CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

210821Orig1s000

OTHER REVIEW(S)

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)

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Date of This Review:	June 25, 2018
Requesting Office or Division:	Division of Transplant and Ophthalmology
Application Type and Number:	NDA 210821
Product Name and Strength:	Tetracaine Hydrochloride Ophthalmic Solution USP, 0.5%
Product Type:	Single-ingredient product
Rx or OTC:	Rx
Applicant/Sponsor Name:	Valeant Pharmaceuticals, c/o Paragon Bioteck, Inc.
FDA Received Date:	March 9, 2018
OSE RCM #:	2018-514
DMEPA Safety Evaluator:	Nasim Roosta, PharmD
DMEPA Team Leader:	Otto L. Townsend, PharmD

Reference ID: 4282550

1 PURPOSE OF REVIEW VS REASON FOR REVIEW

As part of the approval process for Tetracaine Hydrochloride Ophthalmic Solution USP 0.5%, the Division of Transplant and Ophthalmology (DTOP) requested that we review the proposed label and labeling for areas that may lead to medication errors.

2 BACKGROUND/REGULATORY HISTORY

Until the approval of Alcon's preservative-free, single-dose Tetracaine Hydrochloride Ophthalmic Solution 0.5% STERI-UNIT (NDA 208135), there were no FDA-approved Tetracaine Hydrochloride ophthalmic products. The Applicant suggests the presence of a single-dose, one-time use Tetracaine Hydrochloride ophthalmic solution and the absence of a multi-dose, preserved version creates an unmet medical need for such a product. The Applicant proposes to fill their identified unmet medical need by marketing (once approved) their proposed preserved, multi-dose product, Tetracaine Hydrochloride ophthalmic solution USP, 0.5%. We note there are currently other "multi-dose, preserved" tetracaine hydrochloride ophthalmic solution, USP, 0.5% products, but they are not FDA-approved.

3 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 for our label and labeling reviews unless we are aware of medication errors through our routine postmarket safety surveillance

4 FINDINGS AND RECOMMENDATIONS

Tables 2 and 3 below include the identified medication error issues with the submitted label and labeling, DMEPA's rationale for concern, and the proposed recommendation to minimize the risk for medication error.

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Table 2: Identified Issues and Recommendations for Division of Transplant and Ophthalmology (DTOP)

Prescribing Information			
	IDENTIFIED ISSUE	**RATIONALE FOR CONCERN**	**RECOMMENDATION**
Full Prescribing Information			
1.	Section 17, Patient Counseling Information, includes the statement, "Do not touch the dropper tip to any surface as this may contaminate the solution."	Since the proposed indication for the product is procedural anesthesia and would likely be administered by a Healthcare Professional, this instruction seems more appropriate for the Dosage and Administration section.	We defer to DTOP on the appropriateness of including this statement in the Patient Counseling section. If they determine it's inappropriate for this section, we recommend its removal or relocation to the Dosage and Administration section.

Table 3: Identified Issues and Recommendations for Paragon BioTeck (entire table to be conveyed to Applicant)

Container Labels and Carton Labeling			
	IDENTIFIED ISSUE	**RATIONALE FOR CONCERN**	**RECOMMENDATION**
1.	The distributor's name on the principal display panel (PDP) of both the carton and container competes in size and prominence with the product established name and strength.	The product name (proper or established) and strength must be the most prominent information on the PDP to prevent product selection errors.[a]	Reduce the size and prominence of the distributor's name "Paragon BioTeck" so that the product's established name and strength are the most prominent information on the PDP of both the carton and container.
2.	The negative statement [redacted] (b) (4) " is displayed on the container label.	Warning statements should be written using affirmative language. This is recommended due to post-marketing reports that state negative statements (e.g. do not) may have the	Remove the statement [redacted] (b) (4) ". The statement, "FOR OPHTHALMIC USE ONLY", is sufficient to inform the user the intended route of administration.

