CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

215602Orig1s000

OTHER REVIEW(S)

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

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

Memorandum

Date: January 12, 2022

To: Jack Dan, Regulatory Project Manager
Division of Neurology 1 (DN1)

Tracy Peters, PharmD, Associate Director for Labeling, DN1

From: Lynn Panholzer, PharmD, Regulatory Review Officer
Office of Prescription Drug Promotion (OPDP)

CC: Aline Moukhtara, RN, MPH, Team Leader, OPDP

Subject: OPDP Labeling Comments for FLEQSUVY™ (baclofen oral suspension)

NDA: 215602

In response to DN1's consult request dated May 27, 2021, OPDP has reviewed the proposed product labeling (PI) and carton and container labels for the original NDA submission for FLEQSUVY™ (baclofen oral suspension).

Labeling: OPDP reviewed the attached proposed PI received by electronic mail from DN1 on January 4, 2022, and we have no comments at this time.

Carton and Container Labels: OPDP reviewed the attached proposed carton and container labels submitted by the Applicant to the electronic document room on November 23, 2021 (container labels) and December 21, 2021 (carton labels), and we have no comments at this time.

Thank you for your consult. If you have any questions, please contact Lynn Panholzer at (301) 796-0616 or lynn.panholzer@fda.hhs.gov.

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LYNN M PANHOLZER
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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:	January 12, 2022
Requesting Office or Division:	Division of Neurology 1 (DN 1)
Application Type and Number:	NDA 215602
Product Name and Strength:	Fleqsuvy[a] (baclofen oral suspension), 5 mg/mL
Applicant/Sponsor Name:	Azurity Pharmaceuticals, Inc. (Azurity)
OSE RCM #:	2021-728-2
DMEPA 2 Safety Evaluator:	Beverly Weitzman, PharmD
DMEPA 2 Team Leader (Acting):	Stephanie DeGraw, PharmD

1 PURPOSE OF MEMORANDUM

The Applicant submitted revised carton labeling received on December 21, 2021 for Fleqsuvy (baclofen oral suspension) to include the "post-opening expiration date" to be consistent with the container labels. The Division of Neurology 1 (DN 1) requested that we review the revised carton labeling (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.[b]

2 CONCLUSION

The Applicant implemented all of our recommendations and we have no additional recommendations at this time.

[a] The proposed proprietary name Fleqsuvy was found conditionally acceptable on June 30, 2021.
[b] Weitzman B. Label and Labeling Review for Fleqsuvy (NDA 215602). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2021 DEC 8. RCM No.: 2021-728-1.

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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:	December 8, 2021
Requesting Office or Division:	Division of Neurology 1 (DN 1)
Application Type and Number:	NDA 215602
Product Name and Strength:	Fleqsuvy[a] (baclofen oral suspension), 5 mg/mL
Applicant/Sponsor Name:	Azurity Pharmaceuticals, Inc. (Azurity)
OSE RCM #:	2021-728-1
DMEPA 2 Safety Evaluator:	Beverly Weitzman, PharmD
DMEPA 2 Team Leader (Acting):	Stephanie DeGraw, PharmD

1 PURPOSE OF MEMORANDUM

The Applicant submitted revised container labels and carton labeling received on November 23, 2021 for Fleqsuvy (baclofen oral suspension). The Division of Neurology 1 (DN 1) requested that we review the revised container labels and carton labeling (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.[b]

2 ASSESSMENT AND RECOMMENDATIONS

Our review of the revised container labels determined they are acceptable from a medication error perspective. However, the carton labeling can be improved to promote the safe use of the product. Tables 1 below includes the identified medication error issue with the revised carton labeling, our rationale for concern, and the proposed recommendation to minimize the risk for medication error.

[a] The proposed proprietary name Fleqsuvy was found conditionally acceptable on June 30, 2021.
[b] Weitzman B. Label and Labeling Review for Fleqsuvy (NDA 215602). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2021 OCT 28. RCM No.: 2021-728.

Table 1. Identified Issues and Recommendations for Azurity (entire table to be conveyed to Applicant)			
	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
Carton Labeling			
1.	The carton labeling is missing the "post-opening expiration date" statement that is present on the container label.	Omission of the "post opening expiration date" statement on the carton labeling may result in deteriorate drug medication errors.	If space permits, we recommend including the "post-opening expiration date" statement on your carton labeling as presented on your container labels as follows "Date of first opening __/__/__. Discard unused portion 2 months after first opening." Alternatively, if there are space constraints, consider only adding the statement "Discard unused portion 2 months after first opening." We recommend including this information below the storage information on the side panel.

