CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

215092Orig1s000

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:	September 21, 2022
Requesting Office or Division:	Division of Ophthalmology (DO)
Application Type and Number:	NDA 215092
Product Name and Strength:	Omlonti (omidenepag isopropyl) ophthalmic solution, 0.002%
Applicant/Sponsor Name:	Santen Ltd. (Santen)
OSE RCM #:	2020-2455-2
DMEPA 1 Safety Evaluator:	Damon Birkemeier, PharmD
DMEPA 1 Team Leader:	Valerie S. Vaughan, PharmD

1 PURPOSE OF MEMORANDUM

Santen submitted revised container labels, carton labeling, instructions for use (IFU), and prescribing information (PI) received on September 20, 2022 for Omlonti. The Division of Ophthalmology (DO) requested that we review the revised container labels, carton labeling, IFU, and PI for Omlonti (Appendix A) to determine if they are acceptable from a medication error perspective. The revisions are in response to recommendations that we made during previous label and labeling reviews.[a,b]

2 CONCLUSION

Santen clarified the expiration date format they intend to use across their labels and labeling is "EXP YYYY-MM" with all numeric values. Additionally, Santen removed the (b) (4) statement on the container labels to ensure sufficient space is available for the minimally required product information and expiration date. Additionally, Santen revised the "Recommended Dosage" statement on the carton labeling so that it more closely matches the

[a] Birkemeier D. Label and Labeling Review for Omlonti (NDA 215092). Silver Spring (MD): FDA, CDER, OSE, DMEPA 1 (US); 2022 JUN 30. RCM No.: 2020-2455.

[b] Vaughan V. Label and Labeling Review Memo for Omlonti (NDA 215092). Silver Spring (MD): FDA, CDER, OSE, DMEPA 1 (US); 2022 SEP 15. RCM No.: 2022-2455-1.

statement in the PI. Santen implemented all of our recommendations and we have no additional recommendations at this time.

APPENDIX A. IMAGES OF LABEL AND LABELING RECEIVED ON SEPTEMBER 20, 2022

- Prescribing Information (PI) (Image Not Shown) available at: \\CDSESUB1\EVSPROD\nda215092\0029\m1\us\114-labeling\draft\labeling\draft-labeling-text.pdf
- Instructions for Use (IFU) (Image Not Shown) available at: \\CDSESUB1\EVSPROD\nda215092\0029\m1\us\114-labeling\draft\labeling\instruction-for-use.pdf

Container Labels

Commercial

(b) (4)

Sample

(b) (4)

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

---

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

DAMON A BIRKEMEIER
09/21/2022 08:04:25 AM

VALERIE S VAUGHAN
09/21/2022 08:12:44 AM

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:	September 15, 2022
Requesting Office or Division:	Division of Ophthalmology (DO)
Application Type and Number:	NDA 215092
Product Name and Strength:	Omlonti (omidenepag isopropyl) ophthalmic solution, 0.002%
Applicant/Sponsor Name:	Santen Ltd. (Santen)
OSE RCM #:	2020-2455-1
DMEPA 1 Team Leader:	Valerie S. Vaughan, PharmD
DMEPA Associate Director of Nomenclature & Labeling:	Mishale Mistry, PharmD, MPH

1 PURPOSE OF MEMORANDUM

The Applicant submitted revised container labels, carton labeling, and Instructions for Use received on September 9, 2022 for Omlonti. The Division of Ophthalmology (DO) requested that we review the revised container labels, carton labeling, and Instructions for Use for Omlonti (Appendix A) to determine if they are acceptable from a medication error perspective. The revisions are in response to recommendations that we made during a previous label and labeling review.[a]

2 CONCLUSION

The revised container label, carton labeling, and Instructions for Use are unacceptable from a medication error perspective.

A. The Instructions for Use (IFU) was revised to change the expiration abbreviation in the *Storing Omlonti* section from "EXP" to (b) (4) to align with the expiration abbreviation included on the previous submission of the container label and carton labeling. However, the expiration date abbreviation on the container label and carton

[a] Birkemeier, D. Label and Labeling Review for Omlonti (NDA 215092). Silver Spring (MD): FDA, CDER, OSE, DMEPA 1 (US); 2022 JUN 30. RCM No.: 2020-2455.

labeling was subsequently revised to “EXP.” As such, there is a mismatch between the IFU and container label/carton labeling. Select a single abbreviated expiration date format to be used consistently across the IFU, container label, and carton labeling to increase patients’ ability to appropriately cross-reference between the labels and labeling.

B. The container label does not include the linear barcode required per 21 CFR 201.25. Add the linear barcode to the container label.
C. The machine readable 2-D matrix barcode of the product identifier is missing. Add the 2-D matrix barcode in close proximity to the human-readable portion of the product identifier.
D. We acknowledge the intended expiration date format is YYYY-MM. Confusion has occurred with use of alphabetical abbreviations “JU,” which can represent both “June” and “July” and “MA,” which can represent both “March” and “May. Please clarify if the month portion of the expiration will use numeric characters only (e.g., 2022-09).
E. The (b) (4) terminology included on the container label does not align with the “recommended dosage” terminology included in the Prescribing Information. Revise the (b) (4) terminology to “Recommended Dosage.”

