

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

207795Orig1s000

OTHER REVIEW(S)

Division of Transplant and Ophthalmology Products
Associate Director for Labeling Recommendations
of the Prescribing Information

Product Title	Vyzulta (latanoprostene bunod ophthalmic solution) 0.024%
Applicant	Bausch & Lomb, Inc.
Application/Supplement Number	NDA 207795
Type of Application/Submission	Original/ New molecular entity/Class 2 resubmission
Proposed Indication	Reduction of intraocular pressure in patients with open-angle glaucoma or ocular hypertension
Date FDA Received Resubmission	February 24, 2017
Action Date	August 24, 2017
Review Date	June 15, 2017
Reviewer	Jane Filie, M.D.
Project Manager	Lois Almoza

This Associate Director for Labeling (ADL) memorandum provides recommendations for consideration by the management of the Division of Transplant and Ophthalmology Products (DTOP), on the content and format of the prescribing information (PI) to help ensure that the PI:

- Is compliant with Physician Labeling Rule (PLR) and Pregnancy and Lactation Labeling Rule (PLLR) requirements¹
- Is consistent with labeling guidance recommendations² and with CDER/OND best labeling practices and policies
- Conveys the essential scientific information needed for safe and effective use of the product
- Is clinically meaningful and scientifically accurate
- Is a useful communication tool for health care providers
- Is consistent with other PI with the same active moiety, drug class, or similar indication

This is a class 2 resubmission after the applicant received a Complete Response Letter (July 21, 2016), due to deficiencies at the manufacturing site. No labeling was agreed upon in the initial cycle.

¹ See [January 2006 Physician Labeling Rule](#); 21 CFR [201.56](#) and [201.57](#); and [December 2014 Pregnancy and Lactation Labeling Rule](#) available at <https://www.federalregister.gov/documents/2014/12/04/2014-28241/content-and-format-of-labeling-for-human-prescription-drug-and-biological-products-requirements-for>

²See [PLR Requirements for PI](#) website for PLR labeling guidances.

Labeling Related Consults

I. Medication Error and Proprietary Name Assessments, Division of Medication Error Prevention and Analysis, Office of Surveillance and Epidemiology

The Division of Medication Error Prevention and Analysis (DMEPA) reviewed the proposed container label, carton labeling, and PI for Vyzulta ophthalmic solution to determine whether there are safety concerns with respect to preventable medication errors. The primary reviewer Madhuri R. Patel, Pharm.D. and secondary reviewer, Sarah K. Vee, Pharm.D. reviewed the proposed container label, carton labeling concluded that the PI is acceptable from the medication error perspective (see review dated 05/25/2017). Only one recommendation was made to reduce the size of a graphic (the letter “V” on the principal display panel, to improve readability. This will be addressed in the review by the clinical team leader, W. Boyd, M.D.

DMEPA also evaluated the proposed proprietary name “Vyzulta” in the previous cycle, which was resubmitted in this cycle by the applicant. The primary reviewer, Teresa McMillan, Pharm.D. and secondary reviewer Sarah K. Vee, Pharm.D., concluded that the proposed name is acceptable since it will not misbrand the product and does not raise safety concerns (see DMEPA review dated 6/13/17 and review by Meena Ramachandra, Pharm.D., Office of Prescription Drug Promotion dated 04/21/16). The proprietary name “Vyzulta” was granted on 06/14/17.

II. Pregnancy and Lactation Labeling Rule, Division of Pediatric and Maternal Health

The Division of Pediatric and Maternal Health (DPMH) provided assistance with formatting of the label (see review by Melissa Tassinari, Ph.D., Sr. Clinical Advisor dated 07/21/17). The clinical team accepted their suggestion regarding the language for **8.2 Lactation** (see attached label). Other suggestions regarding the nonclinical content of sections 8 and 13 are deferred to the nonclinical team and are addressed in the review by Andrew McDougal, Ph.D.

III. Risk Evaluation and Mitigation Strategy (REMS), Division of Risk Management, Office of Surveillance and Epidemiology

The Division of Risk Management evaluated the need for REMS for latanoprostene bunod ophthalmic solution 0.024%. DRISK and DTOP concurred that this product **does not** require a REMS based on the following:

- The risks of pigmentation of the iris, periorbital tissue (eyelid), and eyelashes, gradual eyelash changes including increased length, thickness, and number of lashes, intraocular inflammation and macular edema can be communicated through labeling.
- Ophthalmology providers, who treat patients for the reduction of intraocular pressure in the setting of open angle glaucoma or ocular hypertension, are familiar

with the risks associated with this proposed formulation and understand the importance of frequent patient monitoring for the reported risks associated with the use of latanoprostene bunod 0.024%.

Labeling Formatting and Content

Formatting and content recommendations were made with the aim of improving clarity and readability of labeling. The edits and recommendations are shown throughout the proposed labeling in track changes and comments. In the attached PI, the ADL recommendations are presented in track changes (maroon) throughout the working version of the applicant's draft PI and comments (in balloons) begin with the bolded acronym "ADL". This version of the PI includes changes proposed by the applicant (green), nonclinical reviewer, Andrew McDougal, Ph.D. (gray), the clinical pharmacology team leader Phillip Colangelo, Ph.D. (blue), statistical reviewer Abel Eshete, Ph.D. (purple), and chemistry team leader Chunchun Zhang, Ph.D. (pink).

This review does not include final edits by the clinical team. The labeling review by the clinical team has not been finalized at the time of this review. The team does not concur with (b) (4) proposed by the applicant in section **14 CLINICAL STUDIES** (b) (4)

. In order to preserve the comments and track changes, the attached labeling may not reflect the final format of the labeling. A clean copy of the **HIGHLIGHTS OF PRESCRIBING INFORMATION** and **FULL PRESCRIBING INFORMATION: CONTENTS** is included in the **APPENDIX**.

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/s/

JANE FILIE
08/02/2017

RENATA ALBRECHT
08/03/2017

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 25, 2017
Requesting Office or Division: Division of Transplant and Ophthalmology Products (DTOP)
Application Type and Number: NDA 207795
Product Name and Strength: Vyzulta (latanoprostene bunod) Ophthalmic Solution, 0.024%
Product Type: Single Ingredient
Rx or OTC: Rx
Applicant/Sponsor Name: Bausch & Lomb, Inc.
Submission Date: February 24, 2017
OSE RCM #: 2017-535
DMEPA Primary Reviewer: Madhuri R. Patel, PharmD
DMEPA Team Leader (Acting): Sarah K. Vee, PharmD

1 REASON FOR REVIEW

The Division of Transplant and Ophthalmology Products (DTOP) requested that we review the proposed container label, carton labeling, and Prescribing Information (PI) for Vyzulta (latanoprostene bunod) Ophthalmic Solution (NDA 207795), submitted by Bausch & Lomb, Inc. on February 24, 2017, to determine if it is acceptable from a medication error perspective.

2 REGULATORY HISTORY

DMEPA previously reviewed the label and labeling for the proposed product, Vyzulta, in RCM 2015-1755 dated June 1, 2016.^a However, NDA 207795 received a Complete Response (CR) on July 21, 2016, due to facilities deficiencies. Thus, the applicant submitted a complete response to the CR along with revised label and labeling on February 24, 2017.

3 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
Human Factors Study	C – N/A
ISMP Newsletters	D – N/A
FDA Adverse Event Reporting System (FAERS)*	E – N/A
Other	F – N/A
Labels and Labeling	G

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

4 OVERALL ASSESSMENT OF THE MATERIALS REVIEWED

We reviewed proposed container label, carton labeling, and Prescribing Information (PI) to determine whether there are any significant concerns in terms of safety related to preventable medication errors. We find the PI and container label acceptable from a medication error perspective. However, we note that the carton labeling can be improved to enhance the readability and prominence of important information (e.g. proprietary name, established name, strength, route of administration).

5 CONCLUSION & RECOMMENDATIONS

DMEPA finds the Prescribing Information and container label acceptable from a medication error perspective. However, we note that the proposed carton labeling can be improved to

^a Rutledge M. Label and Labeling Review for Vyzulta (latanoprostene bunod) NDA 207795. Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2016 JUN 1. RCM No.: 2015-1755.

enhance the readability and prominence of important information (e.g. proprietary name, established name, strength, route of administration).

5.1 RECOMMENDATIONS FOR BAUSCH & LOMB, INC.

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

- A. Reduce the size of the graphic image with the letter “V” on the principal display panel as it competes in size and prominence with the most important information on the carton labeling such as proprietary name, established name, and strength, as per Draft Guidance: Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors, April 2013.

APPENDICES: METHODS & RESULTS FOR EACH MATERIALS REVIEWED

APPENDIX A. PRODUCT INFORMATION/PRESCRIBING INFORMATION

Table 2 presents relevant product information for Vyzulta that Bausch & Lomb, Inc. submitted on February 24, 2017.

Table 2. Relevant Product Information for Vyzulta	
Initial Approval Date	N/A
Active Ingredient	latanoprostene bunod
Indication	reduction of intraocular pressure in patients with open-angle glaucoma or ocular hypertension
Route of Administration	Ophthalmic
Dosage Form	Ophthalmic Solution
Strength	0.024%
Dose and Frequency	One drop in the affected eye(s) once daily in the evening
How Supplied	natural low density polyethylene, 7.5 mL bottle with dropper tip and a turquoise cap filled with a 5 mL fill volume
Storage	Unopened bottle should be stored refrigerated at 2° to 8°C (36° to 46°F). Once a bottle is opened it may be stored at 2° to 25°C (36° to 77°F) for 8 weeks
Container Closure	n/a

APPENDIX B. PREVIOUS DMEPA REVIEWS

B.1 Methods

On May 17, 2017, we searched the L:drive and AIMS using the terms, Vyzulta and latanoprostene bunod, to identify reviews previously performed by DMEPA.