3 CONCLUSION

The revised carton labeling is unacceptable from a medication error perspective. Above, we provided a recommendation in Table 1 for Azurity. We ask that the Division convey Table 1 in its entirety to Azurity, so the recommendation is implemented prior to approval of this NDA.

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LABEL AND LABELING REVIEW
Division of Medication Error Prevention and Analysis 1 (DMEPA 1)
Office of Medication Error Prevention and Risk Management (OMEPRM)
Office of Surveillance and Epidemiology (OSE)
Center for Drug Evaluation and Research (CDER)

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

Date of This Review:	October 28, 2021
Requesting Office or Division:	Division of Neurology 1 (DN 1)
Application Type and Number:	NDA 215602
Product Name and Strength:	Fleqsuvy[a] (baclofen oral suspension), 5 mg/mL
Product Type:	Single Ingredient Product
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	Azurity Pharmaceuticals, Inc. (Azurity)
FDA Received Date:	April 5, 2021 and August 25, 2021
OSE RCM #:	2021-728
DMEPA 1 Safety Evaluator:	Beverly Weitzman, PharmD
DMEPA 1 Team Leader (Acting):	Stephanie DeGraw, PharmD

[a] The proposed proprietary name Fleqsuvy was found conditionally acceptable on June 30, 2021.

1 REASON FOR REVIEW

As part of the approval process for Fleqsuvy (baclofen oral suspension), 5 mg/mL, the Division of Neurology 1 (DN 1) requested that we review the proposed Fleqsuvy prescribing information (PI), container labels and carton labeling for areas of vulnerability that may lead to medication errors.

2 REGULATORY HISTORY AND BACKGROUND

NDA 215602 is a 505(b)(2) and the listed drug product is Lioresal (baclofen) tablet, NDA 017851. Additionally, the currently marketed drug product, Ozobax (baclofen) oral solution, 5 mg/5 mL (1 mg/mL) is referenced by the applicant for labeling comparison purposes only. We note, that Azurity's proposed product differs from the currently marketed product Ozobax oral solution (NDA 208193) with respect to the concentration. See Section 4 below for our assessment of the proposed concentration.

3 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
Comparison between labels and labeling *(shown for comparison purposes only)*	G

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

4 OVERALL ASSESSMENT OF THE MATERIALS REVIEWED

Upon review of the labeling, we note that Azurity proposes a concentration of 5 mg/mL for Fleqsuvy (baclofen oral suspension) which is five times higher than the currently marketed Ozobax (baclofen) oral solution concentration of 5 mg/5 mL (1 mg/mL).

We are concerned that the introduction of the proposed concentration (5 mg/mL) into the marketplace may contribute to wrong dose medication errors with the currently available 5

mg/5 mL (1 mg/mL) concentration (e.g., 5-fold overdose medication errors), especially given that both expressions of strength begin with "5 mg". We issued an information request on August 6, 2021 (see Appendix E) requesting the Applicant provide a risk analysis to characterize the risk of confusion of dosing errors between the currently marketed Ozobax (baclofen) oral solution concentration (1 mg/mL) and the proposed Fleqsuvy (baclofen oral suspension) concentration (5 mg/mL). Specifically, we requested the Applicant include a description of the proposed mitigation strategies (e.g., label/labeling differentiation strategies) and how the proposed strategies will address the identified risks and mitigate the potential for errors.

In their August 25, 2021 response (See Appendix E), the Applicant provided their proposed risk management plan (e.g., Use-Related Risk Analysis and label/labeling differentiation strategies) to address potential risks associated with prescribing, dispensing and administration of Fleqsuvy.[b] In addition, the Applicant provided revised prescribing information (PI), container labels and carton labeling (see Appendix F), based on recommendations made by the ISMP Medication Safety Board in the Label and Risk-Mitigation Review[c] to address potential product selection errors between the two baclofen concentrations and potential wrong dose medication errors. We reviewed the information submitted including revised label and labeling to ensure they support the safe and effective use of the product.

