CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

210872Orig1s000

PRODUCT QUALITY REVIEW(S)

Recommendation: APPROVAL

NDA 210872
Review # 1

Drug Name/Dosage Form	ZuraGard™ (Isopropyl alcohol, 70% v/v)
Strength	70% v/v
Route of Administration	Topical
Rx / OTC Dispensed	OTC
Applicant	Zurex Pharma, Inc.
US agent, if applicable	N/A

SUBMISSION(S) REVIEWED	DOCUMENT DATE	DISCIPLINE(S) AFFECTED
Original	29-June-2018	ONDP
Response to quality IR	11-October-2018	ONDP
Response to quality IR	15-March-2019	ONDP/CDRH

Quality Review Team

DISCIPLINE	REVIEWER	BRANCH/DIVISION
Drug Substance	Jeffrey Medwid, Ph.D.	ONDP/DNDP-II/ Branch VI
Drug Product	Elise Luong, Ph.D.	ONDP/DNDP-II/ Branch VI
Process & facility	Tarun Mehta	OPF/DPAII/BranchVI
Microbiology	Jason God	OPF/DPAII/BranchVI
CDRH	Marc Neubauer	CDRH/ODE
Biopharmaceutics	N/A	
Regulatory Business Process Manager	Teshara Bouie	OPRO/DRBPMI/RBPMBI
Application Technical Lead	Swapan K. De, Ph.D.	ONDP/DNDP-II/ Branch VI
Laboratory (OTR)	NA	NA
Environmental Assessment (EA) and Labeling	Elise Luong, Ph.D.	ONDP/DNDP-II/ Branch VI

Quality Review Data Sheet

1. RELATED/SUPPORTING DOCUMENTS:

A. DMFs/MAF:

DMF #	Type	Holder	Item Referenced	Code[1]	Status[2]	Date Review Completed	Comments
(b) (4)	III		(b) (4)	4	Adequate	N/A	None
	III			4	Adequate	N/A	None
	N/A			4	Adequate	N/A	None

C. [1] Action codes for DMF Table:
D. 1 – DMF Reviewed.
E. Other codes indicate why the DMF was not reviewed, as follows:
F. 2 –Type 1 DMF
G. 3 – Reviewed previously and no revision since last review
H. 4 – Sufficient information in application
I. 5 – Authority to reference not granted
J. 6 – DMF not available
K. 7 – Other (explain under "Comments")
L. [2] Adequate, Inadequate, or N/A (There is enough data in the application, therefore the DMF did not need to be reviewed)

[1] Adequate, Adequate with Information Request, Deficient, or N/A (There is enough data in the application, therefore the DMF did not need to be reviewed

B. Other Documents: *IND, RLD, or sister applications*

DOCUMENT	APPLICATION NUMBER	DESCRIPTION
IND	117045	Isopropyl Alcohol 70% v/v

2. CONSULTS:

DISCIPLINE	STATUS	RECOMMENDATION	DATE	REVIEWER
Biostatistics	NA			
Pharmacology/Toxicology	NA			
CDRH	Adequate	Approval	3/19/2019	Marc Neubauer
Clinical	NA			
Office of Surveillance	NA			

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ASSESSMENT OF THE BIOPHARMACUETICS ..... N/A

ASSESSMENT OF MICROBIOLOGY ..... Micro review Page 1-2

ASSESSMENT OF ENVIRONMENTAL ANALYSIS ..... …. DP41

I.Review of Common Technical Document-Quality (Ctd-Q) Module 1Drug Product N/A

Labeling & Package Insert ..... DP 43-47

Executive Summary (NDA-207964)

I. Recommendations

Regarding Chemistry Manufacturing and Controls, the application may be approved.

A. Recommendation and Conclusion on Approvability

Regarding quality aspects of the submitted application the drug substance, drug product, microbiology, process and facility sections are reviewed and found adequate to support the approval of the application (see attached reviews). In addition, a consult review is performed by CDRH to evaluate the safety and functionality aspects of the drug product, a single-use 10.5-mL plastic applicator containing 70% isopropyl alcohol solution with a sterile barrier system. The CDRH review was found acceptable on 3/19/2019. The drug product is granted a 24-month shelf life when stored at 25°C/60%RH.

B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable

None

II. Summary of Quality Assessments:

This is a 505(b)(2) NDA, relying upon the Food and Drug Administration's findings of safety for ChloraPrep (New Drug Application 020832) as proposed drug product and ChloraPrep. Both contain active ingredient isopropyl alcohol 70% v/v, and have the same dosage form, route of administration, and indication for use.