B.2 Results

Our search identified one previous label and labeling review^b and we confirmed that the previous recommendation was not implemented.

^b Rutledge M. Label and Labeling Review for Vyzulta (latanoprostene bunod) NDA 207795. Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2016 JUN 1. RCM No.: 2015-1755.

APPENDIX C. HUMAN FACTORS STUDY – N/A

APPENDIX D. ISMP NEWSLETTERS – N/A

APPENDIX E. FDA ADVERSE EVENT REPORTING SYSTEM (FAERS) – N/A

APPENDIX F. OTHER – N/A

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/s/

MADHURI R PATEL
05/25/2017

SARAH K VEE
05/25/2017

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: June 1, 2016
Requesting Office or Division: Division of Transplant and Ophthalmology Products (DTOP)
Application Type and Number: NDA 207795
Product Name and Strength: Vyzulta (Latanoprostene bunod) Ophthalmic Solution, 0.024%
Product Type: Single Ingredient
Rx or OTC: Rx
Applicant/Sponsor Name: Valeant Pharmaceuticals North America LLC
Submission Date: July 21, 2015
OSE RCM #: 2015-1755
DMEPA Primary Reviewer: Michelle Rutledge, PharmD
DMEPA Team Leader: Yelena Maslov, PharmD

1 REASON FOR REVIEW

This review evaluates the proposed container label, carton labeling, and prescribing information for Vyzulta (Latanoprostene bunod) Ophthalmic Solution, 0.024%, NDA 207795, for areas of vulnerability and could lead to medication errors. This is a New Drug Application.

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.

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

N/A=not applicable for this review

*We do not typically search FAERS for label and labeling reviews unless we are aware of medication errors through our routine postmarket safety surveillance

3 OVERALL ASSESSMENT OF THE MATERIALS REVIEWED

Valeant Pharmaceuticals North America LLC is seeking approval of Vyzulta Ophthalmic Solution, for the reduction of intraocular pressure in patients with open-angle glaucoma or ocular hypertension. The proposed product will provide an alternative option in the ophthalmological setting for this indication.

We reviewed the proposed label and labeling and identified the following areas of vulnerability to errors.

- Readability and prominence of important information on the carton labeling

4 CONCLUSION & RECOMMENDATIONS

DMEPA concludes that the proposed carton labeling can be improved to increase the readability and prominence of important information.

4.1 RECOMMENDATIONS FOR THE VALEANT PHARMACEUTICALS NORTH AMERICA LLC

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

A. CARTON LABELING

1. Consider reducing the size of the graphic image with letter “V” on the principal display panel as it takes away attention from the most important information on the carton labeling such as proprietary name, established name, and strength statements.

APPENDICES: METHODS & RESULTS FOR EACH MATERIALS REVIEWED

APPENDIX A. PRODUCT INFORMATION/PRESCRIBING INFORMATION

Table 2 presents relevant product information for Vyzulta that Valeant Pharmaceuticals North American LLC submitted on July 21, 2015.

Table 2. Relevant Product Information for Vyzulta	
Initial Approval Date	N/A
Active Ingredient	Latanoprostene bunod ophthalmic solution
Indication	Reduction of intraocular pressure in patients with open angle glaucoma or ocular hypertension
Route of Administration	Topical ophthalmic
Dosage Form	Ophthalmic solution
Strength	0.024%
Dose and Frequency	One drop in the affected eye(s) once daily in the evening
How Supplied	Low density polyethylene, 7.5 mL bottle with dropper tip and a turquoise cap filled with a 5 mL fill volume
Storage	(b) (4) under refrigeration at 2° to 8 °C (36° to 46°F). Protect from light. Protect from freezing.

APPENDIX B. PREVIOUS DMEPA REVIEWS

B.1 Methods

On May 26, 2016, we searched the L: drive using the terms, Vyzulta to identify reviews previously performed by DMEPA.

B.2 Results

Our search identified no previous label and labeling reviews.

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APPENDIX D. ISMP NEWSLETTERS

D.1 Methods

On May 27, we searched the Institute for Safe Medication Practices (ISMP) newsletters using the criteria below, and then individually reviewed each newsletter. We limited our analysis to newsletters that described medication errors or actions possibly associated with the label and labeling.

ISMP Newsletters Search Strategy	
ISMP Newsletter(s)	Acute Care
Search Strategy and Terms	Match Exact Word or Phrase: Vyzulta

D.2 Results

No articles were located.

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/s/

MICHELLE K RUTLEDGE
06/01/2016

YELENA L MASLOV
06/02/2016

Clinical Inspection Summary

Date	April 21, 2015
From	Roy Blay, Ph.D., Reviewer, GCPAB\OSI Janice K. Pohlman, M.D., M.P.H., Team Leader, GCPAB\OSI Kassa Ayalew, M.D., M.P.H., Branch Chief, GCPAB\OSI
To	Lois Almoza, Regulatory Project Manager Lucious Lim, M.D., Medical Officer William Boyd, M.D., Medical Team Leader Division of Transplant and Ophthalmology Products
NDA/BLA #	NDA 207795
Applicant	Bausch & Lomb Inc.
Drug	Vyzulta (latanoprostene bunod ophthalmic solution), 0.024%
NME (Yes/No)	Yes
Therapeutic Classification	Standard Review
Proposed Indication(s)	Reduction of intraocular pressure for patients with open-angle glaucoma or ocular hypertension
Consultation Request Date	August 28, 2015
Summary Goal Date	May 1, 2016
Action Goal Date	July 1, 2016
PDUFA Date	July 21, 2016

1. OVERALL ASSESSMENT OF FINDINGS AND RECOMMENDATIONS

The clinical sites of Drs. Christie and Wirta were inspected in support of this NDA. The final classification of the inspection of Dr. Christie was Voluntary Action Indicated (VAI) due to deviations from protocol in the protocol-specified storage temperature of the test article. Discussion with the chemistry reviewer indicated that the noted temperature excursions would not have affected the stability of the test article. The final classification of the inspection of Dr. Wirta was No Action Indicated (NAI).

Based on the results of the clinical investigator inspections, the study appears to have been conducted adequately, and the data generated by these sites appear acceptable in support of the respective indication.

2. BACKGROUND

The Applicant submitted this NDA to support the use of Vyzulta for the reduction of intraocular pressure (IOP) for patients with open-angle glaucoma or ocular hypertension.

Protocols 769 and 770 entitled, "A Randomized, Multicenter, Double-Masked, Parallel-Group Study Comparing the Safety and Efficacy of BOL-303259-X 0.024% (Latanoprostene Bunod)

Ophthalmic Solution With Timolol Maleate Ophthalmic Solution 0.5% in Subjects With Open-Angle Glaucoma or Ocular Hypertension – APOLLO Study” and “A Randomized, Multicenter, Double-Masked, Parallel-Group Study Comparing the Safety and Efficacy of BOL-303259-X 0.024% (Latanoprostene Bunod) Ophthalmic Solution With Timolol Maleate Ophthalmic Solution 0.5% in Subjects With Open-Angle Glaucoma or Ocular Hypertension – LUNAR Study” respectively, were inspected in support of this application.

The sites of Drs. Christie and Wirta were chosen for inspection based on relatively large study enrollments and a lack of recent inspections.

Protocol 769 was conducted at 47 clinical sites in the United States (US), Bulgaria, and the Czech Republic with first enrollment on January 31, 2013 and an interim data cutoff date of December 19, 2014. The study analyzed a total of 417 subjects. The three-month efficacy phase of this study involved subjects being randomized to either latanoprostene or timolol maleate for 3 months from Visit 3 (Day 0) through Visit 6 (Month 3). The primary objective was to demonstrate that the mean intraocular pressure (IOP) reduction after 3 months (90 days) of treatment with latanoprostene was noninferior to timolol maleate. The sponsor’s conclusion with regard to efficacy was that the mean IOP reduction after 3 months (90 days) of treatment with latanoprostene was non-inferior, and, in fact, superior to treatment with timolol maleate.

Protocol 770 was conducted at 46 domestic and foreign sites comprising 420 randomized subjects with first subject enrollment on January 28, 2013, and the last subject completed on November 26, 2014. The primary objective was to demonstrate that the mean intraocular pressure (IOP) reduction after 3 months (90 days) of treatment with latanoprostene was non-inferior to timolol maleate. The sponsor’s conclusion with regard to efficacy was that the mean IOP reduction after 3 months (90 days) of treatment with latanoprostene was non-inferior to timolol maleate.

3. RESULTS (by site):

Site #/ Name of CI/ Address	Protocol #/ # of Subjects (enrolled)	Inspection Dates	Classification
130785/ William C. Christie, M.D. Scott & Christie and Associates, PC 1101 Freeport Road Pittsburgh, PA 15238 and 105 Brandt Drive Cranberry Township, PA 16066	769/ 35	6-14 Jan 2016	VAI
330042/ David L. Wirta, M.D. Eye Research Foundation 520 Superior Avenue, Suite 235 Newport Beach, CA 92663	770/ 49	17-20 Nov 2015	NAI

Compliance Classifications

NAI = No deviation from regulations.

VAI = Deviation(s) from regulations.

OAI = Significant deviations from regulations. Data unreliable.

Pending = Preliminary classification based on information in 483 or preliminary communication with the field; EIR has not been received from the field, and complete review of EIR is pending. Final classification occurs when the post-inspectional letter has been sent to the inspected entity.