We note that the proposed strength presentation on the revised labels and labeling includes both the strength per 5 mL and strength per mL (i.e., 25 mg per 5 mL (5 mg/mL)) per a recommendation made by ISMP Medication Safety Board. We note that this does not follow the standard strength presentation for products with doses of less than 5 mL. In the case of products with doses less than 5 mL, the strength is usually expressed as "XX mg/mL". However, based on previous post-marketing experience with errors associated with concentrated solutions (e.g., diazepam oral solution vs. oral concentrate and morphine oral solution vs. oral concentrate)[d], the statements of strength were revised such that both the "mg per 5 mL" and the "mg per mL" are specified. Per post-market surveillance, revising the strength presentation in this manner has been effective in mitigating wrong dose medication errors that could potentially lead to overdose or underdose errors. Therefore, the Applicant's approach of expressing the strength of Fleqsuvy as "25 mg per 5mL (5 mg/mL)" conforms with precedence for these types of "concentrated" products.[e,f] Based on the totality of the information stated above, we find the proposed strength expression "25 mg per 5mL (5 mg/mL)" to be acceptable.

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[b] Available via: \\CDSESUB1\evsprod\nda215602\0006\m1\us\use-rltd-rsk-analysis-fleqsuvy.pdf

[c] Available via: \\CDSESUB1\evsprod\nda215602\0006\m1\us\med-safe-brd-lbl-rsk-mit-rev.pdf

[d] Institute for Safe Medication Practices. Safety briefs: FDA Advise-ERR: A new look for Morphine Sulfate 100 mg per 5 mL (20 mg/mL) Oral Solution. ISMP Med Saf Alert Acute Care. 2010;15(3):1-2.

[e] Available via: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=1aaf9375-ae3d-4fed-9cd1-24102e00be1a

[f] Available via: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=4d425667-006b-446d-832c-63040509ad59

Additionally, we notified the Office of Quality Pharmaceutical Quality (OPQ) via email regarding the proposed strength presentation. OPQ deferred to DMEPA for final determination on the presentation of the expression of strength.

5 CONCLUSION AND RECOMMENDATIONS

The proposed prescribing information (PI), container labels, and carton labeling 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 6 for the Division and in Section 7 for Azurity Pharmaceuticals, Inc.

6 RECOMMEDATIONS FOR DIVISION OF NEUROLOGY 1 (DN 1)

Table 2. Identified Issues and Recommendations for Division of Neurology 1 (DN 1)

	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
Full Prescribing Information – Section 2 Dosage and Administration			
1.	The Dosage and Administration section of the PI (Section 2) lacks a statement regarding the use of a dosing device, such as an oral syringe, to accurately measure and administer the prescribed dose and lacks instructions to "shake well before administration."	The lack of information regarding how to accurately measure the prescribed dose may result in a risk of delayed therapy or wrong dose medication errors. Additionally, the lack of instructions to (i.e., shake well) may contribute to wrong technique medication errors.	We recommend adding the following statements, or something similar, under a separate subheading titled "2.3 Important Administration Information" in Section 2 Dosage and Administration: "Measure Fleqsuvy with an appropriate oral dosing syringe provided by a pharmacist" "Shake Fleqsuvy oral suspension well before every administration."
2.	The post-opening expiration date is missing.	There is a risk of deteriorated drug medication errors. opening.	We recommend adding a post-opening expiration statement, such as "Discard the unused portion XX days after first opening [See How Supplied/Storage and Handling]" under a separate subheading titled "2.3 Important Administration

Table 2. Identified Issues and Recommendations for Division of Neurology 1 (DN 1)			
	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
			Information" in Section 2 Dosage and Administration.
Full Prescribing Information – Section 3 Dosage Forms and Strengths			
1.	The Dosage Forms and Strengths section of the PI (Section 3) includes the statements (b) (4) [redacted]." However, Section 3 does not appear to be the appropriate place to include these statements.	We are concerned about the risk for product selection errors and wrong dose medication errors between the different baclofen concentrations (i.e., 25 mg/5 mL (5 mg/mL) vs. 5 mg/5 mL (1 mg/mL)) and are concerned these warning statements may be overlooked in Section 3.	We recommend relocating these statements to the top of 2.1 and revising the statements to read "FLEQSUVY is a concentrated formulation. Verify the strength and dose of the product prior to prescribing, dispensing, and administering."
2.	The dosage form statement does not align with the dosage form statement in Section 16 which states that the product is "concentrated".	We are concerned that the concentration formulation information may be overlooked.	We recommend revising the dosage form statement to read "…baclofen as a concentrated orange to yellow-colored, grape-flavored suspension."
Full Prescribing Information – Section 16 How Supplied/Storage and Handling			
1.	The post-opening expiration date is missing.	There is a risk of deteriorated drug medication errors.	We recommend including a post-opening expiration date statement, such as "Discard the unused portion XX days after first opening." in section 16.2 Storage and Handling.

