CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

213260Orig1s000

OTHER REVIEW(S)

MEMORANDUM

REVIEW OF REVISED LABEL AND LABELING

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

Office of Medication Error Prevention and Risk Management (OMEPRM)

Office of Surveillance and Epidemiology (OSE)

Center for Drug Evaluation and Research (CDER)

Date of This Memorandum:	January 25, 2023
Requesting Office or Division:	Division of Diabetes, Lipid Disorders, and Obesity (DDLO)
Application Type and Number:	NDA 213260
Product Name and Strength:	Atorvaliq (atorvastatin calcium) suspension, 20 mg per 5 mL
Applicant/Sponsor Name:	CMP Development LLC (CMP)
TTT ID #:	2022-726-1
DMEPA 1 Safety Evaluator:	Ariane O. Conrad, PharmD, BCACP, CDCES
DMEPA 1 Team Leader:	Idalia E. Rychlik, PharmD

1 PURPOSE OF MEMORANDUM

The Applicant submitted a revised container label for Atorvaliq on December 16, 2022. The Division of Diabetes, Lipid Disorders, and Obesity (DDLO) requested that we review the revised container label for Atorvaliq (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

The Applicant addressed all of our prior recommendations and we find the proposed container label for Atorvaliq acceptable. We have no additional recommendations at this time.

[a] Conrad, A. Label and Labeling Review for Atorvaliq (NDA 213260). Silver Spring (MD): FDA, CDER, OSE, DMEPA 1 (US); 2022 Dec 6. RCM No.: 2022-726.

APPENDIX A. IMAGE OF LABEL RECEIVED ON DECEMBER 16, 2022

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/s/

ARIANE O CONRAD
01/25/2023 11:42:15 AM

IDALIA E RYCHLIK
01/26/2023 08:45:02 PM

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

PATIENT LABELING REVIEW

Date:	January 19, 2023
To:	Martin White, MS Regulatory Project Manager **Division of Diabetes, Lipid Disorders, and Obesity (DDLO)**
Through:	LaShawn Griffiths, MSHS-PH, BSN, RN Associate Director for Patient Labeling **Division of Medical Policy Programs (DMPP)**
From:	Nyedra W. Booker, PharmD, MPH Senior Patient Labeling Reviewer **Division of Medical Policy Programs (DMPP)**
	Ankur Kalola, PharmD Regulatory Review Officer **Office of Prescription Drug Promotion (OPDP)**
Subject:	Review of Patient Labeling: Patient Package Insert (PPI)
Drug Name (established name):	ATORVALIQ (atorvastatin calcium)
Dosage Form and Route:	oral suspension
Application Type/Number:	NDA 213260
Applicant:	CMP Development LLC

1 INTRODUCTION

On January 13, 2020, CMP Development LLC submitted for the Agency's an original New Drug Application (NDA) for ATORVALIQ (atorvastatin calcium) oral suspension (NDA 213260). This submission relies on the Agency's previous findings of safety and effectiveness in accordance with section 505(b)(2) of the Federal Food, Drug and Cosmetic Act for the listed drug LIPITOR (atorvastatin calcium) tablets distributed by Parke-Davis Division of Pfizer Inc.

On October 16, 2020, the Applicant received a Complete Response (CR) notification due to Product Quality, Facility Inspections and Clinical Pharmacology deficiencies.

On July 31, 2022, the Applicant submitted for the Agency's review a class 2 resubmission in response to the CR action letter dated October 16, 2020.

The proposed indication for ATORVALIQ (atorvastatin calcium) oral suspension is as an adjunct therapy to diet to:

- Reduce the risk of MI, stroke, revascularization procedures, and angina in adult patients without CHD, but with multiple risk factors.
- Reduce the risk of MI and stroke in adult patients with type 2 diabetes without CHD, but with multiple risk factors.
- Reduce the risk of non-fatal MI, fatal and non-fatal stroke, revascularization procedures, hospitalization for CHF, and angina in adult patients with CHD.
- Reduce elevated total-C, LDL-C, apo B, and TG levels and increase HDL-C in adult patients with primary hyperlipidemia (heterozygous familial and nonfamilial) and mixed dyslipidemia.
- Reduce elevated TG in adult patients with hypertriglyceridemia and primary dysbetalipoproteinemia.
- Reduce total-C and LDL-C in patients with homozygous familial hypercholesterolemia (HoFH).
- Reduce elevated total-C, LDL-C, and apo B levels in pediatric patients, 10 years to 17 years of age, with heterozygous familial hypercholesterolemia (HeFH) after failing an adequate trial of diet therapy.

