

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

204822Orig1s000

ADMINISTRATIVE and CORRESPONDENCE
DOCUMENTS

EXCLUSIVITY SUMMARY

NDA # 204822

SUPPL #

HFD #

Trade Name IZBA

Generic Name: Travoprost ophthalmic solution, 0.003%

Applicant Name: Alcon, Inc

Approval Date, If Known: May 15, 2014

PART I IS AN EXCLUSIVITY DETERMINATION NEEDED?

1. An exclusivity determination will be made for all original applications, and all efficacy supplements. Complete PARTS II and III of this Exclusivity Summary only if you answer "yes" to one or more of the following questions about the submission.

a) Is it a 505(b)(1), 505(b)(2) or efficacy supplement?

YES NO

If yes, what type? Specify 505(b)(1), 505(b)(2), SE1, SE2, SE3,SE4, SE5, SE6, SE7, SE8

505(b)(1)

c) Did it require the review of clinical data other than to support a safety claim or change in labeling related to safety? (If it required review only of bioavailability or bioequivalence data, answer "no.")

YES NO

If your answer is "no" because you believe the study is a bioavailability study and, therefore, not eligible for exclusivity, EXPLAIN why it is a bioavailability study, including your reasons for disagreeing with any arguments made by the applicant that the study was not simply a bioavailability study.

If it is a supplement requiring the review of clinical data but it is not an effectiveness supplement, describe the change or claim that is supported by the clinical data:

d) Did the applicant request exclusivity?

YES NO

If the answer to (d) is "yes," how many years of exclusivity did the applicant request?

3

e) Has pediatric exclusivity been granted for this Active Moiety?

YES NO

If the answer to the above question in YES, is this approval a result of the studies submitted in response to the Pediatric Written Request?

IF YOU HAVE ANSWERED "NO" TO ALL OF THE ABOVE QUESTIONS, GO DIRECTLY TO THE SIGNATURE BLOCKS AT THE END OF THIS DOCUMENT.

2. Is this drug product or indication a DESI upgrade?

YES NO

IF THE ANSWER TO QUESTION 2 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8 (even if a study was required for the upgrade).

PART II FIVE-YEAR EXCLUSIVITY FOR NEW CHEMICAL ENTITIES

(Answer either #1 or #2 as appropriate)

1. Single active ingredient product.

Has FDA previously approved under section 505 of the Act any drug product containing the same active moiety as the drug under consideration? Answer "yes" if the active moiety (including other esterified forms, salts, complexes, chelates or clathrates) has been previously approved, but this particular form of the active moiety, e.g., this particular ester or salt (including salts with hydrogen or coordination bonding) or other non-covalent derivative (such as a complex, chelate, or clathrate) has not been approved. Answer "no" if the compound requires metabolic conversion (other than deesterification of an esterified form of the drug) to produce an already approved active moiety.

YES NO

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA# 21257 Travatan

NDA# 21994 Travatan Z

NDA#

2. Combination product.

If the product contains more than one active moiety(as defined in Part II, #1), has FDA previously approved an application under section 505 containing any one of the active moieties in the drug product? If, for example, the combination contains one never-before-approved active moiety and one previously approved active moiety, answer "yes." (An active moiety that is marketed under an OTC monograph, but that was never approved under an NDA, is considered not previously approved.)

YES NO

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA#

NDA#

NDA#

IF THE ANSWER TO QUESTION 1 OR 2 UNDER PART II IS "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8. (Caution: The questions in part II of the summary should only be answered "NO" for original approvals of new molecular entities.)

IF "YES," GO TO PART III.

PART III THREE-YEAR EXCLUSIVITY FOR NDAs AND SUPPLEMENTS

To qualify for three years of exclusivity, an application or supplement must contain "reports of new clinical investigations (other than bioavailability studies) essential to the approval of the application and conducted or sponsored by the applicant." This section should be completed only if the answer to PART II, Question 1 or 2 was "yes."

1. Does the application contain reports of clinical investigations? (The Agency interprets "clinical investigations" to mean investigations conducted on humans other than bioavailability studies.) If

the application contains clinical investigations only by virtue of a right of reference to clinical investigations in another application, answer "yes," then skip to question 3(a). If the answer to 3(a) is "yes" for any investigation referred to in another application, do not complete remainder of summary for that investigation.

YES NO

IF "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8.

2. A clinical investigation is "essential to the approval" if the Agency could not have approved the application or supplement without relying on that investigation. Thus, the investigation is not essential to the approval if 1) no clinical investigation is necessary to support the supplement or application in light of previously approved applications (i.e., information other than clinical trials, such as bioavailability data, would be sufficient to provide a basis for approval as an ANDA or 505(b)(2) application because of what is already known about a previously approved product), or 2) there are published reports of studies (other than those conducted or sponsored by the applicant) or other publicly available data that independently would have been sufficient to support approval of the application, without reference to the clinical investigation submitted in the application.

(a) In light of previously approved applications, is a clinical investigation (either conducted by the applicant or available from some other source, including the published literature) necessary to support approval of the application or supplement?

YES NO

If "no," state the basis for your conclusion that a clinical trial is not necessary for approval AND GO DIRECTLY TO SIGNATURE BLOCK ON PAGE 8:

(b) Did the applicant submit a list of published studies relevant to the safety and effectiveness of this drug product and a statement that the publicly available data would not independently support approval of the application?

YES NO

(1) If the answer to 2(b) is "yes," do you personally know of any reason to disagree with the applicant's conclusion? If not applicable, answer NO.

YES NO

If yes, explain:

(2) If the answer to 2(b) is "no," are you aware of published studies not conducted or sponsored by the applicant or other publicly available data that could independently

demonstrate the safety and effectiveness of this drug product?

YES NO

If yes, explain:

- (c) If the answers to (b)(1) and (b)(2) were both "no," identify the clinical investigations submitted in the application that are essential to the approval:

Study C-11-034 titled "A Multicenter, Double-Masked Study of the Safety and Efficacy of Travoprost Ophthalmic Solution, 0.003% Compared to Travatan in Patients with Open-Angle Glaucoma or Ocular Hypertension"

Studies comparing two products with the same ingredient(s) are considered to be bioavailability studies for the purpose of this section.