1. William C. Christie, M.D.

At this site for Protocol 769, 45 subjects were screened, nine subjects failed screening and one subject withdrew consent, 35 subjects were enrolled in the study, one subject discontinued due to an adverse event, and 34 subjects completed the study. Source data was compared to line listings. The study records of the enrolled subjects were reviewed in detail with respect to randomization, early terminations, adverse events, and intraocular pressures (IOPs). The records of 18 subjects were reviewed for general protocol adherence and reporting of concomitant medications and illnesses. Other records reviewed included, but were not limited to, financial disclosure, delegation of authority, sponsor, monitor, and IRB communications, and test article accountability and storage.

Signed informed consent was obtained from all enrolled subjects prior to study entry. A Form FDA 483 was issued at the conclusion of the inspection noting that the study deviated from protocol in that the refrigerator containing the study drug was at a temperature (0° C) below the specified storage temperature of 2-8° C for at least 31 days at varying intervals, and that there were 19 days where the temperature was not recorded. Follow up with the review chemist indicated there were no stability concerns with the temperature excursions to 0° C. Dr. Christie acknowledged his responsibility for the overall conduct of the study in his written response dated January 26, 2016. For those periods when refrigerator temperatures were not recorded, Dr. Christie said that review of temperature logs prior to and after these periods provided no basis for concluding that temperature excursions occurred in those periods. Dr. Christie appears to have implemented corrective actions to his study practices that should prevent similar findings in future studies.

This finding of improper drug storage conditions would not appear to adversely affect subject safety or data quality. The data generated by this site appear acceptable in support of the respective indication.

2. David L. Wirta, M.D.

At this site for Protocol 770, 72 subjects were screened, 50 subjects were randomized, and 40 subjects completed the study. Per the study report, three subjects were discontinued for noncompliance with the protocol, four subjects experienced adverse events, and three subjects withdrew from the study. Records reviewed included, but were not limited to, informed consent, financial disclosure, medical histories, inclusion/exclusion criteria, concomitant medications, sponsor and IRB communications, and test article storage and accountability. The site was responsible for transferring the source data to electronic Case Report Forms (eCRFs). For primary endpoints and adverse events, source records for all subjects completing the study were compared against data listings.

A Form FDA 483 was not issued at the conclusion of the inspection. Review of the records noted above revealed no significant discrepancies or regulatory violations.

The study appears to have been conducted adequately, and the data generated by this site appear acceptable in support of the respective indication.

{See appended electronic signature page}

Roy Blay, Ph.D.
Good Clinical Practice Assessment Branch
Division of Clinical Compliance Evaluation
Office of Scientific Investigations

CONCURRENCE:

{See appended electronic signature page}

Kassa Ayalew, M.D., M.P.H
Branch Chief
Good Clinical Practice Assessment Branch
Division of Clinical Compliance Evaluation
Office of Scientific Investigations

CC:

Central Doc. Rm.

DTOP/Division Director/Albrecht

DTOP/Medical Team Leader/Boyd

DTOP/MO/Lim

DTOP/Project Manager/Almoza

OSI/Office Director/Burrow

OSI/DCCE/ Division Director/Khin

OSI/DCCE/Branch Chief/Ayalew

OSI/DCCE/Team Leader/Pohlman

OSI/DCCE/GCP Reviewer/Blay

OSI/ GCP Program Analysts/ Patague/Peacock

OSI/Database PM/Walters

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/s/

ROY A BLAY
04/22/2016

KASSA AYALEW
04/22/2016

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

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

Memorandum

Date: April 21, 2016

To: Lois Almoza, Regulatory Health Project Manager
Division of Transplant and Ophthalmology Products (DTOP)

From: Meena Ramachandra PharmD, Regulatory Review Officer
Office of Prescription Drug Promotion (OPDP)

Subject: Vyzulta (latanoprostene bunod ophthalmic solution), 0.024% For
Topical Ophthalmic Use
NDA 207795

As requested in DTOP's consult dated September 3, 2015, OPDP has reviewed the draft PI and proposed carton and container labeling for Vyzulta (latanoprostene bunod ophthalmic solution), 0.024%.

OPDP reviewed the proposed substantially complete version of the PI titled, "draft-labeling-text.doc" accessed via the DTOP SharePoint website on April 14, 2016. OPDP's comments are provided in the attached clean version of the substantially complete labeling.

OPDP has no comments on the version of the proposed carton and container labeling titled "1-14-1-1 Draft Carton Label.pdf" and "1-14-1-1 Draft Container Label.pdf" accessed on the DTOP SharePoint website on April 14, 2016.

Thank you for the opportunity to review and provide comments on this proposed labeling. If you have any questions please contact Meena Ramachandra (240) 402-1348 or Meena.Ramachandra@fda.hhs.gov.

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/s/

MEENA RAMACHANDRA
04/21/2016

RPM FILING REVIEW

(Including Memo of Filing Meeting)

To be completed for all new NDAs, BLAs, and Efficacy Supplements [except SE8 (labeling change with clinical data) and SE9 (manufacturing change with clinical data)]

Application Information		
NDA # 207795 BLA# N/A	NDA Supplement #: S- N/A BLA Supplement #: S- N/A	Efficacy Supplement Category: <input type="checkbox"/> New Indication (SE1) <input type="checkbox"/> New Dosing Regimen (SE2) <input type="checkbox"/> New Route Of Administration (SE3) <input type="checkbox"/> Comparative Efficacy Claim (SE4) <input type="checkbox"/> New Patient Population (SE5) <input type="checkbox"/> Rx To OTC Switch (SE6) <input type="checkbox"/> Accelerated Approval Confirmatory Study (SE7) <input type="checkbox"/> Labeling Change With Clinical Data (SE8) <input type="checkbox"/> Manufacturing Change With Clinical Data (SE9) <input type="checkbox"/> Animal Rule Confirmatory Study (SE10) N/A
Proprietary Name: Vesneo (under review by OSE) Established/Proper Name: latanoprostene bunod Dosage Form: ophthalmic solution Strengths: 0.024%		
Applicant: Bausch & Lomb Inc. Agent for Applicant (if applicable): N/A		
Date of Application: July 21, 2015 Date of Receipt: July 21, 2015 Date clock started after UN: N/A		
PDUFA Goal Date: July 21, 2016		Action Goal Date (if different): N/A
Filing Date: September 19, 2015		Date of Filing Meeting: August 31, 2015
Chemical Classification (original NDAs only) : <input checked="" type="checkbox"/> Type 1- New Molecular Entity (NME); NME and New Combination <input type="checkbox"/> Type 2- New Active Ingredient; New Active Ingredient and New Dosage Form; New Active Ingredient and New Combination <input type="checkbox"/> Type 3- New Dosage Form; New Dosage Form and New Combination <input type="checkbox"/> Type 4- New Combination <input type="checkbox"/> Type 5- New Formulation or New Manufacturer <input type="checkbox"/> Type 7- Drug Already Marketed without Approved NDA <input type="checkbox"/> Type 8- Partial Rx to OTC Switch		
Proposed indication(s)/Proposed change(s): reduction of intraocular pressure in patients with open-angle glaucoma or ocular hypertension		
Type of Original NDA: AND (if applicable) Type of NDA Supplement:		<input checked="" type="checkbox"/> 505(b)(1) <input type="checkbox"/> 505(b)(2) <input type="checkbox"/> 505(b)(1) <input type="checkbox"/> 505(b)(2) N/A
If 505(b)(2): Draft the "505(b)(2) Assessment" review found at: http://inside.fda.gov:9003/CDER/OfficeofNewDrugs/ImmediateOffice/UCM027499		

Type of BLA	<input type="checkbox"/> 351(a) <input type="checkbox"/> 351(k) N/A
<i>If 351(k), notify the OND Therapeutic Biologics and Biosimilars Team</i>	
Review Classification:	<input checked="" type="checkbox"/> Standard <input type="checkbox"/> Priority
<i>The application will be a priority review if:</i>	<input type="checkbox"/> Pediatric WR
<ul style="list-style-type: none"><i>A complete response to a pediatric Written Request (WR) was included (a partial response to a WR that is sufficient to change the labeling should also be a priority review – check with DPMH)</i>	<input type="checkbox"/> QIDP
<ul style="list-style-type: none"><i>The product is a Qualified Infectious Disease Product (QIDP)</i>	<input type="checkbox"/> Tropical Disease Priority Review Voucher
<ul style="list-style-type: none"><i>A Tropical Disease Priority Review Voucher was submitted</i>	<input type="checkbox"/> Pediatric Rare Disease Priority Review Voucher
<ul style="list-style-type: none"><i>A Pediatric Rare Disease Priority Review Voucher was submitted</i>	
Resubmission after withdrawal? NO	Resubmission after refuse to file? NO
Part 3 Combination Product? NO	<input type="checkbox"/> Convenience kit/Co-package
<i>If yes, contact the Office of Combination Products (OCP) and copy them on all Inter-Center consults</i>	<input type="checkbox"/> Pre-filled drug delivery device/system (syringe, patch, etc.)
	<input type="checkbox"/> Pre-filled biologic delivery device/system (syringe, patch, etc.)
	<input type="checkbox"/> Device coated/impregnated/combined with drug
	<input type="checkbox"/> Device coated/impregnated/combined with biologic
	<input type="checkbox"/> Separate products requiring cross-labeling
	<input type="checkbox"/> Drug/Biologic
	<input type="checkbox"/> Possible combination based on cross-labeling of separate products
	<input type="checkbox"/> Other (drug/device/biological product)

<input type="checkbox"/> Fast Track Designation	<input type="checkbox"/> PMC response
<input type="checkbox"/> Breakthrough Therapy Designation <i>(set the submission property in DARRTS and notify the CDER Breakthrough Therapy Program Manager)</i>	<input type="checkbox"/> PMR response:
<input type="checkbox"/> Rolling Review	<input type="checkbox"/> FDAAA [505(o)]
<input type="checkbox"/> Orphan Designation	<input type="checkbox"/> PREA deferred pediatric studies (FDCA Section 505B)
<input type="checkbox"/> Rx-to-OTC switch, Full	<input type="checkbox"/> Accelerated approval confirmatory studies (21 CFR 314.510/21 CFR 601.41)
<input type="checkbox"/> Rx-to-OTC switch, Partial	<input type="checkbox"/> Animal rule postmarketing studies to verify clinical benefit and safety (21 CFR 314.610/21 CFR 601.42)
<input type="checkbox"/> Direct-to-OTC	
Other:	

