CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

208151Orig1s000

PROPRIETARY NAME REVIEW(S)

PROPRIETARY NAME REVIEW

Division of Medication Error Prevention and Analysis (DMEPA)
Office of Medication Error Prevention and Risk Management (OMEPRM)
Office of Surveillance and Epidemiology (OSE)
Center for Drug Evaluation and Research (CDER)

***** This document contains proprietary information that cannot be released to the public*****

Date of This Review:	June 1, 2016
Application Type and Number:	NDA 208151
Product Name and Strength:	Isopto Atropine (atropine sulfate), Ophthalmic solution
Product Type:	Single Ingredient
Rx or OTC:	Rx
Applicant/Sponsor Name:	Alcon Research, Ltd.
Panorama #:	2016-2996074
DMEPA Primary Reviewer:	Michelle Rutledge, PharmD
DMEPA Team Leader:	Yelena Maslov, PharmD
DMEPA Deputy Director:	Lubna Merchant, MS, PharmD

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1 INTRODUCTION

This review evaluates the proposed proprietary name, Isopto Atropine, from a safety and misbranding perspective. The sources and methods used to evaluate the proposed name are outlined in the reference section and Appendix A respectively. The Applicant did not submit an external name study for this proposed proprietary name.

1.1 REGULATORY HISTORY

Isopto Atropine has been in the US market for more than 50 years. However, this product has never been approved by the FDA. As a result, on February 12, 2016, Alcon submitted an NDA for Isopto Atropine (b) (4) and proposed proprietary name review for the product on March 9, 2016.

Following an email correspondence with DMEPA to clarify if Alcon intended to (b) (4), Alcon submitted an amendment to the proprietary name request on May 11, 2016 revising their proposed name to Isopto Atropine (b) (4)

1.2 PRODUCT INFORMATION

The following product information is provided in the March 9, 2016 and May 11, 2016 proprietary name submission.

- Intended Pronunciation: eye-sop'-toe AT-row-peen
- Active Ingredient: atropine sulfate
- Indication of Use:
  - Mydriasis
  - Cycloplegia
  - Amblyopia
  - (b) (4)
- Route of Administration: Topical ophthalmic
- Dosage Form: Ophthalmic solution
- Strength: 1%
- Dose and Frequency: (b) (4)
- How Supplied:
  - 5 mL filled in 8-mL bottles
  - 15 mL filled in 15-mL bottles
- Storage: 2–25°C (36–77°F)
- Container and Closure Systems: low-density polyethylene plastic DROP-TAINER® dispensers with low-density polyethylene tips and polypropylene caps

2 RESULTS

The following sections provide information obtained and considered in the overall evaluation of the proposed proprietary name.

2.1 MISBRANDING ASSESSMENT

The Office of Prescription Drug Promotion (OPDP) determined that the proposed name would not misbrand the proposed product. DMEPA and the Division of Transplant and Ophthalmology Products (DTOP) concurred with the findings of OPDP's assessment of the proposed name.

2.2 SAFETY ASSESSMENT

The following aspects were considered in the safety evaluation of the name.

2.2.1 United States Adopted Names (USAN) Search

There is a USAN stem, -trop-, present in the proposed proprietary name[1]. The USAN stem lists the trop stem as an infix (-'trop-') for atropine derivatives. As noted above, this name has been on the market for over 50 years and the presence of the USAN stem is consistent with the pharmacologic class and has not led to any reported name confusion medication errors.

2.2.2 Components of the Proposed Proprietary Name

In their submission, the Applicant indicated the following regarding the proposed name:

- The Applicant indicated in their submission that the 'Isopto' root name is contrived and originally referred to the product vehicle which contains hypromellose and various salts.
- The applicant states the 'Atropine' modifier identifies the active ingredient (by the root of the established name of the drug substance).