APPENDIX A. IMAGES OF LABEL AND LABELING RECEIVED ON SEPTEMBER 9, 2022

Instructions for Use

Instructions for Use (Image not shown) available at:
\\CDSESUB1\EVSPROD\nda215092\0027\m1\us\114-labeling\draft\labeling\instruction-for-use.pdf

Container labels

Commercial

(b) (4)

Sample

(b) (4)

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

---

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

VALERIE S VAUGHAN
09/15/2022 04:35:05 PM

MISHALE P MISTRY
09/16/2022 08:16:54 AM

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:	June 30, 2022
Requesting Office or Division:	Division of Ophthalmology (DO)
Application Type and Number:	NDA 215092
Product Name and Strength:	omidenepag isopropyl ophthalmic solution, 0.002%
Product Type:	Combination Product (Drug-Device)
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	Santen Ltd. (Santen)
FDA Received Date:	May 6, 2022
OSE RCM #:	2020-2455
DMEPA 1 Safety Evaluator:	Damon Birkemeier, PharmD
DMEPA 1 Team Leader:	Valerie S. Vaughan, PharmD

1 REASON FOR REVIEW

As part of the approval process for omidenepag isopropyl ophthalmic solution, the Division of Ophthalmology (DO) requested that we review the proposed omidenepag isopropyl prescribing information (PI), instructions for use (IFU), container labels and carton labeling for areas of vulnerability that may lead to medication errors.

1.1 REGULATORY HISTORY

Santen submitted NDA 215092 on November 19, 2020, which received a Complete Response (CR) on November 9, 2021, due to facility inspection issues.[a] Thus, Santen submitted a Class 2 Resubmission on May 6, 2022.

2 MATERIALS REVIEWED

Table 1. Materials Considered for this Label and Labeling Review

Material Reviewed	Appendix Section (for Methods and Results)
Product Information/Prescribing Information	A
Previous DMEPA Reviews	B
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 or ISMP Newsletters for our label and labeling reviews unless we are aware of medication errors through our routine postmarket safety surveillance

3 CONCLUSION AND RECOMMENDATIONS

Our evaluation of the proposed omidenepag isopropyl prescribing information did not identify areas of vulnerability that may lead to medication errors. However, the proposed instructions for use, container labels, and carton labeling may be improved to promote the safe use of this product from a medication error perspective. We provide the identified medication error

[a] Smith J. Complete Response for omidenepag isopropyl. Silver Spring (MD): FDA, CDER, OND, DO (US); 2021 NOV 9. NDA 215092.

issues, our rationale for concern, and our proposed recommendations to minimize the risk for medication error in Section 4 for Santen Ltd.

4 RECOMMENDATIONS FOR SANTEN LTD.

Table 2. Identified Issues and Recommendations for Santen Ltd. (entire table to be conveyed to Applicant)

	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
Container Labels and Carton Labeling			
1.	As currently presented, the strength statement appears less prominently in size than the net quantity statement.	The net quantity statement should not compete in size and prominence with important information such as the strength.	Increase the prominence of the strength presentation.
2.	As currently presented, the percentage sign in the strength statement appears to be smaller and offset compared to the strength.	Inconsistency in the font size of the strength statement decreases readability and may cause confusion amongst users.	Ensure all parts of the strength statement (i.e., the numerical part and the percentage sign) are the same font size.
Container Labels			
1.	As currently presented, we note that the container label is missing minimum required information.	Per 21 CFR 201.10(i), small labels are required to include, at a minimum the: • Proprietary name • Established name • Product strength • Identifying lot or control number • Name of manufacturer, packer, or distributor of the drug Additionally, USP requires the label of an official drug product bear an expiration date.	Revise the container label for your product to include the: • Proprietary name • Established name • Product strength • Expiration date • Identifying lot or control number • Name of manufacturer, packer, or distributor of the drug per 21 CFR 201.10(i) and USP. Consider removing the (b) (4) statement on the container label to ensure sufficient space is available for the minimally required product

Table 2. Identified Issues and Recommendations for Santen Ltd. (entire table to be conveyed to Applicant)			
	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
			information and expiration date.
2.	As currently presented, the linear barcode is missing on the container labels.	The drug barcode is often used as an additional verification before drug administration in the hospital setting; therefore, it is an important safety feature that should be part of the label.	Add the product's linear barcode to each individual container label as required per 21 CFR 201.25. Please note, the barcode should be surrounded by sufficient white space to allow scanners to correctly read the barcode. Additionally, the barcode should be placed in an area where it will not be damaged.
Carton Labeling			
1.	The (b) (4) statement uses the terminology (b) (4) Furthermore, the (b) (4) terminology is inconsistent with the terminology "recommended dosage" included in the Prescribing Information.	Inconsistent dosage statements may cause confusion amongst users and potentially cause administration errors.	Revise the (b) (4) statement to be consistent with the terminology in the PI and IFU, modify this statement to state: "Recommended dosage: Instill 1 drop in (b) (4) affected eye once daily in the evening."
2.	As currently presented, the carton labeling for the commercial product does not include a 2-D	In June 2021, FDA finalized guidance on product identifiers required under the Drug Supply Chain Security Act (DSCSA). The	Add the 2-D matrix barcode in close proximity to the human-readable portion of the product identifier.

Table 2. Identified Issues and Recommendations for Santen Ltd. (entire table to be conveyed to Applicant)			
	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
	matrix machine-readable barcode.	Act requires manufacturers and repackagers, respectively, to affix or imprint a product identifier to each package and homogenous case of a product intended to be introduced in a transaction in(to) commerce beginning November 27, 2017, and November 27, 2018, respectively. The product identifier contains the NDC, serial number, lot, and expiration date. The DSCSA guidance on product identifiers recommends the format below for the human-readable portion of the product identifier. The guidance also recommends that the human-readable portion be located near the 2D data matrix barcode.	
3.	As currently presented, the format of the expiration date on the carton labeling is denoted as, "(b) (4) YYYY-MM". It is unclear if the month portion, "MM," of the expiration date format will use alphabetical or numerical characters.	The expiration date should be clearly defined to minimize confusion and risk for deteriorated drug errors. For example, confusion has occurred with use of the alphabetical abbreviation "JU," which can represent both "June" and "July" and the alphabetical abbreviation "MA," which can represent both "March" and "May."	Clarify if you intend to use only numerical characters to express each portion of the expiration date.

