CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

217370Orig1s000

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)

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

Date of This Review:	May 28, 2025
Requesting Office or Division:	Division of Ophthalmology (DO)
Application Type and Number:	NDA 217370
Product Name, Dosage Form, and Strength:	Tryptyr (acoltremon) ophthalmic solution, 0.003%
Applicant Name:	Alcon Laboratories, Inc
FDA Received Date:	May 14, 2025
TTT ID #:	2024-9761-1
DMEPA 1 Safety Evaluator:	Sofanit Getahun, PharmD, BCPS
DMEPA 1 Team Leader:	Valerie S. Vaughan, PharmD

1 PURPOSE OF MEMORANDUM

Alcon Laboratories, Inc submitted revised vial label, trade and professional sample pouch and carton labeling received on May 14, 2025 for Tryptyr. The Division of Ophthalmology (DO) requested that we review the revised vial label, trade and professional sample pouch and carton labeling for Tryptyr (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

Alcon Laboratories, Inc implemented all of our recommendations and we have no additional recommendations at this time. Additionally, Alcon clarified that their intended expiration date format is YYYY-MM, using only numerical characters.

4 Page(s) of Draft Labeling have been Withheld in Full as b4 (CCI/TS) immediately following this page

[a] Getahun, S. Label and Labeling Review for Tryptyr (NDA 217370). Silver Spring (MD): FDA, CDER, OSE, DMEPA 1 (US); 2024 OCT 31. TTT ID: 2024-9761.

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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:	April 21, 2025
To:	Michael Puglisi Senior Regulatory Project Manager **Division of Ophthalmology (DO)**
Through:	Marcia Williams, PhD Team Leader, Patient Labeling **Division of Medical Policy Programs (DMPP)**
From:	Sharon Williams, MSN, BSN, RN Senior Patient Labeling Reviewer **Division of Medical Policy Programs (DMPP)** David Foss, PharmD Regulatory Review Officer **Office of Prescription Drug Promotion (OPDP)**
Subject:	Review of Patient Labeling: Instructions for Use (IFU)
Drug Name (established name):	TRYPTYR (acoltremon ophthalmic solution) 0.003%
Dosage Form and Route:	for topical ophthalmic use
Application Type/Number:	NDA 217370
Applicant:	Alcon Laboratories

1 INTRODUCTION

On May 30, 2024, Alcon Laboratories, Inc. submitted for the Agency's review an original New Drug Application (NDA) for acoltremon ophthalmic solution 0.003%, a potent and selective transient receptor potential cation channel subfamily M member 8 (TRPM8) agonist, for topical ocular administration. Acoltremon ophthalmic solution 0.003% is indicated for the treatment of the signs and symptoms of dry eye disease (DED).

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 July 24, 2024 for DMPP and OPDP to review the Applicant's proposed Instructions for Use (IFU) for TRYPTYR (acoltremon ophthalmic solution) 0.003%.

2 MATERIAL REVIEWED

- Draft TRYPTYR (acoltremon ophthalmic solution) 0.003% IFU received on May 30, 2024, revised by the Review Division throughout the review cycle, and received by DMPP and OPDP on April 16, 2025.
- Draft TRYPTYR (acoltremon ophthalmic solution) 0.003% PI received on May 30, 2024, revised by the Review Division throughout the review cycle and received by DMPP and OPDP on April 16, 2025.

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%. 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 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 meets the criteria as specified in both the FDA Guidance for Useful Written Consumer Medication Information (published July 2006) and

Instructions for Use-Patient Labeling for Human Prescription Drug and Biological Products (published July 2022)

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

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

Memorandum

Date: April 16, 2025

To: Michael Puglisi, Regulatory Project Manager
Division of Ophthalmology (DO)

David Summer, Clinical Reviewer, DO

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

CC: Jim Dvorsky, Team Leader, OPDP

Subject: OPDP Labeling Comments for TRYPTYR (acoltremon ophthalmic solution) 0.003%, for topical ophthalmic use

NDA: 217370

Background:

In response to DO's consult request dated April 15, 2025, OPDP has reviewed the proposed Prescribing Information (PI), Instructions for Use (IFU), and carton and container labeling for the original NDA submission for Tryptyr.

PI/IFU:

OPDP's review of the proposed PI is based on the draft labeling emailed to OPDP on April 14, 2025, and we do not have any comments at this time.

