CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

211759Orig1s000

OTHER REVIEW(S)

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:	March 5, 2025
Requesting Office or Division:	Division of Anesthesiology, Addiction Medicine, and Pain Medicine (DAAP)
Application Type and Number:	NDA 211759
Product Name, Dosage Form, and Strength:	Vyscoxa (celecoxib) Oral Suspension, 10 mg/mL
Product Type:	Single Ingredient Product
Rx or OTC:	Prescription (Rx)
Applicant Name:	CodaDOSE, Inc. (CodaDOSE)
FDA Received Date:	September 30, 2024 and October 23, 2024
TTT ID #:	2024-11920
DMEPA 1 Safety Evaluator:	Susan Hakeem, PharmD
DMEPA 1 Team Leader:	Valerie S. Vaughan, PharmD

1 INTRODUCTION

As part of the approval process for Vyscoxa (celecoxib) Oral Suspension, the Division of Anesthesiology, Addiction Medicine, and Pain Medicine (DAAP) requested that we review the proposed Vyscoxa Prescribing Information (PI), Medication Guide (MG), and container label for areas of vulnerability that may lead to medication errors.

1.1 BACKGROUND

Vyscoxa (celecoxib) is a proposed 505(b)(2) drug product and the Listed Drug (LD) is Celebrex (celecoxib), NDA 020998.

1.2 REGULATORY HISTORY

CodaDOSE, Inc. previously submitted NDA 211759 on March 9, 2018, which received a Refuse to File on April 30, 2018 from the Agency.[a]

On September 30, 2024, CodaDOSE submitted their Class 2 Resubmission of Celecoxib Oral Suspension (NDA 211759) [b] in response to the deficiencies in the Agency's Refuse to File letter.

2 MATERIALS CONSIDERED

This section lists the materials considered for our review.

Table 1. Materials Considered for this Review	
Materials Considered	Appendix Section
Relevant Product Information	A
Labels and Labeling	B
Previous DMEPA Reviews	C

3 CONCLUSION

We evaluated the proposed Medication Guide and determined that it is acceptable from a medication error perspective.

However, the proposed Vyscoxa Prescribing Information and container label 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 Anesthesiology,

[a] Truong, S. FDA Communication: Refuse to File for Vyscoxa (celecoxib) oral suspension (NDA 211759). Silver Spring (MD): FDA, CDER, OND, DAAAP (US); 2018 OCT 8. NDA 211759. Available from: https://darrts.fda.gov/darrts/faces/ViewDocument?documentId=090140af80494917.

[b] Cover Letter: NDA Resubmission for Celecoxib Oral Suspension (NDA 211759). Flowery Beach (GA): CodaDOSE, Inc.; 2024 SEP 30. Available from: \\CDSESUB1\EVSPROD\nda211759\0006\m1\us\1-2-cover-letters\1-2-2-cover-letters.pdf.

Addiction Medicine, and Pain Medicine (DAAP) in Section 4 and for CodaDOSE, Inc. (CodaDOSE) in Section 5.

4 RECOMMENDATIONS FOR THE DIVISION OF ANESTHESIOLOGY, ADDICTION MEDICINE, AND PAIN MEDICINE (DAAP)

Table 2. Identified Issues and Recommendations for the Division of Anesthesiology, Addiction Medicine, and Pain Medicine (DAAP)

	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
Full Prescribing Information – Section 2 Dosage and Administration			
1.	As currently presented in section 2.1 *General Dosing Instructions,* instructions are written in passive voice (e.g., (b) (4)	Passive voice creates ambiguity regarding the correct actions to take.	We recommend revising statements presented in passive voice to active voice. For example, revise (b) (4) (b) (4) (b) (4) (b) (4) to "The maximum single dose is 200 mg (20 mL)."
Full Prescribing Information – Section 3 Dosage Forms and Strengths			
1.	A description of the dosage form is not provided (e.g., color, and clarity).	A description of identifying characteristics of the dosage form is required per 21 CFR 201.57(c)(4)(ii).	Provide a description of identifying characteristics of the oral suspension in accordance with 21 CFR 201.57(c)(4)(ii). For example, white, opaque, aqueous suspension.
Full Prescribing Information – Section 16 How Supplied/Storage and Handling			
1.	The statement, "protect from light" is missing from Section 16 but included on the container label.	Not including the statement, "protect from light" may result in loss of strength or potency, or destructive alteration of the product's characteristics.	Include the statement, "protect from light" in alignment with the container label.