This collaborative review is written by the Division of Medical Policy Programs (DMPP) and the Office of Prescription Drug Promotion (OPDP) in response to a request by the Division of Diabetes, Lipid Disorders, and Obesity (DDLO) on December 13, 2022, and December 6, 2022, respectively, for DMPP and OPDP to review the Applicant's proposed Patient Package Insert (PPI) for ATORVALIQ (atorvastatin calcium) oral suspension.

2 MATERIAL REVIEWED

- Draft ATORVALIQ (atorvastatin calcium) oral suspension PPI received on January 13, 2020, revised by the Review Division throughout the review cycle, and received by DMPP and OPDP on January 12, 2023.
- Draft ATORVALIQ (atorvastatin calcium) oral suspension Prescribing Information (PI) received on January 13, 2020, revised by the Review Division

throughout the review cycle, and received by DMPP and OPDP on January 12, 2023.

- LIPITOR (atorvastatin calcium) tablets, for oral use comparator labeling dated December 7, 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 PPI, we have:

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

4 CONCLUSIONS

The PPI 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 PPI 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 PPI.

Please let us know if you have any questions.

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/s/

NYEDRA W BOOKER
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ANKUR S KALOLA
01/19/2023 08:12:30 AM

LASHAWN M GRIFFITHS
01/19/2023 11:15:02 AM

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

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

Memorandum

Date: January 18, 2023

To: Martin White, Regulatory Project Manager, DDLO

Melinda Wilson, Associate Director for Labeling, DDLO

From: Ankur Kalola, Regulatory Review Officer
Office of Prescription Drug Promotion (OPDP)

CC: Susannah O'Donnell, Team Leader, OPDP

Subject: OPDP Labeling Comments for ATORVALIQ® (atorvastatin calcium) oral suspension

NDA: 213260

Background:
In response to DDLO's consult request dated December 6, 2022, OPDP has reviewed the proposed Prescribing Information (PI), Patient Package Insert (PPI), and carton and container labeling for the original NDA submission for Atorvaliq.

PPI
A combined OPDP and Division of Medical Policy Programs (DMPP) review will be completed for the proposed PPI, 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 sent by DDLO (Martin White) on January 12, 2023, and we do not have any comments at this time.

Thank you for your consult. If you have any questions, please contact Ankur Kalola at 301-796-4530 or Ankur.Kalola@fda.hhs.gov.

31 Page(s) of Draft Labeling have been Withheld in Full as B4 (CCI/TS) immediately following this page

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/s/

ANKUR S KALOLA
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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:	December 6, 2022
Requesting Office or Division:	Division of Diabetes, Lipid Disorders, and Obesity (DDLO)
Application Type and Number:	NDA 213260
Product Name, Dosage Form, and Strength:	Atorvaliq[a] (atorvastatin calcium) suspension, 20 mg per 5 mL (4 mg/mL)
Product Type:	Single Ingredient Product
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	CMP Development LLC (CMP)
FDA Received Date:	August 1, 2022
TTT ID #:	2022-726
DMEPA 1 Safety Evaluator:	Ariane O. Conrad, PharmD, BCACP, CDCES
DMEPA 1 Team Leader:	Idalia E. Rychlik, PharmD

[a] Conrad A. Proprietary Name Review for Atorvaliq (NDA 213260). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2022 Oct 21. PNR ID #: 2022-1044724694.

1 REASON FOR REVIEW

As part of the approval process for Atorvaliq (atorvastatin calcium) suspension, the Division of Diabetes, Lipid Disorders, and Obesity (DDLO) requested that we review the proposed Atorvaliq prescribing information (PI) and container label for areas of vulnerability that may lead to medication errors.

Atorvaliq (NDA 213260) was submitted as a 505(b)(2) NDA and the listed drug is Lipitor (NDA 020702, approved December 17, 1996).

2 MATERIALS REVIEWED

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

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

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

3 OVERALL ASSESSMENT OF THE MATERIALS REVIEWED

We performed a risk assessment of the proposed prescribing information (PI) and container label for Atorvaliq to identify areas of vulnerability that may lead to medication errors and other areas of improvement. We determined that the proposed PI is acceptable; however, we identified some areas of concern for the proposed container labels, and we provide our recommendations below in Section 4.1 for the sponsor.