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

Carton and Container Labeling:

OPDP's review of the proposed carton and container labeling is based on the draft labeling submitted by the sponsor to the electronic document room on April 15, 2025, and we do not have any comments at this time.

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

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DAVID F FOSS
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Clinical Inspection Summary

Date	January 23, 2025
From	Roy Blay, Ph.D. Michele Fedowitz, M.D. Jenn Sellers, M.D., Ph.D. Good Clinical Practice Assessment Branch (GCPAB) Division of Clinical Compliance Evaluation (DCCE) Office of Scientific Investigations (OSI)
To	William Boyd, M.D., Deputy Division Director Rhea Lloyd, M.D., Clinical Team Leader David Summer, M.D., Reviewing M.O. Michael Puglisi, P.M. Division of Ophthalmology
NDA	217370
Applicant	ALCON LABORATORIES, INC.
Drug	Trypter (acoltremon)
NME	Yes
Therapeutic Classification	Receptor (TRPM8) agonist
Proposed Indication(s)	Treatment of signs and symptoms of dry eye disease
Consultation Request Date	24 Jul 2024
Summary Goal Date	4 Apr 2025
Action Goal Date	30 May 2025
PDUFA Date	30 May 2025

I. OVERALL ASSESSMENT OF FINDINGS AND RECOMMENDATIONS

Clinical data from Protocols AR-15512-CS301 and AR-15512-CS302 were submitted to the Agency in support of NDA 217370 for the use of Trypter (acoltremon) for the treatment of signs and symptoms of dry eye disease. Drs. Liu, Anderson, Springs, and Bamba were inspected in support of this NDA.

Based on the results of these inspections, Protocols AR-15512-CS301 and AR-15512-CS302 appear to have been conducted adequately and the data generated by these sites and submitted by the Applicant appear acceptable in support of the respective indication.

II. BACKGROUND

The Applicant submitted this NDA to support the use Trypter (acoltremon), a receptor (TRPM8) agonist, for the treatment of signs and symptoms of dry eye disease.

Inspections were requested of the following protocols in support of this application:

Protocol Numbers and Titles:

Protocol AR-15512-CS301: "A Phase 3 Study Evaluating the Safety and Efficacy of AR-15512, a Cold Thermoreceptor Modulator, for the Treatment of Dry Eye Disease (COMET-2)"

and

Protocol AR-15512-CS302: "A Phase 3 Study Evaluating the Safety and Efficacy of AR-15512, a Cold Thermoreceptor Modulator, for the Treatment of Dry Eye Disease (COMET-3)"

Protocols AR-15512-CS301and AR-15512-CS302

These protocols were very similar in design with both studies being designed to assess the safety, efficacy, and tolerability of Trypter (acoltremon) in the treatment of signs and symptoms of dry eye disease over a 15-week study period.

Both studies shared the same efficacy objectives, treatment schedules, and subject qualification criteria. These protocols were multicenter, randomized, double-blind, placebo-controlled, parallel-group Phase 3 trials whose primary objectives were to evaluate the safety, efficacy, and tolerability of Trypter (acoltremon) compared to placebo for approximately 13 weeks in the treatment signs and symptoms of dry eye disease.

The study consisted of six clinic visits over a period of 15 weeks. Eligible subjects were randomized in a 1:1 ratio to receive Trypter (acoltremon) or vehicle (placebo) once daily for 13 weeks. Clinical assessments of efficacy were conducted at the baseline visit and on Day 7, Day 14, Day 28, and Day 90**.**

The primary efficacy endpoint of the study was the increase (post-drop on Day 14 vs pre-drop at baseline) in unanesthetized Schirmer score on Day 14.

Each protocol was conducted at 23 sites in the US. For Protocol AR-15512-CS301, there were 465 randomized subjects with the first subject being enrolled on 23 May 2022, and the last subject completing the study on 24 July 2023. For Protocol AR-15512-CS302, there were 467 randomized subjects with the first subject being enrolled on 01 August 2022, and the last subject completing on 17 October 2023.

1. **Alex Liu, M.D.**
   East West Eye Institute
   23441 Madison St., Suite 120
   Torrance, CA 90505

   Site: 207
   Protocol: AR-15512-CS301
   Inspection Dates: 07-11 Oct 2024

Dr. Liu was inspected for the conduct of Protocol AR-15512-CS301**.** This was the first inspection of Dr. Liu. At this site, 75 subjects were screened, 58 subjects were enrolled, and 53 subjects completed the study.

