APPLICATION NUMBER:

214965Orig1s000

OTHER REVIEW(S)
PATIENT LABELING REVIEW

Date: June 10, 2021

To: Wendy Streight, PhD
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)

From: Kelly Jackson, PharmD
Patient Labeling Reviewer
Division of Medical Policy Programs (DMPP)

Carrie Newcomer, PharmD
Regulatory Review Officer
Office of Prescription Drug Promotion (OPDP)

Subject: Review of Patient Labeling: Instructions for Use (IFU)

Drug Name (established name): Verkazia (cyclosporine ophthalmic emulsion) 0.1%

Dosage Form and Route: for topical ophthalmic use

Application Type/Number: NDA 214965

Applicant: Santen Inc.
INTRODUCTION

On August 26, 2020, Santen Inc. submitted for the Agency’s review a New Drug Application (NDA) 214965 under section 505(b)(2) of the Federal Food, Drug and Cosmetic Act for Verkazia (cyclosporine ophthalmic emulsion) 0.1% for topical ophthalmic use. The proposed indication for Verkazia (cyclosporine ophthalmic emulsion) 0.1% for topical ophthalmic use is the treatment of vernal keratoconjunctivitis (VKC) in children 4 through 18 years of age.

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 Ophthalmology (DO) on September 15, 2020 and September 30, 2020 respectively, for DMPP and OPDP to review the Applicant’s proposed Instructions for Use (IFU) for Verkazia (cyclosporine ophthalmic emulsion) 0.1% for topical ophthalmic use.

MATERIAL REVIEWED

- Draft Verkazia (cyclosporine ophthalmic emulsion) 0.1% IFU received on August 26, 2020, revised by the Review Division throughout the review cycle, and received by DMPP and OPDP on June 8, 2021.
- Draft Verkazia (cyclosporine ophthalmic emulsion) 0.1% Prescribing Information (PI) received on August 26, 2020, revised by the Review Division throughout the review cycle, and received by DMPP and OPDP on June 8, 2021.

REVIEW METHODS

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

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

In our collaborative review of the 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)
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.
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/s/

KELLY D JACKSON
06/10/2021 12:59:13 PM

JAMES S DVORSKY on behalf of CARRIE A NEWCOMER
06/10/2021 01:29:43 PM

MARCIA B WILLIAMS
06/10/2021 01:40:18 PM

LASHAWN M GRIFFITHS
06/10/2021 01:50:16 PM
Memorandum

Date:       June 9, 2021
To:         Wendy Streight, PhD
            Regulatory Health Project Manager
            Division of Ophthalmology
From:       Carrie Newcomer, Regulatory Review Officer
            Office of Prescription Drug Promotion (OPDP)
CC:         James Dvorsky, Team Leader, OPDP
Subject:    OPDP Labeling Comments for Verkazia® (cyclosporine ophthalmic
            emulsion) 0.1%
NDA:        214965

In response to the Division of Ophthalmology’s (DO) consult request dated September 30,
2020, OPDP has reviewed the proposed product labeling (PI), carton and container labeling,
and Instructions for Use (IFU) for Verkazia® (cyclosporine ophthalmic emulsion) 0.1%
(Verkazia).

**Labeling:** OPDP’s comments on the proposed labeling are based on the draft labeling
received by electronic mail from DO on June 8, 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 DO on June 8, 2021, and we do not have
any comments.

Thank you for your consult. If you have any questions, please contact Carrie Newcomer at 6-1233, or carrie.newcomer@fda.hhs.gov

Reference ID: 4808851
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/s/

CARRIE A NEWCOMER
06/09/2021 12:24:43 PM
I. OVERALL ASSESSMENT OF FINDINGS AND RECOMMENDATIONS

Clinical data from Study VEKTIS (NVG09B113) were submitted to the Agency in support of this New Drug Application (NDA) 214965 for Cyclosporine ophthalmic emulsion 1 mg/ml for the proposed indication. Two clinical investigators (CIs): Drs. Joseph Martel (Site 2101) and Kara Cavuoto (Site 2110) were inspected for Study VEKTIS (NVG09B113).

Based on the results of these CI inspections, Study VEKTIS (NVG09B113) appears 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.