3. In addition to being essential, investigations must be "new" to support exclusivity. The agency interprets "new clinical investigation" to mean an investigation that 1) has not been relied on by the agency to demonstrate the effectiveness of a previously approved drug for any indication and 2) does not duplicate the results of another investigation that was relied on by the agency to demonstrate the effectiveness of a previously approved drug product, i.e., does not redemonstrate something the agency considers to have been demonstrated in an already approved application.

- a) For each investigation identified as "essential to the approval," has the investigation been relied on by the agency to demonstrate the effectiveness of a previously approved drug product? (If the investigation was relied on only to support the safety of a previously approved drug, answer "no.")

Investigation #1 YES NO

Investigation #2 YES NO

If you have answered "yes" for one or more investigations, identify each such investigation and the NDA in which each was relied upon:

- b) For each investigation identified as "essential to the approval", does the investigation duplicate the results of another investigation that was relied on by the agency to support the effectiveness of a previously approved drug product?

Investigation #1 YES NO

Investigation #2 YES NO

If you have answered "yes" for one or more investigation, identify the NDA in which a similar investigation was relied on:

c) If the answers to 3(a) and 3(b) are no, identify each "new" investigation in the application or supplement that is essential to the approval (i.e., the investigations listed in #2(c), less any that are not "new"):

Study C-11-034 titled "A Multicenter, Double-Masked Study of the Safety and Efficacy of Travoprost Ophthalmic Solution, 0.003% Compared to Travatan in Patients with Open-Angle Glaucoma or Ocular Hypertension"

4. To be eligible for exclusivity, a new investigation that is essential to approval must also have been conducted or sponsored by the applicant. An investigation was "conducted or sponsored by" the applicant if, before or during the conduct of the investigation, 1) the applicant was the sponsor of the IND named in the form FDA 1571 filed with the Agency, or 2) the applicant (or its predecessor in interest) provided substantial support for the study. Ordinarily, substantial support will mean providing 50 percent or more of the cost of the study.

a) For each investigation identified in response to question 3(c): if the investigation was carried out under an IND, was the applicant identified on the FDA 1571 as the sponsor?

Investigation #1
IND # 51000 YES ! NO
! Explain:

Investigation #2
IND # YES ! NO
! Explain:

(b) For each investigation not carried out under an IND or for which the applicant was not identified as the sponsor, did the applicant certify that it or the applicant's predecessor in interest provided substantial support for the study?

Investigation #1
!
!
YES ! NO
Explain: ! Explain:

Investigation #2
!
!
YES ! NO
Explain: ! Explain:

(c) Notwithstanding an answer of "yes" to (a) or (b), are there other reasons to believe that the applicant should not be credited with having "conducted or sponsored" the study? (Purchased studies may not be used as the basis for exclusivity. However, if all rights to the drug are purchased (not just studies on the drug), the applicant may be considered to have sponsored or conducted the studies sponsored or conducted by its predecessor in interest.)

YES NO

If yes, explain:

Name of person completing form: Judit Milstein
Title: Chief, Project Management Staff
Date: May 15, 2014

Name of Office/Division Director signing form: Renata Albrecht, MD
Title: Director, Division of Transplant and Ophthalmology Products

Form OGD-011347; Revised 05/10/2004; formatted 2/15/05; removed hidden data 8/22/12;

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

/s/

JUDIT R MILSTEIN
05/16/2014

RENATA ALBRECHT
05/16/2014

NDA 204822

IZBA (travoprost ophthalmic solution), 0.003%

For the reduction of intraocular pressure in patients with open-angle glaucoma and ocular hypertension
Alcon, Inc.

This application provides for a new formulation of travoprost ophthalmic solution; Therefore PREA is not applicable

ACTION PACKAGE CHECKLIST

APPLICATION INFORMATION ¹		
NDA # 204822 BLA #	NDA Supplement # BLA Supplement #	If NDA, Efficacy Supplement Type: <i>(an action package is not required for SE8 or SE9 supplements)</i>
Proprietary Name: IZBA Established/Proper Name: travoprost ophthalmic solution Dosage Form:		Applicant: Alcon, Inc Agent for Applicant (if applicable):
RPM: Judit Milstein		Division: Transplant and Ophthalmology Drug Products
NDA Application Type: <input checked="" type="checkbox"/> 505(b)(1) <input type="checkbox"/> 505(b)(2) Efficacy Supplement: <input type="checkbox"/> 505(b)(1) <input type="checkbox"/> 505(b)(2) BLA Application Type: <input type="checkbox"/> 351(k) <input type="checkbox"/> 351(a) Efficacy Supplement: <input type="checkbox"/> 351(k) <input type="checkbox"/> 351(a)	<p><u>For ALL 505(b)(2) applications, two months prior to EVERY action:</u></p> <ul style="list-style-type: none"> Review the information in the 505(b)(2) Assessment and submit the draft² to CDER OND IO for clearance. Check Orange Book for newly listed patents and/or exclusivity (including pediatric exclusivity) <p><input type="checkbox"/> No changes <input type="checkbox"/> New patent/exclusivity (<i>notify CDER OND IO</i>) Date of check:</p> <p><i>Note: If pediatric exclusivity has been granted or the pediatric information in the labeling of the listed drug changed, determine whether pediatric information needs to be added to or deleted from the labeling of this drug.</i></p>	
❖ Actions		
<ul style="list-style-type: none"> Proposed action- User Fee Goal Date is <u>May 15, 2014</u> 		<input checked="" type="checkbox"/> AP <input type="checkbox"/> TA <input type="checkbox"/> CR
<ul style="list-style-type: none"> Previous actions (<i>specify type and date for each action taken</i>) 		<input checked="" type="checkbox"/> None
❖ If accelerated approval or approval based on efficacy studies in animals, were promotional materials received? Note: Promotional materials to be used within 120 days after approval must have been submitted (for exceptions, see http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm069965.pdf). If not submitted, explain _____		<input type="checkbox"/> Received
❖ Application Characteristics ³		

¹ The **Application Information** Section is (only) a checklist. The **Contents of Action Package** Section (beginning on page 2) lists the documents to be included in the Action Package.

² For resubmissions, 505(b)(2) applications must be cleared before the action, but it is not necessary to resubmit the draft 505(b)(2) Assessment to CDER OND IO unless the Assessment has been substantively revised (e.g., new listed drug, patent certification revised).