Table 2. Identified Issues and Recommendations for Santen Ltd. (entire table to be conveyed to Applicant)			
	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
4.	On the side panel of the carton labeling, the statement, (b) (4) Additionally, the terminology (b) (4) is not consistent with the terminology used in the PI and the IFU (b) (4)	Lack of clarity in beyond-use statement may result in administration of deteriorated drug product.	Revise the beyond-use statement on the carton labeling (b) (4) and include a space for the patient to write the date the bottle was first opened. For example, "Date of first opening __/__/__. Discard unused portion 31 days after opening". We recommend "Date of first opening" so patients won't have to calculate the "Discard after" date. Additionally, the "__/__/__" statement will alert the users to write a complete date (month, day, and year) on the container label and carton labeling.
Instructions for Use			
1.	As currently presented, in the "Storing Omlonti" section of the IFU, the abbreviation used in the expiration date statement "Do not use Omlonti if the expiration date (EXP)…" is inconsistent with the abbreviation on the carton labeling (b) (4)	Inconsistent expiration date formats (i.e., (b) (4) *versus* EXP) may cause confusion amongst users and potentially cause administration errors.	We recommend selecting a single abbreviated expiration date format to use for consistently across the labels and labeling. For example: "Do not use Omlonti if the expiration date (b) (4)…"

APPENDICES: METHODS & RESULTS FOR EACH MATERIAL REVIEWED

APPENDIX A. PRODUCT INFORMATION/PRESCRIBING INFORMATION

Table 3 presents relevant product information for omidenepag isopropyl that Santen Ltd. submitted on May 6, 2022.

Table 3. Relevant Product Information for omidenepag isopropyl	
Initial Approval Date	N/A
Active Ingredient	Omidenepag isopropyl
Indication	Reduction of elevated intraocular pressure in patients with open-angle glaucoma or ocular hypertension
Route of Administration	Ophthalmic
Dosage Form	Ophthalmic solution
Strength	0.002%
Dose and Frequency	One drop in the affected eye(s) once daily in the evening
How Supplied	2.5 mL sterile solution in a 5 mL white low density polyethylene bottle with linear low density polyethylene dropper tips, high density polyethylene screw caps and tamper-evident low density polyethylene overcaps
Storage	Store unopened bottle in the refrigerator at 2°C to 8°C (36°F to 46°F). Once a bottle is opened for use, it can be stored for 31 days at up to 30°C (86°F)

APPENDIX B. PREVIOUS DMEPA REVIEWS

On May 19, 2022, we searched for previous DMEPA reviews relevant to this current review using the terms NDA 215092. Our search identified one previous review[b] and we considered our previous recommendations to see if they are applicable for this current review.

[b] Roosta N. Label and Labeling Review for omidenepag isopropyl (NDA 215092). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2021 MAY 21. RCM No.: 2020-2454.

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 omidenepag isopropyl labels and labeling submitted by Santen Ltd.

- Container labels received on May 6, 2022
- Carton labeling received on May 6, 2022
- Professional Sample Container Labels received on May 6, 2022
- Professional Sample Carton Labeling received on May 6, 2022
- Instructions for Use (Image not shown) received on May 6, 2022, available from \\CDSESUB1\evsprod\nda215092\0023\m1\us\114-labeling\draft\labeling\instruction-for-use-redlined.pdf
- Prescribing Information (Image not shown) received on May 6, 2022, available from \\CDSESUB1\evsprod\nda215092\0023\m1\us\114-labeling\draft\annotated\annotated-draft-labeling-text.pdf

F.2 Label and Labeling Images

Container label

Professional Sample Container Label

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

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

---

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

DAMON A BIRKEMEIER
06/30/2022 04:57:22 PM

VALERIE S VAUGHAN
07/05/2022 09:29:11 AM

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

PATIENT LABELING REVIEW

Date:	August 19, 2021
To:	Jacqueline Smith, MA Regulatory Project Manager **Division of Ophthalmology (DO)**
Through:	LaShawn Griffiths, MSHS-PH, BSN, RN Associate Director for Patient Labeling **Division of Medical Policy Programs (DMPP)** Marcia Williams, PhD Team Leader, Patient Labeling **Division of Medical Policy Programs (DMPP)**
From:	Maria Nguyen, MSHS, BSN, RN Patient Labeling Reviewer **Division of Medical Policy Programs (DMPP)** David Foss, PharmD, MPH, BCPS Regulatory Review Officer **Office of Prescription Drug Promotion (OPDP)**
Subject:	Review of Patient Labeling: Instructions for Use (IFU)
Drug Name (established name):	OMLONTI (omidenepag isopropyl opthalmic solution), 0.002%
Dosage Form and Route:	for topical ophthalmic use
Application Type/Number:	NDA 215092
Applicant:	Santen, Inc.

1 INTRODUCTION

On November 19, 2020, Santen, Inc., submitted for the Agency's review New Drug Application (NDA) #215092 for OMLONTI (omidenepag isopropyl opthalmic solution), 0.002%, for topical opthallmic use. The proposed indication for OMLONTI (omidenepag isopropyl opthalmic solution), 0.002% is the reduction of elevated intraocular pressure (IOP) in patients with open-angle glaucoma or ocular hypertension.

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 Opthalmology (DO) on January 12, 2021, for DMPP and OPDP to review the Applicant's proposed Instructions for Use (IFU) for OMLONTI (omidenepag isopropyl opthalmic solution), 0.002%, for topical opthalmic use.