Collaborative Review Division (if OTC product): N/A

List referenced IND Number(s): IND 73435, (b) (4)

Goal Dates/Product Names/Classification Properties	YES	NO	NA	Comment
PDUFA and Action Goal dates correct in tracking system? <i>If no, ask the document room staff to correct them immediately. These are the dates used for calculating inspection dates.</i>	X	<input type="checkbox"/>		
Are the established/proper and applicant names correct in tracking system? <i>If no, ask the document room staff to make the corrections. Also, ask the document room staff to add the established/proper name to the supporting IND(s) if not already entered into tracking</i>	X	<input type="checkbox"/>		

<i>system.</i>				
Is the review priority (S or P) and all appropriate classifications/properties entered into tracking system (e.g., chemical classification, combination product classification, orphan drug)? <i>Check the New Application and New Supplement Notification Checklists for a list of all classifications/properties at:</i> http://inside.fda.gov:9003/CDER/OfficeofBusinessProcessSupport/ucm163969.htm <i>If no, ask the document room staff to make the appropriate entries.</i>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	Review Priority: S
Application Integrity Policy	YES	NO	NA	Comment
Is the application affected by the Application Integrity Policy (AIP)? <i>Check the AIP list at:</i> http://www.fda.gov/ICECI/EnforcementActions/ApplicationIntegrityPolicy/default.htm	<input type="checkbox"/>	<input checked="" type="checkbox"/>		
If yes, explain in comment column.			<input checked="" type="checkbox"/>	
If affected by AIP, has OC been notified of the submission? If yes, date notified:	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	
User Fees	YES	NO	NA	Comment
Is Form 3397 (User Fee Cover Sheet)/Form 3792 (Biosimilar User Fee Cover Sheet) included with authorized signature?	<input checked="" type="checkbox"/>	<input type="checkbox"/>		
<u>User Fee Status</u> <i>If a user fee is required and it has not been paid (and it is not exempted or waived), the application is unacceptable for filing following a 5-day grace period. Review stops. Send Unacceptable for Filing (UN) letter and contact user fee staff.</i>	Payment for this application (<i>check daily email from UserFeeAR@fda.hhs.gov</i>): <input checked="" type="checkbox"/> Paid <input type="checkbox"/> Exempt (orphan, government) <input type="checkbox"/> Waived (e.g., small business, public health) <input type="checkbox"/> Not required Note: Receipt date for user fee is June 17, 2015			
<i>If the firm is in arrears for other fees (regardless of whether a user fee has been paid for this application), the application is unacceptable for filing (5-day grace period does not apply). Review stops. Send UN letter and contact the user fee staff.</i>	<input checked="" type="checkbox"/> Not in arrears <input type="checkbox"/> In arrears			
User Fee Bundling Policy <i>Refer to the guidance for industry, Submitting Separate Marketing Applications and Clinical Data for Purposes of Assessing User Fees at:</i> http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM079320.pdf	Has the user fee bundling policy been appropriately applied? <i>If no, or you are not sure, consult the User Fee Staff.</i> <input checked="" type="checkbox"/> Yes <input type="checkbox"/> No			
505(b)(2) (NDAs/NDA Efficacy Supplements only)	YES	NO	NA	Comment
Is the application a 505(b)(2) NDA? (<i>Check the 356h form,</i>	<input type="checkbox"/>	<input checked="" type="checkbox"/>		

cover letter, and annotated labeling). If yes , answer the bulleted questions below:							
<ul style="list-style-type: none"> Is the application for a duplicate of a listed drug and eligible for approval under section 505(j) as an ANDA? 				<input type="checkbox"/>	<input type="checkbox"/>	X	
<ul style="list-style-type: none"> Is the application for a duplicate of a listed drug whose only difference is that the extent to which the active ingredient(s) is absorbed or otherwise made available to the site of action is less than that of the reference listed drug (RLD)? [see 21 CFR 314.54(b)(1)]. 				<input type="checkbox"/>	<input type="checkbox"/>	X	
<ul style="list-style-type: none"> Is the application for a duplicate of a listed drug whose only difference is that the rate at which the proposed product's active ingredient(s) is absorbed or made available to the site of action is unintentionally less than that of the listed drug [see 21 CFR 314.54(b)(2)]? <p><i>If you answered yes to any of the above bulleted questions, the application may be refused for filing under 21 CFR 314.101(d)(9). Contact the 505(b)(2) review staff in the Immediate Office of New Drugs for advice.</i></p>				<input type="checkbox"/>	<input type="checkbox"/>	X	
<ul style="list-style-type: none"> Is there unexpired exclusivity on another listed drug product containing the same active moiety (e.g., 5-year, 3-year, orphan, or pediatric exclusivity)? <p>Check the Electronic Orange Book at: http://www.accessdata.fda.gov/scripts/cder/ob/default.cfm</p>				<input type="checkbox"/>	<input type="checkbox"/>	X	
If yes , please list below:							
Application No.	Drug Name	Exclusivity Code	Exclusivity Expiration				
<p><i>If there is unexpired, 5-year exclusivity remaining on another listed drug product containing the same active moiety, a 505(b)(2) application cannot be submitted until the period of exclusivity expires (unless the applicant provides paragraph IV patent certification; then an application can be submitted four years after the date of approval.) Pediatric exclusivity will extend both of the timeframes in this provision by 6 months. 21 CFR 314.108(b)(2). Unexpired, 3-year exclusivity may block the approval but not the submission of a 505(b)(2) application.</i></p>							
Exclusivity	YES	NO	NA	Comment			
Does another product (same active moiety) have orphan exclusivity for the same indication? Check the Orphan Drug Designations and Approvals list at: http://www.accessdata.fda.gov/scripts/opdlisting/opd/index.cfm	<input type="checkbox"/>	X					
If another product has orphan exclusivity , is the product considered to be the same product according to the orphan drug definition of sameness [see 21 CFR 316.3(b)(13)]?	<input type="checkbox"/>	<input type="checkbox"/>	X				
<i>If yes, consult the Director, Division of Regulatory Policy II, Office of Regulatory Policy</i>							
NDAs/NDA efficacy supplements only: Has the applicant requested 5-year or 3-year Waxman-Hatch exclusivity?	X	<input type="checkbox"/>	<input type="checkbox"/>	Applicant requested 5-year exclusivity in original submission dated and received July 21, 2015.			
If yes , # years requested: 5 years							
<i>Note: An applicant can receive exclusivity without requesting it;</i>							

<i>therefore, requesting exclusivity is not required.</i>				
NDAs only: Is the proposed product a single enantiomer of a racemic drug previously approved for a different therapeutic use?	<input type="checkbox"/>	X	<input type="checkbox"/>	
If yes, did the applicant: (a) elect to have the single enantiomer (contained as an active ingredient) not be considered the same active ingredient as that contained in an already approved racemic drug, and/or (b): request exclusivity pursuant to section 505(u) of the Act (per FDAAA Section 1113)? <i>If yes, contact the Orange Book Staff (CDER-Orange Book Staff).</i>	<input type="checkbox"/>	<input type="checkbox"/>	X	
BLAs only: Has the applicant requested 12-year exclusivity under section 351(k)(7) of the PHS Act? <i>If yes, notify Marlene Schultz-DePalo, CDER Purple Book Manager</i> <i>Note: Exclusivity requests may be made for an original BLA submitted under Section 351(a) of the PHS Act (i.e., a biological reference product). A request may be located in Module 1.3.5.3 and/or other sections of the BLA and may be included in a supplement (or other correspondence) if exclusivity has not been previously requested in the original 351(a) BLA. An applicant can receive exclusivity without requesting it; therefore, requesting exclusivity is not required.</i>	<input type="checkbox"/>	<input type="checkbox"/>	X	

Format and Content				
<i>Do not check mixed submission if the only electronic component is the content of labeling (COL).</i>	<input type="checkbox"/> All paper (except for COL) <input checked="" type="checkbox"/> All electronic <input type="checkbox"/> Mixed (paper/electronic)			
	<input checked="" type="checkbox"/> CTD <input type="checkbox"/> Non-CTD <input type="checkbox"/> Mixed (CTD/non-CTD)			
If mixed (paper/electronic) submission, which parts of the application are submitted in electronic format?				
Overall Format/Content	YES	NO	NA	Comment
If electronic submission, does it follow the eCTD guidance? ¹ If not, explain (e.g., waiver granted).	X	<input type="checkbox"/>	<input type="checkbox"/>	
Index: Does the submission contain an accurate comprehensive index?	X	<input type="checkbox"/>		
Is the submission complete as required under 21 CFR 314.50 (NDAs/NDA efficacy supplements) or under 21 CFR 601.2 (BLAs/BLA efficacy supplements) including:	X	<input type="checkbox"/>		

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<http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm072349.pdf>