5 RECOMMENDATIONS FOR CODADOSE, INC. (CODADOSE)

Table 3. Identified Issues and Recommendations for CodaDOSE, Inc. (CodaDOSE) (entire table to be conveyed to Applicant)			
	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
Container Label			
1.	We note the inclusion of a medication guide (MG) as part of the labeling submission; however, the MG statement is missing from the principal display panel (PDP) of the container label.	Per 21 CFR 208.24(d), the label of each container or package, where the container label is too small, of drug product for which a Medication Guide is required under this part shall instruct the authorized dispenser to provide a Medication Guide to each patient to whom the drug product is dispensed and shall state how the Medication Guide is provided. These statements shall appear on the label in a prominent and conspicuous manner.	Ensure the Medication Guide statement appears in accordance with 21 CFR 208.24(d). For example, add "Dispense the accompanying Medication Guide to each patient" to the PDP.
2.	The linear barcode is missing on the container label.	The drug barcode is often used as an additional verification during the medication use process; therefore, it is an important safety feature that should be part of the label and is a requirement per 21 CFR 201.25(c)(2).	Add the product's linear barcode to the container label in accordance with 21CFR 201.25(c)(2). The bar code should be placed in a conspicuous location where it will not be difficult to read because of distorted text. Additionally, the barcode should be placed in an area where it will not be damaged because it appears at the point of label separation (e.g., perforation).

APPENDICES: MATERIALS CONSIDERED FOR THIS REVIEW

APPENDIX A. RELEVANT PRODUCT INFORMATION

Table 4 presents relevant product information for Vyscoxa received on September 30, 2024 from CodaDOSE, and the Listed Drug (LD).

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

Product Name	Vyscoxa	Celebrex[c] (NDA 020998)
Initial Approval Date	NA	December 31, 1998
Active Ingredient	celecoxib	
Indication	Vyscoxa is a nonsteroidal anti-inflammatory drug indicated for these chronic conditions: • Osteoarthritis (OA) • Rheumatoid Arthritis (RA) • Juvenile Rheumatoid Arthritis (JRA) in patients 2 years and older • Ankylosing Spondylitis (AS) Limitations of Use (b) (4) [redacted]	CELEBREX is a nonsteroidal anti-inflammatory drug indicated for: • Osteoarthritis (OA) • Rheumatoid Arthritis (RA) • Juvenile Rheumatoid Arthritis (JRA) in patients 2 years and older • Ankylosing Spondylitis (AS) • Acute Pain (AP) • Primary Dysmenorrhea (PD)
Dosage Form	Oral Suspension	Oral Capsules
Strength	10 mg/mL	50 mg, 100 mg, 200 mg, 400 mg
Route of Administration	Oral	

[c] Celebrex [Prescribing Information]. Drugs@FDA. U.S. Food and Drug Administration. NOV 2024. [cited 2025 FEB 25]. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/020998s058lbl.pdf.

Table 4. Relevant Product Information for Vyscoxa and the Listed Drug (LD).		
Product Name	Vyscoxa	Celebrex[c] (NDA 020998)
Dose and Frequency	• OA: 200 mg (20 mL) once daily or 100 mg (10 mL) twice daily. • RA: 100 mg (10 mL) to 200 mg (20 mL) twice daily. • JRA: 50 mg (5 mL) twice daily in patients 10 kg to 25 kg. 100 mg (10 mL) twice daily in patients more than 25 kg. • AS: 200 mg (20 mL) once daily single dose or 100 mg (10 mL) twice daily. If no effect is observed after 6 weeks, a trial of 200 mg (20 mL) twice daily may be of benefit. Important: Vyscoxa is not recommended at a single dose greater than 200 mg (20 mL). Single doses of the suspension greater than 200 mg (20 mL) may result in celecoxib concentrations higher than expected. For patients who require a single dose over 200 mg (20 mL), use a different celecoxib formulation. Hepatic Impairment: Reduce daily dose by 50% in patients with moderate hepatic impairment (Child-Pugh Class B). Poor Metabolizers of CYP2C9 Substrates: Consider a dose reduction by 50% (or alternative management for JRA) in patients who are known or suspected to be CYP2C9 poor metabolizers. Use the lowest effective dosage for shortest duration consistent with individual patient treatment goals for these chronic conditions.	• OA: 200 mg per day administered as a single dose or as 100 mg twice daily. • RA: 100 mg to 200 mg twice daily. • JRA: pediatric patients (age 2 years and older) is based on weight. For patients ≥10 kg to ≤25 kg the recommended dose is 50 mg twice daily. For patients >25 kg the recommended dose is 100 mg twice daily. For patients who have difficulty swallowing capsules, the contents of a CELEBREX capsule can be added to applesauce. The entire capsule contents are carefully emptied onto a level teaspoon of cool or room temperature applesauce and ingested immediately with water. The sprinkled capsule contents on applesauce are stable for up to 6 hours under refrigerated conditions (2°C to 8°C/35°F to 45°F). • AS: 200 mg daily in single (once per day) or divided (twice per day) doses. If no effect is observed after 6 weeks, a trial of 400 mg daily may be worthwhile. If no effect is observed after 6 weeks on 400 mg daily, a response is not likely and consideration should be given to alternate treatment options. • Management of Acute Pain and Treatment of Primary Dysmenorrhea: 400 mg initially,