2 MATERIAL REVIEWED

- Draft OMLONTI (omidenepag isopropyl opthalmic solution), IFU received by the review division on November 20, 2020, and received by DMPP and OPDP on August 11, 2021.
- Draft OMLONTI (omidenepag isopropyl opthalmic solution) Prescribing Information (PI) received on November 20, 2020, revised by the Review Division throughout the review cycle, and received by DMPP on August 11, 2021.
- Approved LUMIGAN (bimatoprost opthalmic solution) comparator labeling dated September 9, 2020.
- Approved XALATAN (latanoprost opthalmic solution) comparator labeling dated September 1, 2020.
- Approved TRAVATAN Z (travoprost ophthalmic solution) comparator labeling dated April 2, 2020.

3 REVIEW METHODS

To enhance patient comprehension, materials should be written at a 6th to 8th grade reading level, and have a reading ease score of at least 60%.

Additionally, in 2008 the American Society of Consultant Pharmacists Foundation (ASCP) in collaboration with the American Foundation for the Blind (AFB) published *Guidelines for Prescription Labeling and Consumer Medication Information for People with Vision Loss*. The ASCP and AFB recommended using fonts such as Verdana, Arial or APHont to make medical information more accessible for patients with vision loss. We reformatted the IFU document using the Arial font, size 10.

In our collaborative review of the IFU we:

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

4 CONCLUSIONS

The IFU 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 IFU 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 IFU.

Please let us know if you have any questions.

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

---

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

MARIA T NGUYEN
08/19/2021 10:48:45 AM
DMPP-OPDP review of omidenepag isopropyl (OMLONTI) NDA 215092 DMPP-OPDP IFU

DAVID F FOSS
08/19/2021 11:43:20 AM

MARCIA B WILLIAMS
08/19/2021 11:47:13 AM

LASHAWN M GRIFFITHS
08/19/2021 11:52:00 AM

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

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

Memorandum

Date: August 12, 2021

To: Jacquelyn Smith
Regulatory Project Manager
Division of Transplant and Ophthalmology Products (DTOP)

From: David Foss, Regulatory Review Officer
Office of Prescription Drug Promotion (OPDP)

CC: James Dvorsky, Team Leader, OPDP

Subject: OPDP Labeling Comments for (b) (4) (omidenepag isopropyl ophthalmic solution) 0.002%, for topical ophthalmic use

NDA: 215092

In response to DTOP's consult request dated January 12, 2021, OPDP has reviewed the proposed product labeling (PI), Instructions for Use (IFU), and carton and container labeling for the original NDA submission for (b) (4).

Labeling: OPDP's comments on the proposed labeling are based on the draft labeling received by electronic mail from DTOP on August 10, 2021, and are provided below.

A combined OPDP and Division of Medical Policy Programs (DMPP) review will be completed, and comments on the proposed IFU will be sent under separate cover.

Carton and Container Labeling: OPDP has reviewed the attached proposed carton and container labeling received by electronic mail from DTOP on August 11, 2021, and we do not have any comments.

Thank you for your consult. If you have any questions, please contact David Foss at (240) 402-7112 or david.foss@fda.hhs.gov

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

---

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

DAVID F FOSS
08/12/2021 02:03:56 PM

Clinical Inspection Summary

Date	June 09, 2021
From	Ling Yang, M.D., Ph.D., FAAFP Min Lu, M.D., M.P.H., Team Leader Kassa Ayalew, M.D., M.P.H., Branch Chief Good Clinical Practice Assessment Branch (GCPAB) Division of Clinical Compliance Evaluation (DCCE) Office of Scientific Investigations (OSI)
To	Martin Nevitt, M.D., Medical Officer William Boyd, M.D., Clinical Team Leader Jacquelyn Smith, Regulatory Health Project Manager Diana Willard, Chief Project Management Staff Division of Ophthalmology (DO)
NDA #	215092
Applicant	Santen, Inc.
Drug	Omidenepag isopropyl ophthalmic solution, 0.002%
NME (Yes/No)	Yes
Review Priority	Standard
Proposed Indication(s)	Treatment of open angle glaucoma and ocular hypertension
Consultation Request Date	January 12, 2021
Summary Goal Date	July 01, 2021
Action Goal Date	August 29, 2021
PDUFA Date	September 19, 2021

I. OVERALL ASSESSMENT OF FINDINGS AND RECOMMENDATIONS

Clinical data from Studies 011709IN (Spectrum 3 Study) and 011710IN (Spectrum 4 Study) were submitted to the Agency in support of this New Drug Application (NDA 215092) for omidenepag isopropyl ophthalmic solution, 0.002% for the proposed indication. Four clinical investigators (CIs): Drs. El-Roy Dixon (Site 8400025; Study 011709IN), Robert Smyth-Medina (Site 8400296; Study 011709IN), Eugene McLaurin (Site 8400044; Study 011710IN), and Paul James Hartman (Site 8400270; Study 011710IN) were selected for clinical inspections.

The inspections verified the sponsor Santen, Inc. (Santen) submitted clinical data with source records at the CI sites. Based on the results of these CI inspections, Studies 011709IN and 011710IN appear to have been conducted adequately, and the data generated by these sites and submitted by the sponsor appear acceptable in support of the respective indication.

During inspection of Dr. Robert Smyth-Medina's (Site 8400296; Study 011709IN), few inspectional issues related to the sponsor's responsibilities were observed. The observations noted during inspection are:

1) Four adverse events (AEs) the investigator entered in the electronic case report forms (eCRFs) and the electronic database capture (EDC) were not in the sponsor submitted AE list: blurred vision after investigational product (IP) instillation (Subject (b) (6); test arm);

subconjunctival hemorrhage (Subject (b) (6); control arm); posterior subcapsular cataract (Subject (b) (6); test arm); and blepharitis (Subject (b) (6); control arm).

2) Subjects (b) (6) (control arm) and (b) (6) (control arm) withdrew the study due to COVID-19 safety concerns. The data were entered in the eCRF/EDC by the CI but are not listed in the discontinued subjects' list.
3) Nine subjects' protocol deviations entered in the eCRF/EDC were not in the sponsor submitted data listing. The protocol deviations were mostly out of window visit or incomplete assessments due to COVID-19 and loss of IP bottles (3 subjects).