X legible X English (or translated into English) X pagination X navigable hyperlinks (electronic submissions only)				
If no, explain.				
BLAs only: Companion application received if a shared or divided manufacturing arrangement?	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	
If yes, BLA #				
Forms and Certifications				
<i>Electronic forms and certifications with electronic signatures (scanned, digital, or electronic – similar to DARRTS, e.g., /s/) are acceptable. Otherwise, paper forms and certifications with hand-written signatures must be included. Forms include: user fee cover sheet (3397/3792), application form (356h), patent information (3542a), financial disclosure (3454/3455), and clinical trials (3674); Certifications include: debarment certification, patent certification(s), field copy certification, and pediatric certification.</i>				
Application Form	YES	NO	NA	Comment
Is form FDA 356h included with authorized signature per 21 CFR 314.50(a)?	<input checked="" type="checkbox"/>	<input type="checkbox"/>		Submitted in original submission received July 21, 2015.
<i>If foreign applicant, a U.S. agent must sign the form [see 21 CFR 314.50(a)(5)].</i>				
Are all establishments and their registration numbers listed on the form/attached to the form?	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Patent Information (NDAs/NDA efficacy supplements only)	YES	NO	NA	Comment
Is patent information submitted on form FDA 3542a per 21 CFR 314.53(c)?	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	Submitted in original submission received July 21, 2015.
Financial Disclosure	YES	NO	NA	Comment
Are financial disclosure forms FDA 3454 and/or 3455 included with authorized signature per 21 CFR 54.4(a)(1) and (3)?	<input checked="" type="checkbox"/>	<input type="checkbox"/>		Submitted in original submission received July 21, 2015.
<i>Forms must be signed by the APPLICANT, not an Agent [see 21 CFR 54.2(g)].</i>				
<i>Note: Financial disclosure is required for bioequivalence studies that are the basis for approval.</i>				
Clinical Trials Database	YES	NO	NA	Comment
Is form FDA 3674 included with authorized signature?	<input checked="" type="checkbox"/>	<input type="checkbox"/>		Submitted in original submission received July 21, 2015.
<i>If yes, ensure that the application is also coded with the supporting document category, "Form 3674."</i>				

<i>If no, ensure that language requesting submission of the form is included in the acknowledgement letter sent to the applicant</i>				
Debarment Certification	YES	NO	NA	Comment
Is a correctly worded Debarment Certification included with authorized signature? <i>Certification is not required for supplements if submitted in the original application; If foreign applicant, <u>both</u> the applicant and the U.S. Agent must sign the certification [per Guidance for Industry: Submitting Debarment Certifications].</i> <i>Note: Debarment Certification should use wording in FD&C Act Section 306(k)(1) i.e., “[Name of applicant] hereby certifies that it did not and will not use in any capacity the services of any person debarred under section 306 of the Federal Food, Drug, and Cosmetic Act in connection with this application.” Applicant may not use wording such as, “To the best of my knowledge...”</i>	X	<input type="checkbox"/>	<input type="checkbox"/>	
Field Copy Certification (NDAs/NDA efficacy supplements only)	YES	NO	NA	Comment
For paper submissions only: Is a Field Copy Certification (that it is a true copy of the CMC technical section) included? <i>Field Copy Certification is not needed if there is no CMC technical section or if this is an electronic submission (the Field Office has access to the EDR)</i> <i>If maroon field copy jackets from foreign applicants are received, return them to CDR for delivery to the appropriate field office.</i>	<input type="checkbox"/>	<input type="checkbox"/>	X	Electronic Submission Only
Controlled Substance/Product with Abuse Potential	YES	NO	NA	Comment
<u>For NMEs:</u> Is an Abuse Liability Assessment, including a proposal for scheduling, submitted per 21 CFR 314.50(d)(5)(vii)? <i>If yes, date consult sent to the Controlled Substance Staff:</i> <u>For non-NMEs:</u> <i>Date of consult sent to Controlled Substance Staff :</i>	<input type="checkbox"/>	<input type="checkbox"/>	X	
Pediatrics	YES	NO	NA	Comment
<u>PREA</u> Does the application trigger PREA? <i>If yes, notify PeRC@fda.hhs.gov to schedule required PeRC meeting²</i> <i>Note: NDAs/BLAs/efficacy supplements for new active ingredients (including new fixed combinations), new indications, new dosage</i>	X	<input type="checkbox"/>		

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<http://inside.fda.gov:9003/CDER/OfficeofNewDrugs/ImmediateOffice/PediatricandMaternalHealthStaff/ucm027829.htm>

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forms, new dosing regimens, or new routes of administration trigger PREA. All waiver & deferral requests, pediatric plans, and pediatric assessment studies must be reviewed by PeRC prior to approval of the application/supplement.				
If the application triggers PREA, is there an agreed Initial Pediatric Study Plan (iPSP)? <i>If no, may be an RTF issue - contact DPMH for advice.</i>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	Agreement to iPSP issued 1/9/2015 to IND 73435
If required by the agreed iPSP, are the pediatric studies outlined in the agreed iPSP completed and included in the application? <i>If no, may be an RTF issue - contact DPMH for advice.</i>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	Pediatric studies were not required by the agreed iPSP
<u>BPCA:</u> Is this submission a complete response to a pediatric Written Request? <i>If yes, notify Pediatric Exclusivity Board RPM (pediatric exclusivity determination is required)³</i>	<input type="checkbox"/>	<input checked="" type="checkbox"/>		
Proprietary Name	YES	NO	NA	Comment
Is a proposed proprietary name submitted? <i>If yes, ensure that the application is also coded with the supporting document category, "Proprietary Name/Request for Review."</i>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	Proposed Proprietary Name submitted in original submission received July 21, 2015. Supporting document category coded correctly in DARRTS on 8/4/2015.
REMS	YES	NO	NA	Comment
Is a REMS submitted? <i>If yes, send consult to OSE/DRISK and notify OC/OSI/DSC/PMSB via the CDER OSI RMP mailbox</i>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	
Prescription Labeling	<input type="checkbox"/> Not applicable			
Check all types of labeling submitted.	<input checked="" type="checkbox"/> Package Insert (PI) <input type="checkbox"/> Patient Package Insert (PPI) <input type="checkbox"/> Instructions for Use (IFU) <input type="checkbox"/> Medication Guide (MedGuide) <input checked="" type="checkbox"/> Carton labels <input checked="" type="checkbox"/> Immediate container labels <input type="checkbox"/> Diluent <input type="checkbox"/> Other (specify)			
	YES	NO	NA	Comment
Is Electronic Content of Labeling (COL) submitted in SPL format? <i>If no, request applicant to submit SPL before the filing date.</i>	<input checked="" type="checkbox"/>	<input type="checkbox"/>		

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<http://inside.fda.gov:9003/CDER/OfficeofNewDrugs/ImmediateOffice/PediatricandMaternalHealthStaff/ucm027837.htm>

Is the PI submitted in PLR format? ⁴	<input checked="" type="checkbox"/>	<input type="checkbox"/>		
If PI not submitted in PLR format , was a waiver or deferral requested before the application was received or in the submission? If requested before application was submitted , what is the status of the request? <i>If no waiver or deferral, request applicant to submit labeling in PLR format before the filing date.</i>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	
For applications submitted on or after June 30, 2015: Is the PI submitted in PLLR format? ⁵	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
Has a review of the available pregnancy and lactation data been included?	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
For applications submitted on or after June 30, 2015: If PI not submitted in PLLR format , was a waiver or deferral requested before the application was received or in the submission? If requested before application was submitted , what is the status of the request? <i>If no waiver or deferral, request applicant to submit labeling in PLR/PLLR format before the filing date.</i>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	
All labeling (PI, PPI, MedGuide, IFU, carton and immediate container labels) consulted to OPDP?	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	Consult Request dated 9/4/2015
MedGuide, PPI, IFU (plus PI) consulted to OSE/DRISK? (send WORD version if available)	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	
Carton and immediate container labels, PI, PPI sent to OSE/DMEPA and appropriate CMC review office in OPQ (OBP or ONDP)?	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
OTC Labeling	X Not Applicable			
Check all types of labeling submitted.	<input type="checkbox"/> Outer carton label <input type="checkbox"/> Immediate container label <input type="checkbox"/> Blister card <input type="checkbox"/> Blister backing label <input type="checkbox"/> Consumer Information Leaflet (CIL) <input type="checkbox"/> Physician sample <input type="checkbox"/> Consumer sample <input type="checkbox"/> Other (specify)			
	YES	NO	NA	Comment
Is electronic content of labeling (COL) submitted? <i>If no, request in 74-day letter.</i>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	

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<http://inside.fda.gov:9003/CDER/OfficeofNewDrugs/ImmediateOffice/StudyEndpointsandLabelingDevelopmentTeam/ucm025576.htm>

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<http://inside.fda.gov:9003/CDER/OfficeofNewDrugs/ImmediateOffice/StudyEndpointsandLabelingDevelopmentTeam/ucm025576.htm>

Are annotated specifications submitted for all stock keeping units (SKUs)? <i>If no, request in 74-day letter.</i>	<input type="checkbox"/>	<input type="checkbox"/>	X	
If representative labeling is submitted, are all represented SKUs defined? <i>If no, request in 74-day letter.</i>	<input type="checkbox"/>	<input type="checkbox"/>	X	
All labeling/packaging sent to OSE/DMEPA?	<input type="checkbox"/>	<input type="checkbox"/>	X	
Other Consults	YES	NO	NA	Comment
Are additional consults needed? (e.g., IFU to CDRH; QT study report to QT Interdisciplinary Review Team) <i>If yes, specify consult(s) and date(s) sent:</i>	<input type="checkbox"/>	X	<input type="checkbox"/>	
Meeting Minutes/SPAs	YES	NO	NA	Comment
End-of Phase 2 meeting(s)? Date(s): 9/26/2012, 6/11/2013 <i>If yes, distribute minutes before filing meeting</i>	X	<input type="checkbox"/>		
Pre-NDA/Pre-BLA/Pre-Supplement meeting(s)? Date(s): 2/9/2015 <i>If yes, distribute minutes before filing meeting</i>	X	<input type="checkbox"/>		
Any Special Protocol Assessments (SPAs)? Date(s): <i>If yes, distribute letter and/or relevant minutes before filing meeting</i>	<input type="checkbox"/>	<input type="checkbox"/>	X	

ATTACHMENT

MEMO OF FILING MEETING

DATE: August 31, 2015

BACKGROUND: NDA 207795 was submitted on July 21, 2015, for reduction of intraocular pressure for patients in with open-angle glaucoma or of ocular hypertension.