³ Answer all questions in all sections in relation to the pending application, i.e., if the pending application is an NDA or BLA supplement, then the questions should be answered in relation to that supplement, not in relation to the original NDA or BLA. For example, if the application is a pending BLA supplement, then a new *RMS-BLA Product Information Sheet for TBP* must be completed.

Review priority: Standard Priority
 Chemical classification (new NDAs only): 5
 (*confirm chemical classification at time of approval*)

- | | |
|---|---|
| <input type="checkbox"/> Fast Track | <input type="checkbox"/> Rx-to-OTC full switch |
| <input type="checkbox"/> Rolling Review | <input type="checkbox"/> Rx-to-OTC partial switch |
| <input type="checkbox"/> Orphan drug designation | <input type="checkbox"/> Direct-to-OTC |
| <input type="checkbox"/> Breakthrough Therapy designation | |

NDAs: Subpart H

- Accelerated approval (21 CFR 314.510)
 Restricted distribution (21 CFR 314.520)

Subpart I

- Approval based on animal studies

- Submitted in response to a PMR
 Submitted in response to a PMC
 Submitted in response to a Pediatric Written Request

BLAs: Subpart E

- Accelerated approval (21 CFR 601.41)
 Restricted distribution (21 CFR 601.42)

Subpart H

- Approval based on animal studies

- REMS: MedGuide
 Communication Plan
 ETASU
 MedGuide w/o REMS
 REMS not required

Comments:

❖ BLAs only: Ensure <i>RMS-BLA Product Information Sheet for TBP</i> and <i>RMS-BLA Facility Information Sheet for TBP</i> have been completed and forwarded to OPI/OBI/DRM (Vicky Carter)	<input type="checkbox"/> Yes, dates
❖ BLAs only: Is the product subject to official FDA lot release per 21 CFR 610.2 (<i>approvals only</i>)	<input type="checkbox"/> Yes <input type="checkbox"/> No
❖ Public communications (<i>approvals only</i>)	
• Office of Executive Programs (OEP) liaison has been notified of action	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
• Indicate what types (if any) of information were issued	<input checked="" type="checkbox"/> None <input type="checkbox"/> FDA Press Release <input type="checkbox"/> FDA Talk Paper <input type="checkbox"/> CDER Q&As <input type="checkbox"/> Other
❖ Exclusivity	
• Is approval of this application blocked by any type of exclusivity (orphan, 5-year NCE, 3-year, pediatric exclusivity)? • If so, specify the type	<input checked="" type="checkbox"/> No <input type="checkbox"/> Yes
❖ Patent Information (NDAs only)	
• Patent Information: Verify that form FDA-3542a was submitted for patents that claim the drug for which approval is sought.	<input checked="" type="checkbox"/> Verified <input type="checkbox"/> Not applicable because drug is an old antibiotic.
CONTENTS OF ACTION PACKAGE	
Officer/Employee List	
❖ List of officers/employees who participated in the decision to approve this application and consented to be identified on this list (<i>approvals only</i>)	<input checked="" type="checkbox"/> Included
Documentation of consent/non-consent by officers/employees	<input checked="" type="checkbox"/> Included

Action Letters	
❖ Copies of all action letters <i>(including approval letter with final labeling)</i>	Action and date- Approval May 15, 2014
Labeling	
❖ Package Insert <i>(write submission/communication date at upper right of first page of PI)</i>	
<ul style="list-style-type: none"> Most recent draft labeling <i>(if it is division-proposed labeling, it should be in track-changes format)</i> 	<input checked="" type="checkbox"/> Included
<ul style="list-style-type: none"> Original applicant-proposed labeling 	<input checked="" type="checkbox"/> Included
❖ Medication Guide/Patient Package Insert/Instructions for Use/Device Labeling <i>(write submission/communication date at upper right of first page of each piece)</i>	<input type="checkbox"/> Medication Guide <input type="checkbox"/> Patient Package Insert <input type="checkbox"/> Instructions for Use <input type="checkbox"/> Device Labeling <input checked="" type="checkbox"/> None
<ul style="list-style-type: none"> Most-recent draft labeling <i>(if it is division-proposed labeling, it should be in track-changes format)</i> 	<input type="checkbox"/> Included
<ul style="list-style-type: none"> Original applicant-proposed labeling 	<input type="checkbox"/> Included
❖ Labels (full color carton and immediate-container labels) <i>(write submission/communication date on upper right of first page of each submission)</i>	
<ul style="list-style-type: none"> Most-recent draft labeling 	<input checked="" type="checkbox"/> Included
❖ Proprietary Name	
<ul style="list-style-type: none"> Acceptability/non-acceptability letter(s) <i>(indicate date(s))</i> Review(s) <i>(indicate date(s))</i> 	February 19, 2014 February 10, 2014
❖ Labeling reviews <i>(indicate dates of reviews)</i>	RPM: <input checked="" type="checkbox"/> August 30, 2013 DMEPA: <input checked="" type="checkbox"/> March 4, 2014 DMPP/PLT (DRISK): <input checked="" type="checkbox"/> None OPDP: <input checked="" type="checkbox"/> March 31, 2014 SEALD: <input checked="" type="checkbox"/> None CSS: <input checked="" type="checkbox"/> None Other: <input checked="" type="checkbox"/> None
Administrative / Regulatory Documents	
❖ RPM Filing Review ⁴ /Memo of Filing Meeting <i>(indicate date of each review)</i>	September 16, 2013
❖ All NDA 505(b)(2) Actions: Date each action cleared by 505(b)(2) Clearance Committee	<input checked="" type="checkbox"/> Not a (b)(2)
❖ NDAs only: Exclusivity Summary <i>(signed by Division Director)</i>	<input checked="" type="checkbox"/> Included
❖ Application Integrity Policy (AIP) Status and Related Documents http://www.fda.gov/ICECI/EnforcementActions/ApplicationIntegrityPolicy/default.htm	
<ul style="list-style-type: none"> Applicant is on the AIP 	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

⁴ Filing reviews for scientific disciplines are NOT required to be included in the action package.