Table 4. Relevant Product Information for Vyscoxa and the Listed Drug (LD).		
Product Name	Vyscoxa	Celebrex[c] (NDA 020998)
		followed by an additional 200 mg dose if needed on the first day. On subsequent days, the recommended dose is 200 mg twice daily as needed.
How Supplied	16 oz Amber (b) (4) Bottle	• CELEBREX (celecoxib) 50 mg capsules are white, with reverse printed white on red band of body and cap with markings of 7767 on the cap and 50 on the body. • CELEBREX (celecoxib) 100 mg capsules are white, with reverse printed white on blue band of body and cap with markings of 7767 on the cap and 100 on the body. • CELEBREX (celecoxib) 200 mg capsules are white, with reverse printed white on gold band with markings of 7767 on the cap and 200 on the body. • CELEBREX (celecoxib) 400 mg capsules are white, with reverse printed white on green band with markings of 7767 on the cap and 400 on the body.
Storage	Store at room temperature 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].	Store at room temperature 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].

Table 4. Relevant Product Information for Vyscoxa and the Listed Drug (LD).		
Product Name	Vyscoxa	Celebrex[c] (NDA 020998)
Container Closure	16 oz (b) (4) amber Bottle (b) (4) Child Resistant Closure	No Info

APPENDIX B. LABELS AND LABELING

B.1 List of Labels 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 Vyscoxa labels and labeling submitted by CodaDOSE, Inc. (CodaDOSE).

- Prescribing Information received on September 30, 2024, available from \\CDSESUB1\EVSPROD\nda211759\0006\m1\us\1-14-labeling\1-14-1-draft-labeling\1-14-1-3-draft-pi-clean.pdf.
- Annotated Prescribing Information received on September 30, 2024, available from \\CDSESUB1\EVSPROD\nda211759\0006\m1\us\1-14-labeling\1-14-1-draft-labeling\1-14-1-3-draft-pi.pdf.
- Medication Guide received on September 30, 2024, available from file://cdsesub1/evsprod/NDA211759/0009/m1/us/1-14-labeling/1-14-1-draft-labeling/spl/58dfc0a4-4ec2-4762-91da-55ad402608ee.xml.
- Structured Product Label received on October 23, 2024, available from \\CDSESUB1\EVSPROD\nda211759\0009\m1\us\1-14-labeling\1-14-1-draft-labeling\spl\58dfc0a4-4ec2-4762-91da-55ad402608ee.xml.
- Container label received on September 30, 2024.

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

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APPENDIX C. PREVIOUS DMEPA REVIEWS

On February 25, 2025, we searched for previous DMEPA reviews relevant to this current review using the terms, celecoxib. Our search identified three previous review(s)[e,f,g], and we considered our previous recommendations to see if they are applicable for this current review.

[e] Mwangi, F. Label Comprehension Study Protocol Review for celecoxib (IND 122698). Silver Spring (MD): FDA, CDER, OSE, DMEPA 1 (US); 2024 APR 25. TTT ID No.: 2024-7884.

[f] Birkemeier, D. Use-Related Risk Analysis and Comparative Analyses Review for celecoxib (IND 147372). Silver Spring (MD): FDA, CDER, OSE, DMEPA 1 (US); 2022 NOV 23. TTT ID No.: 2022-2418.

[g] Human Factors Validation Study Protocol-Advice for celecoxib (IND 122698) Silver Spring (MD): FDA, CDER, OSE, DMEPA 1 (US); 2024 APR 25. 2024-7884.

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/s/

SUSAN HAKEEM
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VALERIE S VAUGHAN
03/05/2025 03:11:39 PM

DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Division of Pediatrics and Maternal Health
Office of Rare Diseases, Pediatrics, Urologic
and Reproductive Medicine
Office of New Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Silver Spring, MD 20993
Tel 301-796-2200
FAX 301-796-9744

PLLR Labeling Memorandum

Date: March 27, 2025 **Date consulted:** November 22, 2024

From: Kevin Clark, MD, Medical Officer, Maternal Health
Division of Pediatrics and Maternal Health

Through: Tamara Johnson, MD, MS, Team Leader, Maternal Health
Division of Pediatrics and Maternal Health

To: Division of Anesthesiology, Addiction Medicine, and Pain Medicine (DAAP)

Drug: Vyscoxa (celecoxib) Oral Suspension

NDA : NDA 211759

Applicant: CodaDOSE, Inc.

Subject: Pregnancy and Lactation Labeling

Indication(s): For management of the signs and symptoms of osteoarthritis, rheumatoid arthritis, juvenile rheumatoid arthritis, and ankylosing spondylitis.

Materials Reviewed:

- Applicant's resubmission after refuse-to-file, dated September 30, 2024.
- DAAP consult request dated November 22, 2024.
- Applicant's response to Information Request (IR) dated December 26, 2024.