II. BACKGROUND

Santen submitted NDA 214965 for Cyclosporine ophthalmic emulsion 1 mg/ml on 08/26/2020. The proposed indication is for treatment of vernal keratoconjunctivitis (VKC) in pediatric patients. Data from a Phase 3 study VEKTIS (NVG09B113) were submitted to support the approval of the product in the pediatric population.

Study VEKTIS (NVG09B113)

Study NVG09B113 was a multicenter, randomized, double-masked, 3 parallel arms, placebo-controlled study to assess the efficacy and safety of cyclosporine (NOVA22007) 1 mg/mL ophthalmic emulsion administered in pediatric subjects 4 to 18 years with active severe VKC.
The primary study objective was to compare the efficacy of 2 different dosing regimens of NOVA22007 vs. placebo (vehicle) on both the evolution of severe keratitis and the need for rescue medication.

The primary efficacy endpoint was the composite efficacy score at 4 months, defined as the mean of the 4 efficacy scores taken at each monthly visit. Efficacy was assessed monthly during the 4-month treatment period and compared with those at baseline based on: keratitis assessed by the modified Oxford scale; need for rescue medication and occurrence of corneal ulceration. The efficacy score was calculated as following:

- Patient’s score at month X= corneal fluorescein staining (CFS) (Baseline)- CFS (Month X) + penalty (ies)
- Penalty for rescue medication: -1 (per course, with a maximum of 2 courses between 2 scheduled visits)
- Penalty for corneal ulceration: -1 (per occurrence).

After screening, subjects were randomized at a 1:1:1 ratio to 1 of the 3 arms listed below and started the 4-month efficacy evaluation treatment period, with monthly visits. The 3 arms were:

- **High dose**: 1 drop of NOVA22007 4 times a day (morning, noon, afternoon and evening).
- **Low dose**: 1 drop of NOVA22007 twice a day (morning and evening) and 1 drop of placebo twice a day (noon and afternoon).
- **Placebo**: 1 drop of placebo 4 times a day.

Subjects then entered the 8-month safety follow-up period as described below:

- Subjects enrolled at the beginning of the VKC season and randomized to either of the active study treatment arm for the previous 4-month treatment period were continued with the same active study treatment regimen until the end of the VKC allergy season.
- Subjects enrolled at the beginning of the VKC season and randomized to the placebo arm were switched in a blinded fashion at a 1:1 ratio to an active study treatment arm until the end of the VKC allergy season.
- Subjects enrolled late in the VKC season discontinued study treatment (active and placebo) at the end of the VKC allergy season upon the completion of their 4-month efficacy evaluation period.
- Study visits were at Month 6, 8, 10 and 12.

The study randomized a total of 169 subjects in 51 study sites in 11 countries (Croatia-1; France-8; Germany-1; Greece-3; Hungary-3; India-6; Israel-5; Italy-6; Portugal-3; Spain-11; and US-4). The first subject was enrolled on 04/29/2013, and the last subject was completed on 02/01/2016.

**Rationale for Site Selection**

Two CIs: Drs. Joseph Martel (Site 2101) and Kara Cauvuto (Site 2110) were requested for clinical inspection in support of the application. These sites were selected for surveillance inspection because they enrolled a high number of subjects.

**III. RESULTS**

1. **Dr. Joseph Martel, Site 2101**
   Martel Eye Group
Dr. Joseph Martel was inspected on 12/15-17/2020 as a data audit for Study VEKTIS (NVG09B113). This was the second inspection for Dr. Martel. Previous inspection on 04/05/2018 was classified as no action indicated (NAI). The investigator screened 5 subjects and enrolled 4 subjects. All 4 enrolled subjects completed the study. All source records were reviewed for all of the 5 screened 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 (monitoring logs, laboratory tests, concomitant medication use, AEs, etc.), the investigational product (IP) accountability records, visit data, 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 the study subjects, with no significant deficiencies reported. The submitted data were verifiable with source records at the study site. The primary efficacy data were verified. There was no evidence of underreporting of AEs.