4 CONCLUSION & RECOMMENDATIONS

The proposed PI for Atorvaliq is acceptable; however, the container label is not acceptable from a medication error perspective. We have provided recommendations below in Section 4.1.

4.1 RECOMMENDATIONS FOR CMP DEVELOPMENT LLC

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

A. Container Labels

1. We recommend the presentation of the established name to be presented as "atorvastatin calcium" using lowercase letters for improved differentiation from the proprietary name.
2. We note that you propose to present the product strength as "(b) (4)". However, we note that per USP General Chapter <7> Labeling, the label should only express the strength in a single format (e.g., either 20 mg/5 mL or 4 mg/mL. Therefore, considering the dosage recommendations for your product, we recommend that you remove the "(b) (4)" product strength and revise the presentation of the strength to read "20 mg/5 mL".
3. The strength statement lacks prominence as compared to less important information on the label. We note that the use of the purple font on the product strength and its placement next to the large purple block- utilized for the route of administration statement- may impact the prominence and readability of the product strength. Therefore, we recommend that you revise the appearance of the product strength to improve readability and prominence of this information.
4. Decrease the prominence of the statement "Rx only" by removing the bold font and relocating the statement to the bottom of the label so that it is less prominent than other important information on the label.
5. We note the statement "Attention Pharmacist: dispense to patients in original packaging" appears on the PDP; however, the intended meaning and the need for this statement is unclear. Please provide your justification for including this information on the label.
6. We note there is no clear indication regarding the expiration date of the suspension after the bottle is opened by the end user. Please clarify and add the following statement to the side panel in bold font: "Date of first opening __/__/__. Discard unused portion XX days/weeks/months after first opening." We note that the "__/__/__" statement will alert the users to write a complete date (month, day, and year) on the container label.
7. Consider moving the net quantity statement ("150 mL") to the left side of the PDP so that it appears separately from the NDC number and Rx only statement.

APPENDICES: METHODS & RESULTS FOR EACH MATERIALS REVIEWED

APPENDIX A. PRODUCT INFORMATION/PRESCRIBING INFORMATION

Table 2 presents relevant product information for Atorvaliq received on August 1, 2022 from CMP Development LLC, and the listed drug (LD).

Table 2. Relevant Product Information for Atorvaliq and the Listed Drug		
Product Name	Atorvaliq	Lipitor[b]
Initial Approval Date	N/A	December 17, 1996
Active Ingredient	atorvastatin calcium	
Indication	LIPITOR is an HMG-CoA reductase inhibitor indicated as an adjunct therapy to diet to: • Reduce the risk of MI, stroke, revascularization procedures, and angina in adult patients without CHD, but with multiple risk factors (1.1). • Reduce the risk of MI and stroke in adult patients with type 2 diabetes without CHD, but with multiple risk factors (1.1). • Reduce the risk of non-fatal MI, fatal and non-fatal stroke, revascularization procedures, hospitalization for CHF, and angina in adult patients with CHD (1.1). • Reduce elevated total-C, LDL-C, apo B, and TG levels and increase HDL-C in adult patients with primary hyperlipidemia (heterozygous familial and nonfamilial) and mixed dyslipidemia (1.2). • Reduce elevated TG in adult patients with hypertriglyceridemia and primary dysbetalipoproteinemia (1.2). • Reduce total-C and LDL-C in patients with homozygous familial hypercholesterolemia (HoFH) (1.2). • Reduce elevated total-C, LDL-C, and apo B levels in pediatric patients, 10 years to 17 years of age, with heterozygous familial hypercholesterolemia (HeFH) after failing an adequate trial of diet therapy (1.2).	
Route of Administration	oral	
Dosage Form	suspension	tablet
Strength	20 mg per 5 mL (4 mg/mL)	10 mg, 20 mg, 40 mg, and 80 mg
Dose and Frequency	10 to 80 mg once daily	
How Supplied	150 mL bottles	10 mg and 20 mg tablets: • Bottles of 90, 1000, and 5000 tablets • 10 x 10 unit dose blisters 40 mg tablets: • Bottles of 90, 500, and 2500 tablets • 10 x 10 unit dose blisters

[b] Lipitor [Prescribing Information]. Drugs@FDA. U.S. Food and Drug Administration. 2022 Nov 18. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/020702s077lbl.pdf.

