

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*  
**200738Orig1s000**

**OTHER REVIEW(S)**

FOOD AND DRUG ADMINISTRATION  
Center for Drug Evaluation and Research  
Division of Drug Marketing, Advertising, and Communications

## Memorandum

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**\*\*\*Pre-Decisional Agency Information\*\*\***

**Date:** September 30, 2010

**To:** Fariba Izadi, Pharm.D., Regulatory Health Project Manager  
Division of Anti-Infective and Ophthalmology Products

**From:** Christine Corser, Pharm.D., Regulatory Review Officer  
Division of Drug Marketing, Advertising, and Communications

Sheila Ryan, Pharm.D., Group Leader  
Division of Drug Marketing, Advertising, and Communications

**Subject:** Lotemax (loteprednol etabonate ophthalmic ointment) 0.5%  
NDA: 200738

DDMAC has reviewed the proposed product labeling, including the package insert (PI), draft carton label, and draft container label for Lotemax (loteprednol etabonate ophthalmic ointment) 0.5%, dated 9/13/2010, and we offer the following comments. DDMAC has no comment regarding the draft carton label, but recommends adding "For Ophthalmic Use Only" on the draft container label. Please feel free to contact me at (301)796-2653 with any questions or clarifications.

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b4 (CCI/TS) immediately following this page

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/s/

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CHRISTINE G CORSER  
09/30/2010

**MEMORANDUM  
HUMAN SERVICES**

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

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**CLINICAL INSPECTION SUMMARY**

**DATE:** Tuesday, September 07, 2010

**TO:** William Boyd, MD, Cross Discipline Team Leader  
Division of Anti-Infective and Ophthalmology Products

**FROM:** Kassa Ayalew, M.D.  
Good Clinical Practice Branch 2  
Division of Scientific Investigations

**THROUGH:** Tejashri Purohit-Sheth, M.D.  
Branch Chief Good Clinical Practice Branch 2  
Division of Scientific Investigations

**SUBJECT:** Evaluation of Clinical Inspections.

**NDA or BLA:** NDA 200738

**APPLICANT:** Bausch & Lomb Inc.  
8500 Hidden River Parkway  
Tampa, FL 33637  
Contact Person: Julie Townsend, MPH  
Phone: 813.975.7700  
Fax: (813) 975-7757  
E-mail: julie\_townsend@bausch.com

**DRUG:** loteprednol etabonate ophthalmic ointment 0.5% Trade Name: Lotemax

**NME:** No

**THERAPEUTIC CLASSIFICATION:** Standard

**INDICATIONS:** Treatment of post-operative inflammation and pain  
following ocular surgery

CONSULTATION REQUEST DATE: January 22, 2010

PDUFA: October 23, 2010

## I. BACKGROUND:

The sponsor, Bausch & Lomb Incorporation submitted an efficacy supplement application under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Loteprednol Etabonate (LE) Ophthalmic Ointment, 0.5% (Lotemax®) on December 22, 2009 to support a labeling claim for the treatment of post-operative inflammation and pain following ocular surgery. Loteprednol etabonate is a corticosteroid that has been marketed in the United States since 1998 as Lotemax® and Alrex® ophthalmic suspension drug products, and since 2005 in a fixed combination with tobramycin as Zylet®.

The current United States Food and Drug Administration-approved (US FDA-approved) dosage form of LE consists of an aqueous based, low viscosity, preserved (benzalkonium chloride) suspension. Bausch & Lomb has reformulated LE in an ointment formulation to provide (b) (4) alternative ophthalmic delivery dosage form for patients requiring treatment of postoperative inflammation and pain (b) (4).

The Applicant has provided data from two well-controlled pivotal studies (525 and 526) which they believe provide sufficient evidence to support the safety and efficacy of LE Ophthalmic Ointment, 0.5%, for therapy of patients requiring treatment for postoperative inflammation and pain. Both studies were randomized, multicenter, double-masked, parallel group, vehicle-controlled trials that were conducted to evaluate the clinical safety and efficacy of LE Ophthalmic Ointment, 0.5% compared to its vehicle for the treatment of postoperative inflammation and pain following cataract surgery.

### **Protocol No. 525 and Protocol No. 526 : A Randomized, Multicenter, Double-Masked, Parallel-Group Clinical Safety and Efficacy Evaluation of Loteprednol Etabonate Ophthalmic Ointment, 0.5% versus Vehicle for the Treatment of Inflammation Following Cataract Surgery**

The two studies had identical study endpoints, choice of control group, study duration, statistical methods, patient population, and dosage. Eligible subjects were to be randomized to LE Ophthalmic Ointment, 0.5% or to vehicle for the treatment of inflammation and pain following cataract surgery. Subjects were to be instructed to self-administer approximately one-half inch long ribbon of study drug to the lower cul-de-sac of the study eye, four times daily (QID), at approximately 4 hour intervals. The duration of treatment was to be 14 days with the last administration being the fourth dose on the day before Visit 6 (Day 15, ±1 day).