- Subject (b) (6) (control arm)'s Visit 8 was 8 days out of window due to COVID-19.
- Subject (b) (6) (test arm)'s Visit 5 was 5 days out of window and Visit 8 was done over the phone due to COVID-19 and the eye photos were not taken.
- Both Subject (b) (6) (control arm) and Subject (b) (6) (control arm)s' Visit 8 were conducted over the phone and the assessments of vital signs, best corrected visual acuity (BCVA), eye photos, intraocular pressure (IOP) and fundus exam were not completed due to COVID-19.
- Subject (b) (6) (test arm) missed 3 doses of IP between Visit 7 and 8.
- Subject (control arm), Subject (b) (6) (control arm) and Subject (b) (6) (test arm) each lost one bottle of IP.
- Subject (b) (6) (test arm) missed two doses of IP between Visit 6 and 7, and the assessments of vital signs, BCVA, IOP and IP collection were not completed due to COVID-19.

The identified inspectional findings were the responsibilities of the sponsor not Dr. Robert Smyth-Medinas.

II. BACKGROUND

Santen submitted NDA 215092 for omidenepag isopropyl ophthalmic solution, 0.002% (DE-117) on 11/19/2020. The proposed indication is for the treatment of open angle glaucoma (OAG) and ocular hypertension (OHT). Data from two Phase 3 clinical studies 011709IN (Spectrum 3 Study) and 011710IN (Spectrum 4 Study) were submitted to support the approval of the NDA.

Study 011709IN (Spectrum 3 Study)

Study 011709IN was a Phase 3, randomized, double-masked, active-controlled, parallel-group, multi-center study assessing the efficacy and safety of DE-117 ophthalmic solution 0.002% compared with timolol maleate ophthalmic solution 0.5% in subjects with OAG or OHT. The primary study objective was to determine whether DE-117 ophthalmic solution 0.002% given once daily is non-inferior to timolol maleate ophthalmic solution 0.5% given twice daily in reducing the IOP in subjects with OAG or OHT after 3 months of treatment. The primary efficacy endpoint was the IOP in the study eye measured at specified timepoints: 08:00, 10:00 and 16:00 at Week 1, Week 6 and Month 3 (Visits 3, 4, and 5).

The study consisted of a washout period, a double-masked treatment period and an open-label treatment period.

Washout Period (up to 28 days): Eligible subjects discontinued use of all IOP-lowering medications, if any, during the period, with the duration determined according to a specified minimum required for each medication class (up to + 7 days window was allowed). Subjects who discontinued IOP-lowering treatment(s) could be treated with a topical carbonic anhydrase inhibitor (CAI), if deemed necessary for safety; such topical CAI treatment was discontinued one week before the Baseline Visit.

Double-Masked Treatment Period (3 months): Subjects were randomized in a 1:1 ratio to the following regimens:

- Test: DE-117 ophthalmic solution 0.002% QD (20:00) and vehicle QD (08:00), or
- Control: timolol maleate ophthalmic solution 0.5% BID (20:00 and 08:00).

Subjects self-administered the study product. Scheduled visits were at Week 1, Week 6, and Month 3. Ocular assessments were IOP (at 3 scheduled timepoints, 08:00, 10:00, and 16:00), BCVA, slit-lamp biomicroscopy, ophthalmoscopy (at Baseline and Month 3), and deepening of the upper eyelid sulcus (DUES), eyelid, eyelash, and iris assessments (at Baseline and Month 3).

Open-Label Treatment Period (9 months): Adult subjects converted to the single DE-117 0.002% QD arm at Visit 5 (Month 3). Visits were at Month 6, 9 and 12. All subjects dosed with DE-117 QD at 20:00 (± 60 min) starting in the evening of Visit 5 (Month 3) and ending the evening before Visit 8 (Month 12). Ocular assessments included IOP (at 3 timepoints, 08:00, 10:00, and 16:00), BCVA, slit lamp biomicroscopy, ophthalmoscopy (at Month 12 only), DUEs, eyelid, eyelash, and iris assessments (including photos at Month 3 and 12).

The study screened a total of 628 subjects, randomized 426 subjects (413 adults and 13 pediatric subjects) at 49 study sites in the US. The first subject was enrolled on October 04, 2018, and the study was ongoing at the study report cut-off date of September 23, 2020.

Study 011710IN (Spectrum 4 Study)

Study 011710IN was a Phase 3, randomized, double-masked, active-controlled, parallel-group, multicenter study assessing the efficacy and safety of DE-117 ophthalmic solution 0.002% compared with timolol maleate ophthalmic solution 0.5% in subjects with OAG or OHT. The primary study objective was to determine whether DE-117 ophthalmic solution 0.002% given once daily is non-inferior to timolol maleate ophthalmic solution 0.5% given twice daily in reducing the IOP in subjects with glaucoma or OHT after 3 months of treatment. The primary efficacy endpoint was IOP in the study eye at each scheduled timepoint (08:00, 10:00, and 16:00) at Week 1 (Visit 3), Week 6 (Visit 4), and Month 3 (Visit 5).

The study consisted of a washout period and a double-masked treatment period.

Washout Period (up to 28 days): Eligible subjects discontinued the use of all IOP-lowering medications during the period, with the duration determined according to a specified minimum required for each medication class. Subjects who discontinued IOP-lowering treatment(s) could be treated with a topical CAI, if deemed necessary for safety; such topical CAI treatment was discontinued one week before the Baseline visit.

Treatment Period (3 months): Subjects were randomized in a 1:1 ratio to one of the following regimens:

- Test: DE-117 0.002% QD (20:00) and vehicle (08:00) each day.
- Control: Timolol 0.5% BID (20:00 and 08:00 each day).

