

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:
200738Orig1s000

ADMINISTRATIVE and CORRESPONDENCE
DOCUMENTS

EXCLUSIVITY SUMMARY

NDA # 200738

SUPPL #

HFD #

Trade Name Lotemax

Generic Name loteprednol etabonate ophthalmic ointment 0.5%

Applicant Name Bausch & Lomb

Approval Date, If Known 04-15-2011

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 years

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?

Yes

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# 20-583

Lotemax (loteprednol etabonate ophthalmic suspension) 0.5%

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:

Investigation #1 - Study 525; Investigation #2 - Study 526

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"):

Investigation #1 - Study 525; Investigation #2 - Study 526

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 # 32,432 YES !
! ! NO
! Explain:

Investigation #2
IND # 32,432 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: Fariba Izadi, PharmD
Title: Regulatory Project Manager
Date: 04-15-11

Name of Office/Division Director signing form: Wiley A. Chambers, M.D.
Title: Acting Division Director

Form OGD-011347; Revised 05/10/2004; formatted 2/15/05

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

/s/

FARIBA IZADI
04/15/2011

WILEY A CHAMBERS
04/15/2011

1.3.3 Debarment Certification

Bausch & Lomb Incorporated hereby certifies that it did not and will not use in any capacity the services of any person debarred under Section 306 of the Federal Food, Drug and Cosmetic Act in connection with this application.

Julie Townsend
Julie Townsend
Manager, Global Regulatory Affairs

12/21/2009
Date

ACTION PACKAGE CHECKLIST

APPLICATION INFORMATION¹

NDA # 200738 BLA #	NDA Supplement # BLA STN #	If NDA, Efficacy Supplement Type:
Proprietary Name: Lotemax Established/Proper Name: Loteprednol Etabonate Dosage Form: Ophthalmic ointment 0.5%		Applicant: Bausch & Lomb Inc. Agent for Applicant (if applicable):
RPM: Fariba Izadi		Division: Anti-Infective and Ophthalmology
<p>NDAs: 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)</p> <p>(A supplement can be either a (b)(1) or a (b)(2) regardless of whether the original NDA was a (b)(1) or a (b)(2). Consult page 1 of the 505(b)(2) Assessment or the Appendix to this Action Package Checklist.)</p>		<p>505(b)(2) Original NDAs and 505(b)(2) NDA supplements: Listed drug(s) relied upon for approval (include NDA #(s) and drug name(s):</p> <p>Provide a brief explanation of how this product is different from the listed drug.</p> <p>If no listed drug, explain.</p> <p><input type="checkbox"/> This application relies on literature. <input type="checkbox"/> This application relies on a final OTC monograph. <input type="checkbox"/> Other (explain)</p> <p><u>Two months prior to each action, review the information in the 505(b)(2) Assessment and submit the draft to CDER OND IO for clearance. Finalize the 505(b)(2) Assessment at the time of the approval action.</u></p> <p><u>On the day of approval, check the Orange Book again for any new patents or pediatric exclusivity.</u></p> <p><input type="checkbox"/> No changes <input type="checkbox"/> Updated Date of check:</p> <p>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.</p>
<p>❖ Actions</p> <ul style="list-style-type: none"> • Proposed action • User Fee Goal Date is <u>07-25-2011</u> • Previous actions (<i>specify type and date for each action taken</i>) 		<p><input checked="" type="checkbox"/> AP <input type="checkbox"/> TA <input type="checkbox"/> CR</p> <p><input type="checkbox"/> None CR 10-20-10</p>
<p>❖ 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 _____</p>		<p><input type="checkbox"/> Received</p>

¹ The **Application Information** section is (only) a checklist. The **Contents of Action Package** section (beginning on page 5) lists the documents to be included in the Action Package.

❖ Application Characteristics ²	
Review priority: <input checked="" type="checkbox"/> Standard <input type="checkbox"/> Priority Chemical classification (new NDAs only): 3-New Dosage Form <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 NDAs: Subpart H <input type="checkbox"/> Accelerated approval (21 CFR 314.510) <input type="checkbox"/> Restricted distribution (21 CFR 314.520) Subpart I <input type="checkbox"/> Approval based on animal studies <input type="checkbox"/> Submitted in response to a PMR <input type="checkbox"/> Submitted in response to a PMC <input type="checkbox"/> Submitted in response to a Pediatric Written Request Comments: BLAs: Subpart E <input type="checkbox"/> Accelerated approval (21 CFR 601.41) <input type="checkbox"/> Restricted distribution (21 CFR 601.42) Subpart H <input type="checkbox"/> Approval based on animal studies REMS: <input type="checkbox"/> MedGuide <input type="checkbox"/> Communication Plan <input type="checkbox"/> ETASU <input type="checkbox"/> REMS not required	
❖ 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
• Press Office notified of action (by OEP)	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
• Indicate what types (if any) of information dissemination are anticipated	<input checked="" type="checkbox"/> None <input type="checkbox"/> HHS Press Release <input type="checkbox"/> FDA Talk Paper <input type="checkbox"/> CDER Q&As <input type="checkbox"/> Other

² 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.

❖ Exclusivity	
<ul style="list-style-type: none"> Is approval of this application blocked by any type of exclusivity? 	<input checked="" type="checkbox"/> No <input type="checkbox"/> Yes
<ul style="list-style-type: none"> NDA and BLAs: Is there existing orphan drug exclusivity for the "same" drug or biologic for the proposed indication(s)? Refer to 21 CFR 316.3(b)(13) for the definition of "same drug" for an orphan drug (i.e., active moiety). This definition is NOT the same as that used for NDA chemical classification. 	<input checked="" type="checkbox"/> No <input type="checkbox"/> Yes If, yes, NDA/BLA # _____ and date exclusivity expires: _____
<ul style="list-style-type: none"> (b)(2) NDAs only: Is there remaining 5-year exclusivity that would bar effective approval of a 505(b)(2) application? (Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.) 	<input type="checkbox"/> No <input type="checkbox"/> Yes If yes, NDA # _____ and date exclusivity expires: _____
<ul style="list-style-type: none"> (b)(2) NDAs only: Is there remaining 3-year exclusivity that would bar effective approval of a 505(b)(2) application? (Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.) 	<input type="checkbox"/> No <input type="checkbox"/> Yes If yes, NDA # _____ and date exclusivity expires: _____
<ul style="list-style-type: none"> (b)(2) NDAs only: Is there remaining 6-month pediatric exclusivity that would bar effective approval of a 505(b)(2) application? (Note that, even if exclusivity remains, the application may be tentatively approved if it is otherwise ready for approval.) 	<input type="checkbox"/> No <input type="checkbox"/> Yes If yes, NDA # _____ and date exclusivity expires: _____
<ul style="list-style-type: none"> NDAs only: Is this a single enantiomer that falls under the 10-year approval limitation of 505(u)? (Note that, even if the 10-year approval limitation period has not expired, the application may be tentatively approved if it is otherwise ready for approval.) 	<input checked="" type="checkbox"/> No <input type="checkbox"/> Yes If yes, NDA # _____ and date 10-year limitation expires: _____
❖ Patent Information (NDAs only)	
<ul style="list-style-type: none"> Patent Information: Verify that form FDA-3542a was submitted for patents that claim the drug for which approval is sought. If the drug is an old antibiotic, skip the Patent Certification questions. 	<input checked="" type="checkbox"/> Verified <input type="checkbox"/> Not applicable because drug is an old antibiotic.
<ul style="list-style-type: none"> Patent Certification [505(b)(2) applications]: Verify that a certification was submitted for each patent for the listed drug(s) in the Orange Book and identify the type of certification submitted for each patent. 	21 CFR 314.50(i)(1)(i)(A) <input type="checkbox"/> Verified 21 CFR 314.50(i)(1) <input type="checkbox"/> (ii) <input type="checkbox"/> (iii)
<ul style="list-style-type: none"> [505(b)(2) applications] If the application includes a paragraph III certification, it cannot be approved until the date that the patent to which the certification pertains expires (but may be tentatively approved if it is otherwise ready for approval). 	<input type="checkbox"/> No paragraph III certification Date patent will expire _____
<ul style="list-style-type: none"> [505(b)(2) applications] For each paragraph IV certification, verify that the applicant notified the NDA holder and patent owner(s) of its certification that the patent(s) is invalid, unenforceable, or will not be infringed (review documentation of notification by applicant and documentation of receipt of notice by patent owner and NDA holder). (If the application does not include any paragraph IV certifications, mark "N/A" and skip to the next section below (Summary Reviews)). 	<input type="checkbox"/> N/A (no paragraph IV certification) <input type="checkbox"/> Verified

- [505(b)(2) applications] For **each paragraph IV** certification, based on the questions below, determine whether a 30-month stay of approval is in effect due to patent infringement litigation.

Answer the following questions for **each** paragraph IV certification:

- (1) Have 45 days passed since the patent owner's receipt of the applicant's notice of certification?