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

2. Dr. Kara Cauvoto, Site 2110
900 NW 17th Street
Miami, FL 33136

Dr. Kara Cauvoto was inspected on 12/15-18/2020 as a data audit for Study VEKTIS (NVG09B113). This was the first inspection for Dr. Cauvoto. The investigator screened and randomized 3 subjects with 2 subjects completed the study. The first subject was enrolled on 03/20/2014 and the last subject’s last follow-up visit was on 06/20/2015. All source records of the 3 screened subjects were reviewed.

Source records reviewed during the inspection included study protocol and amendments, ICFs, documentation of eligibility criteria and enrollment logs, medical records (monitoring logs, visit reports, laboratory tests, AEs, concomitant medication use, etc.), IP accountability records, paper subjects’ diaries, electronic data capture (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, with no significant deficiencies reported. The submitted data were verifiable with source records at the study site. The primary efficacy endpoint data were verified. There was no evidence of underreporting of AEs or SAEs.

At the end of the inspection, a Form 483 was not issued. Discussed items included the following:
1. The temperature of IP storage area exceeded limits set forth in the protocol for 7 times. During the excursions, IPs were dispensed to subjects prior to the CI’s awareness of the situation.

_Reviewer’s Comments:_ Per the study protocol, IPs must be stored at 39ºF-77ºF. The temperature range of the above mentioned 7 excursions was 78.3ºF -81.9ºF, which are unlikely to affect the stability of the IPs as the sponsor’s stability data sent on 07/22/2014 that the IPs are stable for 36 months when stored at 86ºF.

2. Subject # had two unscheduled visits on and for blood tests. The visits were not documented as unscheduled visits in the eCRF or source documentation.

_Reviewer’s Comments:_ The subject’s visit on was to repeat liver function tests that were mildly elevated at baseline, and the visit on was to obtain a creatine value which was missed during the monthly visit. These are appropriate clinical visits but should have been documented.

In general, this clinical site appeared to be in compliance with GCP. The discussed findings appear unlikely to have significant impacts on the overall efficacy and safety analyses.

{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
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CONCURRENCE:

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Kassa Ayalew, M.D., M.P.H
Branch Chief
Good Clinical Practice Assessment Branch
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CC:
Central Document Room\NDA 214965
DO\Division Director\Wiley Chambers
DO\CDTL\William Boyd
DO\Reviewer\Rhea Lloyd
DO\Project Manager\Wendy Streight
OSI\DCCE\Division Director\Ni Khin
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
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/s/

LING YANG
03/19/2021 03:18:39 PM

MIN LU
03/19/2021 05:02:40 PM

KASSA AYALEW
03/20/2021 09:27:11 AM
**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***

<table>
<thead>
<tr>
<th><strong>Date of This Review:</strong></th>
<th>March 10, 2021</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Requesting Office or Division:</strong></td>
<td>Division of Ophthalmology (DO)</td>
</tr>
<tr>
<td><strong>Application Type and Number:</strong></td>
<td>NDA 214965</td>
</tr>
<tr>
<td><strong>Product Name and Strength:</strong></td>
<td>Verkazia (cyclosporine) ophthalmic emulsion, 0.1%</td>
</tr>
<tr>
<td><strong>Product Type:</strong></td>
<td>Single Ingredient Product</td>
</tr>
<tr>
<td><strong>Rx or OTC:</strong></td>
<td>Prescription (Rx)</td>
</tr>
<tr>
<td><strong>Applicant/Sponsor Name:</strong></td>
<td>Santen, Inc.</td>
</tr>
<tr>
<td><strong>FDA Received Date:</strong></td>
<td>August 26, 2020</td>
</tr>
<tr>
<td><strong>OSE RCM #:</strong></td>
<td>2020-1783</td>
</tr>
<tr>
<td><strong>DMEPA Safety Evaluator:</strong></td>
<td>Nasim Roosta, PharmD</td>
</tr>
<tr>
<td><strong>DMEPA Deputy Director:</strong></td>
<td>Irene Z. Chan, PharmD, BCPS</td>
</tr>
</tbody>
</table>
1 REASON FOR REVIEW
As part of the approval process for Verkazia (cyclosporine) ophthalmic emulsion, the Division of Ophthalmology (DO) requested that we review the proposed Verkazia prescribing information (PI), container label, pouch 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

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

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), container label, pouch 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)