The proprietary name is comprised of two words, the root name 'Isopto' and the modifier 'Atropine'. Alcon is also marketing several products that contain the ('ISOPTO') root name, ISOPTO Carpine, ISOPTO Plain and ISOPTO Tears. All of these products have been on the market since prior to 1962, except ISOPTO Tears that has been marketed since 1975. Although, DMEPA discourages the use of common prefixes such as "Isopto" because the proliferation of use may increase the risk of name confusion between all the "Isopto" products, we note that this product had been on the market for over 50 years as ISOPTO Atropine. As noted in Section 2.2.5., we have not identified any post-marketing cases or signals related to name confusion with this product.

[1]USAN stem search conducted on April 24, 2016.

2.2.3 FDA Name Simulation Studies

Seventy-five practitioners participated in DMEPA's prescription studies. The responses did not overlap with any currently marketed products nor did the responses sound or look similar to any currently marketed products or any products in the pipeline. Appendix B contains the results from the verbal and written prescription studies.

2.2.4 Comments from Other Review Disciplines at Initial Review

In response to the OSE, April 14, 2016 e-mail, the Division of Transplant and Ophthalmic Products (DTOP)) did not forward any comments or concerns relating to the proposed proprietary name at the initial phase of the review.

2.2.5 Medication Error Data Selection of Cases

We searched the FDA Adverse Event Reporting System (FAERS) database using the strategy listed in Table 2 (see Appendix A1 for a description of FAERS database) for name confusion errors involving ***Isopto Atropine*** that would be relevant for this review.

Table 2. FAERS Search Strategy	
Search Date	April 24, 2016
Drug Name	Isopto Atropine [product name]
Event (MedDRA Terms)	**DMEPA Official Proprietary Name Review Search Terms Event List:** Product name confusion (PT) Medication error (PT) Intercepted medication error (PT) Drug dispensing error (PT) Intercepted drug dispensing error (PT) Circumstance or information capable of leading to a medication error (PT)
Date Limits	- 4/24/2016

The search yielded no cases.

2.2.6 Communication of DMEPA's Analysis at Midpoint of Review

DMEPA communicated our findings to the Division of Transplant and Ophthalmology Products (DTOP) via e-mail on May 26, 2016. At that time we also requested additional information or concerns that could inform our review. Per e-mail correspondence from the DTOP on June 1, 2016, they stated no additional concerns with the proposed proprietary name, Isopto Atropine.

3 CONCLUSIONS

The proposed proprietary name is acceptable.

If you have further questions or need clarifications, please contact Janet Higgins, OSE project manager, at 240-402-0330.

3.1 COMMENTS TO THE APPLICANT

We have completed our review of the proposed proprietary name, Isopto Atropine, and have concluded that this name is acceptable.

If any of the proposed product characteristics as stated in your March 9, 2016 and May 11, 2016 submission are altered prior to approval of the marketing application, the name must be resubmitted for review.

4 REFERENCES

1. ***USAN Stems (http://www.ama-assn.org/ama/pub/physician-resources/medical-science/united-states-adopted-names-council/naming-guidelines/approved-stems.page)***

   USAN Stems List contains all the recognized USAN stems.

APPENDICES

Appendix A

FDA's Proprietary Name Risk Assessment evaluates proposed proprietary names for misbranding and safety concerns.

1. **Misbranding Assessment**: For prescription drug products, OPDP assesses the name for misbranding concerns. . For over-the-counter (OTC) drug products, the misbranding assessment of the proposed name is conducted by DNDP. OPDP or DNDP evaluates proposed proprietary names to determine if the name is false or misleading, such as by making misrepresentations with respect to safety or efficacy. For example, a fanciful proprietary name may misbrand a product by suggesting that it has some unique effectiveness or composition when it does not (21 CFR 201.10(c)(3)). OPDP or DNDP provides their opinion to DMEPA for consideration in the overall acceptability of the proposed proprietary name.
2. **Safety Assessment**: The safety assessment is conducted by DMEPA, and includes the following:

a. Preliminary Assessment: We consider inclusion of USAN stems or other characteristics that when incorporated into a proprietary name may cause or contribute to medication errors (i.e., dosing interval, dosage form/route of administration, medical or product name abbreviations, names that include or suggest the composition of the drug product, etc.) See prescreening checklist below in Table 2*. DMEPA defines a medication error as any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer. [2]

[2] National Coordinating Council for Medication Error Reporting and Prevention. http://www nccmerp.org/aboutMedErrors.html. Last accessed 10/11/2007.