Yes No

(Note: The date that the patent owner received the applicant's notice of certification can be determined by checking the application. The applicant is required to amend its 505(b)(2) application to include documentation of this date (e.g., copy of return receipt or letter from recipient acknowledging its receipt of the notice) (see 21 CFR 314.52(e)).

If "Yes," skip to question (4) below. If "No," continue with question (2).

- (2) Has the patent owner (or NDA holder, if it is an exclusive patent licensee) submitted a written waiver of its right to file a legal action for patent infringement after receiving the applicant's notice of certification, as provided for by 21 CFR 314.107(f)(3)?

Yes No

If "Yes," there is no stay of approval based on this certification. Analyze the next paragraph IV certification in the application, if any. If there are no other paragraph IV certifications, skip the rest of the patent questions.

If "No," continue with question (3).

- (3) Has the patent owner, its representative, or the exclusive patent licensee filed a lawsuit for patent infringement against the applicant?

Yes No

(Note: This can be determined by confirming whether the Division has received a written notice from the (b)(2) applicant (or the patent owner or its representative) stating that a legal action was filed within 45 days of receipt of its notice of certification. The applicant is required to notify the Division in writing whenever an action has been filed within this 45-day period (see 21 CFR 314.107(f)(2)).

If "No," the patent owner (or NDA holder, if it is an exclusive patent licensee) has until the expiration of the 45-day period described in question (1) to waive its right to bring a patent infringement action or to bring such an action. After the 45-day period expires, continue with question (4) below.

- (4) Did the patent owner (or NDA holder, if it is an exclusive patent licensee) submit a written waiver of its right to file a legal action for patent infringement within the 45-day period described in question (1), as provided for by 21 CFR 314.107(f)(3)?

Yes No

If "Yes," there is no stay of approval based on this certification. Analyze the next paragraph IV certification in the application, if any. If there are no other paragraph IV certifications, skip to the next section below (Summary Reviews).

If "No," continue with question (5).

<p>(5) Did the patent owner, its representative, or the exclusive patent licensee bring suit against the (b)(2) applicant for patent infringement within 45 days of the patent owner's receipt of the applicant's notice of certification?</p> <p>(Note: This can be determined by confirming whether the Division has received a written notice from the (b)(2) applicant (or the patent owner or its representative) stating that a legal action was filed within 45 days of receipt of its notice of certification. The applicant is required to notify the Division in writing whenever an action has been filed within this 45-day period (see 21 CFR 314.107(f)(2)). If no written notice appears in the NDA file, confirm with the applicant whether a lawsuit was commenced within the 45-day period).</p> <p><i>If "No," there is no stay of approval based on this certification. Analyze the next paragraph IV certification in the application, if any. If there are no other paragraph IV certifications, skip to the next section below (Summary Reviews).</i></p> <p><i>If "Yes," a stay of approval may be in effect. To determine if a 30-month stay is in effect, consult with the OND ADRA and attach a summary of the response.</i></p>	<p><input type="checkbox"/> Yes <input type="checkbox"/> No</p>
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CONTENTS OF ACTION PACKAGE

❖ Copy of this Action Package Checklist ³	Enclosed
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 type="checkbox"/> Included
Action Letters	
❖ Copies of all action letters (<i>including approval letter with final labeling</i>)	Action(s) and date(s) Complete Response 10-20-2010, Approval 04-15-11
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. If it is division-proposed labeling, it should be in track-changes format. 	04-08-2011 FDA proposed/Sponsor proposed 04-11-2011
<ul style="list-style-type: none"> • Original applicant-proposed labeling 	12-22-2009
<ul style="list-style-type: none"> • Example of class labeling, if applicable 	

³ Fill in blanks with dates of reviews, letters, etc.
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<ul style="list-style-type: none"> 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. If it is division-proposed labeling, it should be in track-changes format. 	NA
<ul style="list-style-type: none"> Original applicant-proposed labeling 	NA
<ul style="list-style-type: none"> Example of class labeling, if applicable 	NA
<ul style="list-style-type: none"> ❖ 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 	10-14-2010
<ul style="list-style-type: none"> ❖ 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>) 	06-04-2010 Letter 06-04-2010 Review
<ul style="list-style-type: none"> ❖ Labeling reviews (<i>indicate dates of reviews and meetings</i>) 	<input type="checkbox"/> RPM <input checked="" type="checkbox"/> DMEPA 08-29-2010 <input type="checkbox"/> DRISK <input checked="" type="checkbox"/> DDMAC 09-30-2010 <input type="checkbox"/> CSS <input type="checkbox"/> Other reviews
Administrative / Regulatory Documents	
<ul style="list-style-type: none"> Administrative Reviews (<i>e.g., RPM Filing Review⁴/Memo of Filing Meeting</i>) (<i>indicate date of each review</i>) 	05-06-2010
<ul style="list-style-type: none"> ❖ All NDA (b)(2) Actions: Date each action cleared by (b)(2) Clearance Cmte 	<input checked="" type="checkbox"/> Not a (b)(2)
<ul style="list-style-type: none"> ❖ NDA (b)(2) Approvals Only: 505(b)(2) Assessment (<i>indicate date</i>) 	<input checked="" type="checkbox"/> Not a (b)(2)
<ul style="list-style-type: none"> ❖ NDAs only: Exclusivity Summary (<i>signed by Division Director</i>) 	<input checked="" type="checkbox"/> Included
<ul style="list-style-type: none"> ❖ 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
<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 type="checkbox"/> No <input checked="" 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 <u>06-30-2010</u> If PeRC review not necessary, explain: _____ Pediatric Page/Record (<i>approvals only, must be reviewed by PERC before finalized</i>) 	<input checked="" type="checkbox"/> Included
<ul style="list-style-type: none"> ❖ Debarment certification (original applications only): verified that qualifying language was not used in certification and that certifications from foreign applicants are cosigned by U.S. agent (<i>include certification</i>) 	<input checked="" type="checkbox"/> Verified, statement is acceptable
<ul style="list-style-type: none"> ❖ Outgoing communications (<i>letters (except action letters), emails, faxes, telecons</i>) 	Enclosed

⁴ Filing reviews for scientific disciplines should be filed behind the respective discipline tab.
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❖ Internal memoranda, telecons, etc.	Enclosed
❖ Minutes of Meetings	
• Regulatory Briefing (<i>indicate date of mtg</i>)	<input checked="" type="checkbox"/> No mtg
• If not the first review cycle, any end-of-review meeting (<i>indicate date of mtg</i>)	<input checked="" type="checkbox"/> N/A or no mtg
• Pre-NDA/BLA meeting (<i>indicate date of mtg</i>)	<input type="checkbox"/> No mtg 10-07-2009
• EOP2 meeting (<i>indicate date of mtg</i>)	<input type="checkbox"/> No mtg 07-16-2007
• Other milestone meetings (e.g., EOP2a, CMC pilots) (<i>indicate dates of mtgs</i>)	
❖ Advisory Committee Meeting(s)	<input checked="" type="checkbox"/> No AC meeting
• Date(s) of Meeting(s)	
• 48-hour alert or minutes, if available (<i>do not include transcript</i>)	
Decisional and Summary Memos	
❖ Office Director Decisional Memo (<i>indicate date for each review</i>)	<input checked="" type="checkbox"/> None
Division Director Summary Review (<i>indicate date for each review</i>)	10-20-2010; 04-14-2011
Cross-Discipline Team Leader Review (<i>indicate date for each review</i>)	10-20-2010; 04-14-2011
PMR/PMC Development Templates (<i>indicate total number</i>)	<input checked="" type="checkbox"/> None
Clinical Information⁵	
❖ Clinical Reviews	
• Clinical Team Leader Review(s) (<i>indicate date for each review</i>)	10-20-2010; 04-14-11
• Clinical review(s) (<i>indicate date for each review</i>)	09-27-2010; 04-12-11
• Social scientist review(s) (if OTC drug) (<i>indicate date for each review</i>)	<input 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>)	Page 6 of Clinical Review-08-09-10
❖ 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"/> Not applicable
❖ Risk Management	
• REMS Documents and Supporting Statement (<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
❖ DSI Clinical Inspection Review Summary(ies) (<i>include copies of DSI letters to investigators</i>)	<input type="checkbox"/> None requested 09-13-2010, 03-15-2011

⁵ Filing reviews should be filed with the discipline reviews.