<ul style="list-style-type: none"> This application is on the AIP <ul style="list-style-type: none"> If yes, Center Director's Exception for Review memo (<i>indicate date</i>) If yes, OC clearance for approval (<i>indicate date of clearance communication</i>) 	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No <input type="checkbox"/> Not an AP action
<ul style="list-style-type: none"> Pediatrics (<i>approvals only</i>) <ul style="list-style-type: none"> Date reviewed by PeRC _____ If PeRC review not necessary, explain: <u>This NDA is for a new formulation, therefore PREA does not apply- No presentation at PeRC</u> 	
<ul style="list-style-type: none"> Outgoing communications: letters, emails, and faxes considered important to include in the action package by the reviewing office/division (e.g., clinical SPA letters, RTF letter, etc.) (<i>do not include previous action letters, as these are located elsewhere in package</i>) 	January 17, 2014 December 6, 2013 November 8, 2013 September 16, 2013 August 30, 2013 August 29, 2013 August 28, 2013 August 27, 2013 August 14, 2013 July 24, 2013
<ul style="list-style-type: none"> Internal documents: memoranda, telecons, emails, and other documents considered important to include in the action package by the reviewing office/division (e.g., Regulatory Briefing minutes, Medical Policy Council meeting minutes) 	None
<ul style="list-style-type: none"> Minutes of Meetings <ul style="list-style-type: none"> If not the first review cycle, any end-of-review meeting (<i>indicate date of mtg</i>) Pre-NDA/BLA meeting (<i>indicate date of mtg</i>) EOP2 meeting (<i>indicate date of mtg</i>) Mid-cycle Communication (<i>indicate date of mtg</i>) Late-cycle Meeting (<i>indicate date of mtg</i>) Other milestone meetings (e.g., EOP2a, CMC pilots) (<i>indicate dates of mtgs</i>) 	<input checked="" type="checkbox"/> no mtg <input checked="" type="checkbox"/> No mtg <input checked="" type="checkbox"/> No mtg <input checked="" type="checkbox"/> N/A <input checked="" type="checkbox"/> N/A
<ul style="list-style-type: none"> Advisory Committee Meeting(s) <ul style="list-style-type: none"> Date(s) of Meeting(s) 	<input checked="" type="checkbox"/> No AC meeting
Decisional and Summary Memos	
<ul style="list-style-type: none"> Office Director Decisional Memo (<i>indicate date for each review</i>) 	<input checked="" type="checkbox"/> None
<ul style="list-style-type: none"> Division Director Summary Review (<i>indicate date for each review</i>) 	<input checked="" type="checkbox"/> May 15, 2014
<ul style="list-style-type: none"> Cross-Discipline Team Leader Review (<i>indicate date for each review</i>) 	<input checked="" type="checkbox"/> May 14, 2014
<ul style="list-style-type: none"> PMR/PMC Development Templates (<i>indicate total number</i>) 	<input checked="" type="checkbox"/> None
Clinical	
<ul style="list-style-type: none"> Clinical Reviews <ul style="list-style-type: none"> Clinical Team Leader Review(s) (<i>indicate date for each review</i>) Clinical review(s) (<i>indicate date for each review</i>) Social scientist review(s) (if OTC drug) (<i>indicate date for each review</i>) 	<input checked="" type="checkbox"/> No separate review February 3, 2014 Filing-August 26, 2013 <input checked="" type="checkbox"/> None

❖ Financial Disclosure reviews(s) or location/date if addressed in another review OR If no financial disclosure information was required, check here <input type="checkbox"/> and include a review/memo explaining why not (<i>indicate date of review/memo</i>)	May 19, 2014
❖ Clinical reviews from immunology and other clinical areas/divisions/Centers (<i>indicate date of each review</i>)	<input checked="" type="checkbox"/> None
❖ Controlled Substance Staff review(s) and Scheduling Recommendation (<i>indicate date of each review</i>)	<input checked="" type="checkbox"/> N/A
❖ Risk Management <ul style="list-style-type: none"> REMS Documents and REMS Supporting Document (<i>indicate date(s) of submission(s)</i>) REMS Memo(s) and letter(s) (<i>indicate date(s)</i>) Risk management review(s) and recommendations (including those by OSE and CSS) (<i>indicate date of each review and indicate location/date if incorporated into another review</i>) 	<input checked="" type="checkbox"/> None
❖ OSI Clinical Inspection Review Summary(ies) (<i>include copies of OSI letters to investigators</i>)	<input checked="" type="checkbox"/> March 14, 2014 March 12, 2014-Letter to Investigator March 11, 2014-Letter to Investigator September 9, 2013-Request for Clinical Inspections
Clinical Microbiology <input checked="" type="checkbox"/> None	
❖ Clinical Microbiology Team Leader Review(s) (<i>indicate date for each review</i>)	<input type="checkbox"/> No separate review
Clinical Microbiology Review(s) (<i>indicate date for each review</i>)	<input type="checkbox"/> None
Biostatistics <input type="checkbox"/> None	
❖ Statistical Division Director Review(s) (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> No
Statistical Team Leader Review(s) (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> No separate review
Statistical Review(s) (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> March 27, 2014 Filing-August 27, 2013
Clinical Pharmacology <input type="checkbox"/> None	
❖ Clinical Pharmacology Division Director Review(s) (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> No
Clinical Pharmacology Team Leader Review(s) (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> No separate review
Clinical Pharmacology review(s) (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> December 13, 2013 Filing August 27, 2013
❖ OSI Clinical Pharmacology Inspection Review Summary (<i>include copies of OSI letters</i>)	<input checked="" type="checkbox"/> None requested