7 RECOMMENDATIONS FOR AZURITY PHARMACEUTICALS, INC

Table 3. Identified Issues and Recommendations for Azurity Pharmaceuticals, Inc (entire table to be conveyed to Applicant)			
	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
Container Labels and Carton Labeling			
1.	The strength per mL statement (i.e., 5 mg/mL) as presented in the blue boxes lacks sufficient prominence.	We agree with stating the strength as the amount per 5 mL (25 mg per 5 mL) followed by the amount per mL (5 mg/mL) to minimize the risk of wrong product selection and wrong dose medication errors. However, we are concerned that the per mL expression of strength, 5 mg/mL, may be overlooked due to lack of prominence, and contribute to wrong dose medication errors. For example, the amount per 5 mL (25 mg per 5 mL) may be misinterpreted as the recommended dose the user should take.	We recommend increasing the prominence/size of the per mL expression of strength, 5 mg/mL, as presented in the blue boxes relative to the size of the amount per 5 mL. However, ensure that the amount per 5 mL strength presentation (25 mg per 5 mL) remains more prominent/larger than the expression of strength per mL presentation (5 mg/mL).
2.	The statement "Concentrated Formulation" as presented in the blue boxes lacks prominence.	Lack of prominence of the statement "Concentrated Formulation" may contribute to the risk of wrong product selection errors and wrong dose medication errors between the different baclofen concentrations (i.e., 25 mg/5 mL (5 mg/mL) vs. 5 mg/5 mL (1 mg/mL)).	Consider increasing the prominence of the statement "Concentrated Formulation" in the blue boxes.
3.	The established name does not appear to be at	The established name does not appear to be	Ensure the presentation of the established name is at least half

Table 3. Identified Issues and Recommendations for Azurity Pharmaceuticals, Inc (entire table to be conveyed to Applicant)			
	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
	least half the size of the proprietary name.	presented in accordance with 21 CFR 201.10(g)(2).	the size of the proprietary name per CRF 201.10(g)(2).
4.	The "Each contains" statement is presented as total strength per total volume (i.e., (b) (4) .	In accordance with USP General Chapter <7> which states for liquids, "Official drug products not in unit-dose packaging must be labeled to show quantity of each active moiety or drug substance in each mL or in each gram, or express the percentage of each such ingredient."	Revise the statement " (b) (4) located on the side panel to read "Each mL contains 5 mg of baclofen USP" in accordance with USP General Chapter <7>.
5.	As currently presented, there is no space for healthcare providers or patients to write the post-opening expiration date.	To reduce the risk of deteriorated drug medication errors.	We recommend including a space for healthcare providers or patients to write the date that the product is first opened under the storage information. For example: "Date of first opening __/__/__. Discard unused portion XX days/weeks/months after first opening." We recommend "Date of first opening" so patients do not have to calculate the "Discard after" date. Additionally, the "__/__/__" statement will alert the users to write a complete date (month, day, and year) on the container label and carton labeling. Furthermore, we recommend this statement appear sufficiently prominent, through use of bolding, contrasting font

Table 3. Identified Issues and Recommendations for Azurity Pharmaceuticals, Inc (entire table to be conveyed to Applicant)			
	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
			color, highlighted text, or other means.
6.	The recommended dosage statement can be improved.	To ensure consistency with the prescribing information and across the container labels and carton labeling.	Carton: Revise the statement, (b) (4) to read "Recommended Dosage: See prescribing information." Container: Revise the statement, (b) (4) to read "Recommended Dosage: See prescribing information."
Container Label(s)			
1.	The linear bar code is displayed in a horizontal position.	Barcodes placed in a horizontal position may not scan due to container curvature.[g] The bending of barcodes around a curved surface affects how light reflects off them, and, if it is distorted in such a way, scanners cannot capture the entire barcode.	Consider reorienting the linear barcode to a vertical position to ensure the scannability of the barcode.
Carton Labeling			
1.	The company name "azurity" and logo competes in prominence with critical product information on the principal display panel	Critical product information such as the proprietary name, established name, strength, and dosage form should appear as the most	To increase the prominence of important product information, we recommend relocating the company information to the side panel or decreasing the prominence of the company

[g] Neuenschwander M. et al. Practical guide to bar coding for patient medication safety. Am J Health Syst Pharm. 2003 Apr 15;60(8):768-79.