Version: 8/25/10

Clinical Microbiology <input checked="" type="checkbox"/> None	
❖ Clinical Microbiology Team Leader Review(s) (indicate date for each review)	<input checked="" type="checkbox"/> None
Clinical Microbiology Review(s) (indicate date for each review)	<input checked="" type="checkbox"/> None
Biostatistics <input type="checkbox"/> None	
❖ Statistical Division Director Review(s) (indicate date for each review)	<input checked="" type="checkbox"/> None
Statistical Team Leader Review(s) (indicate date for each review)	Concurred; signature on review
Statistical Review(s) (indicate date for each review)	08-19-2010
Clinical Pharmacology <input type="checkbox"/> None	
❖ Clinical Pharmacology Division Director Review(s) (indicate date for each review)	<input checked="" type="checkbox"/> None
Clinical Pharmacology Team Leader Review(s) (indicate date for each review)	Concurred; signature on review
Clinical Pharmacology review(s) (indicate date for each review)	<input type="checkbox"/> None 08-20-2010
❖ DSI Clinical Pharmacology Inspection Review Summary (include copies of DSI letters)	<input checked="" type="checkbox"/> None
Nonclinical <input type="checkbox"/> None	
❖ Pharmacology/Toxicology Discipline Reviews	
• ADP/T Review(s) (indicate date for each review)	<input checked="" type="checkbox"/> None
• Supervisory Review(s) (indicate date for each review)	Concurred; signature on review
• Pharm/tox review(s), including referenced IND reviews (indicate date for each review)	<input type="checkbox"/> None 07-16-2010
Review(s) by other disciplines/divisions/Centers requested by P/T reviewer (indicate date for each review)	<input checked="" type="checkbox"/> None
❖ Statistical review(s) of carcinogenicity studies (indicate date for each review)	<input checked="" type="checkbox"/> No carc
❖ ECAC/CAC report/memo of meeting	<input checked="" type="checkbox"/> None Included in P/T review, page
❖ DSI Nonclinical Inspection Review Summary (include copies of DSI letters)	<input checked="" type="checkbox"/> None requested
Product Quality <input type="checkbox"/> None	
❖ Product Quality Discipline Reviews	
• ONDQA/OBP Division Director Review(s) (indicate date for each review)	<input checked="" type="checkbox"/> None
• Branch Chief/Team Leader Review(s) (indicate date for each review)	04-08-2011; 04-12-2011
• Product quality review(s) including ONDQA biopharmaceutics reviews (indicate date for each review)	09-30-2010; 04-08-2011; 04-12-2011
❖ Microbiology Reviews	07-02-2010
<input checked="" type="checkbox"/> NDAs: Microbiology reviews (sterility & pyrogenicity) (OPS/NDMS) (indicate date of each review)	
<input type="checkbox"/> BLAs: Sterility assurance, microbiology, facilities reviews (DMPQ/MAPCB/BMT) (indicate date of each review)	
❖ Reviews by other disciplines/divisions/Centers requested by CMC/quality reviewer (indicate date of each review)	<input checked="" type="checkbox"/> None

❖ Environmental Assessment (check one) (original and supplemental applications)	
<input checked="" type="checkbox"/> Categorical Exclusion (<i>indicate review date</i>)(<i>all original applications and all efficacy supplements that could increase the patient population</i>)	See CMC Review #1, 09-22-2010, page 118
<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 checked="" type="checkbox"/> NDAs: Facilities inspections (include EER printout) (<i>date completed must be within 2 years of action date</i>) (<i>only original NDAs and supplements that include a new facility or a change that affects the manufacturing sites⁶</i>)	Date completed: 04-12-2011 <input checked="" type="checkbox"/> Acceptable <input type="checkbox"/> Withhold recommendation <input type="checkbox"/> Not applicable
<input type="checkbox"/> BLAs: TB-EER (<i>date of most recent TB-EER must be within 30 days of action date</i>) (<i>original and supplemental BLAs</i>)	Date completed: <input type="checkbox"/> Acceptable <input type="checkbox"/> Withhold recommendation
❖ NDAs: Methods Validation (<i>check box only, do not include documents</i>)	<input type="checkbox"/> Completed <input type="checkbox"/> Requested <input type="checkbox"/> Not yet requested <input checked="" type="checkbox"/> Not needed (per review)

⁶ 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.
Version: 8/25/10

Appendix to Action Package Checklist

An NDA or NDA supplemental application is likely to be a 505(b)(2) application if:

- (1) It relies on published literature to meet any of the approval requirements, and the applicant does not have a written right of reference to the underlying data. If published literature is cited in the NDA but is not necessary for approval, the inclusion of such literature will not, in itself, make the application a 505(b)(2) application.
- (2) **Or** it relies for approval on the Agency's previous findings of safety and efficacy for a listed drug product and the applicant does not own or have right to reference the data supporting that approval.
- (3) **Or** it relies on what is "generally known" or "scientifically accepted" about a class of products to support the safety or effectiveness of the particular drug for which the applicant is seeking approval. (Note, however, that this does not mean *any* reference to general information or knowledge (e.g., about disease etiology, support for particular endpoints, methods of analysis) causes the application to be a 505(b)(2) application.)

Types of products for which 505(b)(2) applications are likely to be submitted include: fixed-dose combination drug products (e.g., heart drug and diuretic (hydrochlorothiazide) combinations); OTC monograph deviations (see 21 CFR 330.11); new dosage forms; new indications; and, new salts.

An efficacy supplement can be either a (b)(1) or a (b)(2) regardless of whether the original NDA was a (b)(1) or a (b)(2).

An efficacy supplement is a 505(b)(1) supplement if the supplement contains all of the information needed to support the approval of the change proposed in the supplement. For example, if the supplemental application is for a new indication, the supplement is a 505(b)(1) if:

- (1) The applicant has conducted its own studies to support the new indication (or otherwise owns or has right of reference to the data/studies).
- (2) **And** no additional information beyond what is included in the supplement or was embodied in the finding of safety and effectiveness for the original application or previously approved supplements is needed to support the change. For example, this would likely be the case with respect to safety considerations if the dose(s) was/were the same as (or lower than) the original application.
- (3) **And** all other "criteria" are met (e.g., the applicant owns or has right of reference to the data relied upon for approval of the supplement, the application does not rely for approval on published literature based on data to which the applicant does not have a right of reference).

An efficacy supplement is a 505(b)(2) supplement if:

- (1) Approval of the change proposed in the supplemental application would require data beyond that needed to support our previous finding of safety and efficacy in the approval of the original application (or earlier supplement), and the applicant has not conducted all of its own studies for approval of the change, or obtained a right to reference studies it does not own. For example, if the change were for a new indication AND a higher dose, we would likely require clinical efficacy data and preclinical safety data to approve the higher dose. If the applicant provided the effectiveness data, but had to rely on a different listed drug, or a new aspect of a previously cited listed drug, to support the safety of the new dose, the supplement would be a 505(b)(2).
- (2) **Or** the applicant relies for approval of the supplement on published literature that is based on data that the applicant does not own or have a right to reference. If published literature is cited in the supplement but is not necessary for approval, the inclusion of such literature will not, in itself, make the supplement a 505(b)(2) supplement.
- (3) **Or** the applicant is relying upon any data they do not own or to which they do not have right of reference.

If you have questions about whether an application is a 505(b)(1) or 505(b)(2) application, consult with your ODE's ADRA.

Teleconference Date and Time: April 8, 2011
Application Number: NDA 200738
Product Name: Lotemax ophthalmic ointment
Indication: Treatment of post-operative inflammation and pain following ocular surgery
Sponsor/Applicant Name: Bausch & Lomb

Division of Anti-Infective and Ophthalmology participants:

Wiley Chambers, MD	Acting Division Director
William Boyd, MD	Clinical Team Leader
Martin Nevitt, MD	Clinical Reviewer
Fariba Izadi, Pharm.D.	Regulatory Health Project Manager
Leanna Kelly	Consumer Safety Officer

Bausch & Lomb Participants:

Tuyen Ong, MD	Head of Clinical Science
Baldo Sforzolini, MD, VP	Medical, Clinical and Regulatory Sciences
Fang Li, PhD	Associate Director, Regulatory Affairs
Mary Harrell	Manager, Regulatory Affairs
Michael Bailey	Director, Regulatory Affairs
Kristina Quinzi	Project Manager

Discussion:

A teleconference was held between The Division and Bausch & Lomb to discuss edits and revisions to the labeling. The Division recommended changes to Section 6 (Adverse reactions) and section 12.1 (Mechanism of Action). Bausch & Lomb will submit a revised label formally to the NDA.

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/s/

FARIBA IZADI
04/11/2011

Izadi, Fariba

From: Izadi, Fariba
Sent: Friday, April 08, 2011 9:30 AM
To: 'Li, Fang'
Cc: 'Harrell, Mary E'
Subject: NDA 200738 (Lotemax oph oint) draft-labeling-text

Importance: High

Attachments: draft-labeling-text NDA200738 4_6_11.doc



draft-labeling-text
NDA200738 ...

Dear Dr. Li,

Attached, please find the draft labeling for NDA 200738 (Lotemax oph oint). This is your submitted labeling from 10/18/10 with our changes shown in red. Please confirm receipt of this e-mail and inform us if you find this label acceptable. If you have any questions or concerns, we are available for a t-con at 11 AM today.