Nonclinical <input type="checkbox"/> None	
❖ Pharmacology/Toxicology Discipline Reviews	
• ADP/T Review(s) (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> No
• Supervisory Review(s) (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> No separate review
• Pharm/tox review(s), including referenced IND reviews (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> April 3, 2014 Filing August 27, 2013
❖ Review(s) by other disciplines/divisions/Centers requested by P/T reviewer (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> None
❖ Statistical review(s) of carcinogenicity studies (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> No carc
❖ ECAC/CAC report/memo of meeting	<input checked="" type="checkbox"/> None Included in P/T review, page
❖ OSI Nonclinical Inspection Review Summary (<i>include copies of OSI letters</i>)	<input checked="" type="checkbox"/> None requested
Product Quality <input type="checkbox"/> None	
❖ Product Quality Discipline Reviews	
• ONDQA/OBP Division Director Review(s) (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> No
• Branch Chief/Team Leader Review(s) (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> No separate review
• Product quality review(s) including ONDQA biopharmaceutics reviews (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> May 13, 2014 April 20, 2014 March 18, 2014 Filing September 5, 2013 Filing August 21, 2013
❖ Microbiology Reviews <input type="checkbox"/> NDAs: Microbiology reviews (sterility & pyrogenicity) (OPS/NDMS) (<i>indicate date of each review</i>) <input type="checkbox"/> BLAs: Sterility assurance, microbiology, facilities reviews (OMPQ/MAPCB/BMT) (<i>indicate date of each review</i>)	<input type="checkbox"/> Not needed October 28, 2013 Filing: August 27, 2013
❖ Reviews by other disciplines/divisions/Centers requested by CMC/quality reviewer (<i>indicate date of each review</i>)	<input checked="" type="checkbox"/> None
❖ Environmental Assessment (check one) (original and supplemental applications)	
<input type="checkbox"/> Categorical Exclusion (<i>indicate review date</i>)(<i>all original applications and all efficacy supplements that could increase the patient population</i>)	
<input type="checkbox"/> Review & FONSI (<i>indicate date of review</i>)	
<input type="checkbox"/> Review & Environmental Impact Statement (<i>indicate date of each review</i>)	
❖ Facilities Review/Inspection	
<input type="checkbox"/> NDAs: Facilities inspections (include EER printout or EER Summary Report only; do NOT include EER Detailed Report; date completed must be within 2 years of action date) (<i>only original NDAs and supplements that include a new facility or a change that affects the manufacturing sites⁵</i>)	Date completed: <input checked="" type="checkbox"/> Acceptable <input type="checkbox"/> Withhold recommendation <input type="checkbox"/> Not applicable
<input type="checkbox"/> BLAs: TB-EER (date of most recent TB-EER must be within 30 days of action date) (<i>original and supplemental BLAs</i>)	Date completed: <input type="checkbox"/> Acceptable <input type="checkbox"/> Withhold recommendation

⁵ i.e., a new facility or a change in the facility, or a change in the manufacturing process in a way that impacts the Quality Management Systems of the facility.

❖ NDAs: Methods Validation (*check box only, do not include documents*)

- Completed
- Requested
- Not yet requested
- N/A (per review)

Day of Approval Activities	
❖ For all 505(b)(2) applications: • Check Orange Book for newly listed patents and/or exclusivity (including pediatric exclusivity)	<input type="checkbox"/> No changes <input type="checkbox"/> New patent/exclusivity (<i>Notify CDER OND IO</i>)
• Finalize 505(b)(2) assessment	<input type="checkbox"/> Done
❖ Send a courtesy copy of approval letter and all attachments to applicant by fax or secure email	<input checked="" type="checkbox"/> Done
❖ If an FDA communication will issue, notify Press Office of approval action after confirming that applicant received courtesy copy of approval letter	<input type="checkbox"/> Done
❖ Ensure that proprietary name, if any, and established name are listed in the <i>Application Product Names</i> section of DARRTS, and that the proprietary name is identified as the “preferred” name	<input checked="" type="checkbox"/> Done
❖ Ensure Pediatric Record is accurate	<input checked="" type="checkbox"/> Done
❖ Send approval email within one business day to CDER-APPROVALS	<input checked="" type="checkbox"/> Done

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/s/

JUDIT R MILSTEIN
05/23/2014
NDA 204822-Action Package Checklist



NDA 204822

**PROPRIETARY NAME REQUEST
CONDITIONALLY ACCEPTABLE**

Alcon Research, Ltd
6201 South Freeway
Fort Worth, TX 76124-2099

ATTENTION: Naj Sharif, PhD
Global Regulatory Project Manager

Dear Dr. Sharif:

Please refer to your New Drug Application (NDA), dated, July 12, 2013, and received, July 15, 2013, submitted under section 505(b)(1) of the Federal Food, Drug, and Cosmetic Act for Travoprost Ophthalmic Solution, 0.003% .

We also refer to your November 22, 2013 correspondence, received, November 25, 2013, requesting review of your proposed proprietary name, Izba. We have completed our review of the proposed proprietary name, Izba, and have concluded that it is acceptable.

If **any** of the proposed product characteristics as stated in your November 22, 2013, submission are altered prior to approval of the marketing application, the proprietary name should be resubmitted for review.

If you have any questions regarding the contents of this letter or any other aspects of the proprietary name review process, contact Karen Townsend, Safety Regulatory Project Manager in the Office of Surveillance and Epidemiology, at (301) 796-5413. For any other information regarding this application, contact Judit Milstein, Regulatory Project Manager, in the Office of New Drugs at (301) 796-0763.

Sincerely,

{See appended electronic signature page}

Kellie A. Taylor, Pharm.D., MPH
Deputy Director
Office of Medication Error Prevention and Risk Management
Office of Surveillance and Epidemiology
Center for Drug Evaluation and Research

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/s/

TODD D BRIDGES on behalf of KELLIE A TAYLOR
02/19/2014



NDA 204822

INFORMATION REQUEST

Alcon Research, Ltd.
Attention: Naj Sharif, Ph.D.
Global Regulatory Project Manager
6201 South Freeway
Fort Worth, TX 76134-2099

Dear Dr. Sharif:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Travoprost Ophthalmic Solution.

We are reviewing the Chemistry, Manufacturing, and Controls section of your submission and have the following comments and information requests. We request a prompt written response by January 29, 2014, in order to continue our evaluation of your NDA.

Regarding your Dec. 18, 2013 response to the agency's CMC Information Request dated Dec. 6, 2013, we have the following recommendations:

1. Revise 3.2.P.5.6 to reflect the revised drug product specifications.

2.



If you have any questions, call Navdeep Bhandari, Regulatory Health Project Manager, at (240) 402 -3815.