		80 mg tablets: • Bottles of 90, 500, and 2500 tablets • 8 x 8 unit dose blisters
Storage	Store at 20° C – 25° C (68° F–77° F); excursions permitted to 15° C to 30° C (59° F to 86° F). [See USP Controlled Room Temperature].	Store at controlled room temperature 20 -25°C (68 -77°F) [see USP].
Container Closure	amber glass bottles with a child-resistant closure	Bottles, unit dose blister packs

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,[c] along with postmarket medication error data, we reviewed the following Atorvaliq labels and labeling submitted by CMP Development LLC.

- Container label received on August 1, 2022
- Prescribing Information received on August 1, 2022, available from \\CDSESUB1\EVSPROD\nda213260\0016\m1\us\1-14-labeling\1-14-1-draft-labeling\1-14-1-3-draft-pi.docx

B.2 Label and Labeling Images

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

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/s/

ARIANE O CONRAD
12/06/2022 12:45:01 PM

IDALIA E RYCHLIK
12/06/2022 02:30:45 PM

M E M O R A N D U M

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

DATE: 10/11/2022

TO: Division of Diabetes, Lipid Disorders, and Obesity (DDLO)
Office of Cardiology, Hematology, Endocrinology and Nephrology (OCHEN)

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 213260

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) inspected the clinical site in November 2021, which falls within the surveillance interval. The inspection was conducted under the following submission: (b) (4).

The following discussion item was addressed with the site during the inspection:

- (b) (4)

OSIS determined the finding did not impact the safety, rights and welfare of study subjects and concluded that the reviewed studies were reliable.

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 Site

Facility Type	Facility Name	Facility Address
Clinical	Cliantha Research, Ltd.	Cliantha Corporate, TP 86, FP 28/1, Off S.P. Ring Road, Sarkhej, Ahmedabad, Gujarat, India
Analytical	(b) (4)	

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/s/

JOSHUA L PEREZ
11/01/2022 01:33:14 PM

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

REVIEW DEFERRAL MEMORANDUM

Date:	November 10, 2020
To:	Richard E. Whitehead Regulatory Project Manager **Division of Diabetes, Lipid Disorders, and Obesity (DLO)**
Through:	LaShawn Griffiths, MSHS-PH, BSN, RN Associate Director for Patient Labeling **Division of Medical Policy Programs (DMPP)**
From:	Sharon W. Williams, MSN, BSN, RN Senior Patient Labeling Reviewer **Division of Medical Policy Programs (DMPP)**
Subject:	Review Deferred: Patient Package Information (PPI)
Drug Name (established name):	atorvastatin calcium
Dosage Form and Route:	oral suspension
Application Type/Number:	NDA 213260
Applicant:	CMP Development LLC

1 INTRODUCTION

On January 13, 2020, CMP Development LLC submitted for the Agency's review a New Drug Application (NDA) for atorvastatin calcium oral suspension. The purpose of the submission was to seek approval for the use of an oral suspension to:

- Reduce the risk of MI, stroke, revascularization procedures, and angina in adult patients without CHD, but with multiple risk factors
- Reduce the risk of MI and stroke in adult patients with type 2 diabetes without CHD, but with multiple risk factors
- Reduce the risk of non-fatal MI, fatal and non-fatal stroke, revascularization procedures, hospitalization for CHF, and angina in adult patients with CHD
- Reduce elevated total-C, LDL-C, apo B, and TG levels and increase HDL-C in adult patients with primary hyperlipidemia (heterozygous familial and nonfamilial) and mixed dyslipidemia
- Reduce elevated TG in adult patients with hypertriglyceridemia and primary dysbetalipoproteinemia
- Reduce total-C and LDL-C in patients with homozygous familial hypercholesterolemia (HoFH)
- Reduce elevated total-C, LDL-C, and apo B levels in pediatric patients, 10 years to 17 years of age, with heterozygous familial hypercholesterolemia (HeFH) after failing an adequate trial of diet therapy

On January 17, 2020 the Division of Diabetes, Lipid Disorders, and Obesity (DLO) requested that the Division of Medical Policy Programs (DMPP) review the Applicant's proposed PPI for atorvastatin calcium oral suspension.

This memorandum documents the DMPP review deferral of the Applicant's proposed PPI for atorvastatin calcium oral suspension.