Best regards,

Fariba Izadi, Pharm.D.
Regulatory Health Project Manager
Division of Anti-Infective and Ophthalmology Products
Phone: (301) 796-0563
Fax: (301) 796-9881
E-mail: Fariba.Izadi@fda.hhs.gov

4 Page(s) of draft labeling have been Withheld in Full as b4 (CCI/TS)
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/s/

FARIBA IZADI
04/11/2011



NDA 200738

**ACKNOWLEDGE –
CLASS 2 RESPONSE**

Bausch & Lomb Incorporated
Attention: Fang Li, Ph.D., RAC
Associate Director, Brand
Director, Global Regulatory Affairs, Pharmaceuticals
7 Giralda Farms, Suite 1001
Madison, NJ 07940

Dear Dr. Li:

We acknowledge receipt on January 25, 2011, of your January 21, 2011, resubmission of your new drug application submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Lotemax (loteprednol etabonate ophthalmic ointment) 0.5%.

We consider this a complete, class 2 response to our October 20, 2010, action letter. Therefore, the user fee goal date is July 25, 2011.

If you have any questions, call Fariba Izadi, Pharm.D., Regulatory Health Project Manager at (301) 796-0563.

Sincerely,

{See appended electronic signature page}

Maureen Dillon-Parker
Chief, Project Management Staff
Division of Anti-Infective and Ophthalmology Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

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/s/

MAUREEN P DILLON PARKER
03/01/2011

Izadi, Fariba

From: Li, Fang [Fang.Li@bausch.com]
Sent: Thursday, December 09, 2010 4:05 PM
To: Izadi, Fariba
Subject: RE: NDA 200738 (Lotemax oph oint)-Preliminary Response

Dear Dr. Izadi:

We confirm that we received the communication below. We will get back to you regarding whether we still want the teleconference.

Best regards,
Fang

Fang Li, Ph.D., RAC
Associate Director, Brand
Global Regulatory Affairs
Pharmaceuticals
BAUSCH+LOMB
Phone: 973-360-6459
Fax: 973-360-6403
Cell: 862-812-8219
e-mail: fang.li@bausch.com

From: Izadi, Fariba [mailto:Fariba.Izadi@fda.hhs.gov]
Sent: Thursday, December 09, 2010 4:02 PM
To: Li, Fang
Cc: Harrell, Mary E
Subject: NDA 200738 (Lotemax oph oint)-Preliminary Response

Dear Dr. Li,

Below is our preliminary response to your question for our scheduled December 14, 2010 teleconference concerning NDA 200738 (Lotemax Oph Oint). If you are satisfied with this response and wish to forego the teleconference, please let me know. We will not, however, be able to discuss any new information or answer new questions during the meeting. If you wish to present additional information or questions, a new meeting should be requested.

Question 1: Does the Agency agree with the proposed approach to respond to deficiency #2 identified in the complete response letter?

FDA Response: [The proposed approach in the meeting package is appropriate. Please include all specific details in your submission including full study results and the revised drug product specification in the amendment.](#)

Best regards,

Reference ID: 2876990

12/13/2010

Fariba Izadi, Pharm.D.
Regulatory Health Project Manager
Division of Anti-Infective and Ophthalmology Products
Phone: (301) 796-0563
Fax: (301) 796-9881
E-mail: Fariba.Izadi@FDA.HHS.GOV

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/s/

FARIBA IZADI
12/13/2010



NDA 200738

MEETING REQUEST GRANTED

Bausch & Lomb Incorporated
Attention: Michael Bailey
Director, Global Regulatory Affairs, Pharmaceuticals
7 Giralda Farms, Suite 1001
Madison, NJ 07940

Dear Mr. Bailey:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Lotemax (loteprednol etabonate ophthalmic ointment) 0.5%.

We also refer to your November 30, 2010, correspondence requesting a teleconference to discuss your planned response to the Complete Response letter dated October 20, 2010. Based on the statement of purpose, objectives, and proposed agenda, we consider the meeting a type B meeting.

The teleconference is scheduled as follows:

Date: December 14, 2010

Time: 3:00 PM to 3:30 PM

Phone Arrangements: Please provide a CALL-IN NUMBER and PASSCODE

Division of Anti-Infective and Ophthalmology Attendees:

Wiley A. Chambers, MD	Acting Director
William Boyd, MD	Medical Team Leader
Fariba Izadi, Pharm.D.	Regulatory Health project Manager
Lin Qi, PhD	Product Quality Reviewer
Linda Ng, PhD	Pharmaceutical Assessment Lead
Steven Miller, PhD	ONDQA Branch Chief II

If you have any questions, call Fariba Izadi, Pharm.D., Regulatory Health Project Manager at (301) 796-0563.

Sincerely,

{See appended electronic signature page}

Maureen Dillon-Parker
Chief, Project Management Staff
Division of Anti-Infective and Ophthalmology Products
Office of Antimicrobial Products
Center for Drug Evaluation and research

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/s/

MAUREEN P DILLON PARKER
12/07/2010

Izadi, Fariba

From: Izadi, Fariba
Sent: Monday, September 27, 2010 4:11 PM
To: 'Harrell, Mary E'
Subject: NDA 200738 (Loteprednol etabonate)

Attachments: FDA draft label lotemax 9_27_10.doc

Dear Ms. Harrell,

Attached, please find the draft labeling and draft carton and container comments for NDA 200738 (Loteprednol etabonate ophthalmic ointment 0.5%). Please note that all manufacturing facilities for the drug substance and the drug product are expected to be in compliance with current good manufacturing practice before this or any application may be approved.

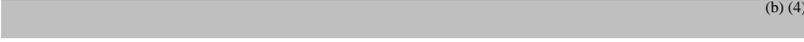
Best regards,

Fariba Izadi, Pharm.D.
Regulatory Health Project Manager
Division of Anti-Infective and Ophthalmology Products
Phone: (301) 796-0563
Fax: (301) 796-9881
E-mail: Fariba.Izadi@fda.hhs.gov



FDA draft label
lotemax 9_27_1...

The carton and container draft labeling should be revised as follows:

1.  (b) (4)
2. *As currently presented, the manufacturer statement 'Bausch & Lomb' is as prominent the proprietary name. The most prominent information on the principal display panel should be the proprietary name immediately followed by the established name, dosage form and strength. Decrease the prominence of the manufacturer statement and relocate it away from the proprietary name in the carton and container.*
3. *As currently presented the carton labeling lacks the expiration date and lot number. Include this information on all carton labeling.*
4. *Revise so that the established name is printed in letters that are at least half as large as the letters comprising the proprietary name, and the established name has a prominence commensurate with the prominence with which such proprietary name, taking into account all pertinent factors, including typography, layout, contrast, and other printing features in accordance with 21 CFR 201.10 (g)(2).*
5. *Increase the prominence of the product strength. The most prominent information on the principal display panel should be the proprietary name immediately followed by the established name, dosage form and strength.*
6. *Increase the prominence of the statement 'Sample-Not for Resale' located on the principal display panel.*
7.  (b) (4)
8. *Revise the statement "Do not use if bottom ridge of tube cap is exposed" to be consistent with the revised draft*

package insert, "Do not use if seal of tube cap is broken."

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/s/

FARIBA IZADI
09/28/2010

Cuff, Althea

From: Cuff, Althea
Sent: Thursday, August 12, 2010 7:35 AM
To: 'mary_harrell@bausch.com'
Cc: Izadi, Fariba
Subject: NDA 200738- (Loteprednol Etabonate Ophthalmic Ointment) Information Request

Dear Ms. Harrell,

We have the following information request from our CMC reviewer:

Please include the dose uniformity test and acceptance criteria in the drug product specification for stability and submit test procedure and acceptance criteria. We recommend that dosing samples be taken from top, middle, and bottom of each tube in multiple tubes to demonstrate homogeneity.

Please confirm receipt of this e-mail and formally submit your response to the NDA.

Thanks,

Althea M. Cuff
Regulatory Health Project Manager
FDA/CDER/OPS/ONDQA
Phone (301) 796-4061

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
----- NDA-200738	----- ORIG-1	----- BAUSCH AND LOMB INC	----- LOTEPREDNOL ETABONATE OINTMENT, 0.5%

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/s/

ALTHEA CUFF
08/12/2010

Izadi, Fariba

From: Harrell, Mary E [Mary_Harrell@bausch.com]
Sent: Friday, June 25, 2010 1:17 PM
To: Izadi, Fariba
Subject: RE: NDA 200738 (Lotemax) Information request.

I confirm receipt of this communication.

From: Izadi, Fariba [mailto:Fariba.Izadi@fda.hhs.gov]
Sent: Friday, June 25, 2010 9:32 AM
To: Harrell, Mary E
Subject: NDA 200738 (Lotemax) Information request.

Dear Mary,

We are reviewing your application for NDA 200738 (Lotemax) and have the following recommendations and information requests from our Product Quality team.

Because you have observed settling during storage of the physician's sample, please include a test and acceptance criteria for dose uniformity in the drug product specification. We recommend that this test be designed to monitor potency variation within the tube that may develop during storage.

Please confirm receipt of this e-mail and formally submit your response to the NDA.