Sincerely,

{See appended electronic signature page}

Rapti D. Madurawe, Ph.D.
Branch Chief, Branch V
Division of New Drug Quality Assessment II
Office of New Drug Quality Assessment
Center for Drug Evaluation and Research

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/s/

RAPTI D MADURawe
01/17/2014



NDA 204822

INFORMATION REQUEST

Alcon Research, Ltd.
Attention: Naj Sharif, Ph.D.
Global Regulatory Project Manager
6201 South Freeway
Fort Worth, TX 76134-2099

Dear Dr. Sharif:

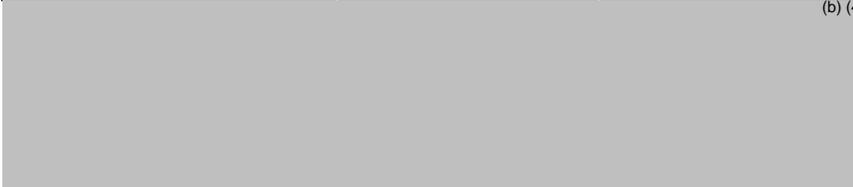
Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Travoprost Ophthalmic Solution.

We are reviewing the Chemistry, Manufacturing, and Controls section of your submission and have the following comments and information requests. We request a prompt written response by December 18, 2013, in order to continue our evaluation of your NDA.

1)  (b) (4)

2)  (b) (4)

3) The proposed acceptance criteria for  (b) (4) in the drug product specifications are not supported by the available batch release and stability data. Please revise the acceptance criteria as follows:

Compound	NDA proposed limit	FDA proposed limit
 (b) (4)		

- 4) Please verify if the method numbers listed in Table 3.2.P.5.2-1 for Travoprost Identity are correct; i.e., Alcon QA Belgium Technical Procedure# (b) (4) for TLC and (b) (4) for UHPLC methods, respectively. If incorrect, please update Table 3.2.P.5.2-1 with the correct reference method numbers.
- 5) The container closure system is sterilized using (b) (4). Please provide information on the potential (b) (4) levels of (b) (4) in the drug product.
- 6) Please update Module 1, section 1.4.1 to include DMF (b) (4) and its Letter of Authorization (LOA) which are currently provided in Module 3, section 3.2.P.7.

If you have any questions, call Navdeep Bhandari, Regulatory Health Project Manager, at (240) 402 -3815.

Sincerely,

{See appended electronic signature page}

Rapti D. Madurawe, Ph.D.
Branch Chief, Branch V
Division of New Drug Quality Assessment II
Office of New Drug Quality Assessment
Center for Drug Evaluation and Research

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/s/

BALAJEE SHANMUGAM
12/06/2013

From: [Sharif, Naj](#)
To: [Bhandari, Navdeep](#)
Subject: RE: 204822 Email to applicant
Date: Tuesday, September 03, 2013 10:32:59 AM

Thank you.
Naj

From: Bhandari, Navdeep [mailto:Navdeep.Bhandari@fda.hhs.gov]
Sent: Tuesday, September 03, 2013 6:59 AM
To: Sharif, Naj
Subject: RE: 204822 Email to applicant

Good morning,
I am confirming receipt of the information you provided to me regarding facilities. If there are any more issues I will let you know.
Thank you,
Navi

From: Sharif, Naj [mailto:naj.sharif@alcon.com]
Sent: Friday, August 30, 2013 12:18 PM
To: Bhandari, Navdeep
Subject: RE: 204822 Email to applicant
Importance: High

Hi Navi,

Did you receive my e-mail and from yesterday? **Please confirm that there are no more issues regarding Section 1.4.4. information.**

Thank you & best regards,
Naj

From: Sharif, Naj
Sent: Thursday, August 29, 2013 2:49 PM
To: 'Navdeep Bhandari@fda.hhs.gov'
Cc: 'judit.milstein@fda.hhs.gov'
Subject: 204822 Email to applicant

Dear Navi,

We've done some more chasing up to confirm the information you requested.

1. Actually, the FDA website clearly shows the Alcon-Couvreur FEI# and address as I provided in the Table (see screen shots below of your website). So, the data I provided is correct and the FEI# exists.
2. I was unable to reach anyone at (b) (4). However, there were two documents online at their website that confirmed the address in the Table I provided & shown in your e-mail below (specifically (b) (4)). In addition, this is one of the same addresses in use by our purchasing group for (b) (4). The (b) (4) address in a previous application had (b) (4) as part of the postcode (zip code). Please look at their websites for address conformation (see directly below for their websites)

(b) (4)

I hope these issues are now resolved. Please confirm.

Thank you & best regards,
Naj

Naj Sharif, PhD
Global Regulatory Project Manager
Glaucoma Products & Exploratory Projects
Alcon Research, Ltd. (Mail-TC-45)
6201 South Freeway, Fort Worth, TX 76134-2099.
Tel: +1 817-568-6494 | naj.sharif@alcon.com


a Novartis company



From: Bhandari, Navdeep [mailto:Navdeep.Bhandari@fda.hhs.gov]
Sent: Thursday, August 29, 2013 11:14 AM
To: Sharif, Naj
Subject: FW: 204822 Email to applicant

Good afternoon Naj,

Thank you for submitting the new chart but unfortunately it still seems to be incorrect. Below is the chart I received from you and highlighted is the information that requires clarification .

1. The FEI number provided for S.A. Alcon-Couvreur N.V. does not exist.

Please provide the correct FEI number for this facility.

2. The FEI number for [Redacted]

(b) (4)

Please confirm the address is correct and specifically [Redacted] (b) (4).

We require a response immediately to enable us evaluate the filability of the NDA. Please ensure all information you submit are accurate.

FACILITIES INFORMATION FOR NDA 204822 (Updated Aug. 27, 2013)

Travoprost Ophthalmic Solution 0.003%

Manufacturing Facility or Supplier/Contractor	DMF#	CFN# or FEI # or DUNS#	Function	Contact	Address	Telephone/ Fax/ E-mail	Ready for Inspection ?
Alcon Manufacturing, Ltd ASPEX Sterile Manufacturing Facility	N/A	CFN# 1610287	Drug Product Manufacturer	Wilma Taylor-Nunn	6201 South Freeway Fort Worth, Texas 76134-2099 USA	Tel: (817) 551-3058 Fax: (817) 302-4337 wilma.taylor-nunn@alcon.com	Yes
S.A. Alcon-Couvreur NV	N/A	3002037047	Drug Product Manufacturer	Frederik Buysse	Rijksweg 14 B-2870 Puurs Belgium	Tel: 32 38 90 27 78 Fax: 32 3890 2825 frederik.buysse@alcon.com	Yes

(b) (4)

Navi Bhandari, Pharm D
Regulatory Health Project Manager
Office of New Drug Quality Assessment
OPS/CDER/FDA
240-402-3815

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/s/

NAVDEEP BHANDARI
11/08/2013



NDA 204822

**FILING COMMUNICATION –
NO FILING REVIEW ISSUES IDENTIFIED**

Alcon Research, Ltd.
Attention: Naj Sharif, PhD
Global Regulatory Project Management
6201 South Freeway
Fort Worth, TX 76134-2099

Dear Dr. Sharif:

Please refer to your New Drug Application (NDA) dated July 12, 2013, received July 15, 2013, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act, for travoprost ophthalmic solution, 0.003%.