The study files of the 53 subjects completing the study were reviewed**,** including the verification of the primary and secondary efficacy endpoints, and the reporting of adverse events. Subject records reviewed included study eligibility, informed consent, randomization, protocol deviations, discontinuations, and concomitant medications.

Study related documents reviewed included the Form 1572, IRB, sponsor, and monitor correspondence, training documentation, delegation logs, investigational product (IP) receipt, storage, accountability, and administration records, electronic records including access controls and audit trails, and financial disclosures.

The inspection compared the source documents with the data listings, and no significant discrepancies were observed. Adherence to the regulations and the investigational plan appeared adequate.

2. Erik Anderson, M.D.
Vision Institute
320 E. Fontanero St., Ste. 201
Colorado Springs, CO 80907

Site: 219
Protocol: AR-15512-CS301
Inspection Dates: 17-19 Dec 2024

Dr. Anderson was inspected for the conduct of Protocol AR-15512-CS301**.** This was the first inspection of Dr. Anderson. At this site, 104 subjects were screened, 35 subjects were enrolled, and 27 subjects completed the study.

The study files of 29 of the 35 subjects were reviewed for verification of the primary efficacy endpoint. Of the 27 subjects completing the study, the complete source data was reviewed for 23 subjects, in addition to the verification of the primary efficacy endpoint and safety data for the remaining four subjects completing the study. Subject records reviewed included study eligibility, informed consent, and protocol deviations.

Study related documents reviewed included the Form 1572, IRB and monitor correspondence, training documentation, delegation logs, investigational product (IP) receipt, dispensation, and storage records, and financial disclosures.

The inspection compared the source documents with the data listings, and no significant discrepancies were observed. Adherence to the regulations and the investigational plan appeared adequate.

3. Clark Springs, M.D.
Wilmington Eye
1176 E. Cutlar Crossing
Leland, NC 28451

Site: 311
Protocol: AR-15512-CS302
Inspection Dates: 18-21 Nov 2024

Dr. Springs was inspected for the conduct of Protocol AR-15512-CS302**.** This was the first inspection of Dr. Springs. At this site, 109 subjects were screened, 86 subjects were screen failures, 23 subjects were enrolled and randomized to the study, 20 subjects completed the study, and three subjects withdrew from the study.

The study files of all 23 randomized subjects were reviewed**,** including the verification of the primary efficacy endpoint and the reporting of adverse events. Subject records reviewed included study eligibility, informed consent, randomization, protocol deviations, and concomitant medications.

Study related documents reviewed included the Form 1572, IRB, sponsor, and monitor correspondence, training documentation, delegation logs, investigational product (IP) receipt, storage, accountability, dispensation, and return records, electronic records including access controls and audit trails, and financial disclosures.

The inspection compared the source documents and electronic case report forms (eCRFs) with the data listings, and no significant discrepancies were observed. Adherence to the regulations and the investigational plan appeared adequate.

4. Sonya Bamba, M.D.
Wyse Eyecare
900 Skokie Blvd, Suite 150
Northbrook, IL 60062

Site: 316
Protocol: AR-15512-CS302
Inspection Dates:14-20 Nov 2024

Dr. Bamba was inspected for the conduct of Protocol AR-15512-CS302. This was the first inspection of Dr. Bamba. At this site, 132 subjects were screened, 27 subjects were enrolled, and randomized, and one subject withdrew from the study.

The study files of all 27 randomized subjects were reviewed**,** including the verification of the primary efficacy endpoint and the reporting of adverse events. Subject records reviewed included study eligibility, informed consent, randomization, protocol deviations, discontinuations, and concomitant medications.

Study related documents reviewed included the Form 1572, IRB, sponsor, and monitor correspondence, training documentation, delegation logs, investigational product (IP) receipt, storage, accountability, and dispensation records, electronic records including access controls and audit trails, and financial disclosures.

The inspection compared the source documents with the data listings, and no significant discrepancies were observed. Adherence to the regulations and the investigational plan appeared adequate.