Subjects self-administered the study product. Visits were at Week 1, Week 6, and Month 3. Ocular assessments were IOP (at three scheduled timepoints, 08:00, 10:00, and 16:00), BCVA, slit-lamp biomicroscopy, ophthalmoscopy (at Baseline and Month 3), DUEs, eyelid, eyelash, and iris assessments including photos (at Baseline and Month 3).

The study screened a total of 590 subjects and randomized 417 subjects at 33 study sites in the US. Of the 417 subjects randomized, 8 subjects were inadvertently randomized (4 to DE-117 and 4 to timolol) prior to the completion of screening and failed screening; the error was identified upon randomization and the subjects were not dosed. Thus, a total of 409 randomized subjects (204 to the DE-117 arm and 205 to the timolol arm) received ≥ 1 dose of the assigned study medication. No pediatric subjects were enrolled as planned. The first subject was enrolled on October 03, 2018, and the last subject completed the study on October 23, 2019.

Rationale for Site Selection
Four CIs: Drs. El-Roy Dixon (Site 8400025; Study 011709IN), Robert Smyth-Medina (Site 8400296; Study 011709IN), Eugene McLaurin (Site 8400044; Study 011710IN), and Paul James Hartman (Site 8400270; Study 011710IN) were requested for inspection in support of the application. These sites were selected based on enrolling a high number of patients to the study treatment arms that may have an impact in the review division's clinical decision-making process.

III. RESULTS

1. El-Roy Dixon, M.D., Site 8400025

806 North Jefferson Street
Albany, GA 31701

This CI was inspected on 02/22-24/2021 as a data audit for Study 011709IN. This was the initial inspection for Dr. Dixon.

The study site screened a total of 32 subjects and enrolled 30 subjects, with 28 subjects completed the study. The first subject was enrolled on 11/12/2018 and the last subject's last dosing was on 08/27/2019. All source records were reviewed for all of the 30 enrolled subjects.

Source records reviewed during the inspection included the study protocol and amendments, informed consent forms (ICFs), documentation of eligibility criteria and enrollment logs, medical records (including visit data, monitoring logs, laboratory tests, AEs, concomitant medication use), the IP accountability records, paper CRFs with eCRF enters/audits and the EDC, protocol deviations and related regulatory documents [e.g., institutional review board (IRB) approvals and communications, staff training logs, financial disclosures and delegation of authority].

The inspection found adequate source documentation for inspected study subjects, with no significant deficiencies reported. The submitted data were verifiable with source records at the study site. The primary efficacy data source was verified. There was no evidence of underreporting of AEs.

At the end of the inspection, a Form 483 (Inspectional Observations) was not issued. Items discussed were:

- On the ICFs of Subjects (b) (6) and (b) (6), the name, signature and date of the study personnel who explained the ICFs were missing.
- Discrepancy between the source document (listed as # 36186) and the IP accountability log (listed as # 36188) for Subject (b) (6) at Visit 5 on (b) (6).

In general, this clinical site appeared to be in compliance with Good Clinical Practice (GCP) except the observations noted above. These observations appear unlikely to have significant impacts on the overall efficacy and safety results.

2. Robert Smyth-Medina, M.D., Site 8400296
11550 Indian Hill Road, Suite 341
Mission Hills, CA 91345

This CI was inspected on 03/22-26/2021 as a data audit for Study 011709IN. This was the second inspection for Dr. Smyth-Medina. Previous inspection in April 2015 was classified as no action indicated (NAI). The study site screened a total of 41 subjects, enrolled 31 subjects, with 22 subjects completed the study (2 subjects withdrew due to COVID-19 safety concerns). The first subject was enrolled on 11/27/2018 and the last subject's last follow-up visit was on 07/21/2020. All source records of the 31 enrolled subjects were reviewed.

Source records reviewed during the inspection included study protocol and amendments, ICFs, documentation of eligibility criteria and enrollment logs, medical records (including monitoring logs, visits data, laboratory tests, AEs, concomitant medication use), IP accountability records, paper CRFs with eCRFs entries and EDC signature process, protocol deviations, and related regulatory documents (e.g., IRB approvals and communications, staff training logs, financial disclosures and delegation of authority).

The inspection found adequate source documentation for inspected study subjects, with no significant deficiencies reported. The submitted data were verifiable with source records at the study site. The primary efficacy data source was verified. There was no evidence of underreporting of AEs.

In general, this clinical site appeared to be in compliance with GCP except the items noted above. These findings appear unlikely to have significant impacts on the overall efficacy and safety results.

3. Eugene B. McLaurin, M.D., Site 8400044
6060 Primacy Parkway, Suite 200
Memphis, TN 38119-5770

This CI was inspected on 03/29-04/02/2021 as a data audit for Study 011710IN. This was the third inspection for Dr. McLaurin. Previous inspections in September 2015 and March 2019 were both NAI.

The study site screened a total of 49 subjects and enrolled 43 subjects, with all 43 subjects completed the study. The first subject was enrolled on 11/08/2018 and the last subject's last follow-up visit was on 09/19/2019. All source records were reviewed for 12 of the 43 enrolled subjects.

Source records reviewed during the inspection included the study protocol and amendments, ICFs, documentation of eligibility criteria and enrollment logs, medical records (including monitoring logs, visit reports, laboratory tests, AEs, concomitant medication use), the IP accountability records, paper CRF with eCRFs entries/audit and EDC, protocol deviations and related regulatory documents (e.g., IRB approvals and communications, staff training logs, financial disclosures and delegation of authority).

The inspection found adequate source documentation for inspected study subjects with no significant deficiencies reported. The submitted data were verifiable with source records at the study site. The primary efficacy data source was verified. There was no evidence of underreporting of AEs.

At the end of the inspection, a Form 483 was not issued. There were no discussion items. In general, this clinical site appeared to be in compliance with GCP.