We have completed our filing review and have determined that your application is sufficiently complete to permit a substantive review. Therefore, in accordance with 21 CFR 314.101(a), this application is considered filed 60 days after the date we received your application. The review classification for this application is **Standard**. Therefore, the user fee goal date is May 15, 2014.

We are reviewing your application according to the processes described in the Guidance for Review Staff and Industry: Good Review Management Principles and Practices for PDUFA Products. Therefore, we have established internal review timelines as described in the guidance, which includes the timeframes for FDA internal milestone meetings (e.g., filing, planning, mid-cycle, team and wrap-up meetings). Please be aware that the timelines described in the guidance are flexible and subject to change based on workload and other potential review issues (e.g., submission of amendments). We will inform you of any necessary information requests or status updates following the milestone meetings or at other times, as needed, during the process. If major deficiencies are not identified during the review, we plan to communicate proposed labeling and, if necessary, any postmarketing commitment requests by April 24, 2014.

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

Because none of these criteria apply to your application, PREA requirements are inapplicable.

PROMOTIONAL MATERIAL

You may request advisory comments on proposed introductory advertising and promotional labeling. Please submit, in triplicate, a detailed cover letter requesting advisory comments (list each proposed promotional piece in the cover letter along with the material type and material identification code, if applicable), the proposed promotional materials in draft or mock-up form with annotated references, and the proposed package insert (PI). Submit consumer-directed, professional-directed, and television advertisement materials separately and send each submission to:

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion (OPDP)
5901-B Ammendale Road
Beltsville, MD 20705-1266

Do not submit launch materials until you have received our proposed revisions to the package insert (PI), and you believe the labeling is close to the final version.

For more information regarding OPDP submissions, please see <http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm>. If you have any questions, call OPDP at 301-796-1200.

If you have any questions, call Judit Milstein, Chief, Project Management Staff, at (301) 796-0763.

Sincerely,

{See appended electronic signature page}

Renata Albrecht, MD
Director
Division of Transplant and Ophthalmology Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

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/s/

RENATA ALBRECHT
09/16/2013

NDA 204822
Travoprost ophthalmic solution, 0.003%
Alcon Research, Inc.

Dear Dr. Sharif,

We completed the initial formatting review of the labeling included in your NDA submission dated July 12, 2013, and identified the following deficiencies:

In the HIGHLIGHTS OF PRESCRIBING INFORMATION:

1. Highlights limitation statement: the sentence stating “IZBA (travoprost ophthalmic solution) 0.003% should be placed starting a new paragraph.
2. The CONTRAINDICATIONS heading is missing. Although there are no contraindications listed in your package insert, the inclusion of such heading is a requirement. Please, include the CONTRAINDICATIONS heading, followed by a statement: none

In the FULL PRESCRIBING INFORMATION (FPI)

3. You presented the cross references in CAPITAL font (e.g., see PATIENT COUNSELING INFORMATION, 17.3). The preferred presentation for cross-references in the FPI is the section heading followed by the numerical identifier in italics (e.g.,[*see Patient Counseling Information (17.3)*]). Please, revise the formatting of the cross references all throughout the labeling accordingly.

We request that you submit revised labeling as described above either by December 13, 2013, or at the time of the initial labeling negotiations, whichever comes first.

If you have any questions regarding this communication, please contact me at (301) 796-0763.

Sincerely,

Judit Milstein
Chief, Project Management Staff
Division of Transplant and Ophthalmology
Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research
Food and Drug Administration

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/s/

JUDIT R MILSTEIN

08/30/2013

NDA 204822-Formatting comments on initial labeling submission

From: Bhandari, Navdeep
To: naj.sharif@alcon.com
Bcc: Shanmugam_Balajee
Subject: FW: 204822 Email to applicant
Date: Thursday, August 29, 2013 12:14:00 PM

Good afternoon Naj,

Thank you for submitting the new chart but unfortunately it still seems to be incorrect. Below is the chart I received from you and highlighted is the information that requires clarification.

1. The FEI number provided for S.A. Alcon-Couvreur N.V. does not exist.

Please provide the correct FEI number for this facility.

2. The FEI number fo [REDACTED] (b) (4)

Please confirm the address is correct and specifically [REDACTED] (b) (4).

We require a response immediately to enable us evaluate the filability of the NDA. Please ensure all information you submit are accurate.

FACILITIES INFORMATION FOR NDA 204822 (Updated Aug. 27, 2013)

Travoprost Ophthalmic Solution 0.003%

Manufacturing Facility or Supplier/Contractor	DMF#	CFN# or FEI # or DUNS#	Function	Contact	Address	Telephone/ Fax/ E-mail	Ready for Inspection ?
Alcon Manufacturing, Ltd ASPEX Sterile Manufacturing Facility	N/A	CFN# 1610287	Drug Product Manufacturer	Wilma Taylor-Nunn	6201 South Freeway Fort Worth, Texas 76134-2099 USA	Tel: (817) 551-3058 Fax: (817) 302-4337 wilma.taylor-nunn@alcon.com	Yes
S A Alcon-Couvreur N V	N/A	3002037047	Drug Product Manufacturer	Frederik Buysse	Rijksweg 14 B-2870 Puurs Belgium	Tel: 32 38 90 27 78 Fax: 32 3890 2825 frederik.buysse@alcon.com	Yes
[REDACTED]							

Navi Bhandari, Pharm.D
 Regulatory Health Project Manager
 Office of New Drug Quality Assessment
 OPS/CDER/FDA
 240-402-3815

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/s/

NAVDEEP BHANDARI
08/29/2013

From: Milstein, Judit
To: [Reese, Richard \(richard.reese@alcon.com\)](mailto:reese.richard@alcon.com)
Subject: Your NDA 204822-Travoprost-Request from statistics reviewer
Date: Wednesday, August 28, 2013 10:51:00 AM

NDA 204822

Travoprost ophthalmic solution, 0.003%

Alcon Research

Richard,

Find enclosed a request for information from your statistical reviewer:

In the Efficacy section (Section 9.7.13) of the clinical study report under subsection *Sensitivity Analyses*, you stated that:

“In order to support the robustness of the LOCF imputation method for missing data, *additional imputation methods* were used to impute missing values for dropouts and missing data for both IOP and IOP change from baseline at on-therapy study visits for the primary efficacy analysis using the ITT analysis set”

However, we couldn't find any detail description of the additional imputation methods and the associated results in the clinical study report. Please clarify.