2 CONCLUSIONS

On October 16, 2020, DLO issued a Complete Response (CR) letter, due to product quality, facility inspections, and clinical pharmacology. Therefore, DMPP defers comment on the Applicant's patient labeling at this time. A final review will be performed if the Applicant resubmits the application. Please send us a new consult request at such time.

Please notify us if you have any questions.

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/s/

SHARON W WILLIAMS
11/10/2020 08:34:48 AM

LASHAWN M GRIFFITHS
11/10/2020 08:40:33 AM

MEMORANDUM

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

Date of This Memorandum:	July 14, 2020
Requesting Office or Division:	Division of Diabetes, Lipid Disorders, and Obesity (DDLO)
Application Type and Number:	NDA 213260
Product Name and Strength:	(b) (4) (atorvastatin calcium) oral suspension, 20 mg/5 mL (4 mg/mL)
Applicant/Sponsor Name:	CMP Development, LLC
OSE RCM #:	2020-135-1
DMEPA Safety Evaluator:	Melina Fanari, R.Ph.
DMEPA Team Leader:	Sevan Kolejian, PharmD, MBA

1 PURPOSE OF MEMORANDUM

The Applicant submitted a revised container label received on July 7, 2020 for (b) (4) DDLO requested that we review the revised container label for (b) (4) (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

Our previous review also included recommendations related to a proposed carton labeling which is no longer being proposed by the Applicant as stated in the July 7, 2020 submission.

The revised container label is acceptable from a medication error perspective and we have no additional recommendations at this time.

[a] Fanari, M. Label and Labeling Review for (b) (4) (NDA 213260). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2020 May 29. RCM No.: 2020-135.

APPENDIX A. IMAGES OF LABEL AND LABELING RECEIVED ON JULY 7, 2020
available in EDR: \\CDSESUB1\evsprod\NDA213260\0011\m1\us\1-14-labeling

Container Label

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/s/

MELINA N FANARI
07/14/2020 02:57:21 PM

SEVAN H KOLEJIAN
07/14/2020 03:10:00 PM

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

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

Date of This Review:	May 29, 2020
Requesting Office or Division:	Division of Diabetes, Lipid Disorders, and Obesity (DDLO)
Application Type and Number:	NDA 213260
Product Name, Dosage Form, and Strength:	(b) (4) [a](atorvastatin calcium) oral suspension, 20 mg/5 mL (4 mg/mL)
Product Type:	Single Ingredient Product
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	CMP Development, LLC
FDA Received Date:	January 13, 2020
OSE RCM #:	2020-135
DMEPA Safety Evaluator:	Melina Fanari, RPh
DMEPA Team Leader:	Sevan Kolejian, PharmD, MBA

[a] Request for proposed proprietary name (b) (4) was submitted on April 13, 2020. The name is currently under review.

1 REASON FOR REVIEW

As part of the 505(b)(2) NDA approval for [redacted] (b) (4) (atorvastatin calcium) oral suspension, the Division of Diabetes, Lipid Disorders, and Obesity (DDLO) requested that we review the proposed [redacted] (b) (4) Prescribing Information (PI), Patient Prescribing Information (PPI), container label and carton labeling for areas of vulnerability that may lead to medication errors.

2 MATERIALS REVIEWED

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

Table 1. Materials Considered for this Label and Labeling Review

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

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

3 FINDINGS AND RECOMMENDATIONS

Tables 2 and 3 below include the identified medication error issues with the submitted Prescribing Information (PI), Patient prescribing Information (PPI), container label and carton labeling, our rationale for concern, and the proposed recommendation to minimize the risk for medication error.

Table 2. Identified Issues and Recommendations for Division of Division of Diabetes, Lipid Disorders, and Obesity (DDLO)

	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
Full Prescribing Information – Section 16 How Supplied/Storage and Handling			
1.	Information on product description is missing, such as color and flavor.	Improve product identification.	Update this section to include the product description of suspension (color, flavor).

Table 2. Identified Issues and Recommendations for Division of Division of Diabetes, Lipid Disorders, and Obesity (DDLO)			
	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
Full Prescribing Information – Section 17 Patient Counseling Information			
1.	Statement to use an appropriate oral syringe is missing.	Decrease risk of wrong dose errors.	Add the following statements to section 17: "Instruct patients or caregivers to use an oral dosing syringe to correctly measure the prescribed amount of medication. Inform patients that oral dosing syringes may be obtained from their pharmacy."
Patient Prescribing Information			
1.	Statement to use an appropriate oral syringe is missing.	Decrease risk of wrong dose error.	Add the following statements to "How should I take [DRUGNAME}?" section of the patient information: "Use an oral dosing syringe to correctly measure your dose. Ask your pharmacist for an oral dosing syringe if you do not have one."