- DPMH Review of Velyntra (tramadol hydrochloride 44 mg/celecoxib 56 mg), NDA 213426, by Christos Mastroyannis, MD, dated February 20, 2020, DARRTS Reference ID: 4563282[1]
- DPMH Review of Amlodipine Besylate and Celecoxib fixed dose combination tablets, NDA 210045, by Christos Mastroyannis, MD, dated May 7, 2018, DARRTS Reference ID: 4258383[1]
- DPMH NSAIDs PLLR template, dated March 16, 2015, by Melissa Tassinari Ph.D., DABT, DARRTS Reference ID: 3715387

Consult Question:
"We are requesting maternal health team consult to review section 8 (PLLR) of the draft label."

INTRODUCTION and BACKGROUND
On September 30, 2024, the Applicant (CodaDOSE, Inc.) resubmitted a New Drug Application after Refuse-to-File (April 2018) for Vyscoxa (celecoxib) oral suspension under Section 505(b)(2) of the Food, Drug, and Cosmetic Act. The Applicant proposes to rely on FDA's findings of safety and efficacy from the listed drug (LD), Celebrex (celecoxib) capsules, 200 mg (NDA 020998), which was initially approved in 1998. Because the Applicant was not able to demonstrate bioequivalence of celecoxib oral suspension to the LD at individual doses greater than 200 mg, the Applicant is not seeking approval for dosages greater than 200 mg twice daily. As such, the Applicant is not seeking approval for the indications of acute pain or primary dysmenorrhea for which the LD is approved. The Applicant is seeking approval of their product for the management of the signs and symptoms of osteoarthritis (OA), rheumatoid arthritis (RA), juvenile rheumatoid arthritis (JRA), and ankylosing spondylitis (AS).

DAAP consulted the Division of Pediatrics and Maternal Health on November 20, 2024, to assist with the Pregnancy, Lactation, and Females and Males of Reproductive Potential subsections of labeling to comply with the Pregnancy and Lactation Labeling Rule (PLLR).

REVIEW
The reader is referred to previous DPMH labeling reviews mentioned above for celecoxib-containing products and for the non-steroidal anti-inflammatory drugs (NSAIDs) PLLR template. Review of published literature by the Applicant and DPMH from 2015 to present as well as currently approved labeling for the LD Celebrex did not identify any new safety concerns related to celecoxib use during pregnancy and lactation, or its effect on human fertility. As this is a 505(b)(2) NDA, the Applicant did not conduct a review of the pharmacovigilance database for the LD Celebrex.

In their response to an information request dated December 26, 2024, the Applicant proposed the following changes to labeling:

[1] The DPMH reviews for Velyntra and Amlodipine/Celecoxib were part of the materials reviewed but was not a source relied upon for the labeling recommendations in this consult review.

- Premature closure of fetal ductus arteriosus: removed "at about 30 weeks gestation or later" and added [redacted] (b) (4)
- Oligohydramnios/Neonatal renal impairment: removed "at about 20 weeks of gestation or later" and added [redacted] (b) (4) [redacted] (b) (4)

The Applicant's review of published literature from 2015 to present identified the American College of Rheumatology Guidelines which were published in April 2020. The Applicant proposed the above changes to labeling based on these guidelines. However, the current labeling language is based on a Drug Safety Communication (DSC) issued in October 2020. The specific gestational ages included in labeling are based on safety data reviewed by the Agency prior to issuance of the DSC. As such, DPMH recommends that labeling language be reverted back to previously approved language regarding gestational ages for risk windows for premature closure of the fetal ductus arteriosus and oligohydramnios/neonatal renal impairment. Over decades of use of celecoxib since initial approval of the LD, the safety profile and risks of celecoxib use during pregnancy are well established. In addition, there are available data regarding the concentration of celecoxib in breastmilk which are already presented in labeling. As such, DPMH does not recommend postmarketing requirements (PMRs) for pregnancy safety or lactation studies.

CONCLUSIONS
DPMH reviewed published literature and currently approved labeling for celecoxib and found no new safety information that warrants changes to labeling. As discussed above, DPMH disagrees with the Applicant's proposed modifications to labeling and recommends that existing labeling language from the LD be maintained.

RECOMMENDATIONS
DPMH reviewed and/or revised subsections 5.11, 8.1, 8.2, 8.3 and 17 in Vyscoxa (celecoxib) labeling for compliance with the PLLR (see below). DPMH refers to the final NDA action for final labeling.

DPMH Proposed Pregnancy and Lactation Labeling

Comment to the Applicant:
We acknowledge the rationale you provided for these proposed changes, citing the American College of Rheumatology Guidelines which were published in April 2020. However, the current labeling language is based on a Drug Safety Communication (DSC) issued in October 2020. The specific gestational ages included in labeling are based on safety data reviewed by the Agency prior to issuance of the DSC. As such, we reverted back to the previously existing language throughout the labeling regarding gestational ages for risk windows for premature closure of the fetal ductus arteriosus and oligohydramnios/neonatal renal impairment.