REVIEW TEAM:

Discipline/Organization	Names		Present at filing meeting? (Y or N)
Regulatory Project Management	RPM:	Lois Almoza, MS	Y
	CPMS/TL:	Diana Willard	Y
Cross-Discipline Team Leader (CDTL)	William Boyd, MD		Y
Division Director	Renata Albrecht, MD		Y
Deputy Director	Wiley Chambers, MD		Y
Office Director/Deputy	John Farley		Y
Clinical	Reviewer:	Lucious Lim, MD	Y
	TL:	William Boyd, MD	Y
Clinical Microbiology (<i>for antimicrobial products</i>)	Reviewer:		
	TL:		
Clinical Pharmacology	Reviewer:	Yongheng Zhang, PhD	Y
	TL:	Philip Colangelo, PhD	Y
• Genomics	Reviewer:		
• Pharmacometrics	Reviewer:		
Biostatistics	Reviewer:	Abel Eshete, PhD	Y
	TL:	Yan Wang, PhD	Y

Nonclinical (Pharmacology/Toxicology)	Reviewer:	Andrew McDougal, PhD	Y
	TL:	Lori Kotch, PhD	Y
Statistics (carcinogenicity)	Reviewer:		
	TL:		
Product Quality (CMC) Review Team:	ATL:	Anamitro Banerjee, PhD	Y
	RBPM:		
• Drug Substance	Reviewer:	Gaetan Ladouceur, PhD	N
• Drug Product	Reviewer:	Chunchun Zhang, PhD	N
• Process	Reviewer:	Sung Kim, PhD	N
• Microbiology	Reviewer:	Daniel Schu, PhD	Y
• Facility	Reviewer:	Denise DiGiulio, PhD	N
• Biopharmaceutics	Reviewer:	Om Anand, PhD	Y
• Immunogenicity	Reviewer:		
• Labeling (BLAs only)	Reviewer:		
• Branch Chiefs		Balajee Shanmugam, PhD	N
OMP/OMPI/DMPP (Patient labeling: MG, PPI, IFU)	Reviewer:		
	TL:		
OMP/OPDP (PI, PPI, MedGuide, IFU, carton and immediate container labels)	Reviewer:		
	TL:		
OSE/DMEPA (proprietary name, carton/container labels)	Reviewer:	Michelle Rutledge, PhD	Y
	TL:		
OSE/DRISK (REMS)	Reviewer:		
	TL:		
OC/OSI/DSC/PMSB (REMS)	Reviewer:		
	TL:		

Bioresearch Monitoring (OSI)	Reviewer:		
	TL:		
Controlled Substance Staff (CSS)	Reviewer:		
	TL:		
Other reviewers/disciplines			
<ul style="list-style-type: none"> • Discipline <p>*For additional lines, highlight this group of cells, copy, then paste: select "insert as new rows"</p>	Reviewer:		
	TL:		
Other attendees			
*For additional lines, right click here and select "insert rows below"			

FILING MEETING DISCUSSION:

<p>GENERAL</p> <ul style="list-style-type: none"> • 505(b)(2) filing issues: <ul style="list-style-type: none"> ○ Is the application for a duplicate of a listed drug and eligible for approval under section 505(j) as an ANDA? ○ Did the applicant provide a scientific "bridge" demonstrating the relationship between the proposed product and the referenced product(s)/published literature? <p>Describe the scientific bridge (e.g., information to demonstrate sufficient similarity between the proposed product and the listed drug(s) such as BA/BE studies or to justify reliance on information described in published literature):</p> 	<p>X Not Applicable</p> <p><input type="checkbox"/> YES <input type="checkbox"/> NO</p> <p><input type="checkbox"/> YES <input type="checkbox"/> NO</p>
<ul style="list-style-type: none"> • Per reviewers, are all parts in English or English translation? <p>If no, explain:</p>	<p>X YES</p> <p><input type="checkbox"/> NO</p>
<ul style="list-style-type: none"> • Electronic Submission comments <p>List comments:</p>	<p><input type="checkbox"/> Not Applicable</p> <p>X No comments</p>

<p>CLINICAL</p> <p>Comments:</p>	<p><input type="checkbox"/> Not Applicable <input checked="" type="checkbox"/> FILE <input type="checkbox"/> REFUSE TO FILE</p> <p><input type="checkbox"/> Review issues for 74-day letter <input checked="" type="checkbox"/> NONE</p>
<p>• Clinical study site(s) inspections(s) needed?</p> <p>If no, explain:</p>	<p><input checked="" type="checkbox"/> YES <input type="checkbox"/> NO</p>
<p>• Advisory Committee Meeting needed?</p> <p>Comments:</p> <p><i>If no, for an NME NDA or original BLA, include the reason. For example:</i></p> <ul style="list-style-type: none"> ○ <i>this drug/biologic is not the first in its class</i> ○ <i>the clinical study design was acceptable</i> ○ <i>the application did not raise significant safety or efficacy issues</i> ○ <i>the application did not raise significant public health questions on the role of the drug/biologic in the diagnosis, cure, mitigation, treatment or prevention of a disease</i> 	<p><input type="checkbox"/> YES Date if known: <input type="text"/></p> <p><input checked="" type="checkbox"/> NO <input type="checkbox"/> To be determined</p> <p>Reason: the application did not raise significant safety or efficacy issues</p>
<p>• If the application is affected by the AIP, has the division made a recommendation regarding whether or not an exception to the AIP should be granted to permit review based on medical necessity or public health significance?</p> <p>Comments:</p>	<p><input checked="" type="checkbox"/> Not Applicable <input type="checkbox"/> YES <input type="checkbox"/> NO</p>
<p>CONTROLLED SUBSTANCE STAFF</p> <p>• Abuse Liability/Potential</p> <p>Comments:</p>	<p><input checked="" type="checkbox"/> Not Applicable <input type="checkbox"/> FILE <input type="checkbox"/> REFUSE TO FILE</p> <p><input type="checkbox"/> Review issues for 74-day letter</p>
<p>CLINICAL MICROBIOLOGY</p> <p>Comments:</p>	<p><input checked="" type="checkbox"/> Not Applicable <input type="checkbox"/> FILE <input type="checkbox"/> REFUSE TO FILE</p> <p><input type="checkbox"/> Review issues for 74-day letter</p>

<p>CLINICAL PHARMACOLOGY</p> <p>Comments:</p>	<p><input type="checkbox"/> Not Applicable <input checked="" type="checkbox"/> FILE <input type="checkbox"/> REFUSE TO FILE</p> <p><input type="checkbox"/> Review issues for 74-day letter <input checked="" type="checkbox"/> NONE</p>
<ul style="list-style-type: none"> Clinical pharmacology study site(s) inspections(s) needed? 	<p><input type="checkbox"/> YES <input checked="" type="checkbox"/> NO</p>
<p>BIOSTATISTICS</p> <p>Comments:</p>	<p><input type="checkbox"/> Not Applicable <input checked="" type="checkbox"/> FILE <input type="checkbox"/> REFUSE TO FILE</p> <p><input type="checkbox"/> Review issues for 74-day letter <input checked="" type="checkbox"/> NONE</p>
<p>NONCLINICAL (PHARMACOLOGY/TOXICOLOGY)</p> <p>Comments:</p>	<p><input type="checkbox"/> Not Applicable <input checked="" type="checkbox"/> FILE <input type="checkbox"/> REFUSE TO FILE</p> <p><input type="checkbox"/> Review issues for 74-day letter <input checked="" type="checkbox"/> NONE</p>
<p>PRODUCT QUALITY (CMC)</p> <p>Comments:</p>	<p><input type="checkbox"/> Not Applicable <input checked="" type="checkbox"/> FILE <input type="checkbox"/> REFUSE TO FILE</p> <p><input type="checkbox"/> Review issues for 74-day letter <input checked="" type="checkbox"/> NONE</p>
<p><u>New Molecular Entity</u> (NDAs only)</p> <ul style="list-style-type: none"> Is the product an NME? 	<p><input checked="" type="checkbox"/> YES <input type="checkbox"/> NO</p>
<p><u>Environmental Assessment</u></p> <ul style="list-style-type: none"> Categorical exclusion for environmental assessment (EA) requested? <p>If no, was a complete EA submitted?</p> <p>Comments:</p>	<p><input checked="" type="checkbox"/> YES <input type="checkbox"/> NO</p> <p><input type="checkbox"/> YES <input type="checkbox"/> NO</p>

<p><u>Facility Inspection</u></p> <ul style="list-style-type: none"> Establishment(s) ready for inspection? <p>Comments:</p>	<p><input type="checkbox"/> Not Applicable</p> <p><input checked="" type="checkbox"/> YES</p> <p><input type="checkbox"/> NO</p>
<p><u>Facility/Microbiology Review (BLAs only)</u></p> <p>Comments:</p>	<p><input checked="" type="checkbox"/> Not Applicable</p> <p><input type="checkbox"/> FILE</p> <p><input type="checkbox"/> REFUSE TO FILE</p> <p><input type="checkbox"/> Review issues for 74-day letter</p>
<p><u>CMC Labeling Review (BLAs only)</u></p> <p>Comments:</p>	<p><input checked="" type="checkbox"/> Not Applicable</p> <p><input type="checkbox"/> Review issues for 74-day letter</p>
<p>APPLICATIONS IN THE PROGRAM (PDUFA V) (NME NDAs/Original BLAs)</p> <ul style="list-style-type: none"> Were there agreements made at the application's pre-submission meeting (and documented in the minutes) regarding certain late submission components that could be submitted within 30 days after receipt of the original application? If so, were the late submission components all submitted within 30 days? 	<p><input type="checkbox"/> N/A</p> <p><input type="checkbox"/> YES</p> <p><input checked="" type="checkbox"/> NO</p> <p><input type="checkbox"/> YES</p> <p><input type="checkbox"/> NO</p>
<ul style="list-style-type: none"> What late submission components, if any, arrived after 30 days? 	<p>N/A</p>
<ul style="list-style-type: none"> Was the application otherwise complete upon submission, including those applications where there were no agreements regarding late submission components? 	<p><input checked="" type="checkbox"/> YES</p> <p><input type="checkbox"/> NO</p>
<ul style="list-style-type: none"> Is a comprehensive and readily located list of all clinical sites included or referenced in the application? 	<p><input checked="" type="checkbox"/> YES</p> <p><input type="checkbox"/> NO</p>