Best regards,

Fariba Izadi, Pharm.D.
Regulatory Health Project Manager
Division of Anti-Infective and Ophthalmology Products
Phone: (301) 796-0563
Fax: (301) 796-9881
E-mail: Fariba.Izadi@FDA.HHS.GOV

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Thank You

6/25/2010

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-200738	ORIG-1	BAUSCH AND LOMB INC	LOTEPREDNOL ETABONATE OINTMENT, 0.5%

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/s/

FARIBA IZADI
06/25/2010

A Teleconference was held on May 24, 2010 with the sponsor to clarify and discuss the Pediatric statement to be included in the proposed labeling for Lotemax ointment. The sponsor's proposed revision to the labeling provided to the Division via e-mail on May 14, 2010 was not acceptable.



The sponsor has committed to re-evaluate their pediatric plan and submit a new proposal.

FDA ATTENDEES

Division of Anti-Infective and Ophthalmology Products:

Wiley Chambers, MD Acting Division Director
William Boyd, MD Medical Team Leader
Sonal Wadhwa, MD Medical Reviewer
Fariba Izadi, Pharm.D. Regulatory Health Project Manager

Bausch & Lomb Attendees

Dr. Tuyen Ong, Clinical Affairs
Dr. Angele Singh, Clinical Affairs
Dr. Fang Li, Regulatory Affairs
Ms. Mary Harrell, Regulatory Affairs

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
----- NDA-200738	----- ORIG-1	----- BAUSCH AND LOMB INC	----- LOTEPREDNOL ETABONATE OINTMENT, 0.5%

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/s/

FARIBA IZADI
06/04/2010

Izadi, Fariba

From: Izadi, Fariba
Sent: Wednesday, June 09, 2010 10:55 AM
To: 'Harrell, Mary E'
Subject: NDA 200738 (Lotemax oph ointment)-Comments and Information requests.

Dear Mary,

We are reviewing your submission for NDA 200738 and have the following comments and information requests from our product quality and statistical team.

Statistics:

We were unable to reproduce your efficacy rates for studies 525 and 526 for the hierarchical primary efficacy endpoints:

1. The proportion of subjects with complete resolution of anterior chamber cells and flare at Visit 5 (Postoperative Day 8)
2. The proportion of subjects with Grade 0 (no) pain at Visit 5 (Postoperative Day 8).

The differences in your efficacy rates and our efficacy rates are very small, less than 1% (see Table 1 and Table 2).

In the following we provide both our analyses and the your analyses:

Reviewer's analysis:

Table 1: Rates between drug and vehicle (reviewers)

Endpoint	Protocol 525(N=400): Drug vs. placebo (p-value)	Protocol 526(N=405): Drug vs. placebo (p-value)
Complete resolutions and flare at visit 5	49/201(24.38 %) vs. 26/199 (13.07) (p-value 0.0038)	66 / 203(32.35 %) vs. 21/202(10.45 %) (p-value<0.0001)
Grade 0 pain at visit 5	157/201 (78.11 %) vs. 89/199 (44.72 %) (p-value <0.0001)	151/203 (74.02 %) vs. 81/ 202 (40.30%) (p-value <0.0001)

Sponsor's analysis:

Table 2: Rates between drug and vehicle (sponsor's)

Endpoint	Protocol 525(N=400): Drug vs. placebo (p-value)	Protocol 526(N=405): Drug vs. placebo (p-value)
Complete resolutions and flare at visit 5	48/201(23.9%) vs. 27/199 (13.6%) (p-value 0.0082)	64/ 203(31.5%) vs. 23/202(11.4%) (p-value<0.0001)
Grade 0 pain at visit 5	156/201 (77.6%) vs. 90/199 (45.2%) (p-value <0.0001)	149/203 (73.4%) vs. 83/ 202 (41.1%) (p-value <0.0001)

Please clarify the discrepancies in the efficacy rates. I have used the following SAS program (for study 525) based on adeff.xpt file ([in NDA200738\0002\m5\datasets\525](#) submitted on 2/18/2010) . The SAS program for study 526 is similar

to that of study 525.

```
LIBNAME NEWDATA "C:\analysis";
```

```
data eff_525;  
set newdata.adeff;  
run;  
proc contents;  
run;
```

```
data new;  
set eff_525;  
keep ITT OCPAIN TRTAN TRTA TRTRAND VISITNUM ANTREACT CMP_CF1 G0_PNIS G0_PN1 G0_PN2 G0  
_PN2S CMP_CF2 G0_PN2;  
if visitnum=5;  
run;
```

```
/* trtan: treatment arms; CMP_CF1: Complete resolution of Cells and Flare (ITT imputation)*/
```

```
title 'Study 525: CMP_CF1: Complete resolution of Cells and Flare (ITT imputation) analysis';  
proc freq;  
tables trtan*CMP_CF1/all;  
run;
```

```
title 'Study 525: Grade 0 pain (ITT imputation) analysis';  
/* trtan: treatment arms; G0PN1: Grade 0 Pain (ITT imputation)*/  
proc freq;  
tables trtan*G0_PN1/all;  
run;
```

Chemistry:

1. For proper drug release control, it is recommended that testing and acceptance criteria for “Particle Size Distribution” be included in the drug product specification.
2. Please specify the USP requirements in the acceptance criteria for “Metal Particles” in the drug product specification, and report the results with a numeric value.
3. Provide complete analytical procedures for methods PS-1013, PS-1006, PS-1003, C-1204. If the “local procedure” for US product is the USP procedure, then the analytical procedure needs not be supplied.
4. Why are the acceptance criteria for related compounds listed in the drug substance stability data for the more recent Lots (010310, 020825, 030331, and 050249) inconsistent with those in the proposed drug substance specification? Please correct in future submissions.

Please confirm receipt of this e-mail.

Best regards,

Fariba Izadi, Pharm.D.
Regulatory Health Project Manager
Division of Anti-Infective and Ophthalmology Products
Phone: (301) 796-0563
Fax: (301) 796-9881
E-mail: Fariba.Izadi@FDA.HHS.GOV

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
----- NDA-200738	----- ORIG-1	----- BAUSCH AND LOMB INC	----- LOTEPREDNOL ETABONATE OINTMENT, 0.5%

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/s/

FARIBA IZADI
06/11/2010

Izadi, Fariba

From: Izadi, Fariba
Sent: Monday, May 24, 2010 4:33 PM
To: 'Harrell, Mary E'
Subject: NDA 200738 (Loteprednol Etabonate oph oint) Information request.

Dear Mary,

We are reviewing your submission for NDA 200738 (Loteprednol Etabonate Ophthalmic Ointment 0.5%) and have the following information request from our Pharmacology/Toxicology team.

Please submit The Toxicokinetics data from the 28-day rabbit ocular toxicity study as soon as possible.

Best regards,

Fariba Izadi, Pharm.D.
Regulatory Health Project Manager
Division of Anti-Infective and Ophthalmology Products
Phone: (301) 796-0563
Fax: (301) 796-9881
E-mail: Fariba.Izadi@FDA.HHS.GOV

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
----- NDA-200738	----- ORIG-1	----- BAUSCH AND LOMB INC	----- LOTEPREDNOL ETABONATE OINTMENT, 0.5%

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/s/

FARIBA IZADI
06/11/2010



NDA 200738

**PROPRIETARY NAME REQUEST
CONDITIONALLY ACCEPTABLE**

Bausch & Lomb, Incorporated.
8500 Hidden River Parkway
Tampa, Florida 33637

ATTENTION: Julie Townsend, MPH
Manager, Global Regulatory Affairs

Dear Ms. Townsend:

Please refer to your New Drug Application (NDA) dated December 22, 2009, received December 23, 2009, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Loteprednol Etabonate Ophthalmic Ointment, 0.5%.

We also refer to your March 4, 2010, correspondence, received March 8, 2010, requesting review of your proposed proprietary name, Lotemax. We have completed our review of the proposed proprietary name, Lotemax and have concluded that it is acceptable.

If **any** of the proposed product characteristics as stated in your March 4, 2010, 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 Brantley Dorch, Safety Regulatory Project Manager in the Office of Surveillance and Epidemiology, at (301) 796-0150. For any other information regarding this application contact the Office of New Drugs (OND) Regulatory Project Manager, Fariba Izadi, at (301) 796-0563.

Sincerely,

{See appended electronic signature page}

Denise P. Toyer, Pharm.D.
Deputy Director
Division of Medication Error Prevention and Analysis
Office of Surveillance and Epidemiology
Center for Drug Evaluation and Research

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-200738	ORIG-1	BAUSCH AND LOMB INC	LOTEPREDNOL ETABONATE OINTMENT, 0.5%

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/s/

DENISE P TOYER
06/04/2010

Izadi, Fariba

From: Izadi, Fariba
Sent: Monday, May 24, 2010 12:22 PM
To: 'Harrell, Mary E'
Subject: NDA 200738 Lotemax Ointment

Dear Mary,

Please be reminded that we have asked for the efficacy and safety re-analysis without investigator Sall as additional sensitivity analyses. It is not necessary to revise summary Tables in the NDA, replace Modules, or revise labeling. Please formally submit these additional efficacy and safety analyses excluding Investigator Sall to the NDA. We will be happy to discuss this today if necessary.