{See appended electronic signature page}

Roy Blay, Ph.D.
Good Clinical Practice Assessment Branch
Division of Clinical Compliance Evaluation
Office of Scientific Investigations

CONCURRENCE: {See appended electronic signature page}

Michele Fedowitz, M.D.
Team Leader,
Good Clinical Practice Assessment Branch
Division of Clinical Compliance Evaluation
Office of Scientific Investigations

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Jenn Sellers, M.D., Ph.D.
Branch Chief
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CC:
Central Doc. Rm.
DO/Division Director/Charles Ganley
DO/Deputy Director/William Boyd
DO/Medical Team Leader/Rhea Lloyd
DO/MO/David Summer
DO/Project Manager/Michael Puglisi
OSI/Office Director/David Burrow
OSI/Deputy Director/Laurie Muldowney
OSI/DCCE/Division Director/Kassa Ayalew
OSI/DCCE/GCPAB/Branch Chief/Jenn Sellers
OSI/DCCE/GCPAB/Team Leader/Michele Fedowitz
OSI/DCCE/GCPAB Reviewer/Roy Blay
OSI/DCCE/GCPAB/Program Analyst/Yolanda Patague

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USE-RELATED RISK ANALYSIS
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)

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Date of This Review:	January 17, 2025
Requesting Office or Division:	Division of Ophthalmology (DO)
Application Type and Number:	NDA 217370
Product Type:	Combination Product (Drug-Device)
Product Name, Dosage Form and Strength:	Tryptyr[1] (acoltremon) ophthalmic solution, 0.003%
Device Constituent:	single-use vial
Rx or OTC:	Rx
Applicant/Sponsor Name:	Alcon Laboratories, Inc. (Alcon)
Submission Date:	May 30, 2024
OSE TTT #:	2024-10462
DMEPA 1 Safety Evaluator:	Vraj Patel, PharmD
DMEPA 1 Team Leader:	Murewa Oguntimein, PhD, MHS, CPH, MCHES
DMEP 1 Associate Director for Human Factors:	Ariane O. Conrad, PharmD, BCACP, CDCES, FISMP

[1]The proprietary name, Tryptyr, was found conditionally acceptable on August 20, 2024 (PNR ID# 2024-1044725819).

1 REASON FOR REVIEW

The review evaluates the failure mode and effect analysis (hereafter, referred to as use-related risk analysis (URRA)) submitted under NDA 217370 for Tryptyr (acoltremon) single-use vial to determine whether Alcon needs to submit a human factors (HF) validation study results to support their marketing application.

1.1 MATERIALS REVIEWED

We considered the materials listed in Table 1 for this review.

Table 1. Materials Considered for this Review	
Material Reviewed	Section/ Appendix
Product Information	Section 1.2
Background Information Previous HF Reviews (DMEPA)	Section 1.3
Use Related Risk Analysis	Appendix A
Information Requests Issued During the Review	Appendix B - N/A
Product Sample, Labels and Labeling and Packaging	Appendix C – N/A

N/A=not applicable for this review

1.2 PRODUCT DESCRIPTION

Table 2 presents relevant product information for Tryptyr that Alcon submitted on May 30, 2024.

Table 2. Relevant Product Information for Tryptyr	
Application Number	NDA 217370
Initial Approval Date	N/A
Active Ingredient	Acoltremon
Indication	Treatment of Dry Eye Disease (DED)
Route of Administration	Ophthalmic
Dosage Form	Ophthalmic Solution
Strength	0.003%
Dose and Frequency	One drop twice daily in each eye (approximately 12 hours apart).

Table 2. Relevant Product Information for Tryptyr	
How Supplied	Supplied as a sterile, clear to slightly opalescent, and colorless solution (b) (4) in a low-density polyethylene (LDPE), single-(b) (4) vial with a 0.4 mL fill. One strip of 5 single-(b) (4) vials is packaged in a foil pouch with twelve (12) pouches in a carton. • NDC 00658-595-02; Carton of 60 Single-(b) (4) Vials.
Storage	Store refrigerated at 2°C to 8°C (36°F to 46°F), (b) (4). After opening the carton, (b) (4) may be stored refrigerated or at room temperature at 2°C to 25°C (36°F to 77°F) (b) (4) should be used within 30 days, not to exceed the expiration date printed on the carton and pouch. After opening each foil pouch, the (b) (4) should be used within 7 days, not to exceed the expiration date printed on the vial.
Container Closure/Device Constituent	Five (5) single (b) (4) vials (b) (4) 

Table 2. Relevant Product Information for Tryptyr	
	Single-(b) (4) vial: <u>New vial</u> <u>Used vial</u>  
Intended users	Adult patients, lay caregivers
Intended use environments	Non-clinical (i.e., Home)

1.3 RELEVANT REGULATORY HISTORY RELATED TO THE PROPOSED PRODUCT'S HUMAN FACTORS DEVELOPMENT PROGRAM

On September 09, 2024, we searched for previous DMEPA reviews and FDA/ Alcon interactions relevant to this current review using the terms, "*acoltremon*". See details below.