The DSC can be found at https://www.fda.gov/safety/medical-product-safety-information/nonsteroidal-anti-inflammatory-drugs-nsaids-drug-safety-communication-avoid-use-nsaids-pregnancy-20

(b) (4)

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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: January 31, 2025

To: Rigoberto A. Roca, MD
Director
Division of Anesthesiology, Addiction Medicine, and Pain Medicine
Office of New Drugs

Partha Roy, Ph.D.
Director
Office of Bioequivalence
Office of Generic Drugs

From: Rubén C. Ayala, Pharm.D.
Lead Pharmacokineticist
New Drug Study Integrity (DNDSI)
Office of Study Integrity and Surveillance (OSIS)

Through: Arindam Dasgupta, Ph.D.
Deputy Division Director, DNDSI, OSIS

Subject: Review of analytical inspection conducted at (b) (4) (b) (4)

1. Inspection summary

OSIS inspected the analytical portion of studies NON-RESPONSIVE NON-RESPONSIVE, NON-RESPONSIVE (ANDA NON-RESPONSIVE, and 915/22 (NDA 211759) conducted at (b) (4)

Form FDA 483 was issued at the inspection close-out. However, after reviewing the Establishment Inspection Report (EIR), exhibits, and the site's response to Form FDA 483, I have no concerns with the reliability of analytical data generated from all three audited studies.

2. Inspected studies:

NDA 211759

Study Number: 915/22
Study Title: "Single dose crossover comparative bioavailability and food effect study of celecoxib 10 mg/1 mL oral suspension versus Celebrex (celecoxib) 200 mg capsules following the administration of a 200 mg dose in healthy adult volunteers/ fasting and fed state."
Sample analysis: (b) (4)

NON-RESPONSIVE

3. Inspection scope:

I inspected (b) (4) located at (b) (4) (b) (4) from (b) (4).

3.1 Previous inspection:

The previous OSIS analytical inspection of (b) (4) was conducted in (b) (4) At the conclusion of the inspection, Form FDA 483 was not issued. However, the following three discussion items were conveyed. The final classification was NAI.

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(b) (4)

Attachments

Attachment 1: Form FDA 483

Attachment 2: Site response to Form FDA 483

Exhibits

Exhibit 1: Batch (b) (4)
(b) (4)

Exhibit 2: (b) (4)
(b) (4)

Exhibit 3: Batch ID# (b) (4)
(b) (4)

Exhibits 4 and 5: Batch ID# (b) (4)
(b) (4)

Exhibits 5 and 6: Batch ID# (b) (4)

Rubén C. Ayala, Pharm.D.
Lead Pharmacokineticist

Draft: RCA 1/31/2025
Edit: AD 01/31/2025

Analytical site FEI: (b) (4)
OSIS File #: (b) (4)
eNSpect Assignment ID: (b) (4)
eNSpect OpID: (b) (4)

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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:	June 17, 2025
To:	Namrata Thakkar, PharmD, BCPS Regulatory Project Manager **Division of Anesthesiology, Addiction Medicine, and Pain Medicine (DAAP)**
Through:	Barbara Fuller, MSN, BSN, RN Team Leader, Patient Labeling **Division of Medical Policy Programs (DMPP)**
From:	Maria Nguyen, MSHS, BSN, RN Senior Patient Labeling Reviewer **Division of Medical Policy Programs (DMPP)** LaToya Sheneé Toombs, PharmD, CPH Regulatory Review Officer **Office of Prescription Drug Promotion (OPDP)**
Subject:	Review of Patient Labeling: Medication Guide (MG)
Drug Name (established name):	VYSCOXA (celecoxib)
Dosage Form and Route:	oral suspension
Application Type/Number:	NDA 211759
Applicant:	codaDOSE, Inc.

1 INTRODUCTION

On September 30, 2024, codaDOSE, Inc. resubmitted for the Agency's review New Drug Application (NDA) 211759 for VYSCOXA (celecoxib) oral suspension in response to a Refuse to File (RFT) dated April 13, 2018. This is a 505(b)(2) application which references CELEBREX (celecoxib) capsules (NDA 020998). VYSCOXA (celecoxib) oral suspension is a nonsteroidal anti-inflammatory drug (NSAID) proposing indications for these chronic conditions:

- Osteoarthritis
- Rheumatoid arthritis
- Juvenile rheumatoid arthritis
- Ankylosing spondylitis

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 Anesthesiology, Addiction Medicine, and Pain Medicine (DAAP) on November 20, 2024 and November 29, 2024, for DMPP and OPDP, respectively, to review the Applicant's proposed Medication Guide (MG) for VYSCOXA (celecoxib) oral suspension.