Best Regards,

Fariba Izadi, Pharm.D.
Regulatory Health Project Manager
Division of Anti-Infective and Ophthalmology Products
Phone: (301) 796-0563
Fax: (301) 796-9881
E-mail: Fariba.Izadi@FDA.HHS.GOV

From: Harrell, Mary E [mailto:Mary_Harrell@bausch.com]
Sent: Friday, May 21, 2010 2:30 PM
To: Izadi, Fariba
Cc: Li, Fang
Subject: RE: NDA 200738 Lotemax Ointment

Dear Dr. Izadi:

Reference is made to your e-mail on May 10, 2010 advising Bausch & Lomb to re-analyze the efficacy and safety data for each clinical trial submitted in the NDA 200738 for Lotemax (loteprednol etabonate ophthalmic ointment, 0.5%) that had the Sall Research Medical Center (Dr. Kenneth Sall) as one of the investigators. You mentioned that this re-analysis should be done with all data from that site removed from the database. Dr. Sall's site participated and enrolled 36 subjects (18 in active, 18 in placebo group) in Study 525 only. At this time, Bausch & Lomb has performed a re-analysis of the efficacy data for the primary endpoints and found that the results provide no difference in the conclusion presented in the original NDA.

We have not performed re-analysis of the safety data yet. The safety population for this submission included all subjects who received at least one dose of study drug. As all subjects participating at Dr. Sall's site were treated and exposed to either, Loteprednol Etabonate Ophthalmic Ointment, 0.5% or Vehicle (b) (4)

In the tables attached to this communication please find the results from the original analysis (Table TGF: LE-ISE-2-1-table-tgf.pdf) for Study 525 and our re-analysis (Table TKA: LE-ISE-2-1-table-tka.pdf) for the overall efficacy data for Studies 525 and 526, without the data from Dr. Sall's site.

As shown in the original analysis (Table TGF), significantly more LE Ointment subjects than Vehicle subjects had complete resolution of cells and flare; 27.7% (112/404) vs. 12.5% (50/401), (p<0.0001) for the studies combined,

5/25/2010

and 23.9% (48/201) vs. 13.6% (27/199), (p=0.0082) for the individual study 525. Once the 36 subjects from Dr. Sall were removed similar results are observed (Table TKA); 28.5% (110/386) vs. 13.1% (50/383), (p<0.0001) for the studies combined, and 25.1% (46/183) vs. 14.9% (27/181), (p=0.0149) for the individual study 525.

Additionally, significantly more LE Ointment subjects than Vehicle subjects reported Grade 0 (no) pain. The original results from Table TGF; 75.5% (305/404) vs. 43.1% (173/401), (p<0.0001) for the studies combined, and 77.6% (156/201) vs. 45.2% (90/199), (p<0.0001) for the individual study 525. Once the 36 subjects from Dr. Sall were removed similar results are observed (Table TKA); 74.6% (288/386) vs. 41.0% (157/383), (p<0.0001) for the studies combined, and 76.0% (139/183) vs. 40.9% (74/181), (p<0.0001) for the individual study 525.

Bausch & Lomb would like to propose to revise all the efficacy tables in the NDA (Module 2 and Module 5) and update the labeling (Module 1) to reflect the changes of the data. Is this proposal acceptable to the Agency?

I look forward to hearing from you.

Best regards,
Mary

From: Izadi, Fariba [mailto:Fariba.Izadi@fda.hhs.gov]
Sent: Thursday, May 20, 2010 1:22 PM
To: Harrell, Mary E
Subject: NDA 200738 Lotemax Ointment

Dear Mary,

We are reviewing your submission for NDA 200738 and request response to the e-mail sent on Monday, May 10, 2010 (below) as soon as possible. Please let us know when you are planning to address the following issues.

Best regards,

Fariba Izadi, Pharm.D.
Regulatory Health Project Manager
Division of Anti-Infective and Ophthalmology Products
Phone: (301) 796-0563
Fax: (301) 796-9881
E-mail: Fariba.Izadi@FDA.HHS.GOV

From: Izadi, Fariba
Sent: Monday, May 10, 2010 4:25 PM
To: 'Harrell, Mary E'
Subject: NDA 200738 Lotemax Ointment

Dear Mary,

Please provide a re-analysis of the efficacy and safety data for each clinical trial submitted in the NDA 200738 for Lotemax that had the Sall Research Medical Center (Dr. Kenneth Sall) as one of the investigators. This re-analysis should be done with all data from that site removed from the database.

Best regards,

Fariba Izadi, Pharm.D.

5/25/2010

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
----- NDA-200738	----- ORIG-1	----- BAUSCH AND LOMB INC	----- LOTEPREDNOL ETABONATE OINTMENT, 0.5%

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/s/

FARIBA IZADI
05/28/2010

Izadi, Fariba

From: Izadi, Fariba
Sent: Monday, May 10, 2010 4:25 PM
To: 'Harrell, Mary E'
Subject: NDA 200738 Lotemax Ointment

Dear Mary,

Please provide a re-analysis of the efficacy and safety data for each clinical trial submitted in the NDA 200738 for Lotemax that had the Sall Research Medical Center (Dr. Kenneth Sall) as one of the investigators. This re-analysis should be done with all data from that site removed from the database.

Best regards,

Fariba Izadi, Pharm.D.
Regulatory Health Project Manager
Division of Anti-Infective and Ophthalmology Products
Phone: (301) 796-0563
Fax: (301) 796-9881
E-mail: Fariba.Izadi@FDA.HHS.GOV

Please confirm receipt of this e-mail.

Application
Type/Number

Submission
Type/Number

Submitter Name

Product Name

NDA-200738

ORIG-1

BAUSCH AND
LOMB INC

LOTEPREDNOL ETABONATE
OINTMENT, 0.5%

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/s/

FARIBA IZADI
05/21/2010

Izadi, Fariba

From: Izadi, Fariba
Sent: Friday, May 14, 2010 11:26 AM
To: 'Harrell, Mary E'
Subject: NDA 200738 (Loteprednol Etabonate Ophthalmic Ointment 0.5%) Requests and Recommendations

Dear Mary,

We are reviewing your submission for NDA 200738 (Loteprednol Etabonate Ophthalmic Ointment 0.5%) and have the following requests and recommendations:

Chemistry:

1. The structure shown in Fig. 3.2.S.3.1-6 is incorrect and does not show stereochemistry as clearly as the drawing in Fig. 3.2.S.3.1-5. Please provide a revised discussion and figure in the "Potential Isomerism" section that more clearly shows the stereochemistry at atoms 17, 11 and 10.
2. Please clarify which tests are performed by B&L on the in-coming non-sterile material from (b) (4) and on the sterile material.
3. Because release and stability tests are to be performed by B&L, it is recommended that B&L perform routine tests for reference standards.
4. Please rename (b) (4) to "Any Individual Unspecified Impurity" in the drug substance and drug product specifications according to the ICH nomenclature.
5. It is recommended that the acceptance criteria for Any Individual Unspecified Impurity in the drug product specification be tightened to NMT (b) (4).
6. Please clarify how (b) (4) is controlled in the ointment manufacturing process.

Best regards,

Fariba Izadi, Pharm.D.
Regulatory Health Project Manager
Division of Anti-Infective and Ophthalmology Products
Phone: (301) 796-0563
Fax: (301) 796-9881
E-mail: Fariba.Izadi@FDA.HHS.GOV

Please confirm receipt of this e-mail.

Application
Type/Number

Submission
Type/Number

Submitter Name

Product Name

NDA-200738

ORIG-1

BAUSCH AND
LOMB INC

LOTEPREDNOL ETABONATE
OINTMENT, 0.5%

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/s/

FARIBA IZADI
05/18/2010

Izadi, Fariba

From: Izadi, Fariba
Sent: Tuesday, May 04, 2010 11:49 AM
To: 'Harrell, Mary E'
Subject: RE: NDA 200738 Lotemax Ointment

Dear Mary,

Thank you for your e-mail. Since the pediatric study is being waived for safety reasons, you need to submit revised labeling which includes a Warning statement regarding the use of LOTEMAX ointment in pediatric patients because of its potential effects regarding amblyopia. Please submit all the documents formally to the NDA by June 1, 2010.

Best regards,

Fariba Izadi, Pharm.D.
Regulatory Health Project Manager
Division of Anti-Infective and Ophthalmology Products
Phone: (301) 796-0563
Fax: (301) 796-9881
E-mail: Fariba.Izadi@FDA.HHS.GOV

From: Harrell, Mary E [mailto:Mary_Harrell@bausch.com]
Sent: Thursday, April 29, 2010 4:57 PM
To: Izadi, Fariba
Cc: Harrell, Mary E
Subject: RE: NDA 200738 Lotemax Ointment

Dear Fariba,

Based on new information received recently during a Sponsor held advisory board meeting, Bausch & Lomb requests a pediatric waiver for Lotemax (loteprednol etabonate ophthalmic ointment, 0.5%). Please see attached courtesy copy of formal filing document to be sent tomorrow April 30, 2010.