- On December 19, 2023, Aerie Pharmaceuticals (Aerie) submitted a Type B Pre-NDA meeting request under IND 147005 with regards to the development program being conducted by Aerie for their proposed product acoltremon. The teleconference with Aerie was held on March 4, 2024.
    - On February 13, 2024, we sent a human factors (HF) use-related risk analysis advice letter informing Aerie they do not have to submit an HF validation study with their future marketing application.[2]
    - In addition, we referenced the advice documented in the February 13, 2024 letter and reiterated that an HF validation study does not need to be submitted with their future marketing application in the March 26, 2024 meeting minutes[3].
- On May 30, 2024, Alcon[4] submitted new drug application (NDA) 217370 for Tryptyr (acoltremon) 0.0003% vial for the treatment of Dry Eye Disease. This submission included the URRA, which is the subject of this review.

2 OVERALL ASSESSMENT OF MATERIALS REVIEWED

The section below provides our evaluation of the URRA. The URRA was evaluated to identify use-related hazards associated with the proposed product use and the measures implemented to reduce those risks.

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[2] Fashina, O. Human factors use-related risk analysis advice letter for acoltremon. Silver Spring (MD): FDA, Cder, OND (US); 2024 Feb 13. IND 147005.

[3] Connis, N. Meeting Minutes for acoltremon. Silver Spring (MD): FDA, CDER, OND (US); 2024 Mar 26. IND 147005.

[4] In the NDA 217370 for Tryptyr (acoltremon) 0.0003% vial Cover letter, it stated Alcon acquired Aerie in November 2022 and the IND was submitted under Aerie while the NDA was submitted under Alcon. Cover letter for NDA 217370 for Tryptyr (acoltremon). Fort Worth (TX); Alcon Laboratories Inc. 2024 May 30. Available from: \\CDSESUB1\EVSPROD\nda217370\0001\m1\us\m1-2-cover-letter.pdf.

2.1 USE-RELATED RISK ANALYSIS

Alcon submitted a URRA for their proposed product, Tryptyr, which identified and evaluated the tasks involved in the use of the product, the errors that users might commit, the tasks they might fail to perform, and the potential negative consequences of use errors. Alcon proposes that a human factors validation study is not needed to be submitted to support the safe and effective use of Tryptyr. The Sponsor's justification notes that "*The AR-15512 combination product is simple to use and no different than other marketed prescription ophthalmic unit-dose products (e.g., Cequa, Xiidra, Restasis)*". Thus, based on the URRA and the supporting information from the predicate products, it is concluded that a Human Factors validation study is not required for AR-15512 ophthalmic solution.[5]

We reviewed the URRA for Tryptyr and, based on the information we have at this time, the tasks evaluated appear to be comprehensive and appropriate based on what Alcon proposes for the design and intended use of this product. Furthermore, for the tasks evaluated in the URRA, we did not identify any additional use-related issues that were not analyzed. Based on the Alcon's identified use-related risks for Tryptyr, we find that that the introduction of this proposed product is not expected to raise new or different risks compared to similar marketed products.

We note that the DMEPA 1 nomenclature and labeling review team evaluated product specific label and labeling under a separate cover.[6]

3 CONCLUSION

Our review of the use-related risk analysis determined that the tasks evaluated appear to be comprehensive and appropriate based on Alcon's design of Tryptyr. As such, we agree with Alcon's justification for not submitting human factors (HF) validation study results as part of their marketing application. We have no HF recommendations for this marketing application.

[5] NDA 217370 URRA Human Factors Submission. Fort Worth (TX): Alcon Laboratories; 2024 May 30. Available from: \\CDSESUB1\EVSPROD\nda217370\0001\m5\53-clin-stud-rep\535-rep-effic-safety-stud\dry-eye-disease\5354-other-stud-rep\r-02202\study-report-body.pdf.