2 MATERIAL REVIEWED

- Draft VYSCOXA (celecoxib) MG received on September 30, 2024, revised by the Review Division throughout the review cycle, and received by DMPP and OPDP on June 16, 2025.
- Draft VYSCOXA (celecoxib) Prescribing Information (PI) received on September 30, 2024, revised by the Review Division throughout the review cycle, and received by DMPP and OPDP on June 16, 2025.
- Approved CELEBREX (celecoxib), capsule comparator labeling dated November 21, 2024.
- Approved ELYXYB (celecoxib), oral solution comparator labeling dated November 21, 2024.

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%.

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/

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DMPP-OPDP review of celecoxib (VYSCOXA) NDA 211759 MG

LATOYA S TOOMBS
06/18/2025 08:12:09 AM

BARBARA A FULLER
06/18/2025 08:29:17 AM

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

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

Memorandum

Date: June 24, 2025

To: Robert Shibuya, Clinical Reviewer
Division of Anesthesiology, Addiction Medicine, and Pain Medicine (DAAP)

Namrata Thakkar, Regulatory Project Manager, DAAP

Lisa Basham, Associate Director for Labeling, DAAP

From: L. Sheneé Toombs, Regulatory Review Officer
Office of Prescription Drug Promotion (OPDP)

CC: Sam Skariah, Team Leader, OPDP

Subject: OPDP Labeling Comments for VYSCOXA™ (celecoxib) oral suspension

NDA: NDA 211759

In response to DAAP's consult request dated November 29, 2024. OPDP has reviewed the proposed product labeling (PI), Medication Guide, and carton and container labeling for the original NDA submission for VYSCOXA™ (celecoxib) oral suspension.

PI/Medication Guide:
OPDP's review of the proposed PI is based on the draft labeling emailed to OPDP on June 17, 2025, and our comments are provided below.

A combined OPDP and Division of Medical Policy Programs (DMPP) review was completed for the proposed Medication Guide, and comments were sent under separate cover on June 18, 2025.

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 September 30, 2024 and our comments are provided below.

Thank you for your consult. If you have any questions, please contact Sheneé Toombs at (301) 796-4174 or latoya.toombs@fda.hhs.gov.

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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: July 18, 2025

TO: Leah Crisafi, M.D.
Director
Division of Anesthesia, Addiction Medicine, and Pain Medicine (DAAP)
Office of Neuroscience (ON)
Office of New Drugs (OND)

FROM: Makini Cobourne-Duval, Ph.D.
Division of Generic Drug Study Integrity (DGDSI)
Office of Study Integrity and Surveillance (OSIS)

THROUGH: Seongeun (Julia) Cho, Ph.D.
Director
DGDSI
OSIS

SUBJECT: Review of Clinical Inspection of Quinta-Analytica, Prague, Czech Republic

1. Inspection Summary

The Office of Study Integrity and Surveillance (OSIS) arranged a clinical inspection of study 915/22 under NDA 211759 and IND 122698 conducted at Quinta-Analytica, Prague, Czech Republic.

No Form FDA 483 was issued at the inspection close-out. However, there were two discussion items addressed at the inspection close-out. After reviewing the inspectional findings, exhibits provided in EIR, and the firm's response to the discussion items per the EIR, there are no concerns regarding the reliability of the data or human subject protection for inspected study 915/22.

2. Inspected Studies:

NDA 211759

Study Number: 915/22
Study Title: "Single Dose Crossover Comparative Bioavailability and Food Effect Study of Celecoxib 10 mg/1 mL Oral Suspension Versus Celebrex (Celecoxib) 200

mg Capsules Following the Administration of a 200 mg Dose in Healthy Adult Volunteers/Fasting and Fed State"

Dates of study conduct: 8/14/2023 – 9/1/2023

Clinical Investigator: Petr Budera, M.D., Ph.D.
Clinical site: Quinta-Analytica
Prazska 1486/18c, 102 00 Prague 10
Central Bohemian Region
Czech Republic

3. Inspectional Findings

Quinta-Analytica, Prague, Czech Republic

ORA investigator Kathryn Suttling inspected Petr Budera, M.D., Ph.D. at Quinta-Analytica, Prazska 1486/18c, 102 00 Prague 10, Central Bohemian Region, Czech Republic from May 19-23, 2025. As of December 31, 2024, Dr. Budera is no longer employed at the site. He was not present for the inspection and the site was unable to reach him.

3.1 Previous Inspection

This was the first OSIS inspection of Clinical Investigator Petr Budera, M.D., Ph.D. under the BA/BE program. The previous OSIS inspection of the clinical site, Quinta-Analytica, was conducted from October 30 – November 3, 2022. At the conclusion of that inspection, Form FDA 483 was not issued. However, there were 4 discussion items regarding 1) facility access control measures in the subject housing wards, i.e. no written procedures for ensuring locked windows and the presence of drop ceilings, 2) good clinical practice (GCP) documentation issues, 3) an unsigned informed consent form for one subject, and 4) not selecting and isolating retention samples from each shipment prior to performing the studies. The final classification was VAI.