To be eligible for randomization, each subject had to have a sum of anterior chamber cell and flare measures, each on a 0-4 scale, of at least three at Postoperative Day 1. The sum of anterior chamber cell and flare measures was also identified as Anterior Chamber Reaction (ACR) in the study protocol.

The primary efficacy endpoints for this study were the proportion of subjects with complete resolution of anterior chamber cells & flare at Visit 5 (Postoperative Day 8) and the proportion of subjects with Grade 0 pain at Visit 5 (Postoperative Day 8).

Two domestic clinical sites were inspected in support of this application.

**II. RESULTS (by Site):**

<b>Name of CI, IRB, or Sponsor Location</b>	<b>Protocol # Site # # of Subjects</b>	<b>Inspection Date</b>	<b>Final Classification</b>
<b>Kenneth Sall, MD</b> SALL RESEARCH MEDICAL CENTER, INC. 11423 187 <sup>h</sup> St., Suite 200 Artesia, CA. 90701	Study 525 Site #962193 36 Subjects	3/26/2010- 4/7/2010	Pending  Interim Classification: VAI
<b>ARTHUR M. FISHMAN, M.D.</b> Eye Surgery Associates 603 North Flamingo Road, Suite 250 Pembroke Pines, FL 33028	Study 526 Site #986169 47 Subjects	5/17/2010- 5/24/2010	Pending  Interim Classification: NAI

Key to Classifications

NAI = No deviation from regulations.

VAI = Deviation(s) from regulations.

OAI = Significant deviations from regulations. Data unreliable.

Pending = Preliminary classification based on information in 483 or preliminary communication with the field and/or EIR has not been received from the field and/or complete review of EIR is pending.

- 1. Kenneth Sall, MD**  
 SALL RESEARCH MEDICAL CENTER, INC.  
 11423 187<sup>h</sup> St., Suite 200  
 Artesia, CA. 90701

**a. What was inspected?**

This inspection was conducted in accordance with Compliance Program 7348.811, between 3/26/2010- 4/7/2010.

A total of 48 subjects were screened and 36 subjects were enrolled and completed the

study. Records for 15 subjects were reviewed during the inspection. The inspection evaluated informed consent and included review of source documents. Study subject files were reviewed for verification of: 1) entry criteria, 2) diagnosis of target disease, 3) efficacy variables, and 4) adequacy adverse experience reporting. In addition, drug accountability records, IRB approval and dates, and sponsor monitoring records were reviewed. There were no limitations to the inspection.

**b. General observations/commentary:**

The inspection of Dr. Sall's site revealed that the studies were not conducted in accordance with the investigational plan. A Form FDA 483, Inspectional Observations, was issued to this investigator, for:

Failure to conduct the study according to the signed investigator statement and the investigational plan [21 CFR 312.60]. Specifically, three employees performed duties not delegated to them (screening visits, post surgery visit, visual acuity and refraction evaluations).

*DSI Reviewer Comments: The clinical investigator failed to appropriately document delegation of study related duties to authorized personnel. Although, the CI failed to appropriately document this delegation, of study related duties to authorized personnel, it appears that they were qualified to do the work based on their training and CVs. The failure to document this delegation was reportedly an administrative error.*

**c. Assessment of data integrity:**

Although regulatory violations were noted as above, it is unlikely based on the nature of the violations that they significantly affect the reliability of safety and efficacy data. Based on the provided EIR for this site and Dr. Sall's responses regarding the regulatory violations during the inspection, which were documented in the EIR, data derived from Dr. Sall's site are considered reliable.

**2. Arthur M. Fishman, M.D.**

Eye Surgery Associates  
603 North Flamingo Road, Suite 250  
Pembroke Pines, FL 33028  
Phone: (954) 431-2777 Fax: (954) 431-2110

**a. What was inspected?**

This inspection was conducted in accordance with Compliance Program 7348.811 between 5/17/2010-5/24/2010.

A total of 53 subjects were screened and enrolled and 47 subjects completed the study. Six subjects were screen failures. No subject withdrew from the study. Records for 18 of the 47 subjects were reviewed during the inspection.