Table 3. Identified Issues and Recommendations for CMP Development, LLC (entire table to be conveyed to Applicant)			
	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
ALL Carton Labeling and Container Labels			
1.	Established name lacks prominence compared to proprietary name.	Per 21 CFR 201.10(g)(2).	The established name lacks prominence commensurate with the proprietary name. Increase the prominence of the established name taking into account all pertinent factors, including typography, layout, contrast, and other printing

Table 3. Identified Issues and Recommendations for CMP Development, LLC (entire table to be conveyed to Applicant)			
	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
			features in accordance with 21 CFR 201.10(g)(2).
2.	Strength presentation doesn't include mg/mL.	Minimize wrong dose errors.	Revise the product strength presentation as follows: 20 mg/5 mL (b) (4)
3.	'Dispense in original container' statement is missing.	Per 21 CFR 201.100 (b)(7).	Add the following statement to the principle display panel: "Attention Pharmacist: Dispense to patients in original packaging."
4.	Unapproved proprietary name Atorvaliq utilized throughout the container label and carton labeling, was found unacceptable by DMEPA under IND 137915 on December 18, 2019 due to potential confusion with another name that was also under review.	Incorrect product name. The Applicant submitted request for proprietary name, (b) (4) on April 13, 2020.	Remove the proposed proprietary name, Atorvaliq. Until a new name is found to be conditionally acceptable, the placeholder, "TRADENAME" may be used. Once a proprietary name is found conditionally acceptable, the placeholder "Tradename" must be replaced with the proprietary name on the container labels and carton labeling and the revised labels and labeling must be submitted to the Agency for review.
5.	Usual dosage statement requires revisions.	Per 21 CFR 201.55.	Revise the usual dosage statement to read as follows: "Recommended Dosage: See prescribing information."
Container Label			
1.	Net quantity statement is too prominent compared to strength statement.	Decrease risk of numerical confusion between strength and net quantity.	Consider decreasing the net quantity statement such as it is less prominent than the product strength statement.

Table 3. Identified Issues and Recommendations for CMP Development, LLC (entire table to be conveyed to Applicant)			
	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
2.	NDC number is on side panel.	Increase proper product identification.	Consider relocating NDC number to the principle display panel (PDP).
3.	Manufacturer statement is too prominent compared to important information on the label.	Detracts reader away from important information such as proprietary name and strength.	Consider removing or decrease the manufacturer statement on the principle display panel. We note the manufacturer information already exists on the side panel.
4.	The product identifier required under the drug supply chair security act (DSCSA) is missing, although present on container label.	DSCSA requires manufacturers and repackages, respectively, to affix or imprint a product identifier to each package and homogeneous case of a product intended to be introduced in a transaction in (to) commerce beginning November 27, 2017, and November 27, 2018, respectively.	We recommend that you review the draft guidance to determine if the product identifier requirements apply to your product's labeling. The draft guidance is available from: https://www.fda.gov/ucm/groups/fdagov-public/@fdagov-drugs-gen/documents/document/ucm621044.pdf

4 CONCLUSION

Our evaluation of the proposed (b) (4) Prescribing Information (PI), Patient Prescribing Information (PPI), container label and carton labeling identified areas of vulnerability that may lead to medication errors. Above, we have provided recommendations in Error! Reference source not found.Table 2 for the Division and Table 3 for the Applicant. We ask that the Division convey Table 3 in its entirety to CMP Development, LLC so that recommendations are implemented prior to approval of this NDA.

APPENDICES: METHODS & RESULTS FOR EACH MATERIALS REVIEWED

APPENDIX A. PRODUCT INFORMATION/PRESCRIBING INFORMATION

Table 2 presents relevant product information for [redacted] (b) (4) received on January 13, 2020 from CMP Development, LLC, and the listed drug (LD).