If you should have questions regarding this communication please do not hesitate to contact me.

Best regards,

*Mary Harrell
Global Regulatory Affairs
Bausch & Lomb Incorporated
7 Giralda Farms Suite 1001
Madison, New Jersey 07940
Telephone: 973-360-6462
email: mary_harrell@bausch.com*

From: Harrell, Mary E
Sent: Wednesday, April 28, 2010 4:53 PM
To: 'Izadi, Fariba'

5/14/2010

Cc: Harrell, Mary E
Subject: NDA 200738 Lotemax Ointment

Dear Fariba,

This communication is to serve as confirmation that I did receive on the morning of April 27, 2010 your voicemail message sent the afternoon of April 26, 2010, that included a message from William Boyd regarding the deferral request for the proposed pediatric study included in the original NDA filing for Lotemax Ointment. I do understand the information contained therein and am preparing a response to this request that will be provided tomorrow, April 29, 2010. I apologize for the delay in this communication.

Best regards,

*Mary Harrell
Global Regulatory Affairs
Bausch & Lomb Incorporated
7 Giralda Farms Suite 1001
Madison, New Jersey 07940
Telephone: 973-360-6462
email: mary_harrell@bausch.com*

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Thank You

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-200738	ORIG-1	BAUSCH AND LOMB INC	LOTEPREDNOL ETABONATE OINTMENT, 0.5%

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/s/

FARIBA IZADI
05/14/2010

Izadi, Fariba

From: Izadi, Fariba
Sent: Wednesday, May 12, 2010 10:49 AM
To: 'Harrell, Mary E'
Subject: NDA 200738 Lotemax Ointment

Dear Mary,

The Pediatric Waiver request dated April 30, 2010, is noted. The proposed revision to the labeling is not acceptable. (b) (4)

Revised labeling similar to the following should be submitted to the NDA. The labeling should not be submitted in SPL format. It should be formally submitted in PLR format.

Under WARNINGS AND PRECAUTIONS:

5.X Amblyopia

LOTEMAX (loteprednol etabonate ophthalmic ointment), 0.5% should not be used in children following ocular surgery. Its use may interfere with amblyopia treatment by hindering the child's ability to see out of the operated eye.

Under USE IN SPECIFIC POPULATIONS

8.4 Pediatric Use

LOTEMAX (loteprednol etabonate ophthalmic ointment), 0.5% should not be used in children following ocular surgery because its use may interfere with amblyopia treatment by hindering the child's ability to see out of the operated eye.

Regards.

Fariba Izadi, Pharm.D.
Regulatory Health Project Manager
Division of Anti-Infective and Ophthalmology Products
Phone: (301) 796-0563
Fax: (301) 796-9881
E-mail: Fariba.Izadi@FDA.HHS.GOV

Please confirm the receipt of this e-mail.

From: Harrell, Mary E [mailto:Mary_Harrell@bausch.com]
Sent: Tuesday, May 11, 2010 3:55 PM
To: Izadi, Fariba
Cc: Boyd, William M; Chambers, Wiley A
Subject: RE: NDA 200738 Lotemax Ointment

Dear Fariba,

Bausch & Lomb is providing response to the Agency regarding the pediatric study waiver request submitted to our original NDA and the recent request (via email dated May 4, 2010) for a statement to be included in the labeling regarding the use of Lotemax ointment in the pediatric population. Please review

5/14/2010

the proposed addition to the labeling shown below (highlighted in Blue for ease of review).

Current labeling statement

8.4 Pediatric Use

Safety and effectiveness in pediatric patients have not been established.

Proposed labeling statement

8 USE IN SPECIFIC POPULATIONS

8.4 Pediatric Use

Safety and effectiveness in pediatric patients have not been established.

(b) (4)

(b) (4)

The text will be added to Section 8 "Use In Specific Populations" ([8.4 Pediatric Use](#)) of the labeling. Bausch & Lomb will submit the proposed statement to NDA 200738. Please let us know your comments.

Regards,
Mary

From: Izadi, Fariba [mailto:Fariba.Izadi@fda.hhs.gov]
Sent: Tuesday, May 04, 2010 11:49 AM
To: Harrell, Mary E
Subject: RE: NDA 200738 Lotemax Ointment

Dear Mary,

Thank you for your e-mail. Since the pediatric study is being waived for safety reasons, you need to submit revised labeling which includes a Warning statement regarding the use of LOTEMAX ointment in pediatric patients because of its potential effects regarding amblyopia. Please submit all the documents formally to the NDA by June 1, 2010.

Best regards,

Fariba Izadi, Pharm.D.
Regulatory Health Project Manager
Division of Anti-Infective and Ophthalmology Products
Phone: (301) 796-0563
Fax: (301) 796-9881
E-mail: Fariba.Izadi@FDA.HHS.GOV

From: Harrell, Mary E [mailto:Mary_Harrell@bausch.com]
Sent: Thursday, April 29, 2010 4:57 PM
To: Izadi, Fariba
Cc: Harrell, Mary E

Subject: RE: NDA 200738 Lotemax Ointment

Dear Fariba,

Based on new information received recently during a Sponsor held advisory board meeting, Bausch & Lomb requests a pediatric waiver for Lotemax (loteprednol etabonate ophthalmic ointment, 0.5%). Please see attached courtesy copy of formal filing document to be sent tomorrow April 30, 2010.

If you should have questions regarding this communication please do not hesitate to contact me.
Best regards,

Mary Harrell
Global Regulatory Affairs
Bausch & Lomb Incorporated
7 Giralda Farms Suite 1001
Madison, New Jersey 07940
Telephone: 973-360-6462
email: mary_harrell@bausch.com

From: Harrell, Mary E
Sent: Wednesday, April 28, 2010 4:53 PM
To: 'Izadi, Fariba'
Cc: Harrell, Mary E
Subject: NDA 200738 Lotemax Ointment

Dear Fariba,

This communication is to serve as confirmation that I did receive on the morning of April 27, 2010 your voicemail message sent the afternoon of April 26, 2010, that included a message from William Boyd regarding the deferral request for the proposed pediatric study included in the original NDA filing for Lotemax Ointment. I do understand the information contained therein and am preparing a response to this request that will be provided tomorrow, April 29, 2010. I apologize for the delay in this communication.

Best regards,

Mary Harrell
Global Regulatory Affairs
Bausch & Lomb Incorporated
7 Giralda Farms Suite 1001
Madison, New Jersey 07940
Telephone: 973-360-6462
email: mary_harrell@bausch.com

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Thank You

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Thank You

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-200738	ORIG-1	BAUSCH AND LOMB INC	LOTEPREDNOL ETABONATE OINTMENT, 0.5%

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/s/

FARIBA IZADI
05/14/2010



NDA 200738

**ACKNOWLEDGE
ADDRESS CHANGE**

Bausch and Lomb Incorporated
Attention: Michael Bailey
Director, Global Regulatory affairs, Pharmaceuticals
7 Giralda Farms, Suite 1001
Madison, NJ 07940

Dear Mr. Bailey:

We acknowledge receipt on March 08, 2010 of your March, 04, 2010 correspondence notifying the Food and Drug Administration that the address for this application has been changed from

8500 Hidden River Parkway
Tampa, FL 33637

to

7 Giralda Farms, Suite 1001
Madison, NJ 07940

for the following new drug application:

NDA 200738 for Lotemax (lopteprednol etabonate ophthalmic ointment, 0.5%).

We have revised our records to reflect this change.

Please cite the NDA number listed above 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 Anti-Infective and Ophthalmology Products
5901-B Ammendale Road
Beltsville, MD 20705-1266

If you have any questions, call Fariba Izadi, Pharm.D., Regulatory Health Project Manager at (301) 796-0563.

Sincerely,

{See appended electronic signature page}

Maureen Dillon-Parker
Chief, Project Management Staff
Division of Anti-Infective and Ophthalmology Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-200738	GI-1	BAUSCH AND LOMB INC	LOTEPREDNOL ETABONATE OINTMENT, 0.5%

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/s/

MAUREEN P DILLON PARKER
04/02/2010



NDA 200738

FILING COMMUNICATION

Bausch & Lomb Incorporated
Attention: Julie Townsend, MPH
Manager, Global Regulatory Affairs
8500 Hidden River Parkway
Tampa, FL 33637

Dear Ms. Townsend:

Please refer to your new drug application (NDA) dated December 22, 2009, received December 23, 2009, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act, for Lotemax (loteprednol etabonate ophthalmic ointment) 0.5%.

We also refer to your submission(s) dated January 26, and February 4, 2010.

We have completed our filing review and have determined that your application is sufficiently complete to permit a substantive review. Therefore, this application was considered filed 60 days after the date we received your application in accordance with 21 CFR 314.101(a). The review classification for this application is **Standard**. The user fee goal date is October 23, 2010.

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 draft proposed labeling and, if necessary, any postmarketing requirement/commitment requests by July 26, 2010.