<ul style="list-style-type: none">• Is a comprehensive and readily located list of all manufacturing facilities included or referenced in the application?	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO
--	--

REGULATORY PROJECT MANAGEMENT	
Signatory Authority: John Farley, MD, MPH	
Date of Mid-Cycle Meeting (for NME NDAs/BLAs in “the Program” PDUFA V): December 8, 2015	
21st Century Review Milestones (listing review milestones in this document is optional):	
Comments:	
REGULATORY CONCLUSIONS/DEFICIENCIES	
<input type="checkbox"/>	The application is unsuitable for filing. Explain why:
<input checked="" type="checkbox"/>	The application, on its face, appears to be suitable for filing. <u>Review Issues:</u> X No review issues have been identified for the 74-day letter. <input type="checkbox"/> Review issues have been identified for the 74-day letter. <u>Review Classification:</u> X Standard Review <input type="checkbox"/> Priority Review
ACTION ITEMS - <u>NONE</u>	
<input type="checkbox"/>	Ensure that any updates to the review priority (S or P) and classifications/properties are entered into the electronic archive (e.g., chemical classification, combination product classification, orphan drug).
<input type="checkbox"/>	If RTF, notify everyone who already received a consult request, OSE PM, and RBPM
<input type="checkbox"/>	If filed, and the application is under AIP, prepare a letter either granting (for signature by Center Director) or denying (for signature by ODE Director) an exception for review.
<input type="checkbox"/>	If priority review, notify applicant in writing by day 60 (see CST for choices)
<input type="checkbox"/>	Send review issues/no review issues by day 74
<input type="checkbox"/>	Conduct a PLR format labeling review and include labeling issues in the 74-day letter
<input type="checkbox"/>	Update the PDUFA V DARRTS page (for applications in the Program)
<input type="checkbox"/>	Other

Annual review of template by OND ADRAAs completed: September 2014

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

LOIS A ALMOZA
09/17/2015

DIANA M WILLARD
09/17/2015

REGULATORY PROJECT MANAGER PHYSICIAN'S LABELING RULE (PLR) FORMAT REVIEW OF THE PRESCRIBING INFORMATION

Application: NDA 206911

Application Type: New NDA

Name of Drug/Dosage Form: Vesneo (latanoprostene bunod ophthalmic solution), 0.024%

Applicant: Bausch & Lomb Inc.

Receipt Date: July 21, 2015

Goal Date: July 21, 2016

1. Regulatory History and Applicant's Main Proposals

This NDA was dated and received July 21, 2015. The proposed indication is for the reduction of intraocular pressure for patients with open-angle glaucoma of ocular hypertension.

2. Review of the Prescribing Information

This review is based on the applicant's July 21, 2015, submitted Word format of the prescribing information (PI). The applicant's proposed PI was reviewed in accordance with the labeling format requirements listed in the "Selected Requirements for Prescribing Information (SRPI)" checklist (see the Appendix).

3. Conclusions/Recommendations

SRPI format deficiencies were identified in the review of this PI. For identified deficiencies see below.

See item 22.

All SRPI format deficiencies of the PI will be conveyed to the applicant in an advice letter or during scheduled labeling negotiations.

Appendix

The Selected Requirement of Prescribing Information (SRPI) is a 42-item, drop-down checklist of important format elements of the prescribing information (PI) based on labeling regulations (21 CFR 201.56 and 201.57) and guidances.

Highlights

Selected Requirements of Prescribing Information

See Appendix A for a sample tool illustrating the format for the Highlights.

HIGHLIGHTS GENERAL FORMAT

- YES** 1. Highlights (HL) must be in a minimum of 8-point font and should be in two-column format, with ½ inch margins on all sides and between columns.

Comment:

- YES** 2. The length of HL must be one-half page or less unless a waiver has been granted in a previous submission. The HL Boxed Warning does not count against the one-half page requirement.
Instructions to complete this item: If the length of the HL is one-half page or less, select “YES” in the drop-down menu because this item meets the requirement. However, if HL is longer than one-half page, select “NO” unless a waiver has been granted.

Comment:

- YES** 3. A horizontal line must separate HL from the Table of Contents (TOC). A horizontal line must separate the TOC from the FPI.

Comment:

- YES** 4. All headings in HL must be **bolded** and presented in the center of a horizontal line (each horizontal line should extend over the entire width of the column as shown in Appendix A). The headings should be in UPPER CASE letters.

Comment:

- YES** 5. White space should be present before each major heading in HL. There must be no white space between the HL Heading and HL Limitation Statement. There must be no white space between the product title and Initial U.S. Approval. See Appendix A for a sample tool illustrating white space in HL.

Comment:

- YES** 6. Each summarized statement or topic in HL must reference the section(s) or subsection(s) of the Full Prescribing Information (FPI) that contain more detailed information. The preferred format is the numerical identifier in parenthesis [e.g., (1.1)] at the end of each summarized statement or topic.

Comment:

- YES** 7. Section headings must be presented in the following order in HL:

Section	Required/Optional
• Highlights Heading	Required
• Highlights Limitation Statement	Required
• Product Title	Required
• Initial U.S. Approval	Required
• Boxed Warning	Required if a BOXED WARNING is in the FPI
• Recent Major Changes	Required for only certain changes to PI*
• Indications and Usage	Required
• Dosage and Administration	Required
• Dosage Forms and Strengths	Required
• Contraindications	Required (if no contraindications must state “None.”)
• Warnings and Precautions	Not required by regulation, but should be present
• Adverse Reactions	Required
• Drug Interactions	Optional

Selected Requirements of Prescribing Information

• Use in Specific Populations	Optional
• Patient Counseling Information Statement	Required
• Revision Date	Required

* RMC only applies to the BOXED WARNING, INDICATIONS AND USAGE, DOSAGE AND ADMINISTRATION, CONTRAINDICATIONS, and WARNINGS AND PRECAUTIONS sections.

Comment:

HIGHLIGHTS DETAILS

Highlights Heading

- YES** 8. At the beginning of HL, the following heading must be **bolded** and should appear in all UPPER CASE letters: “**HIGHLIGHTS OF PRESCRIBING INFORMATION**”.

Comment:

Highlights Limitation Statement

- YES** 9. The **bolded** HL Limitation Statement must include the following verbatim statement: “**These highlights do not include all the information needed to use (insert name of drug product) safely and effectively. See full prescribing information for (insert name of drug product).**” The name of drug product should appear in UPPER CASE letters.

Comment:

Product Title in Highlights

- YES** 10. Product title must be **bolded**.

Comment:

Initial U.S. Approval in Highlights

- YES** 11. Initial U.S. Approval in HL must be **bolded**, and include the verbatim statement “**Initial U.S. Approval:**” followed by the **4-digit year**.

Comment:

Boxed Warning (BW) in Highlights

- N/A** 12. All text in the BW must be **bolded**.

Comment:

- N/A** 13. The BW must have a heading in UPPER CASE, containing the word “**WARNING**” (even if more than one warning, the term, “**WARNING**” and not “**WARNINGS**” should be used) and other words to identify the subject of the warning (e.g., “**WARNING: SERIOUS INFECTIONS and ACUTE HEPATIC FAILURE**”). The BW heading should be centered.

Comment:

- N/A** 14. The BW must always have the verbatim statement “*See full prescribing information for complete boxed warning.*” This statement should be centered immediately beneath the heading and appear in *italics*.

Comment:

- N/A** 15. The BW must be limited in length to 20 lines (this includes white space but does not include the BW heading and the statement “*See full prescribing information for complete boxed warning.*”).

Selected Requirements of Prescribing Information

Comment:

Recent Major Changes (RMC) in Highlights

- N/A** 16. RMC pertains to only the following five sections of the FPI: BOXED WARNING, INDICATIONS AND USAGE, DOSAGE AND ADMINISTRATION, CONTRAINDICATIONS, and WARNINGS AND PRECAUTIONS. RMC must be listed in the same order in HL as the modified text appears in FPI.

Comment:

- N/A** 17. The RMC must include the section heading(s) and, if appropriate, subsection heading(s) affected by the recent major change, together with each section's identifying number and date (month/year format) on which the change was incorporated in the PI (supplement approval date). For example, "Warnings and Precautions, Acute Liver Failure (5.1) --- 9/2013".

Comment:

- N/A** 18. The RMC must list changes for at least one year after the supplement is approved and must be removed at the first printing subsequent to one year (e.g., no listing should be one year older than revision date).

Comment:

Indications and Usage in Highlights

- YES** 19. If a product belongs to an established pharmacologic class, the following statement is required under the Indications and Usage heading in HL: "(Product) is a (name of established pharmacologic class) indicated for (indication)".

Comment:

Dosage Forms and Strengths in Highlights

- N/A** 20. For a product that has several dosage forms (e.g., capsules, tablets, and injection), bulleted subheadings or tabular presentations of information should be used under the Dosage Forms and Strengths heading.