4. Paul James Hartman, M.D., Site 8400270
2100 S. Clinton Avenue
Rochester, NY 14618

This CI was inspected on 02/22-26/2021 as a data audit for Study 011710IN. This was the initial inspection for Dr. Hartman.

The study site screened a total of 51 subjects and enrolled 48 subjects, with 45 subjects completed the study. The first subject was enrolled on 09/27/2018 and the last subject's last dosing was on 06/25/2019. ICFs were reviewed for all of the 51 screened subjects. All source records were reviewed for 16 of the 48 enrolled subjects.

Source records reviewed during the inspection included the study protocol and amendments, ICFs, documentation of eligibility criteria and enrollment logs, medical records (including monitoring logs, visit reports, laboratory tests, AEs, concomitant medication use), the IP accountability records, CRFs with eCRF entries/audit and the EDC, protocol deviations and related regulatory documents (e.g., IRB approvals and communications, staff training logs, financial disclosures and

delegation of authority).

The inspection found adequate source documentation for inspected study subjects, with no significant deficiencies reported. The submitted data were verifiable with source records at the study site. The primary efficacy data source was verified. There was no evidence of underreporting of AEs. Subject (b) (6) had a serious adverse event (SAE) of myocardial infarction and died on (b) (6). This SAE was reported to the IRB and FDA timely.

At the end of the inspection, a Form 483 was not issued. There was one discussion item:

- Subject (b) (6) had a past medical history of chronic obstructive lung disease and met the exclusion criteria that should not be enrolled. The subject was dosed on (b) (6), experienced an AE of photophobia on (b) (6) and was removed from the study on (b) (6) This protocol deviation was reported to the IRB and was submitted to FDA.

In general, this clinical site appeared to be in compliance with GCP except the discussion item noted above. These observations appear unlikely to have significant impacts on the overall efficacy and safety results.

{See appended electronic signature page}

Ling Yang, M.D., Ph.D.
Good Clinical Practice Assessment Branch
Division of Clinical Compliance Evaluation
Office of Scientific Investigations

CONCURRENCE:

{See appended electronic signature page}

Min Lu, M.D., M.P.H.
Team Leader
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.\NDA 215092
DO\Division Director\Wiley Chambers
DO\CDTL\William Boyd
DO\Reviewer\Martin Nevitt
DO\Project Manager\Jaquelyn Smith
DO\Project Manager\Diana Willard
OSI\DCCE\Division Director\Kassa Ayalew
OSI\DCCE\GCPAB\Branch Chief\Kassa Ayalew
OSI\DCCE\GCPAB\Team Leader\Min Lu
OSI\DCCE\GCPAB\Reviewer\Ling Yang
OSI\DCCE\Program Analysts\Yolanda Patague

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

LING YANG
06/09/2021 01:28:08 PM

MIN LU
06/09/2021 01:55:15 PM

KASSA AYALEW
06/10/2021 01:24:17 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 21, 2021
Requesting Office or Division:	Division of Ophthalmology (DO)
Application Type and Number:	NDA 215092
Product Name and Strength:	Omidenepag isopropyl, ophthalmic solution, 0.002%
Product Type:	Single Ingredient Product
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	Santen Ltd. (Santen)
FDA Received Date:	November 19, 2020
OSE RCM #:	2020-2454
DMEPA Safety Evaluator:	Nasim Roosta, PharmD
DMEPA Team Leader:	Valerie S. Vaughan, PharmD

1 REASON FOR REVIEW

As part of the approval process for Omidenepag isopropyl ophthalmic solution, the Division of Ophthalmology (DO) requested that we review the proposed Omidenepag isopropyl prescribing information (PI), Instructions for Use (IFU), container label and carton labeling for areas of vulnerability that may lead to medication errors.

2 MATERIALS REVIEWED

Table 1. Materials Considered for this Label and Labeling Review

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

N/A=not applicable for this review

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

3 FINDINGS AND RECOMMENDATIONS

Tables 2 and 3 below include the identified medication error issues with the submitted prescribing information (PI), Instructions for Use (IFU), 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 Ophthalmology (DO)

	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
Prescribing Information – Section 2 Dosage and Administration			
1.	Section 2 of the PI does not instruct the user to 'gently shake the bottle' before use.	There is a lack of consistency with the IFU. Additionally, if patient does not shake the bottle prior to administration as instructed in the IFU, they	In Section 2 of PI, include instruction to gently shake bottle prior to administration.

Table 2. Identified Issues and Recommendations for Division of Ophthalmology (DO)			
	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
		may not receive full dose/benefit of product.	
Full Prescribing Information – Section 16 How Supplied/Storage and Handling			
1.	As currently presented, the units of temperature measurement (Centigrade and Fahrenheit) are not included following the first numeric degree measurement in the temperature ranges.	The lower temperatures in the ranges may be overlooked.	We recommend revising the storage statement to include the Centigrade symbol (°C) and Fahrenheit symbol (°F) following each numeric degree measurement of temperature ranges. For example, "Store unopened bottle(s) in the refrigerator at 36°F - 46°F (2°C - 8°C)".
Instructions for Use (IFU)			
1.	As currently presented in the "Storing (b) (4)" section of the IFU, the units of temperature measurement (Centigrade and Fahrenheit) are not included following the first numeric degree measurement in the temperature ranges.	The lower temperatures in the ranges may be overlooked.	We recommend revising the storage statement to include the Centigrade symbol (°C) and Fahrenheit symbol (°F) following each numeric degree measurement of temperature ranges. Also consider stating the Fahrenheit temperature range before the Celsius. For example, "36°F -46°F (2°C - 8°C)".
2.	Step 8 within the Using (b) (4) section of the IFU, uses the terminology (b) (4) in the sentence "Gently squeeze (b) (4)	The terminology (b) (4) is inconsistent with the terminology used in Section 2 "Dosage and Administration".	To provide consistency, replace the terminology (b) (4) For example, "The recommended dosage is one drop in the affected eye(s) once daily in the evening."
3.	Step 10 within the Using (b) (4) section of the IFU, uses the terminology (b) (4) in the sentence "After (b) (4) press	Using the terminology (b) (4) could lead to misinterpretation (b) (4)	For clarity, we recommend revising the statement to: "After using (b) (4)

Table 2. Identified Issues and Recommendations for Division of Ophthalmology (DO)			
	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
	the corner of your eye closest to your nose (b) (4) for 2 minutes."		