Study subject files were reviewed for verification of: 1) entry criteria, 2) diagnosis of target disease, 3) efficacy variables, and 4) adequacy of adverse experience reporting. In addition, drug accountability records, IRB approval and dates, and sponsor monitoring records were reviewed. There were no limitations to the inspection.

**b. General observations/commentary:**

The inspection of Dr. Fishman's site did not reveal regulatory violations. A Form FDA 483, Inspectional Observations, was not issued.

**c. Assessment of data integrity:**

Based on the provided Establishment Inspection Report (EIR) for this site, data derived from Dr. Fishman's site are considered acceptable.

**IV. OVERALL ASSESSMENT OF FINDINGS AND RECOMMENDATIONS**

Two domestic clinical sites were inspected in support of the application. No significant regulatory violations were noted during the inspection of Dr. Fishman and although regulatory violations were noted during the inspection of Dr. Sall, these are not considered likely to importantly impact data reliability. In general, the studies appear to have been conducted adequately and the data in support of the NDA appear reliable.

Final headquarters classifications for all inspections are pending at this time. An addendum to this clinical inspection summary will be forwarded to the review division should there be a change in the final classification or additional observations of clinical and regulatory significance are discovered after reviewing the EIRs.

*{See appended electronic signature page}*

Kassa Ayalew, M.D.  
Good Clinical Practice Branch II  
Division of Scientific Investigations

CONCURRENCE:

*{See appended electronic signature page}*

Tejashri Purohit-Sheth, M.D.  
Branch Chief  
Good Clinical Practice Branch II  
Division of Scientific Investigations

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/

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KASSA AYALEW  
09/13/2010

TEJASHRI S PUROHIT-SHETH  
09/13/2010



**Department of Health and Human Services  
Public Health Service  
Food and Drug Administration  
Center for Drug Evaluation and Research  
Office of Surveillance and Epidemiology**

Date: August 28, 2010

To: Wiley Chambers, MD, Acting Director  
Division of Anti-infective and Ophthalmology Products

Through: Denise Toyer, PharmD, Deputy Director  
Division of Medication Error Prevention and Analysis

From: Kristina A. Toliver, PharmD, Team Leader  
Division of Medication Error Prevention and Analysis

Subject: Label and Labeling Review

Drug Name: Lotemax (Loteprednol Ophthalmic Ointment) 0.5%

Application Type/Number: NDA 200738

Applicant: Bausch & Lomb Incorporated

OSE RCM #: 2010-52

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## **1 INTRODUCTION**

This review is written in response to a January 8, 2010 request from the Division of Anti-Infective and Ophthalmology Products for evaluation of the labels and labeling for Lotemax (Loteprednol Etabonate Ophthalmic Ointment), 0.5% to identify areas that could contribute to medication errors. The Applicant submitted proposed container labels, carton and insert labeling for our review.

Lotemax Ophthalmic Solution (NDA 020583) was approved on March 9, 1998 and is indicated for the treatment of steroid responsive inflammatory condition of the palpebral and bulbar conjunctiva, cornea and anterior segment of the globe and for the treatment of post-operative inflammation following ocular surgery. Lotemax Ophthalmic Ointment shares the same active ingredient as Lotemax Ophthalmic Solution. However, Lotemax Ophthalmic Ointment will only be indicated for treatment of post-operative inflammation following ocular surgery. DMEPA did not review the labels and labeling for Lotemax Ophthalmic Solution.

## **2 METHODS AND MATERIALS**

The Division of Medication Error Prevention and Analysis used Failure Mode and Effects Analysis (FMEA)<sup>1</sup> in our evaluation of the container labels, carton and insert labeling that were submitted on December 23, 2009 (see Appendices A and B).

### **2.1 FDA ADVERSE EVENT REPORTING SYSTEM (AERS)**

Since Lotemax ophthalmic suspension, 0.5% is currently marketed, DMEPA searched the FDA Adverse Event Reporting System (AERS) database to determine if there are any medication errors associated with the labels and labeling confusion with the currently marketed product Lotemax that may be an indication of potential label or labeling confusion with the ophthalmic ointment. The search was conducted using the active ingredient 'loteprednol', trade name 'Lotemax' and the verbatim terms 'lotemax%. The MedDRA high level terms (HLT) 'Maladministrations', 'Medication Errors due to Accidental Exposures' and Medication Errors NEC' and the preferred terms 'Overdose' and 'Product Quality Issue' were used perform the search.

The reports were manually reviewed to determine if a medication error occurred. Duplicate reports were combined. The cases that described a medication error were categorized by type of error. We reviewed the cases within each category to identify factors that contributed to the medication errors. If a root cause was associated with the labels or labeling of the product, the case was considered pertinent to this review. Those reports that did not describe a medication error or did not describe an error applicable to this review (e.g. errors related to accidental exposures, intentional overdoses, etc.) were excluded from further analysis.