Facility review with "acceptable recommendation" is completed on 13 February, 2019. The originally proposed proprietary name 'ZuraPrep' was not acceptable by DMEPA (see review dated September 25, 2018). However, newly proposed name "ZuraGard" is found acceptable (see DMEPA review dated March 1, 2019).

A. Drug Product [] Quality Summary

1. **Strength: Isopropyl alcohol 70% v/v**

2. **Description/Commercial Image:**

Indication of the drug product is to use as a single use, patient preoperative skin prepation solution in presurgical settings as an antiseptic/antimicrobial agent to reduce the bacteria that potentially can cause skin infection. The components of the proposed formulation include (b) (4) isopropyl alcohol, citric acid (b) (4) (b) (4) (b) (4), methylparaben, propylparaben, methylene blu (b) (4), and purified water. The bactericidal activity of alcohols (such as isopropyl alcohol) is accomplished by dissolving the plasma membrane of the cell wall, leading to release of intracellular components, denaturing of proteins, and inhibition of deoxyribonucleic acid, ribonucleic acid, protein, and peptidoglycan synthesis.

The drug product comprises a single-use 10.5-mL plastic applicator containing

70% isopropyl alcohol solution with a sterile barrier system to ensure that the applicator surfaces are sterile. The solution is applied topically to the patient using back and forth strokes of the sponge for approximately 30 seconds on dry surgical sites and approximately 2 minutes on moist surgical sites. The solution is allowed to dry for a minimum of 3 minutes on dry, hairless sites or up to 1 hour in hair. To highlight the coverage area once applied to the skin, the drug product formulation includes an excipien (b) (4) methylene blue (b) (4)
The finished product is packaged in a primary container closure system (b) (4)
(b) (4)

3. Summary of Product Design

The formulation of isopropyl alcohol 70% Solution i (b) (4)
(b) (4)
(b) (4) The manufacturing process has evolved from (b) (4) (b) (4)
(b) (4) The commercial batch formula reflects the proposed composition. There are no differences from the registration batch formula and the commercial batch formula. There is (b) (4) used in the manufacturing process. Microbiological quality is tested in accordance with USP <61> and <62>, using acceptance criteria established according to the guidelines of USP <1111> (b) (4)
(b) (4)

List of Excipients:

(b) (4) Isopropyl alcoho (b) (4)
(b) (4) and Purified water.

4. Process Selection (Unit Operations Summary)

The finished product manufacturing process is similar manufacturing process to NDA 21,669 which is also a Chlorhexidine Gluconate 2% Topical Cloth product. The selection was primarily becaus (b) (4)
(b) (4)

(b) (4)

5. **Container Closure**:

ZuraGard solution is packaged into a single use 10.5-mL applicator container closure system. It is comprised o (b) (4)

(b) (4)

(b) (4)

10.5 mL Applicator

6. **Expiration Date & Storage Conditions**

The drug product is granted a 24-month shelf life when stored at 25ºC/60%RH. The storage statement will be written as "Store betwee (b) (4); (b) (4) 15-30ºC (59-86ºF (b) (4)

(b) (4)

7. **List of co-packaged components: None**

B. Summary of Drug Product Intended Use

Proprietary Name of the Drug Product	(b) (4)
Non Proprietary Name of the Drug Product	Isopropyl Alcohol 70% v/v
Non Proprietary Name of the Drug Substance	Isopropyl Alcohol
Proposed Indication(s) including Intended Patient Population	Patient preoperative skin preparation, for the preparation of the skin prior to surgery and to help reduce bacteria that can potentially cause skin infection
Duration of Treatment	Single use topical application:
Maximum Daily Dose	N/A
Alternative Methods of Administration	None

C. Biopharmaceutics Considerations

1. BCS Classification: Not applicable (BCS class is determined only when applicant proposed the product as BCS Class I.
   - Drug Substance:
   - Drug Product:

2. Biowaivers/Biostudies (For NDA only)
   - Biowaiver Requests: No
   - PK studies: Yes
   - IVIVC: No

D. Novel Approaches

E. Any Special Product Quality Labeling Recommendations

Established name of the drug product:
Isopropyl alcohol 70% v/v surgical solution

F. Life Cycle Knowledge Information (see table below)

Risk Assessment:

Product attribute/CQA	Factors that can impact the CQA	Probability (O)	Severity of Effect (S)	Detectability (D)	FMECA RPN Number	Comment
Assay, stability	• Formulation • Raw materials • Process parameters • Scale/equipments • Site	2	3	2	12	Controlled with specifications

Physical stability (API)	• Formulation • Raw materials • Process parameters • Scale/equipment • Site	2	2	2	8	Stable based on limited data provided.
Microbial Limits	• Formulation • Raw materials • Process parameters • Scale/equipment • Site	2	2	2	8	Controlled with specifications.