Per the EIR, the OII investigator noted that the ward continues to have drop ceilings. No corrective actions were necessary regarding the removal of drop ceilings or the maintenance of written procedures for ensuring locked windows in the subject housing ward. The site corrected the previously cited retention sample issue via the implementation of an SOP for retention sample selection. OII identified no repeat issues regarding the retention samples nor any issues with informed consent forms. However, multiple instances of GCP documentation issues were

noted again and cited as a discussion item in the current inspection.

3.2 Current Inspection

The current inspection included auditing the following items:

-Case report forms (CRFs)
-Informed consent process
-Subject eligibility criteria verification
-Protocol adherence
-Ethics Committee approvals and correspondence
-Investigational product accountability records and reserves
-Randomization and dosing
-Source data verification
-Adverse event reporting
-Relevant site facilities

3.3 Inspection findings

At the conclusion of the inspection, investigator Kathryn Suttling did not issue Form FDA 483 to the clinical site. However, there were two discussion items addressed at the inspection close-out. The discussion items, the firm's response per the EIR, and my evaluation are presented below.

3.3.1. Discussion Items

Discussion item 1:
Multiple instances of the failure to follow Good Clinical Practice in their documentation practices during the study:

a) There were no initials documented next to one of the "clinically not significant" comments on Vital Signs Record on which multiple individuals would record study data
b) One of the vital signs measurements for Subject (b) (6) (Period 3, 72-hour interval) in the Vital Signs Record was recorded >10 minutes outside scheduled window without documenting the justification/explanation as required by the firm's procedures
c) The handwriting for the time documented for a blood sampling for Subject (b) (6) (Period 1, Interval 17) on the Sample Time Record was difficult to read. The apparent handwrit n time (21:18) of blood sample collection for subject (b) (6) (period 1, interval 17) in the Sample Time Records document is after the time recorded in the Centrifuge Record document (21:12) for the same subject.

d) There was no fluid intake volume reco ed in the Fluid Intake Registration Form for Subject (b) (6) during period 2, interval 25.50.

OSIS Evaluation:
The protocol states that the clinical data will be primarily collected on paper source documents promptly, accurately, and legibly in line with the respective SOPs.

Regarding item (a), the study protocol does not require the staff member to sign their initials on the paper source documents when recording study data. For Vital Signs Record cited in the discussion item, the pertinent details of date and time of the blood pressure and heart rate measurements were recorded and the document was signed and dated by the CI just below the "clinically not significant" comment. Therefore, I conclude item (a) is not a protocol violation and has no impact on the reliability of the study data.

Regarding item (b), the exhibit confirms that one of the vital signs measurements for a Subject (b) (6) was taken >10 minutes (21 minutes) outside of the scheduled window. The protocol states that the vital signs will be measured with allowance up to +10 minutes from the scheduled time. Thus, item (b) is a protocol violation. However, there is no requirement in the protocol that a justification/explanation must be documented in cases when the 10-minute allowance is exceeded. Given the isolated incidence in this case for the single set of vital signs measurements for this single subject, I conclude this issue cited in item (b) is unlikely to have any impact on the study PK data.

Regarding item (c), in my review of the Sample Time Record, I found the handwritten times to be clear and easy to read. From my review of the exhibits, I confirmed that the time of blood sample collection for Subject (b) (6) (period 1, interval 17) in the Sample Time Records document (21:18) is after the time recorded in the Centrifuge Record document (21:12) for that same subject, implying the sample for Subject (b) (6) was centrifuged before it was drawn. Given the context of the documents, however, it is likely there was a documentation error of the recorded blood sampling time in the Sample Time Record where "21:18" was documented instead of the intended "21:10" which was the scheduled time. Since this discussion item may be attributed to a likely documentation error on the Sample Time Record and was an isolated occurrence, I conclude that item (c) has no impact on the integrity of the data.

Regarding item (d) (i.e., fluid intake), the protocol states the subjects' fluid consumption will be specifically documented for both periods for each subject in the Fluid Intake Registration Form. It does not require that the fluid intake volume be

documented. Although no fluid intake volume was recorded for Subject (b) (6) during period 2, interval 25.50, the Fl d Intake Form documents the time and confirms that Subject (b) (6) received fruit tea w/sugar at the correct timepoint. Therefore, I conclude that item (d) is not a protocol violation and has no impact on the study data integrity.

Firm's Response:
The firm's management stated that, regarding item (a), from the handwriting they could identify the individual who wrote the "clinically not significant" comment(s) and that items (c) and (d) have been corrected (on the source document during the inspection). Per the EIR, no further comments/response was provided regarding item (b) cited in this discussion item.

Discussion item 2:
An out-of-range heart rate (HR) measurement for Subject (b) (6) (Period 3, 48-hour) was not evaluated for clinical significance and there was no documentation recording whether the investigator was notified of its occurrence.