[6] Getahun, S. Label and Labeling Review for Tryptyr (NDA 217370). Silver Spring (MD): FDA, CDER, OSE, DMEPA 1 (US) 2024 Oct 31. TTT ID No. 2024-9761.

APPENDICES: METHODS & RESULTS FOR EACH MATERIALS REVIEWED

APPENDIX A. URRA AND HF-RELATED SUPPORTING DOCUMENTS

The failure mode and effects analysis for Tryptyr can be accessible in EDR via: \\CDSESUB1\EVSPROD\nda217370\0001\m5\53-clin-stud-rep\535-rep-effic-safety-stud\dry-eye-disease\5354-other-stud-rep\r-02202\study-report-body.pdf.

Justification for Excluding Human Factors Study for Tryptyr can be accessible in EDR via: \\CDSESUB1\EVSPROD\nda217370\0001\m5\53-clin-stud-rep\535-rep-effic-safety-stud\dry-eye-disease\5354-other-stud-rep\r-02202\study-report-body.pdf.

APPENDIX B. INFORMATION REQUESTS ISSUED DURING THE REVIEW

N/A

APPENDIX C. LABELS AND LABELING AND PACKAGING

N/A

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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)

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Date of This Review:	October 31, 2024
Requesting Office or Division:	Division of Ophthalmology (DO)
Application Type and Number:	NDA 217370
Product Name, Dosage Form, and Strength:	Tryptyr[a] (acoltremon) ophthalmic solution, 0.003%
Product Type:	Combination Product (Drug-Device)
Rx or OTC:	Prescription (Rx)
Applicant Name:	Alcon Laboratories, Inc
FDA Received Date:	May 30, 2024
TTT ID #:	2024-9761
DMEPA 1 Safety Evaluator:	Sofanit Getahun, PharmD, BCPS
DMEPA 1 Team Leader:	Valerie S. Vaughan, PharmD

[a] The proprietary name for this NDA, Tryptyr was found conditionally acceptable on August 22, 2024

1 INTRODUCTION

As part of the approval process for Tryptyr (acoltremon) ophthalmic solution, the Division of Ophthalmology (DO) requested that we review the proposed Tryptyr Prescribing Information (PI), Instructions for Use (IFU), container label, trade and professional sample pouch and carton labeling for areas of vulnerability that may lead to medication errors.

2 MATERIALS REVIEWED

This section lists the materials considered for our review of NDA 217370.

Table 1. Materials Considered for this Label and Labeling Review	
Material(s) Reviewed	Appendix Section
Relevant Product Information	A
Labels and Labeling	B

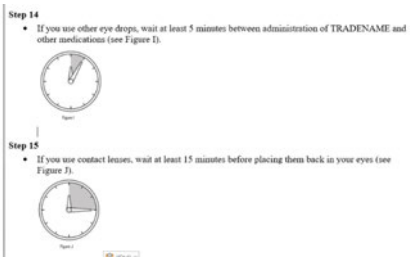
3 CONCLUSION

The proposed Tryptyr Prescribing Information (PI), Instructions for Use (IFU), container label, trade and professional sample pouch and carton labeling may be improved to promote safe use of this product from a medication error perspective. We provide the identified medication error issues, our rationale for concern, and our proposed recommendations to minimize the risk for medication error for the Division of Ophthalmology (DO) in Section 4 and for Alcon Laboratories, Inc in Section 5.

Note that DMEPA 1 is evaluating the Use Related Risk Analaysis under separate cover and based on the outcome of that review, additional label and labeling comments may be forthcoming.

4 RECOMMENDATIONS FOR THE DIVISION OF OPHTHALMOLOGY (DO)

Table 2. Identified Issues and Recommendations for the Division of Ophthalmology (DO)			
	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
General			
1.	As currently presented, the proprietary name is denoted by the placeholder "TRADENAME" throughout the PI. The proposed proprietary name "Tryptyr" was found conditionally acceptable on August 22, 2024. Remove the placeholder "TRADENAME" and replace with the conditionally acceptable name "Tryptyr."		
2.	As currently presented, we note that the package type term "single (b) (4)" is used throughout the prescribing information,	Our Office of Pharmaceutical Quality (OPQ) colleagues confirmed that the correct package type term should be "single dose."	Revise the package type term to "single dose" throughout the labels and labeling.