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<sup>1</sup> Institute for Healthcare Improvement (IHI). Failure Modes and Effects Analysis. Boston. IHI:2004.

### 3 RESULTS

#### 3.1 FDA ADVERSE EVENT REPORTING SYSTEM (AERS)

The AERS search retrieved a total of 17 cases were retrieved from the AERS search conducted on April 30, 2010. Fifteen (n=15) of the cases were not relevant to this review for the following reasons.

- Lotemax was not the suspect drug (n=7)
- Concerns from healthcare practitioners of potential name confusion between a (b) (4) (b) (4) and the currently marketed product Lanoxin (n=4)
- Wrong drug error where a bottle of Tobramycin was dispensed in a Lotemax carton. The bottle was returned to the manufacturer because it was thought that this was a manufacturing issue. However, the manufacturer indicated that it was impossible for this to occur due to the fact that the Lotemax was manufactured and packaged four months after the Tobramycin lot in question and the Tobramycin bottle is larger than the Lotemax bottle and could not have fit through the packaging line. Further causality could not be determined (n=1)
- Wrong drug error where a practitioner in a physician's office accidentally picked a bottle of Proparacaine Ophthalmic Solution off of the counter and put it in the patient's Lotemax carton instead of the patient's open bottle of Lotemax. There are multiple Proparacaine Ophthalmic Solution on the market and the reporter did not include the manufacturer in the report, therefore it can not be determined if the labels look similar.
- Adverse events that were not a result of medication errors (n=2).

In the remaining two cases, reporters complained that the container labels and carton labeling for Lotemax Ophthalmic Solution lack information pertaining to the 'Rx Only' statement (n=1) and lack of a warning statement with regards to use of Lotemax with contact lenses (n=1).

The first case (ISR # 3255060-0) occurred in 1999 where a pharmacist reported that the container labels and carton labeling lacked the statement '*Caution: Federal law prohibits dispensing without a prescription*'. As part of the FDA's Modernization Act of 1997 (FDAMA) the legend statement '*Caution: Federal law prohibits dispensing without a prescription*' was replaced with the phrase 'Rx Only' on the label of prescription drug products. Thus, DMEPA has no comments on this matter since the labels and labeling for the currently marketed ophthalmic solution and the proposed ointment both bear the 'Rx only' statement on their labels and labeling.

The final case (ISR # 3465975-6,) states that in 2000, a patient experienced a loss in visual acuity, discharge, migraine headaches, blurry, burning, itching and dry eyes as a result of administering Lotemax and TobraDex into her eyes while wearing soft contact lenses. The reporter states that the patient was not aware that she could not administer the product with soft contact lenses because the container labels and carton labeling lack the bolded statement 'DO NOT USE THIS PRODUCT WITH SOFT CONTACT LENSES' and the only warning statement is not prominent to patients because it is embedded in the package insert labeling. DMEPA notes that the *Precaution (Information for Patients) Section* of the currently approved package insert labeling for the ophthalmic solution contains the statement '*As with all ophthalmic preparations containing benzalkonium chloride, patients should be advised not to wear contact lenses when using Lotemax*'; and, *Section 17 (Patient Counseling Information)* in the insert labeling for the proposed ointment contains the statement '*Patients should be advised not to wear contact lenses during their course of therapy with Lotemax ointment.*' DMEPA notes that the container labels and carton labeling for the ophthalmic solution and the proposed ointment do not bear these statements. However, similar products such as Alrex (Loteprednol Etabonate Ophthalmic Suspension) and Flarex

(Fluorometholone Acetate Ophthalmic Suspension) also lack this statement on container labels and labeling. Thus, DMEPA does not have any recommendations regarding the lack of this statement on container labels and labeling at this time. We will continue to monitor AERS for these types of errors.

#### 4 RECOMMENDATIONS

We provide recommendations on the insert labeling in Section 4.1, *Comments to the Division*. Section 4.2, *Comments to the Applicant*, contains our recommendations for the container labels and carton labeling. We request the recommendations in Section 4.2 be communicated to the Applicant, prior to approval.

Please copy the Division of Medication Error Prevention and Analysis on any communication to the Applicant with regard to this review. If you have questions or need clarifications, please contact OSE Project Managers, Brantley Dorch at 301-796-0150.