<table>
<thead>
<tr>
<th>IDENTIFIED ISSUE</th>
<th>RATIONALE FOR CONCERN</th>
<th>RECOMMENDATION</th>
</tr>
</thead>
</table>
| Full Prescribing Information- Section 2 Dosage and Administration
1. The administration instructions do not instruct the user to shake the container prior to administration. | Failure to properly shake an emulsion may result in an overdose or underdose. Additionally, we note that the Instructions for Use instruct patients to “gently shake the single-dose container.” | Add the “gently shake” instruction to Section 2, Dosage and Administration. |
Full Prescribing Information – Section 16 How Supplied/Storage and Handling

1. The storage temperature statement does not include the temperature conversion to Celsius.

Some facilities may store based on either Celsius or Fahrenheit; therefore, including both Celsius and Fahrenheit temperatures may better facilitate correct storage.

We recommend adding the corresponding storage temperature in Celsius.

For example: “...

Instructions for Use (IFU)

1. The storage temperature statement, in the section labeled “Storing Verkazia”, does not include the temperature conversion to Celsius.

Some facilities may store based on either Celsius or Fahrenheit; therefore, including both Celsius and Fahrenheit temperatures may better facilitate correct storage.

Consider adding the corresponding storage temperature in Celsius.

For example: “...

Table 3. Identified Issues and Recommendations for Santen, Inc. (entire table to be conveyed to Applicant)

<table>
<thead>
<tr>
<th>IDENTIFIED ISSUE</th>
<th>RATIONALE FOR CONCERN</th>
<th>RECOMMENDATION</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pouch Label and Carton Labeling</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. The established name is not at least half the size of the proprietary name.</td>
<td>In accordance with 21 CFR 201.10(g)(2), the established name should be printed in letters that are at</td>
<td>Revise the established name to be in accordance with 21 CFR 201.10(g)(2).</td>
</tr>
<tr>
<td>IDENTIFIED ISSUE</td>
<td>RATIONALE FOR CONCERN</td>
<td>RECOMMENDATION</td>
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<tr>
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<tr>
<td></td>
<td>least half as large as the letters comprising the proprietary name and be of commensurate prominence to the proprietary name.</td>
<td></td>
</tr>
<tr>
<td>2. The net quantity (“5”) appears more prominently than the strength statement on the pouch label and carton labeling.</td>
<td>The net quantity statement should not compete in size and prominence with important information such as the strength.</td>
<td>Increase the prominence of the strength presentation on the pouch label and the carton labeling.</td>
</tr>
<tr>
<td>3. The format for expiration date is not defined.</td>
<td>Clearly defining the expiration date will minimize confusion and risk for deteriorated drug medication errors.</td>
<td>Identify the expiration date format you intend to use. 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-MMMM-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-MMMM 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.</td>
</tr>
<tr>
<td>4. The storage temperature statement on both the pouch label and carton labeling does not include</td>
<td>Some facilities may store based on either Celsius or Fahrenheit; therefore, including both Celsius and</td>
<td>We recommend adding the corresponding storage temperature in Celsius.</td>
</tr>
<tr>
<td>IDENTIFIED ISSUE</td>
<td>RATIONALE FOR CONCERN</td>
<td>RECOMMENDATION</td>
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<tr>
<td>the temperature conversion to Celsius.</td>
<td>Fahrenheit temperatures may better facilitate correct storage.</td>
<td>For example: “__&quot;.</td>
</tr>
<tr>
<td>5. The route of administration is missing on the PDP of the pouch label and carton labeling.</td>
<td>Stating the route of administration clearly on the PDP of the pouch label and carton label will help minimize the risk of the product being administered via the wrong route.</td>
<td>Per 21 CFR 201.100(b)(3), add the route of administration statement without the use of abbreviations to the PDP of the pouch label and carton labeling. For consistency, use the same statement that is in the PI and IFU: “For topical ophthalmic use&quot;.</td>
</tr>
<tr>
<td>6. The pouch label and carton labeling do not include a statement alerting the patient to shake the contents of the single-dose container prior to administration.</td>
<td>Failure to properly shake an emulsion may result in an overdose or underdose.</td>
<td>We recommend adding a statement to alert the user to shake the contents of the single-dose container prior to administration, as stated in the IFU. For example: “gently shake the single-dose container&quot;.</td>
</tr>
</tbody>
</table>