Table 2. Identified Issues and Recommendations for the Division of Ophthalmology (DO)			
	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
	container label, pouch, and carton labeling		
Instructions for Use (IFU)			
1.	We note (b) (4) for the carton and foil pouch once opened differ from the printed expiration date. However, as currently presented, we note Step 1 and Step 4 do not include instructions directing the user (b) (4) (b) (4).	Lack of instruction may result in use of deteriorated product medication errors.	We recommend including a bullet under Step 1 and Step 4 which direct users (b) (4) (b) (4) once carton is opened and once the foil pouch is opened, respectively.
2.	As currently presented, Figure I corresponds to Step 14 of the IFU, however, it is listed under Step 15, along with Figure J which is the figure that corresponds to Step 15. (b) (4)	Such presentation lacks clarity and may result in medication errors related to wrong administration technique.	We recommend relocating Figure I such that it is listed under the corresponding step. For example:  Step 14 • If you use other eye drops, wait at least 5 minutes between administration of TRADENAME and other medications (see Figure I). Step 15 • If you use contact lenses, wait at least 15 minutes before placing them back in your eyes (see Figure J).

5 RECOMMENDATIONS FOR ALCON LABORATORIES, INC

Note that additional label and labeling comments may be forthcoming when we have completed our evaluation of your Use Related Risk Analysis.

Table 3. Identified Issues and Recommendations for Alcon Laboratories, Inc (entire table to be conveyed to Applicant)			
	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
Container Label, Trade and Professional Sample Pouch and Carton Labeling			
1.	As currently presented, the format for the expiration date is not defined.	We are unable to assess the proposed expiration date format from a medication safety perspective.	To minimize confusion and reduce the risk for deteriorated drug medication errors, we recommend identifying 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-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 forward slash to separate the portions of the expiration date. See *Guidance for Industry: Product Identifiers under the Drug Supply Chain Security Act*

Table 3. Identified Issues and Recommendations for Alcon Laboratories, Inc (entire table to be conveyed to Applicant)			
	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
			- Questions and Answers (June 2021).
2.	As currently presented, the proprietary name is denoted by the placeholder "TRADENAME."	The proposed proprietary name "Tryptyr" was found conditionally acceptable on August 22, 2024.	Remove the placeholder "TRADENAME" and replace with the conditionally acceptable name "Tryptyr." Additionally, consider presenting the proprietary name in a single color.
Carton Labeling			
1.	As currently presented, the route of administration does not appear prominently.	Critical product information such as the proprietary name, established name along with the product strength, route of administration and warning or cautionary statements should be the most prominent information on the PDP.	We recommend increasing the prominence of the route of administration and relocating it to appear on the next line following the established name and strength. See *Guidance for Industry: Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors (May 2022).*[b]
2.	As currently presented, the statement of dosage on the professional sample and trade pouch and carton labeling can be improved such that the frequency of doses is included.	To improve clarity and support safe and effective use of the product.	We recommend revising the statement of dosage such that the frequency of administration is included. For example: *"Place one drop in each eye twice daily (approximately 12 hours apart)."*
3.	As currently presented, we note that the product identifier is not included	The Drug supply Chain Security Act (DSCSA) requires, for certain prescription products, that	We recommend that you review the guidance to determine if the product identifier requirements apply

[b] Guidance for Industry: Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors. May 2022. Available from: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/safety-considerations-container-labels-and-carton-labeling-design-minimize-medication-errors.

Table 3. Identified Issues and Recommendations for Alcon Laboratories, Inc (entire table to be conveyed to Applicant)			
	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
	on the trade carton labeling.	the smallest saleable unit display a human-readable and machine-readable (2D data matrix barcode) product identifier. The DSCSA guidance on product identifier recommends a machine-readable (2D data matrix barcode) product identifier and a human-readable product identifier. The guidance also recommends the format of the human-readable portion be located near the 2D data matrix barcode as the following: NDC: [insert NDC] Serial: [insert serial number] LOT: [insert lot number] EXP: [insert expiration date]	to your product's labeling. See *Guidance for Industry: Product Identifiers under the Drug Supply Chain Security Act – Questions and Answers* (July 2021).[c] If you determine that the product identifier requirements apply to your product's labeling, add a placeholder for the product identifier on the trade carton labeling. Additionally, we recommend you ensure there is sufficient white space between the linear barcode and 2-D matrix barcode to allow barcode scanners the ability to correctly read each barcode.
4.	As currently presented, we note the (b) (4) for the product once the carton is opened *versus* when the foil pouch is opened are different. However, the storage statement on the carton labeling does not clarify that storage up to 30	We are concerned that this presentation lacks clarity, and as such introduces the risk of wrong storge medication errors. The storage statement should be clearly stated to mitigate the risk of storage errors	We recommend revising the storage statement to better clarify storage in the unopened pouch. Additionally, we recommend including the units of measurement following each numeric portion of the temperature range. For example: *"After opening, TRADENAME can be stored*