OSIS Evaluation:
The protocol states that the Investigator should be notified immediately if HR is outside the 50-90 bpm range prior to dosing and at the scheduled timepoints after dosing. The protocol also states that the Investigator should assess clinical significance of each deviation from the HR ran . The provided exhibit confirms that the HR for Subject (b) (6) at the 48-hour timepoint exceeded the range at 95 bpm. There was no indication in the Vital Signs record that the out-of-range HR was identified, reported to the investigator, or evaluated for clinical significance. Therefore, I conclude that this discussion item is a protocol violation. However, given the mild deviation outside the HR range established by the protocol and the isolated occurrence of this event, I conclude that this protocol violation is unlikely to impact the study PK data. Since there was not evaluation for clinical significance during the study, I advise the review division to evaluate the slightly elevated HR for Subject (b) (6) (Period 3, 48-hour) for any possible impact on subject safety.

Firm's Response:
The firm's management acknowledged the discussion item and stated they will correct it.

Makini Cobourne-Duval, Ph.D.
Pharmacologist

Draft: MCD 6/18/2025, 7/15/2025, 7/16/2025, 7/17/2025, 7/18/2025
Edit: HI 7/17/2025, 7/18/2025; JC 7/17/2025, 7/18/2025

OSIS File #: BE 10454

eNSpect Assignment ID: 257436
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MEMORANDUM
REVIEW OF REVISED LABEL AND LABELING

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

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Date of This Review:	July 18, 2025
Requesting Office or Division:	Division of Anesthesiology, Addiction Medicine, and Pain Medicine (DAAP)
Application Type and Number:	NDA 211759
Product Name, Dosage Form, and Strength:	Vyscoxa (celecoxib) Oral Suspension, 10 mg/mL
Applicant Name:	CodaDOSE, Inc.
FDA Received Date:	June 30, 2025
TTT ID #:	2024-11920-1
DMEPA 1 Safety Evaluator:	Susan Hakeem, PharmD
DMEPA 1 Team Leader:	Damon Birkemeier, PharmD, FISMP

1 PURPOSE OF MEMORANDUM

CodaDOSE, Inc. submitted a revised container label received on June 30, 2025 for Vyscoxa. The Division of Anesthesiology, Addiction Medicine, and Pain Medicine (DAAP) requested that we review the revised container label for Vyscoxa (Appendix A) to determine if it is 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

CodaDOSE, Inc. implemented all of our previous recommendations, however, the revised container label is unacceptable 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 3 for CodaDOSE, Inc.

3 RECOMMENDATIONS FOR CODADOSE, INC.

A. Container Label

1. As currently presented, the container label includes the addition of (b) (4) (b) (4) However, we recommend revising this statement so that the end-user is prompted to write the beyond-use date, which is the date the opened product must be discarded, to minimize the risk of deteriorated drug medication errors. For example: Revise (b) (4) to "Discard after ___/____/____".
2. You have previously indicated that the expiration date will be presented as "YYYY-MM-DD". However, it is not clear if you intend to use only numeric characters as a part of the expiration date format. We are aware of postmarketing reports indicating confusion around the expiration date format when it is presented in alphanumeric characters (e.g., 2021 MA). These postmarketing reports have indicated uncertainty of whether the characters "MA" represent March or May. Thus, please confirm how the month of the expiration date will be defined. 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.

[a] Hakeem, S. Label and Labeling Review for Vyscoxa (NDA 211759). Silver Spring (MD): FDA, CDER, OSE, DMEPA 1 (US); 2025 MAR 05. TTT ID: 2024-11920.

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MEMORANDUM
REVIEW OF REVISED LABEL AND LABELING

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

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Date of This Review:	July 29, 2025
Requesting Office or Division:	Division of Anesthesiology, Addiction Medicine, and Pain Medicine (DAAP)
Application Type and Number:	NDA 211759
Product Name, Dosage Form, and Strength:	Vyscoxa (celecoxib) Oral Suspension, 10 mg/mL
Applicant Name:	CodaDOSE, Inc.
FDA Received Date:	July 24, 2025
TTT ID #:	2024-11920-2
DMEPA 1 Safety Evaluator:	Susan Hakeem, PharmD
DMEPA 1 Team Leader:	Valerie S. Vaughan, PharmD

1 PURPOSE OF MEMORANDUM

CodaDOSE, Inc. submitted a revised container label received on July 24, 2025 for Vyscoxa. The Division of Anesthesiology, Addiction Medicine, and Pain Medicine (DAAP) requested that we review the revised container label for Vyscoxa (Appendix A) to determine if it is 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

CodaDOSE, Inc. confirms that the format for the expiration date YYYY/MM/DD will only include numerical characters. Additionally, CodaDOSE, Inc. implemented all of our recommendations and we have no additional recommendations at this time.

[a] Hakeem, S. Label and Labeling Review Memo for Vyscoxa (NDA 211759). Silver Spring (MD): FDA, CDER, OSE, DMEPA 1 (US); 2025 JUL 18. TTT ID: 2024-11920-1.

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