##### 4.1 COMMENTS TO THE DIVISION

###### 4.1.1 Package Insert Labeling (*Highlights of Prescribing Information and Full Prescribing Information*)

1. Remove the statement [REDACTED] (b)(4), from the Heading in the *Highlights of Prescribing Information*.
2. Revise the *Dosage Forms and Strength* sections to read 'loteprednol etabonate ophthalmic ointment, 0.5%'.

##### 4.2 COMMENTS TO THE APPLICANT

###### A. General Comments (Container Labels and Carton Labeling)

1. [REDACTED] (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.
3. As currently presented the carton labeling lacks the expiration date and lot number. Include this information on all carton labeling.

###### B. Carton Labeling (Professional Sample and Trade)

1. 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).

2. 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.
3. 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.
4. Relocate the statement 'For Ophthalmic Use Only', from the side panel to the principal display panel so that the route of administration is in a place where patients and/or caregivers can see it.
5. Increase the prominence of the statement 'Sample-Not for Resale' located on the principal display panel.
6. Consider modifying the blue color used on the carton labeling as it is the same color used for Lotemax Ophthalmic solution. The use of the same color for both dosage forms increases the potential for selection of the wrong dosage form from pharmacy shelves.

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immediately following this page

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/

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KRISTINA C ARNWINE  
08/28/2010

DENISE P TOYER  
08/29/2010

**RPM FILING REVIEW**  
(Including Memo of Filing Meeting)

**To be completed for all new NDAs, BLAs, and Efficacy Supplements (except SE8 and SE9)**

<b>Application Information</b>		
NDA # 200738 BLA#	NDA Supplement #:S- BLA STN #	Efficacy Supplement Type SE-
Proprietary Name: Lotemax Established/Proper Name: Loteprednol etabonate Dosage Form: ophthalmic ointment Strengths: 0.5%		
Applicant: Bausch & Lomb Agent for Applicant (if applicable):		
Date of Application: 12-22-09 Date of Receipt: 12-23-09 Date clock started after UN:		
PDUFA Goal Date: 10-23-10	Action Goal Date (if different): 10-23-10	
Filing Date: 02-21-10	Date of Filing Meeting: 01-27-10	
Chemical Classification: (1,2,3 etc.) (original NDAs only) 3		
Proposed indication(s)/Proposed change(s): Treatment of post-operative inflammation and pain following ocular surgery.		
Type of Original NDA: AND (if applicable) Type of NDA Supplement:	<input checked="" type="checkbox"/> 505(b)(1) <input type="checkbox"/> 505(b)(2) <input type="checkbox"/> 505(b)(1) <input type="checkbox"/> 505(b)(2)	
<b><i>If 505(b)(2): Draft the "505(b)(2) Assessment" form found at:  <a href="http://inside.fda.gov:9003/CDER/OfficeofNewDrugs/ImmediateOffice/ucm027499.html">http://inside.fda.gov:9003/CDER/OfficeofNewDrugs/ImmediateOffice/ucm027499.html</a>            and refer to Appendix A for further information.</i></b>		
Review Classification:	<input checked="" type="checkbox"/> Standard <input type="checkbox"/> Priority  <input type="checkbox"/> Tropical Disease Priority Review Voucher submitted	
<b><i>If the application includes a complete response to pediatric WR, review classification is Priority.</i></b>  <b><i>If a tropical disease priority review voucher was submitted, review classification is Priority.</i></b>		
Resubmission after withdrawal? <input type="checkbox"/>	Resubmission after refuse to file? <input type="checkbox"/>	
Part 3 Combination Product? <input type="checkbox"/> <b><i>If yes, contact the Office of Combination Products (OCP) and copy them on all Inter-Center consults</i></b>	<input type="checkbox"/> Drug/Biologic <input type="checkbox"/> Drug/Device <input type="checkbox"/> Biologic/Device	
<input type="checkbox"/> Fast Track <input type="checkbox"/> Rolling Review <input type="checkbox"/> Orphan Designation  <input type="checkbox"/> Rx-to-OTC switch, Full <input type="checkbox"/> Rx-to-OTC switch, Partial <input type="checkbox"/> Direct-to-OTC	<input type="checkbox"/> PMC response <input type="checkbox"/> PMR response: <input type="checkbox"/> FDAAA [505(o)] <input type="checkbox"/> PREA deferred pediatric studies [21 CFR 314.55(b)/21 CFR 601.27(b)] <input type="checkbox"/> Accelerated approval confirmatory studies (21 CFR 314.510/21 CFR 601.41) <input type="checkbox"/> Animal rule postmarketing studies to verify clinical	