Comment:

Contraindications in Highlights

- YES** 21. All contraindications listed in the FPI must also be listed in HL or must include the statement "None" if no contraindications are known. Each contraindication should be bulleted when there is more than one contraindication.

Comment:

Adverse Reactions in Highlights

- NO** 22. For drug products other than vaccines, the verbatim **bolded** statement must be present: "**To report SUSPECTED ADVERSE REACTIONS, contact (insert name of manufacturer) at (insert manufacturer's U.S. phone number) or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch**".

Selected Requirements of Prescribing Information

Comment: www.fda.gov/medwatch is underlined

Patient Counseling Information Statement in Highlights

YES 23. The Patient Counseling Information statement must include one of the following three **bolded** verbatim statements that is most applicable:

If a product **does not** have FDA-approved patient labeling:

- “**See 17 for PATIENT COUNSELING INFORMATION**”

If a product **has** FDA-approved patient labeling:

- “**See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling**”
- “**See 17 for PATIENT COUNSELING INFORMATION and Medication Guide**”

Comment:

Revision Date in Highlights

YES 24. The revision date must be at the end of HL, and should be **bolded** and right justified (e.g., “**Revised: 9/2013**”).

Comment:

Selected Requirements of Prescribing Information

Contents: Table of Contents (TOC)

See Appendix A for a sample tool illustrating the format for the Table of Contents.

YES 25. The TOC should be in a two-column format.

Comment:

YES 26. The following heading must appear at the beginning of the TOC: “**FULL PRESCRIBING INFORMATION: CONTENTS**”. This heading should be in all UPPER CASE letters and **bolded**.

Comment:

N/A 27. The same heading for the BW that appears in HL and the FPI must also appear at the beginning of the TOC in UPPER CASE letters and **bolded**.

Comment:

YES 28. In the TOC, all section headings must be **bolded** and should be in UPPER CASE.

Comment:

YES 29. In the TOC, all subsection headings must be indented and not bolded. The headings should be in title case [first letter of all words are capitalized except first letter of prepositions (through), articles (a, an, and the), or conjunctions (for, and)].

Comment:

YES 30. The section and subsection headings in the TOC must match the section and subsection headings in the FPI.

Comment:

YES 31. In the TOC, when a section or subsection is omitted, the numbering must not change. If a section or subsection from 201.56(d)(1) is omitted from the FPI and TOC, the heading “FULL PRESCRIBING INFORMATION: CONTENTS” must be followed by an asterisk and the following statement must appear at the end of TOC: “*Sections or subsections omitted from the full prescribing information are not listed.”

Comment:

Selected Requirements of Prescribing Information

Full Prescribing Information (FPI)

FULL PRESCRIBING INFORMATION: GENERAL FORMAT

- YES** 32. The **bolded** section and subsection headings in the FPI must be named and numbered in accordance with 21 CFR 201.56(d)(1) as noted below (section and subsection headings should be in UPPER CASE and title case, respectively). If a section/subsection required by regulation is omitted, the numbering must not change. Additional subsection headings (i.e., those not named by regulation) must also be **bolded** and numbered.

BOXED WARNING
1 INDICATIONS AND USAGE
2 DOSAGE AND ADMINISTRATION
3 DOSAGE FORMS AND STRENGTHS
4 CONTRAINDICATIONS
5 WARNINGS AND PRECAUTIONS
6 ADVERSE REACTIONS
7 DRUG INTERACTIONS
8 USE IN SPECIFIC POPULATIONS
8.1 Pregnancy
8.2 Labor and Delivery
8.3 Nursing Mothers
8.4 Pediatric Use
8.5 Geriatric Use
9 DRUG ABUSE AND DEPENDENCE
9.1 Controlled Substance
9.2 Abuse
9.3 Dependence
10 OVERDOSAGE
11 DESCRIPTION
12 CLINICAL PHARMACOLOGY
12.1 Mechanism of Action
12.2 Pharmacodynamics
12.3 Pharmacokinetics
12.4 Microbiology (by guidance)
12.5 Pharmacogenomics (by guidance)
13 NONCLINICAL TOXICOLOGY
13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility
13.2 Animal Toxicology and/or Pharmacology
14 CLINICAL STUDIES
15 REFERENCES
16 HOW SUPPLIED/STORAGE AND HANDLING
17 PATIENT COUNSELING INFORMATION

Comment:

- YES** 33. The preferred presentation for cross-references in the FPI is the section (not subsection) heading followed by the numerical identifier. The entire cross-reference should be in *italics* and enclosed within brackets. For example, “[*see Warnings and Precautions (5.2)*]” or “[*see Warnings and Precautions (5.2)*]”.

Comment:

N/A

Selected Requirements of Prescribing Information

34. If RMCs are listed in HL, the corresponding new or modified text in the FPI sections or subsections must be marked with a vertical line on the left edge.

Comment:

FULL PRESCRIBING INFORMATION DETAILS

FPI Heading

- YES** 35. The following heading must be **bolded** and appear at the beginning of the FPI: “**FULL PRESCRIBING INFORMATION**”. This heading should be in UPPER CASE.

Comment:

BOXED WARNING Section in the FPI

- N/A** 36. In the BW, all text should be **bolded**.

Comment:

- N/A** 37. The BW must have a heading in UPPER CASE, containing the word “**WARNING**” (even if more than one Warning, the term, “**WARNING**” and not “**WARNINGS**” should be used) and other words to identify the subject of the Warning (e.g., “**WARNING: SERIOUS INFECTIONS and ACUTE HEPATIC FAILURE**”).

Comment:

CONTRAINDICATIONS Section in the FPI

- N/A** 38. If no Contraindications are known, this section must state “None.”

Comment:

ADVERSE REACTIONS Section in the FPI

- YES** 39. When clinical trials adverse reactions data are included (typically in the “Clinical Trials Experience” subsection of ADVERSE REACTIONS), the following verbatim statement or appropriate modification should precede the presentation of adverse reactions:

“Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.”

Comment:

- N/A** 40. When postmarketing adverse reaction data are included (typically in the “Postmarketing Experience” subsection of ADVERSE REACTIONS), the following verbatim statement or appropriate modification should precede the presentation of adverse reactions:

“The following adverse reactions have been identified during post-approval use of (insert drug name). Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.”

Comment:

PATIENT COUNSELING INFORMATION Section in the FPI

- YES** 41. Must reference any FDA-approved patient labeling in Section 17 (PATIENT COUNSELING INFORMATION section). The reference should appear at the beginning of Section 17 and

Selected Requirements of Prescribing Information

include the type(s) of FDA-approved patient labeling (e.g., Patient Information, Medication Guide, Instructions for Use).

Comment:

- YES** 42. FDA-approved patient labeling (e.g., Medication Guide, Patient Information, or Instructions for Use) must not be included as a subsection under section 17 (PATIENT COUNSELING INFORMATION). All FDA-approved patient labeling must appear at the end of the PI upon approval.

Comment:

Selected Requirements of Prescribing Information

Appendix A: Format of the Highlights and Table of Contents

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use [DRUG NAME] safely and effectively. See full prescribing information for [DRUG NAME].

[DRUG NAME (nonproprietary name) dosage form, route of administration, controlled substance symbol]
Initial U.S. Approval: [year]

WARNING: [SUBJECT OF WARNING]

See full prescribing information for complete boxed warning.

- [text]
- [text]

RECENT MAJOR CHANGES

[section (X.X)] [m/year]
[section (X.X)] [m/year]

INDICATIONS AND USAGE

[DRUG NAME] is a [name of pharmacologic class] indicated for [text]

DOSAGE AND ADMINISTRATION

- [text]
- [text]

DOSAGE FORMS AND STRENGTHS

[text]

CONTRAINDICATIONS

- [text]
- [text]

WARNINGS AND PRECAUTIONS

- [text]
- [text]

ADVERSE REACTIONS

Most common adverse reactions (incidence > x%) are [text].

To report SUSPECTED ADVERSE REACTIONS, contact [name of manufacturer] at [phone #] or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DRUG INTERACTIONS

- [text]
- [text]

USE IN SPECIFIC POPULATIONS

- [text]
- [text]

See 17 for PATIENT COUNSELING INFORMATION [and FDA-approved patient labeling OR and Medication Guide].

Revised: [m/year]

FULL PRESCRIBING INFORMATION: CONTENTS*

WARNING: [SUBJECT OF WARNING]

1 INDICATIONS AND USAGE

2 DOSAGE AND ADMINISTRATION

2.1 [text]

2.2 [text]

3 DOSAGE FORMS AND STRENGTHS

4 CONTRAINDICATIONS

5 WARNINGS AND PRECAUTIONS

5.1 [text]

5.2 [text]

6 ADVERSE REACTIONS

6.1 [text]

6.2 [text]

7 DRUG INTERACTIONS

7.1 [text]

7.2 [text]

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

8.2 Labor and Delivery

8.3 Nursing Mothers

8.4 Pediatric Use

8.5 Geriatric Use

9 DRUG ABUSE AND DEPENDENCE

9.1 Controlled Substance

9.2 Abuse

9.3 Dependence

10 OVERDOSAGE

11 DESCRIPTION

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

12.2 Pharmacodynamics

12.3 Pharmacokinetics

12.4 Microbiology

12.5 Pharmacogenomics

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

13.2 Animal Toxicology and/or Pharmacology

14 CLINICAL STUDIES

14.1 [text]

14.2 [text]

15 REFERENCES

16 HOW SUPPLIED/STORAGE AND HANDLING

17 PATIENT COUNSELING INFORMATION

*Sections or subsections omitted from the full prescribing information are not listed.

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

LOIS A ALMOZA
08/27/2015

WILLIAM M BOYD
08/27/2015