We would appreciate your response no later than September 6, 2013. Please, let me know if this timeline is not feasible.

Thank you

Judit Milstein

Chief, Project Management Staff

DTOP/OAP/CDER

Food and Drug Administration

10903 New Hampshire Avenue

Building 22, Room 6180

Silver Spring, MD 20993

Phone: 301-796-0763

Fax: 301-796-9881

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/s/

JUDIT R MILSTEIN

08/28/2013

NDA 204822-Information request

From: Bhandari, Navdeep
To: "[Sharif, Naj](#)"
Cc: [Bhandari, Navdeep](#)
Subject: NDA 204822 Information Request
Date: Tuesday, August 27, 2013 9:47:00 AM
Importance: High

Good morning Naj,

Please provide a comprehensive list of facilities for both drug substance and drug product manufacture with relevant information (FEI #, contact information, facility address, contact phone number/fax number and contact email address) by **COB** Friday August 30, 2013.

Please provide me with a courtesy copy at the time of the official submission. Note: Official submissions are due by COB of due date in order to be reviewed during this review cycle.

Regards,

Navi Bhandari, Pharm.D
Regulatory Health Project Manager
Office of New Drug Quality Assessment
OPS/CDER/FDA
240-402-3815

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/s/

NAVDEEP BHANDARI
08/27/2013



NDA 204822

INFORMATION REQUEST

Alcon Research, Ltd.
Attention: Naj Sharif, PhD
Global Regulatory Project Manager
6201 South Freeway
Fort Worth, TX 76134-2099

Dear Dr. Sharif:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act Travoprost Ophthalmic Solution, 0.003%.

We also refer to your submission dated July 15, 2013.

We are reviewing the Chemistry, Manufacturing, and Controls section of your submission and have the following comments and information requests. We request a prompt written response by August 16, 2013, in order to continue our evaluation of your NDA.

Chemistry IR

Section 1.4.4. of the NDA does not list (b) (4) but does so in Section 2.3.S.2. Please submit, preferably in a table, all facilities with address, CFN #, function, contact information and include a statement on the readiness of the facilities for CGMP inspection to replace the existing table presented in Section 1.4.4.

If you have any questions, call Navdeep Bhandari, Regulatory Health Project Manager, at (240) 402 -3815.

Sincerely,

{See appended electronic signature page}

Rapti D. Madurawe, Ph.D.
Branch Chief, Branch V
Division of New Drug Quality Assessment II
Office of New Drug Quality Assessment
Center for Drug Evaluation and Research

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/s/

DOROTA M MATECKA
08/14/2013



NDA 204822

NDA ACKNOWLEDGMENT

Alcon Research, Ltd.
Attention: Naj Sharif, PhD
Global Regulatory Project Management
6201 South Freeway
Fort Worth, TX 76134-2099

Dear Dr. Sharif:

We have received your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for the following:

Name of Drug Product: Travoprost ophthalmic solution, 0.003%

Date of Application: July 12, 2013

Date of Receipt: July 15, 2013

Our Reference Number: NDA 204822

Unless we notify you within 60 days of the receipt date that the application is not sufficiently complete to permit a substantive review, we will file the application on September 13, 2013, in accordance with 21 CFR 314.101(a).

If you have not already done so, promptly submit the content of labeling [21 CFR 314.50(l)(1)(i)] in structured product labeling (SPL) format as described at <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>. Failure to submit the content of labeling in SPL format may result in a refusal-to-file action under 21 CFR 314.101(d)(3). The content of labeling must conform to the content and format requirements of revised 21 CFR 201.56-57.

You are also responsible for complying with the applicable provisions of sections 402(i) and 402(j) of the Public Health Service Act (PHS Act) [42 USC §§ 282 (i) and (j)], which was amended by Title VIII of the Food and Drug Administration Amendments Act of 2007 (FDAAA) (Public Law No, 110-85, 121 Stat. 904).

The NDA number provided above should be cited at the top of the first page of all submissions to this application. Send all submissions, electronic or paper, including those sent by overnight mail or courier, to the following address:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Transplant and Ophthalmology Products
5901-B Ammendale Road
Beltsville, MD 20705-1266

All regulatory documents submitted in paper should be three-hole punched on the left side of the page and bound. The left margin should be at least three-fourths of an inch to assure text is not obscured in the fastened area. Standard paper size (8-1/2 by 11 inches) should be used; however, it may occasionally be necessary to use individual pages larger than standard paper size. Non-standard, large pages should be folded and mounted to allow the page to be opened for review without disassembling the jacket and refolded without damage when the volume is shelved. Shipping unbound documents may result in the loss of portions of the submission or an unnecessary delay in processing which could have an adverse impact on the review of the submission. For additional information, please see <http://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/DrugMasterFilesDMFs/ucm073080.htm>.

Secure email between CDER and applicants is useful for informal communications when confidential information may be included in the message (for example, trade secrets or patient information). If you have not already established secure email with the FDA and would like to set it up, send an email request to SecureEmail@fda.hhs.gov. Please note that secure email may not be used for formal regulatory submissions to applications.

If you have any questions, call me at 301-796-0763.

Sincerely,

{See appended electronic signature page}

Judit Milstein
Chief, Project Management Staff
Division of Transplant and Ophthalmology
Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

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/s/

JUDIT R MILSTEIN

07/24/2013

NDA 204822-Acknowledgment letter