Other:	benefit and safety (21 CFR 314.610/21 CFR 601.42)			
Collaborative Review Division (if OTC product):				
List referenced IND Number(s): IND 32432, IND 36209. (b) (4)				
<b>Goal Dates/Names/Classification Properties</b>	<b>YES</b>	<b>NO</b>	<b>NA</b>	<b>Comment</b>
PDUFA and Action Goal dates correct in tracking system? <i>If not, ask the document room staff to correct them immediately. These are the dates used for calculating inspection dates.</i>	x			
Are the proprietary, established/proper, and applicant names correct in tracking system? <i>If not, ask the document room staff to make the corrections. Also, ask the document room staff to add the established/proper name to the supporting IND(s) if not already entered into tracking system.</i>	x			
Are all classification properties [e.g., orphan drug, 505(b)(2)] entered into tracking system? <i>If not, ask the document room staff to make the appropriate entries.</i>	x			
<b>Application Integrity Policy</b>	<b>YES</b>	<b>NO</b>	<b>NA</b>	<b>Comment</b>
Is the application affected by the Application Integrity Policy (AIP)? <i>Check the AIP list at: <a href="http://www.fda.gov/ICECI/EnforcementActions/ApplicationIntegrityPolicy/default.htm">http://www.fda.gov/ICECI/EnforcementActions/ApplicationIntegrityPolicy/default.htm</a></i>		x		
<b>If yes, explain in comment column.</b>				
<b>If affected by AIP, has OC/DMPQ been notified of the submission? If yes, date notified:</b>				
<b>User Fees</b>	<b>YES</b>	<b>NO</b>	<b>NA</b>	<b>Comment</b>
Is Form 3397 (User Fee Cover Sheet) included with authorized signature?	x			
<u>User Fee Status</u> <i>If a user fee is required and it has not been paid (and it is not exempted or waived), the application is unacceptable for filing following a 5-day grace period. Review stops. Send UN letter and contact user fee staff.</i>	Payment for this application: <input checked="" type="checkbox"/> Paid <input type="checkbox"/> Exempt (orphan, government) <input type="checkbox"/> Waived (e.g., small business, public health) <input type="checkbox"/> Not required			
<i>If the firm is in arrears for other fees (regardless of whether a user fee has been paid for this application), the application is unacceptable for filing (5-day grace period does not apply). Review stops. Send UN letter and contact the user fee staff.</i>	Payment of other user fees: <input checked="" type="checkbox"/> Not in arrears <input type="checkbox"/> In arrears			
<i>Note: 505(b)(2) applications are no longer exempt from user fees pursuant to the passage of FDAAA. All 505(b) applications, whether 505(b)(1) or 505(b)(2), require user fees unless otherwise waived or exempted (e.g., small business waiver, orphan exemption).</i>				

505(b)(2) (NDAs/NDA Efficacy Supplements only)	YES	NO	NA	Comment																
Is the application for a duplicate of a listed drug and eligible for approval under section 505(j) as an ANDA?			x																	
Is the application for a duplicate of a listed drug whose only difference is that the extent to which the active ingredient(s) is absorbed or otherwise made available to the site of action less than that of the reference listed drug (RLD)? (see 21 CFR 314.54(b)(1)).			x																	
Is the application for a duplicate of a listed drug whose only difference is that the rate at which the proposed product's active ingredient(s) is absorbed or made available to the site of action is unintentionally less than that of the listed drug (see 21 CFR 314.54(b)(2))?  <i>Note: If you answered yes to any of the above questions, the application may be refused for filing under 21 CFR 314.101(d)(9).</i>			x																	
Is there unexpired exclusivity on the active moiety (e.g., 5-year, 3-year, orphan or pediatric exclusivity)? <b>Check the Electronic Orange Book at:</b> <a href="http://www.fda.gov/cder/ob/default.htm">http://www.fda.gov/cder/ob/default.htm</a>  <b>If yes, please list below:</b>			x																	
<table border="1"> <thead> <tr> <th>Application No.</th> <th>Drug Name</th> <th>Exclusivity Code</th> <th>Exclusivity Expiration</th> </tr> </thead> <tbody> <tr><td> </td><td> </td><td> </td><td> </td></tr> <tr><td> </td><td> </td><td> </td><td> </td></tr> <tr><td> </td><td> </td><td> </td><td> </td></tr> </tbody> </table>	Application No.	Drug Name	Exclusivity Code	Exclusivity Expiration																
Application No.	Drug Name	Exclusivity Code	Exclusivity Expiration																	
<i>If there is unexpired, 5-year exclusivity remaining on the active moiety for the proposed drug product, a 505(b)(2) application cannot be submitted until the period of exclusivity expires (unless the applicant provides paragraph IV patent certification; then an application can be submitted four years after the date of approval.) Pediatric exclusivity will extend both of the timeframes in this provision by 6 months. 21 CFR 108(b)(2). Unexpired, 3-year exclusivity will only block the approval, not the submission of a 505(b)(2) application.</i>																				
Exclusivity	YES	NO	NA	Comment																
Does another product have orphan exclusivity for the same indication? <b>Check the Electronic Orange Book at:</b> <a href="http://www.fda.gov/cder/ob/default.htm">http://www.fda.gov/cder/ob/default.htm</a>		x																		
<b>If another product has orphan exclusivity</b> , is the product considered to be the same product according to the orphan drug definition of sameness [21 CFR 316.3(b)(13)]?  <i>If yes, consult the Director, Division of Regulatory Policy II, Office of Regulatory Policy (HFD-007)</i>			x																	
Has the applicant requested 5-year or 3-year Waxman-Hatch exclusivity? (NDAs/NDA efficacy supplements only)  <b>If yes, # years requested:</b> 3 years –Marketing Exclusivity  <i>Note: An applicant can receive exclusivity without requesting it; therefore, requesting exclusivity is not required.</i>	x																			