### Container Label

<p>| 1. The container label does not include the product’s established name, strength, name of manufacturer, packer or distributor of the drug, identifying lot number. | Lack of product identifying characteristics could lead to wrong drug errors. | Include the product's established name, strength, name of manufacturer, packer or distributor of the drug, identifying lot number and expiration date (if not imprinted on plastic of single-dose container). If lot number and expiration date are to be imprinted on the single-dose container, please specify the location and format. |
| 2. It is unclear if the individual vials will include an expiration date. | Including the expiration date on the individual vials will help to minimize the risk of administering deteriorated drug product in instances when the vials | We recommend including the expiration date on the individual vial label. FDA recommends that the human-readable expiration date on the drug package label include a year, month, and non- |</p>
<table>
<thead>
<tr>
<th>IDENTIFIED ISSUE</th>
<th>RATIONALE FOR CONCERN</th>
<th>RECOMMENDATION</th>
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<tr>
<td>are separated from the primary and secondary packaging.</td>
<td>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.</td>
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**Carton Labeling**

1. The carton labeling does not include the machine readable 2D data matrix barcode product identifier.

   The DSCSA requires certain prescription drugs to have a human-readable and machine-readable (2D data matrix barcode) product identifier on the smallest saleable unit (usually the carton) for tracking and tracing purposes.

   NDC: [insert product’s NDC]
   SERIAL: [insert product’s serial number]

   We recommend that you review the draft guidance to determine if the product identifier requirements apply to your product’s labeling. See Draft Guidance for Industry: Product Identifiers under the Drug Supply Chain Security Act - Questions and Answers (September 2018).²

   Note that the draft guidance recommends that the human-readable portion be located near the 2D data matrix barcode.

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² When final, this guidance will represent FDA’s current thinking on this topic. For the most recent version of a guidance, check the FDA guidance web page at [https://www.fda.gov/regulatory-information/search-fda-guidance-documents](https://www.fda.gov/regulatory-information/search-fda-guidance-documents).
Table 3. Identified Issues and Recommendations for Santen, Inc. (entire table to be conveyed to Applicant)

<table>
<thead>
<tr>
<th>IDENTIFIED ISSUE</th>
<th>RATIONALE FOR CONCERN</th>
<th>RECOMMENDATION</th>
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<tbody>
<tr>
<td>LOT: [insert product’s lot number]</td>
<td></td>
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<tr>
<td>EXP: [insert product’s expiration date]</td>
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</table>

4 CONCLUSION

Our evaluation of the proposed Verkazia prescribing information (PI), container label, pouch 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, Inc. 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 Verkazia that Santen, Inc. submitted on August 26, 2020.

<table>
<thead>
<tr>
<th>Table 4. Relevant Product Information for Verkazia</th>
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<tbody>
<tr>
<td><strong>Initial Approval Date</strong></td>
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<tr>
<td><strong>Active Ingredient</strong></td>
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<tr>
<td><strong>Indication</strong></td>
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<tr>
<td><strong>Route of Administration</strong></td>
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<tr>
<td><strong>Dosage Form</strong></td>
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<tr>
<td><strong>Strength</strong></td>
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<tr>
<td><strong>Dose and Frequency</strong></td>
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<tr>
<td><strong>How Supplied</strong></td>
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<tr>
<td><strong>Storage</strong></td>
</tr>
<tr>
<td><strong>Container Closure</strong></td>
</tr>
</tbody>
</table>
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, along with postmarket medication error data, we reviewed the following Verkazia labels and labeling submitted by Santen, Inc.:

- Container label received on August 26, 2020
- Carton labeling received on August 26, 2020
- Pouch label received on August 26, 2020
- Instructions for Use received on August 26, 2020
- Prescribing Information (Image not shown) received on September 2, 2020, available from: \CDSESUB1\evsprod\nda214965\0003\m1\us\114-labeling\draft\labeling\draft-labeling-text.docx

F.2 Label and Labeling Images

Container label

Pouch Label:
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
03/10/2021 11:09:58 AM

IRENE Z CHAN
03/10/2021 11:29:59 AM