Table 3. Identified Issues and Recommendations for Azurity Pharmaceuticals, Inc (entire table to be conveyed to Applicant)			
	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
	and back panel of the carton labeling.	prominent information on the principal display panel in accordance with 21 CFR 201.15.	information on the principal display panel and back panel.

APPENDICES: METHODS & RESULTS FOR EACH MATERIAL REVIEWED

APPENDIX A. PRODUCT INFORMATION/PRESCRIBING INFORMATION

Table 4 presents relevant product information for Fleqsuvy (baclofen oral suspension), 5 mg/mL that Azurity Pharmaceuticals, Inc. submitted on April 5, 2021 and, the currently marketed drug and listed drug (LD).

Table 4. Relevant Product Information for Fleqsuvy (baclofen oral suspension), 5 mg/mL, Currently Marketed Drug, Ozobax[h] and the Listed Drug, Lioresal[i]

Product Name	Fleqsuvy *(new concentration)*	Ozobax (NDA 208193) *(Marketed drug)*	Lioresal (NDA 017851) *(Listed drug)*
Initial Approval Date	N/A	September 18, 2019	November 22, 1977
Active Ingredient	Baclofen	Baclofen	Baclofen
Indication	• For the treatment of spasticity resulting from multiple sclerosis, particularly for the relief of flexor spasms and concomitant pain, clonus, and muscular rigidity. • May also be of some value in patients with spinal cord injuries and other spinal cord diseases.	• For the treatment of spasticity resulting from multiple sclerosis, particularly for the relief of flexor spasms and concomitant pain, clonus, and muscular rigidity. • May also be of some value in patients with spinal cord injuries and other spinal cord diseases.	• Lioresal is useful for the alleviation of signs and symptoms of spasticity resulting from multiple sclerosis, particularly forthe relief of flexor spasms and concomitant pain, clonus, and muscular rigidity • Lioresal may also be of some value in patients with spinal cord injuries and other spinal cord diseases.
Route of Administration	Oral	Oral	Oral
Dosage Form	Oral Suspension	Oral Solution	Tablet
Strength	25 mg/5 mL (5 mg/mL) [Concentrated formulation]	5 mg/5 mL (1 mg/mL)	10 mg and 20 mg

[h] Ozobax (baclofen) Oral Suspension (NDA 208193) Prescribing Information. Available in Drugs@FDA under NDA 208193: https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/208193s000lbl.pdf

[i] Lioresal (baclofen) Tablet (017851) Prescribing Information. Available in DARRTS under NDA 017851/annual report-32: \\fdswa150\NONECTD\N17851\Y_032\2006-01-13\N17851\labeling\spl\Lioresal.xml

Dose and Frequency	Initiate with a low dosage, preferably in divided doses, administered orally. The following gradually increasing dosage regimen is suggested, but should be adjusted based on clinical response and tolerability: • 5 mL (5 mg) three times a day for three days • 10 mL (10 mg) three times a day for three days • 15 mL (15 mg) three times a day for three days • 20 mL (20 mg) three times a day for three days Additional increases may be necessary up to the maximum recommended dosage of 80 mg daily (20 mg four times a day).	Initiate with a low dosage, preferably in divided doses, administered orally. The following gradually increasing dosage regimen is suggested, but should be adjusted based on clinical response and tolerability: • 5 mL (5 mg) three times a day for three days • 10 mL (10 mg) three times a day for three days • 15 mL (15 mg) three times a day for three days • 20 mL (20 mg) three times a day for three days Additional increases may be necessary up to the maximum recommended dosage of 80 mg daily (20 mg four times a day).	The determination of optimal dosage requires individual titration. Start therapy at a low dosage and increase gradually until optimum effect is achieved (usually between 40-80 mg daily). The following dosage titration schedule is suggested: 5 mg t.i.d. for 3 days 10 mg t.i.d. for 3 days 15 mg t.i.d. for 3 days 20 mg t.i.d. for 3 days Thereafter additional increases may be necessary but the total daily dose should not exceed a maximum of 80 mg daily (20 mg q.i.d.).
How Supplied	An orange to yellow grape-flavored Suspension: 120 mL and 300 mL bottles	It is a clear, colorless solution with a grape aroma and is supplied in bottles of 473 mL	10 mg and 20 mg tablets in bottles of 100 and box of 100 (strips of 10)
Storage	Store at controlled room temperature: 20°C to 25°C (68°F to 77°F)	Must be refrigerated. Store at 2°C to 8°C (36°F to 46°F). Dispense in a tight, light-resistant container with a child-resistant closure.	Do not store above 30°C (86°F). Dispense in tight container (USP).
Container Closure	High Density Polyethylene (HDPE) bottles with white, polypropylene, CRC with a foam liner and heat induction layered inner seal	16 ounce round amber container white (b) (4) CRC with induction seal and foil liner	N/A