***Table 2- Prescreening Checklist for Proposed Proprietary Name**

	Answer the questions in the checklist below. Affirmative answers to any of these questions indicate a potential area of concern that should be carefully evaluated as described in this guidance.
Y/N	**Is the proposed name obviously similar in spelling and pronunciation to other names?**
	Proprietary names should not be similar in spelling or pronunciation to proprietary names, established names, or ingredients of other products.
Y/N	**Are there medical and/or coined abbreviations in the proprietary name?**
	Proprietary names should not incorporate medical abbreviations (e.g., QD, BID, or others commonly used for prescription communication) or coined abbreviations that have no established meaning.
Y/N	**Are there inert or inactive ingredients referenced in the proprietary name?**
	Proprietary names should not incorporate any reference to an inert or inactive ingredient in a way that might create an impression that the ingredient's value is greater than its true functional role in the formulation (21 CFR 201.10(c)(4)).
Y/N	**Does the proprietary name include combinations of active ingredients?**
	Proprietary names of fixed combination drug products should not include or suggest the name of one or more, but not all, of its active ingredients (see 21 CFR 201.6(b)).
Y/N	**Is there a United States Adopted Name (USAN) stem in the proprietary name?**
	Proprietary names should not incorporate a USAN stem in the position that USAN designates for the stem.
Y/N	**Is this proprietary name used for another product that does not share at least one common active ingredient?**
	Drug products that do not contain at least one common active ingredient should not use the same (root) proprietary name.
Y/N	**Is this a proprietary name of a discontinued product?**
	Proprietary names should not use the proprietary name of a discontinued product if that discontinued drug product does not contain the same active ingredients.

Appendix A1: Description of FAERS

The FDA Adverse Event Reporting System (FAERS) is a database that contains information on adverse event and medication error reports submitted to FDA. The database is designed to support the FDA's postmarket safety surveillance program for drug and therapeutic biologic products. The informatic structure of the FAERS database adheres to the international safety reporting guidance issued by the International Conference on Harmonisation. FDA's Office of Surveillance and Epidemiology codes adverse events and medication errors to terms in the Medical Dictionary for Regulatory Activities (MedDRA) terminology. Product names are coded using the FAERS Product Dictionary. More information about FAERS can be found at: http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Surveillance/AdverseDrugEffects/default.htm.

Appendix B: Prescription Simulation Samples and Results

Figure 1. Isopto Atropine Study (Conducted on March 25, 2016)

Handwritten Requisition Medication Order	Verbal Prescription
Medication Order: Isopto Atropine 1% One or two drops topically Outpatient Prescription: Isopto Atropine 1% UAD #1	Isopto Atropine 1% Use as directed #1

FDA Prescription Simulation Responses (Aggregate 1 Rx Studies Report)

286 People Received Study
75 People Responded

Study Name: Isopto Atropine 1%

INTERPRETATION	OUTPATIENT	VOICE	INPATIENT	TOTAL
Total	20	26	29	

DSOPTO ATROPINE	0	0	1	1
EYESOPTO ATROPINE	0	1	0	1
ISOCTOACTROPINE	0	1	0	1
ISOPTO ATROPHENE	0	1	0	1
ISOPTO ATROPINE	14	11	24	49
ISOPTO ATROPINE 1%	6	3	4	13
ISOPTOATROPINE	0	4	0	4
ISOPTO-ATROPINE	0	2	0	2
ISOPTRO ATROPINE 1%	0	1	0	1
ISOTOATROPINE 1%	0	1	0	1
ISOTOP ATROPINE 1%	0	1	0	1

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/s/

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