Table 2. Relevant Product Information for [redacted] (b) (4) and the Listed Drug		
Product Name	[redacted] (b) (4)	**Lipitor**[b]
Initial Approval Date	N/A	1996
Active Ingredient	atorvastatin calcium	atorvastatin calcium
Indication	-Reduce the risk of MI, stroke, revascularization procedures, and angina in adult patients without CHD, but with multiple risk factors. -Reduce the risk of MI and stroke in adult patients with type 2 diabetes without CHD, but with multiple risk factors. -Reduce the risk of non-fatal MI, fatal and non-fatal stroke, revascularization procedures, hospitalization for CHF, and angina in adult patients with CHD. -Reduce elevated total-C, LDL-C, apo B, and TG levels and increase HDL-C in adult patients with primary hyperlipidemia (heterozygous familial and nonfamilial) and mixed dyslipidemia. -Reduce elevated TG in adult patients with hypertriglyceridemia and primary dysbetalipoproteinemia. -Reduce total-C and LDL-C in patients with homozygous	-Reduce the risk of MI, stroke, revascularization procedures, and angina in adult patients without CHD, but with multiple risk factors. -Reduce the risk of MI and stroke in adult patients with type 2 diabetes without CHD, but with multiple risk factors. -Reduce the risk of non-fatal MI, fatal and non-fatal stroke, revascularization procedures, hospitalization for CHF, and angina in adult patients with CHD. -Reduce elevated total-C, LDL-C, apo B, and TG levels and increase HDL-C in adult patients with primary hyperlipidemia (heterozygous familial and nonfamilial) and mixed dyslipidemia. -Reduce elevated TG in adult patients with hypertriglyceridemia and primary dysbetalipoproteinemia. -Reduce total-C and LDL-C in patients with homozygous

[b] Lipitor [Prescribing Information]. Drugs@FDA. U.S. Food and Drug Administration. 2020 May 18. Available from: https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/020702s074lbl.pdf.

	familial hypercholesterolemia (HoFH). -Reduce elevated total-C, LDL-C, and apo B levels in pediatric patients, 10 years to 17 years of age, with heterozygous familial hypercholesterolemia (HeFH) after failing an adequate trial of diet therapy.	familial hypercholesterolemia (HoFH). -Reduce elevated total-C, LDL-C, and apo B levels in pediatric patients, 10 years to 17 years of age, with heterozygous familial hypercholesterolemia (HeFH) after failing an adequate trial of diet therapy.
Route of Administration	oral	oral
Dosage Form	Oral suspension	Tablet
Strength	20 mg/5 mL (4 mg/mL)	10 mg, 20 mg, 40 mg and 80 mg
Dose and Frequency	10 mg to 80 mg once daily	10 mg to 80 mg once daily
How Supplied	150 glass bottle	Bottles of 90, 500, 1000, 2500 or 5000 tablets and unit dose blisters
Storage	Stored at room temperature 20°C to 25°C (68°F to 77°F.	Stored at room temperature 20°C to 25°C (68°F to 77°F).

APPENDIX B. PREVIOUS DMEPA REVIEWS

On May 18, 2020, we searched for previous DMEPA reviews relevant to this current review using the terms, IND 137915. Our search did not identify any previous relevant review.

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,[c] along with postmarket medication error data, we reviewed the following (b) (4) labels and labeling submitted by CMP Development, LLC.

- Container label received on January 13, 2020
- Carton labeling received on January 13, 2020
- Prescribing Information and Patient Prescribing Information (Image not shown) received on January 13, 2020, available from \\cdsesub1\evsprod\NDA213260\0000\m1\us\1-14-labeling\1-14-1-draft-labeling

F.2 Label and Labeling Images

Container Labels

(b) (4)

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

1 Page(s) of Draft Labeling has been Withheld in Full as B4 (CCI/TS) immediately following this page

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/s/

MELINA N FANARI
05/29/2020 10:26:17 AM

SEVAN H KOLEJIAN
05/29/2020 11:24:57 AM

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: 3/19/2020

TO: Division of Metabolism and Endcrinology Products
Office of Drug Evaluation II

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 213260

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

Rationale

The clinical and analytical inspections occured in (b) (4), which falls within the surveillance interval. The inspections were conducted under the following submissions: (b) (4)

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

Therefore, an inspection is not warranted at this time.

Inspection Sites

Facility Type	Facility Name	Facility Address
Clinical	Veeda Clinical Research Pvt., Ltd.	Shivalik Plaza, Near I.I.M., Ambawadi, Ahmedabad, Gujarat, India
Analytical	(b) (4)	

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/s/

FOLAREMI ADEYEMO
03/19/2020 09:09:03 AM