APPENDIX E. INFORMATION REQUEST

E.1 Information Request (ISSUED August 6, 2021)

Dear Mr. Beckloff,

We refer to NDA 215602 received on April 5, 2021, for Fleqsuvy (baclofen) Oral Suspension. We note your proposed concentration for Fleqsuvy (baclofen) Oral Suspension is 5 mg/mL, which is five times higher than the currently marketed Ozobax (baclofen) Oral Solution concentration of 1 mg/mL. We are concerned that the introduction of your proposed concentration (5 mg/mL) into the marketplace may increase the potential for wrong dose medication errors with the currently available 1 mg/mL concentration (e.g., 5-fold overdose medication errors). In order to address this concern, we recommend you conduct a risk analysis to characterize the risks of confusion and dosing errors between the currently marketed Ozobax (baclofen) Oral Solution concentration (1 mg/mL) and your proposed concentration (5 mg/mL).

To facilitate our efficient review, please submit your proposed risk analysis, including a description of your proposed mitigation strategies (e.g., label/labeling differentiation strategies) and explain how your proposed strategies will address the identified risks and mitigate the potential for errors. Please submit your response by close of business, August 23, 2021.

E.2 Response (Received August 25, 2021):

Response available via docuBridge via
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The Applicant responded to DMEPA's information request (IR) on August 25, 2021. In their response, the Applicant provided a risk management plan including a description of their risk mitigation strategies (e.g., label/labeling differentiation strategies) to address potential product selection errors and wrong dose medication errors. In addition, the Applicant provided revised prescribing information (PI), container labels and carton labeling, for our review (see Appendix F), to address potential mix-ups between the two baclofen concentrations and potential for wrong dose medication errors. The risk management plan (Non-REMS) includes the following:

1. Use-Related Risk Analysis (URRA) and Label/Labeling Differentiation Strategies
   Available in DocuBridge via: \\CDSESUB1\evsprod\nda215602\0006\m1\us\use-rltd-rsk-analysis-fleqsuvy.pdf

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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,[j] along with postmarket medication error data, we reviewed the following Fleqsuvy (baclofen oral suspension), 5 mg/mL labels and labeling submitted by Azurity Pharmaceuticals, Inc. received August 25, 2021.

- Proposed Container labels
- Proposed Carton labeling
- Prescribing Information (Image not shown)

  Refer to link in docuBridge for Prescribing Information (Track and Clean):

  \\CDSESUB1\evsprod\nda215602\0006\m1\us\baclofen-pi-tracked- changes.docx
  \\CDSESUB1\evsprod\nda215602\0006\m1\us\baclofen-pi.docx

F.2 Label and Labeling Images

(b) (4)

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

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

DATE: 7/14/2021

TO: Division of Neurology I (DN I)
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 215602

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

Rationale

Frontage, Secaucus: The Office of Regulatory Affairs (ORA) inspected the site in October 2018, which falls within the surveillance interval. The inspection was conducted under the following submission: (b) (4)

(b) (4): OSIS inspected the site in (b) (4) which falls within the surveillance interval. The inspection was conducted under the following submissions: (b) (4).

The final classification for both inspections was No Action Indicated (NAI).

Therefore, based on the rationale described above, inspections are not warranted at this time.

Inspection Sites

Facility Type	Facility Name	Facility Address
Clinical	Frontage Clinical Services, Inc.	200 Meadowlands Parkway, Secaucus, NJ
Analytical	(b) (4)	

Ting Wang -S

Digitally signed by Ting Wang -S
DN: c=US, o=U.S. Government, ou=HHS, ou=FDA, ou=People, cn=Ting Wang -S, 0.9.2342.19200300.100.1.1=2000956299
Date: 2021.07.14 08:43:23 -04'00'

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TING WANG
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