[a] Guidance for Industry: Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors. Food and Drug Administration. 2013. Available from http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM349009.pdf

		opposite of the intended meaning because the word (b) (4)' can be overlooked and misinterpreted as an affirmative action.[a]	

5 CONCLUSION

Our evaluation of the proposed label and 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 the Applicant so that recommendations are implemented prior to approval of this NDA.

APPENDICES: METHODS & RESULTS FOR EACH MATERIALS REVIEWED

APPENDIX A. PRODUCT INFORMATION/PRESCRIBING INFORMATION

Table 4 presents relevant product information for Tetracaine Hydrochloride Ophthalmic Solution USP that Paragon BioTeck submitted on March 9, 2018.

Table 4 presents relevant product information for Tetracaine Hydrochloride Ophthalmic Solution USP that Paragon BioTeck submitted on March 9, 2018, and the listed drug (LD).

Table 4. Relevant Product Information for Tetracaine Hydrochloride Ophthalmic Solution 0.5% STERI-UNIT and Tetracaine Hydrochloride Ophthalmic Solution USP 0.5%

Product Name	**Tetracaine Hydrochloride Ophthalmic Solution 0.5% STERI-UNIT (NDA 208135)**	**Tetracaine Hydrochloride Ophthalmic Solution USP 0.5%**
Initial Approval Date	2/29/2016	N/A
Active Ingredient	Tetracaine Hydrochloride	Tetracaine Hydrochloride
Indication	For procedures requiring a rapid and short-acting topical ophthalmic anesthetic.	For procedures requiring a rapid and short-acting topical ophthalmic anesthetic.
Route of Administration	Ophthalmic	Ophthalmic
Dosage Form	Solution	Solution
Strength	0.5%	0.5%
Dose and Frequency	One drop topically in the eye(s) as needed. Discard unused portion	One drop topically in the eye(s) as needed.
How Supplied	Tetracaine Hydrochloride Ophthalmic Solution 0.5% STERI-UNITS® is supplied as single patient use, 4 mL filled in 4-mL natural medium-or low-density polyethylene plastic DROPTAINER® dispensers in a carton of 12. Each sterilized DROP-TAINER® dispenser is packaged in a clear PVC and Tyvek blister.	Tetracaine Hydrochloride Ophthalmic Solution USP, 0.5% is supplied as a sterile, aqueous, topical ophthalmic solution with a fill volume of 15 mL in a 15 mL low-density polyethylene plastic dropper bottle.
Storage	Storage: Store at 2°C to 25°C (36°F to 77°F). Protect from light. Do not use if solution contains crystals, cloudy, or discolored.	Storage: Store at 15°C to 25°C (59°F to 77°F). Protect from light. Do not use if solution contains crystals, cloudy, or discolored.

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Container Closure	Each droptainer contains a natural low density polyethylene tip with a white polypropylene cap.	Each bottle has a low-density polyethylene dropper tip and a white polypropylene cap.

APPENDIX B. PREVIOUS DMEPA REVIEWS

B.1 Methods

On May 17, 2018, we searched the L:drive and AIMS using the term, Tetracaine to identify reviews previously performed by DMEPA.

B.2 Results

Our search identified one previous review[b]; however, the review was for the referenced product (tetracaine hydrochloride ophthalmic solution 0.5% STERI-UNIT) and is not applicable to this review.

APPENDIX F. LABELS AND LABELING

F.1 List of Labels and Labeling Reviewed

Using the principles of human factors and Failure Mode and Effects Analysis,[c] along with postmarket medication error data, we reviewed the following Tetracaine Hydrochloride Ophthalmic Solution, USP 0.5% labels and labeling submitted by Paragon BioTeck on March 9, 2018.

- Container label
- Carton labeling
- Prescribing Information (Image not shown)

F.2 Label and Labeling Images

[b] Rutledge, Michelle. Label and Labeling Review for Tetracaine Hydrochloride NDA 208135. Silver Spring (MD): FDA, CDER, OSE, DMEPA (US);2016 JAN 06. RCM No.: 2015-1593.

[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

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

/s/

NASIM N ROOSTA
06/25/2018

OTTO L TOWNSEND
06/25/2018