitant AED over at least 6 weeks is recommended. 2.3 Dosage Information for Patients with Renal Impairment: For patients with mild to moderate renal impairment, no dosage adjustment is necessary. For patients with severe renal impairment [creatinine clearance (CLCR) less than 30 mL/min as estimated by the Cockcroft-Gault equation for adults; CLCR less than 30 mL/min/1.73m2 as estimated by the Schwartz equation for pediatric patients] or end-stage renal disease, a reduction of 25% of the maximum dosage is recommended.	Hemodialysis: Lacosamide Extended-Release Capsules is effectively removed from plasma by hemodialysis. Following a 4-hour hemodialysis treatment, dosage supplementation of up to 50% should be considered. Concomitant Strong CYP3A4 or CYP2C9 Inhibitors: Dose reduction may be necessary in patients with renal impairment who are taking strong inhibitors of CYP3A4 and CYP2C9. 2.4 Dosage Information for Patients with Hepatic Impairment For patients with mild or moderate hepatic impairment, (b) (4) Lacosamide Extended-Release Capsules use is not recommended in patients with severe hepatic impairment. Concomitant Strong CYP3A4 and CYP2C9 Inhibitors: Dose reduction may be necessary in patients with hepatic impairment who are taking strong inhibitors of CYP3A4 and CYP2C9.

	In all patients with renal impairment, the dose titration should be performed with caution. Hemodialysis: VIMPAT is effectively removed from plasma by hemodialysis. Following a 4-hour hemodialysis treatment, dosage supplementation of up to 50% should be considered. Concomitant Strong CYP3A4 or CYP2C9 Inhibitors: Dose reduction may be necessary in patients with renal impairment who are taking strong inhibitors of CYP3A4 and CYP2C9. 2.4 Dosage Information for Patients with Hepatic Impairment For patients with mild or moderate hepatic impairment, a reduction of 25% of the maximum dosage is recommended. The dose titration should be performed with caution in patients with hepatic impairment. VIMPAT use is not recommended in patients with severe hepatic impairment. Concomitant Strong CYP3A4 and CYP2C9 Inhibitors: Dose reduction may be necessary in patients with hepatic impairment who are taking strong inhibitors of CYP3A4 and CYP2C9.	
How Supplied	Film coated tablet: bottles containing 60 tablets and carton containing 6 x 10 unit- dose cards	Lacosamide Extended-Release Capsules (b) (4) • 100 mg are (b) (4) yellow opaque cap and white opaque body with “A” printed in black ink on the cap and “100” printed in black ink on the body,

		containing white or off-white beads. They are supplied as follows: Bottles of 60 • 150 mg are brown opaque cap and white opaque body with “A” printed in black ink on the cap and “150” printed in black ink on the body, containing white or off-white beads. They are supplied as follows: Bottles of 60 • 200 mg are blue opaque cap and white opaque body with “A” printed in black ink on the cap and “200” printed in black ink on the body, containing white or off-white beads. They are supplied as follows: Bottles of 60
Storage	Store at 20°C to 25°C (68°F to 77°F); excursions permitted between 15°C to 30°C (59°F to 86°F). [See USP Controlled Room Temperature]	
Container Closure	Film coated tablet: High density polyethylene (HDPE) bottle with polypropylene (PP) child-resistant cap (CRC)	HDPE bottles with (b) (4) caps

APPENDIX E. INFORMATION REQUEST

E.1 Information Request (Issued December 14, 2022)

You stated that: [redacted] (b) (4)

E.2 Response (Received December 20, 2022):

Aucta acknowledges the agency's comment. Aucta proposes to revise the statement from [redacted] (b) (4) to "Lacosamide extended release capsules may be taken with or without food. Lacosamide extended release capsules should be swallowed whole with liquid. Do not chew or crush capsules." [redacted] (b) (4) Section 1.14 Proposed Package Insert (word, pdf, side-by-side comparison) and section 3.2.P.2 of Product Development Report (PDR) have been updated accordingly.

IR response available in docuBridge via:
\\CDSESUB1\EVSPROD\nda216185\0006\m1\us\aucta-response-to-ir-003.pdf

Excerpt from PI Submitted on December 20, 2022 (Section 12.3 Pharmacokinetics):

Effect of food
Compared to the fasted state, high-fat meal [redacted] (b) (4) has no effect on the C_{max}, T_{max} and AUC of PROPRIETARY NAME. Hence, PROPRIETARY NAME can be taken with or without food.

APPENDIX F. LABELS AND LABELING

F.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 Motpoly XR labels and labeling submitted by Aucta Pharmaceuticals, Inc.

- Container labels received on September 28, 2022
- Prescribing Information and medication guide (Image not shown) received on December 20, 2022, available from
  Clean: \\CDSESUB1\EVSPROD\nda216185\0006\m1\us\aucta-pi-pdf-122022.pdf
  Annotated comparison with RLD, Vimpat:
  \\CDSESUB1\EVSPROD\nda216185\0006\m1\us\aucta-pi-sbs.pdf

F.2 Label and Labeling Images

Container labels

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

1 Page of Draft Labeling has been Withheld in Full as b4 (CCI/TS) immediately following this page

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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
02/02/2023 01:21:32 PM

STEPHANIE L DEGRAW
02/02/2023 03:09:06 PM