Is the proposed product a single enantiomer of a racemic drug previously approved for a different therapeutic use ( <i>NDA</i> s only)?		x		
<b>If yes</b> , did the applicant: (a) elect to have the single enantiomer (contained as an active ingredient) not be considered the same active ingredient as that contained in an already approved racemic drug, and/or (b): request exclusivity pursuant to section 505(u) of the Act (per FDAAA Section 1113)?  <i>If yes, contact Mary Ann Holovac, Director of Drug Information, OGD/DLPS/LRB.</i>			x	

Format and Content				
<i>Do not check mixed submission if the only electronic component is the content of labeling (COL).</i>	<input type="checkbox"/> All paper (except for COL) <input checked="" type="checkbox"/> All electronic <input type="checkbox"/> Mixed (paper/electronic)  <input checked="" type="checkbox"/> CTD <input type="checkbox"/> Non-CTD <input type="checkbox"/> Mixed (CTD/non-CTD)			
<b>If mixed (paper/electronic) submission</b> , which parts of the application are submitted in electronic format?				
<b>Overall Format/Content</b>	<b>YES</b>	<b>NO</b>	<b>NA</b>	<b>Comment</b>
<b>If electronic submission</b> , does it follow the eCTD guidance <sup>1</sup> ? <b>If not</b> , explain (e.g., waiver granted).	x			
<b>Index:</b> Does the submission contain an accurate comprehensive index?	x			
Is the submission complete as required under 21 CFR 314.50 ( <i>NDA</i> s/ <i>NDA efficacy supplements</i> ) or under 21 CFR 601.2 ( <i>BLA</i> s/ <i>BLA efficacy supplements</i> ) including:  <input checked="" type="checkbox"/> legible <input checked="" type="checkbox"/> English (or translated into English) <input checked="" type="checkbox"/> pagination <input checked="" type="checkbox"/> navigable hyperlinks (electronic submissions only)  <b>If no</b> , explain.	x			
<b>Controlled substance/Product with abuse potential:</b> Is an Abuse Liability Assessment, including a proposal for scheduling, submitted?  <i>If yes, date consult sent to the Controlled Substance Staff:</i>			x	
<b>BLAs only:</b> Companion application received if a shared or divided manufacturing arrangement?  <b>If yes</b> , BLA #			x	