At this time we are notifying you that we have not identified any potential review issues; Please note that our filing review is only a preliminary evaluation of the application and is not indicative of deficiencies that may be identified during our review.

We do, however, request that you submit the following information:

1. The dosing regimen of loteprednol etabonate ophthalmic ointment 0.5%

is described as “apply approximately ½ inch ribbon into the conjunctival sac(s) four times daily for 14 days.” However, the exact amount of loteprednol etabonate in the ½ inch ribbon of ointment is not provided. This information is needed for calculating the multiples of animal dose to human dose (in mg/kg/day) in the label. Please provide the calculation(s) for how the figures in the proposed label were derived.

2. Provide representative Certificate of Analysis for white petrolatum and mineral oil.
3. To demonstrate the drug product stability during shipping, provide testing results from either a 3 months accelerated stability study at 40°C, a low/high temperature cycling study, or another appropriate study.

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 in pediatric patients unless this requirement is waived, deferred, or inapplicable.

Pediatric studies conducted under the terms of section 505B of the Federal Food, Drug, and Cosmetic Act (the Act) may also qualify for pediatric exclusivity under the terms of section 505A of the Act. If you wish to qualify for pediatric exclusivity please consult Division of Anti-Infective and Ophthalmology Products. Please note that satisfaction of the requirements in section 505B of the Act alone may not qualify you for pediatric exclusivity under 505A of the Act.

We acknowledge receipt of your request for a full deferral of pediatric studies for this application. Once we have reviewed your request and the application, we will notify you of our decision.

If you have any questions, call Fariba Izadi, Pharm.D., Regulatory Health Project Manager at (301) 796-0563.

Sincerely,

{See appended electronic signature page}

Wiley A. Chambers, M.D.
Acting Director
Division of Anti-Infective and Ophthalmology Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-200738	ORIG-1	BAUSCH AND LOMB INC	LOTEPREDNOL ETABONATE OINTMENT, 0.5%

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/s/

WILEY A CHAMBERS
03/04/2010

REQUEST FOR DDMAC LABELING REVIEW CONSULTATION

****Please send immediately following the Filing/Planning meeting****

TO:

CDER-DDMAC-RPM

FROM: (Name/Title, Office/Division/Phone number of requestor)

Fariba Izadi, Pharm.D.
Regulatory Health Project Manager
Division of Anti-Infective and Ophthalmology Products
Phone: (301) 796-0563
Fax: (301) 796-9881
E-mail: Fariba.Izadi@FDA.HHS.GOV

REQUEST DATE
February 17, 2010

IND NO.

NDA/BLA NO.
200738

TYPE OF DOCUMENTS
Original

NAME OF DRUG

Loteprednol Etabonate Ophthalmic ointment

PRIORITY CONSIDERATION

Standard

CLASSIFICATION OF DRUG

Ophthalmic

DESIRED COMPLETION DATE

(Generally 1 week before the wrap-up meeting)

July 5, 2010

NAME OF FIRM:

Bausch & Lomb

PDUFA Date: October 23, 2010

TYPE OF LABEL TO REVIEW

TYPE OF LABELING:

(Check all that apply)

PACKAGE INSERT (PI)

PATIENT PACKAGE INSERT (PPI)

CARTON/CONTAINER LABELING

MEDICATION GUIDE

INSTRUCTIONS FOR USE(IFU)

TYPE OF APPLICATION/SUBMISSION

ORIGINAL NDA/BLA

IND

EFFICACY SUPPLEMENT

SAFETY SUPPLEMENT

LABELING SUPPLEMENT

PLR CONVERSION

REASON FOR LABELING CONSULT

INITIAL PROPOSED LABELING

LABELING REVISION

EDR link to submission:

<\\CDSESUB1\EVSPROD\NDA0200738\0200738.enx>

Please Note: There is no need to send labeling at this time. DDMAC reviews substantially complete labeling, which has already been marked up by the CDER Review Team. The DDMAC reviewer will contact you at a later date to obtain the substantially complete labeling for review.

COMMENTS/SPECIAL INSTRUCTIONS:

Mid-Cycle Meeting: [Insert Date] May 21, 2010

Labeling Meetings: [Insert Dates]TBA

Wrap-Up Meeting: [Insert Date] July 12, 2010

SIGNATURE OF REQUESTER Fariba Izadi, Pharm.D

SIGNATURE OF RECEIVER

METHOD OF DELIVERY (Check one)

eMAIL

HAND

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
----- NDA-200738	----- ORIG-1	----- BAUSCH AND LOMB INC	----- LOTEPREDNOL ETABONATE OINTMENT, 0.5%

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/s/

FARIBA IZADI
02/17/2010

Izadi, Fariba

From: Townsend, Julie [Julie_Townsend@bausch.com]
Sent: Wednesday, January 27, 2010 3:45 PM
To: Izadi, Fariba
Subject: RE: NDA 200738 (Loteprednol etabonate) Information Request

Hi Fariba,

I acknowledge receipt of your email and will begin working with my team to address the items listed below.

Thanks and best regards,
Julie

From: Izadi, Fariba [mailto:Fariba.Izadi@fda.hhs.gov]
Sent: Wednesday, January 27, 2010 3:22 PM
To: Townsend, Julie
Subject: NDA 200738 (Loteprednol etabonate) Information Request

Dear Ms. Townsend,

We acknowledge section 1.9.2 of your NDA submission [REDACTED] (b) (4)
Please provide us with additional information as soon as possible.

[REDACTED] (b) (4)

In addition, we have the following information requests from our statistics team.

We couldn't locate the following items for studies 525 and 526. Please provide them as soon as possible to assist us in reviewing your NDA effectively and timely.

1. All the derived datasets (in .xpt format) and the related define document.
2. The define document for the SAS programs used to produce the study results.
3. The subgroup analysis results for the individual studies.

The review team will appreciate it if you can send us your responses by February 4, 2010. Please confirm receipt of this email.

Best Regards.

Fariba Izadi, Pharm.D.
Regulatory Health Project Manager
Division of Anti-Infective and Ophthalmology Products
Phone: (301) 796-0563
Fax: (301) 796-9881

1/28/2010

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
----- NDA-200738	----- ORIG-1	----- BAUSCH AND LOMB INC	----- LOTEPREDNOL ETABONATE OINTMENT, 0.5%

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/s/

FARIBA IZADI
01/28/2010



NDA 200738

NDA ACKNOWLEDGMENT

Bausch & Lomb Incorporated
Attention: Julie Townsend, MPH
Manager, Global Regulatory Affairs
8500 Hidden River Parkway
Tampa, FL 33637

Dear Ms. Townsend:

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: Lotemax (Loteprednol etabonate ophthalmic ointment 0.5%)

Date of Application: December 22, 2009

Date of Receipt: December 23, 2009

Our Reference Number: NDA 200738

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 February 21, 2010 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.

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 Anti-Infective 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>

If you have any questions, call Fariba Izadi, Pharm.D., Regulatory Health Project Manager at (301) 796-0563.

Sincerely,

{See appended electronic signature page}

Maureen Dillon-Parker
Chief, Project Management Staff
Division of Anti-Infective and Ophthalmology Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-200738	ORIG-1	BAUSCH AND LOMB INC	LOTEPREDNOL ETABONATE OINTMENT, 0.5%

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/s/

MAUREEN P DILLON PARKER
01/15/2010

MEMORANDUM

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

DATE: 1/14/09, 5:30 pm

TO: Julie Townsend, MPH, Manager, Global Regulatory Affairs
Bausch and Lomb, Ph: 813-866-2299

THROUGH : Jeannie David, Regulatory Project Manager, ONDQA

FROM: Jeannie David, Regulatory Project Manager, ONDQA

SUBJECT: Memo of Telecon: Request for clarification on establishments information

APPLICATION/DRUG: NDA 200,738 / loteprednol etabonate ophthalmic ointment, 0.5%

**Memo of Telecon:

The following clarifications were requested in a telephone conversation from Jeannie David, RPM, ONDQA, to Julie Townsend, Bausch and Lomb, regarding establishment information submitted to the original NDA on FDA Form 356h Attachment:

1. Informally provide (FYI, via email) inspection history for [REDACTED] (b) (4), to enable the FDA to cross-reference relevant sites in our database system.
2. Provide a local contact for [REDACTED] (b) (4), or confirm that the contact listed in [REDACTED] (b) (4) is appropriate.
3. Provide fax numbers and/or email address for all of the contacts for each manufacturing and testing facility listed.
4. Verify the correct CFN number for [REDACTED] (b) (4)
5. Verify the correct street address for [REDACTED] (b) (4)
6. Provide any changes that result from 2. - 5. above as an amendment to the NDA, updating the FDA Form 356h Attachment, and the relevant tables in Modules 2.3.S.1, 2.3.P.3, 3.2.S.2, and 3.2.P.3.

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-200738	ORIG-1	BAUSCH AND LOMB INC	LOTEPREDNOL ETABONATE OINTMENT, 0.5%

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/s/

JEANNIE C DAVID
01/14/2010