Table 3. Identified Issues and Recommendations for Santen Ltd. (Santen) (entire table to be conveyed to Applicant)			
	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
Container Label and Carton Labeling			
1.	The format for expiration date does not match on the container label and the carton labeling.	Clearly defining the expiration date will minimize confusion and risk for deteriorated drug medication errors.	Identify the expiration date format you intend to use that is consistent for both the container label and the carton labeling. FDA recommends that the human-readable expiration date on the drug package label include a year, month, and non-zero day. FDA recommends that the expiration date appear in YYYY-MM-DD format if only numerical characters are used or in YYYY-MMM-DD if alphabetical characters are used to represent the month. If there are space limitations on the drug package, the human-readable text may include only a year and month, to be expressed as: YYYY-MM if only numerical characters are used or YYYY-MMM if alphabetical characters are used to represent the month. FDA recommends that a hyphen or a space be used to separate the portions of the expiration date.
Container Label			
1.	The container label is missing the product's identifying lot or control number.	The lot or control number is required to appear on the container label per 21 CFR 201.10(i).	Include the products identifying lot or control number on the container label, per 21 CFR 201.10(i). Additionally, to ensure sufficient space, consider removing (b) (4)

Table 3. Identified Issues and Recommendations for Santen Ltd. (Santen) (entire table to be conveyed to Applicant)			
	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
			(b) (4) from the container label.
2.	(b) (4) inconsistent with the prescribing information and the carton labeling.	(b) (4)	If this statement is retained, and in order to be consistent with the prescribing information and carton labeling, (b) (4) (b) (4)
3.	As currently presented, the linear barcode is missing on the container labels.	The drug barcode is often used as an additional verification before drug administration in the hospital setting; therefore, it is an important safety feature that should be part of the label.	Add the product's linear barcode to each individual container label as required per 21 CFR 201.25. Please note, the barcode should be surrounded by sufficient white space to allow scanners to correctly read the barcode. Additionally, the barcode should be placed in an area where it will not be damaged.
Carton Labeling			
1.	As currently presented, the strength statement appears less prominently in size than the net quantity displayed on the PDP carton labeling.	The net quantity statement should not compete in size and prominence with important information such as the strength.	Increase the prominence of the strength presentation on the carton labeling.
2.	On the side panel of the carton labeling, the statement, (b) (4) and is not a	Lack of clarity in beyond-use statement may result in administration of deteriorated drug product.	Revise the beyond-use statement on the carton labeling (b) (4) and include a space for the patient to write the date the bottle was first opened. For example, "Date of first opening __/__/__. Discard unused portion 1 month after opening". We recommend "Date of first opening" so patients won't have to

Table 3. Identified Issues and Recommendations for Santen Ltd. (Santen) (entire table to be conveyed to Applicant)			
	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
	representation of usual beyond-use language.		calculate the "Discard after" date. Additionally, the "__/__/__" statement will alert the users to write a complete date (month, day, and year) on the container label and carton labeling.

4 CONCLUSION

Our evaluation of the proposed Omidenepag isopropyl prescribing information (PI), Instructions for Use (IFU), container label and carton labeling identified areas of vulnerability that may lead to medication errors. Above, we have provided recommendations in Table 2 for the Division and Table 3 for the Applicant. We ask that the Division convey Table 3 in its entirety to Santen Ltd. (Santen) so that recommendations are implemented prior to approval of this NDA.

APPENDICES: METHODS & RESULTS FOR EACH MATERIAL REVIEWED

APPENDIX A. PRODUCT INFORMATION/PRESCRIBING INFORMATION

Table 4 presents relevant product information for Omidenepag isopropyl that Santen Ltd. (Santen) submitted on November 19, 2020.

Table 4. Relevant Product Information for Omidenepag isopropyl	
Initial Approval Date	N/A
Active Ingredient	omidenepag isopropyl
Indication	Treatment of open-angle glaucoma or ocular hypertension
Route of Administration	Ophthalmic
Dosage Form	Ophthalmic solution
Strength	0.002%
Dose and Frequency	1 drop into the affected eye(s) once daily in the evening.
How Supplied	2.5 mL solution in a 5 mL bottle
Storage	Store the product under refrigeration at 2° to 8°C (36° to 46° F). (b) (4) [redacted]
Container Closure	(b) (4) [redacted]

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,[a] along with postmarket medication error data, we reviewed the following Omidenepag isopropyl labels and labeling submitted by Santen Ltd. (Santen).

- Container label received on November 19, 2020
- Carton labeling received on November 19, 2020
- Instructions for Use (Image not shown) received on November 19, 2020, available at: \\CDSESUB1\evsprod\nda215092\0001\m1\us\114-labeling\draft\labeling\instruction-for-use.pdf
- Prescribing Information (Image not shown) received on November 19, 2020, available at: \\CDSESUB1\evsprod\nda215092\0001\m1\us\114-labeling\draft\labeling\draft-labeling-text.docx

F.2 Label and Labeling Images

Container label:

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

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

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

NASIM N ROOSTA
05/21/2021 11:36:30 AM

VALERIE S VAUGHAN
05/21/2021 11:44:17 AM