Life Cycle Knowledge Information related to Post-Approval Changes (b) (4)

(b) (4)

OVERALL ASSESSMENT AND SIGNATURES: EXECUTIVE SUMMARY

Regarding Chemistry Manufacturing and Controls, the application may be approved.

Application Technical Lead Signature:

Swapan K. De -S

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DN: c=US, o=U.S. Government, ou=HHS, ou=FDA, ou=People, cn=Swapan K. De -S, 0.9.2342.19200300.100.1.1=1300132497
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{For NDA only}

R Regional Information

1.14 Labeling

ZuraPrep IPA is an OTC product, the Office of Nonprescription Drug Product is responsible for labeling reviews to ensure compliance with OTC labeling requirements. ONDP reviews the CMC information for consistency with information provided in the NDA. The drug established name and CMC information in the provided labeling are accurate. On 09/20/18, the labeling review team concluded that the proposed proprietary name ZuraPrep™ is unacceptable. The applicant proposed another proprietary name ZuraGard™ and updated all labels with the new name on 02/15/19.

Carton

(b) (4)

[redacted]

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(b) (4)

[redacted]

Reviewer's Assessment:

(1) The labeling should be revised to state the standard storage language: "Store (b) (4) [redacted] (b) (4) 15-30°C (59-86°F (b) (4) [redacted] (b) (4)

(2) The labeling should include a statement 'Do not use when the sponge is already wet upon opening the package'.

Labeling will be finalized through OND during labeling negotiations with the applicant.

List of Deficiencies: None.

Primary Labeling Reviewer Name and Date: Elise Luong, Ph.D.; 12/17/18.

Secondary Reviewer Name and Date (and Secondary Summary, as needed): Danae Christodoulou, Ph.D., I concur with the reviewer's assessment; 02/25/19.

Elise Luong

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Danae Christodoulou

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M E M O R A N D U M

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

DATE: 10 January 2018

TO: NDA 210-872

FROM: Jason God, Ph.D.

THROUGH: Denise Miller, Senior Microbiologist

SUBJECT: DMA review of NDA 210872
Submission Date: 29 June 2018
Quality Microbiology assessment for ZuraPrep™ (70% v/v isopropyl alcohol).

The subject submission provides for the initial marketing of a non-sterile 70% v/v isopropyl alcohol solution which is contained in an applicator body equipped with a sponge applicator tip (proprietary name: ZuraPrep™). ZuraPrep™ is intended for preoperative skin preparation in a presurgical setting as an antiseptic/antimicrobial agent to reduce the microbial load on the skin and the risk of infection. Since the drug product solution is non-sterile, a review of the manufacturing process and facility is not necessary.

(b) (4) (b) (4) (b) (4) . CDRH conducted the review of the (b) (4)

It is noted that the isopropyl alcohol solution i (b) (4) with methylparaben and propylparaben. (b) (4) content is tested at release and during stability. The applicant does not state that antimicrobial effectiveness testing will be performed. As the drug product is labeled for single use with instructions to discard the applicator and any unused solution after use, no further information will be requested.

Th (b) (4) pouch serves as the sterile barrier and its integrity is assessed visually at release and during long-term stability at 3, 6, 9, 12, 18 and 24 months. Additional assessment is performed by ASTM F1929, Method B (b) (4) at 18 and 24 months during long-term stability. Review of container-closure integrity was performed by CDRH.

Release and stability microbial limits for the isopropyl alcohol solution comply with USP (b) (4) for a cutaneous product: TAMC: NMT (b) (4) CFU/g, TYMC: NMT (b) (4) CFU/g, absence of *Staphylococcus aureus* and *Pseudomonas aeruginosa*. Testing will be performed per USP <61>

and <62>. Microbial limits will be tested on long-term stability samples at 0, 12 and 24 months (proposed expiration is 24 months). The applicant has committed to placing the first 3 production-scale batches on long-term and accelerated stability and to place at least 1 product batch on long-term stability annually thereafter.

ADEQUATE

END

Jason God

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Denise Miller

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Swapan De

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