[c] Guidance for Industry: Product Identifiers Under the Drug Supply Chain Security Act - Questions and Answers. 2021. Available from: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/product-identifiers-under-drug-supply-chain-security-act-questions-and-answers

Table 3. Identified Issues and Recommendations for Alcon Laboratories, Inc (entire table to be conveyed to Applicant)			
	IDENTIFIED ISSUE	**RATIONALE FOR CONCERN**	**RECOMMENDATION**
	days is if the product is in an unopened pouch.		*refrigerated or at room temperature up to 30 days in the unopened foil pouch, 2°C to 25°C (36°F to 77°F).* *Date **carton** first opened __/__/__.* *See additional discard instructions on the pouch."*
5.	There is a (b) (4) (b) (4) on the professional sample and trade carton labeling. (b) (4)	(b) (4)	Delete, move, and/or decrease (b) (4)
Pouch Labeling			
1.	As currently presented, a space is not provided for users to write in the date of first opening of the pouch.	Lack of an allotted space to write in the date of first opening of the pouch may lead to storage and administration errors, for example, use of vials beyond 7 days.	We recommend including a space for patients to write in the date when the pouch is first opened. For example, "Date of first opening __/__/__". The "__/__/__" statement will alert users to write a complete date (month, day, and year) on the pouch labeling.

APPENDICES: METHODS & RESULTS FOR EACH MATERIALS REVIEWED

APPENDIX A. RELEVANT PRODUCT INFORMATION

Table 4 presents relevant product information for acoltremon received on May 30, 2024 from Alcon Laboratories, Inc.

Table 4. Relevant Product Information for acoltremon	
Initial Approval Date	N/A
Active Ingredient	acoltremon
Indication	Treatment of the signs and symptoms of dry eye disease (DED).
Dosage Form	ophthalmic solution
Strength	0.003%
Route of Administration	Topical ophthalmic
Dose and Frequency	Instill one drop twice daily in each eye (approximately 12 hours apart).
How Supplied	Low-density polyethylene (LDPE), single-(b) (4) vial with a 0.4 mL fill. One strip of 5 single-(b) (4) vials is packaged in a foil pouch with twelve (12) pouches in a carton. NDC 00658-595-02; Carton of 60 Single-(b) (4) Vials.
Storage	Store refrigerated at 2°C to 8°C (36°F to 46°F), (b) (4) (b) (4). After opening the carton, (b) (4) may be stored refrigerated or at room temperature at 2°C to 25°C (36°F to 77°F) (b) (4) should be used within 30 days, not to exceed the expiration date printed on the carton and pouch. After opening each foil pouch, the (b) (4) should be used within 7 days, not to exceed the expiration date printed on the vial.
Container Closure	\\CDSESUB1\EVSPROD\nda217370\0001\m3\32-body-data\32p-drug-prod\acoltremon-ophthalmic-solution\32p7-cont-closure-sys\container-closure-system-(b) (4).pdf

APPENDIX B. LABELS AND LABELING

B.1 List of Labels and Labeling Reviewed

Using the principles of human factors and Failure Mode and Effects Analysis,[d] along with postmarket medication error data, we reviewed the following Tryptyr labels and labeling submitted by Alcon Laboratories, Inc.

- Prescribing Information received on May 30, 2024, available from: \\CDSESUB1\EVSPROD\nda217370\0001\m1\us\m1-14-1-3-draft-labeling-text.docx
- Container label received on May 30, 2024
- Carton labeling received on May 30, 2024
- Pouch labeling received on May 30, 2024
- Professional Sample Carton Labeling received on May 30, 2024
- Professional Sample Pouch labeling received on May 30, 2024

B.2 Container Label(s) and Carton Labeling Images

Container label

3 Page(s) of Draft Labeling have been Withheld in Full as b4 (CCI/TS) immediately following this page

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

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/s/

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