<b>Forms and Certifications</b>				
<p><i>Electronic forms and certifications with electronic signatures (scanned, digital, or electronic – similar to DARRTS, e.g., /s/) are acceptable. Otherwise, <b>paper</b> forms and certifications with hand-written signatures must be included. <b>Forms</b> include: user fee cover sheet (3397), application form (356h), patent information (3542a), financial disclosure (3454/3455), and clinical trials (3674); <b>Certifications</b> include: debarment certification, patent certification(s), field copy certification, and pediatric certification.</i></p>				
<b>Application Form</b>	<b>YES</b>	<b>NO</b>	<b>NA</b>	<b>Comment</b>
<p>Is form FDA 356h included with authorized signature?</p> <p><i>If foreign applicant, <b>both</b> the applicant and the U.S. agent must sign the form.</i></p>	x			
<p>Are all establishments and their registration numbers listed on the form/attached to the form?</p>	x			
<b>Patent Information (NDAs/NDA efficacy supplements only)</b>	<b>YES</b>	<b>NO</b>	<b>NA</b>	<b>Comment</b>
<p>Is patent information submitted on form FDA 3542a?</p>	x			
<b>Financial Disclosure</b>	<b>YES</b>	<b>NO</b>	<b>NA</b>	<b>Comment</b>
<p>Are financial disclosure forms FDA 3454 and/or 3455 included with authorized signature?</p> <p><i>Forms must be signed by the APPLICANT, not an Agent.</i></p> <p><i>Note: Financial disclosure is required for bioequivalence studies that are the basis for approval.</i></p>	x			
<b>Clinical Trials Database</b>	<b>YES</b>	<b>NO</b>	<b>NA</b>	<b>Comment</b>
<p>Is form FDA 3674 included with authorized signature?</p>	x			
<b>Debarment Certification</b>	<b>YES</b>	<b>NO</b>	<b>NA</b>	<b>Comment</b>
<p>Is a correctly worded Debarment Certification included with authorized signature? (<i>Certification is not required for supplements if submitted in the original application</i>)</p> <p><i>If foreign applicant, <b>both</b> the applicant and the U.S. Agent must sign the certification.</i></p> <p><i>Note: Debarment Certification should use wording in FD&amp;C Act section 306(k)(1) i.e., “[Name of applicant] 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.” Applicant may not use wording such as, “To the best of my knowledge...”</i></p>	x			

<b>Field Copy Certification (NDAs/NDA efficacy supplements only)</b>	<b>YES</b>	<b>NO</b>	<b>NA</b>	<b>Comment</b>
<p><b>For paper submissions only:</b> Is a Field Copy Certification (that it is a true copy of the CMC technical section) included?</p> <p><i>Field Copy Certification is not needed if there is no CMC technical section or if this is an electronic submission (the Field Office has access to the EDR)</i></p> <p><i>If maroon field copy jackets from foreign applicants are received, return them to CDR for delivery to the appropriate field office.</i></p>			X	All Electronic NDA

<b>Pediatrics</b>	<b>YES</b>	<b>NO</b>	<b>NA</b>	<b>Comment</b>
<p><b><u>PREA</u></b></p> <p>Does the application trigger PREA?</p> <p><i>If yes, notify PeRC RPM (PeRC meeting is required)</i></p> <p><i>Note: NDAs/BLAs/efficacy supplements for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration trigger PREA. All waiver &amp; deferral requests, pediatric plans, and pediatric assessment studies must be reviewed by PeRC prior to approval of the application/supplement.</i></p>	X			
<p><b>If the application triggers PREA</b>, are the required pediatric assessment studies or a full waiver of pediatric studies included?</p>		X		
<p><b>If studies or full waiver not included</b>, is a request for full waiver of pediatric studies OR a request for partial waiver and/or deferral with a pediatric plan included?</p> <p><i>If no, request in 74-day letter</i></p>	X			
<p><b>If a request for full waiver/partial waiver/deferral is included</b>, does the application contain the certification(s) required under 21 CFR 314.55(b)(1), (c)(2), (c)(3)/21 CFR 601.27(b)(1), (c)(2), (c)(3)</p> <p><i>If no, request in 74-day letter</i></p>		X		Information request was sent to the sponsor on 1-27-10. The sponsor responded back on 02-04-10
<p><b><u>BPCA</u> (NDAs/NDA efficacy supplements only):</b></p> <p>Is this submission a complete response to a pediatric Written Request?</p> <p><i>If yes, notify Pediatric Exclusivity Board RPM (pediatric exclusivity determination is required)</i></p>		X		

<b>Proprietary Name</b>	<b>YES</b>	<b>NO</b>	<b>NA</b>	<b>Comment</b>
Is a proposed proprietary name submitted?  <i>If yes, ensure that it is submitted as a separate document and routed directly to OSE/DMEPA for review.</i>	x			
<b>Prescription Labeling</b>	<input type="checkbox"/> <b>Not applicable</b>			
Check all types of labeling submitted.	<input checked="" type="checkbox"/> Package Insert (PI) <input type="checkbox"/> Patient Package Insert (PPI) <input type="checkbox"/> Instructions for Use (IFU) <input type="checkbox"/> Medication Guide (MedGuide) <input checked="" type="checkbox"/> Carton labels <input checked="" type="checkbox"/> Immediate container labels <input type="checkbox"/> Diluent <input type="checkbox"/> Other (specify)			
	<b>YES</b>	<b>NO</b>	<b>NA</b>	<b>Comment</b>
Is Electronic Content of Labeling (COL) submitted in SPL format?  <i>If no, request in 74-day letter.</i>	x			
Is the PI submitted in PLR format?	x			
<b>If PI not submitted in PLR format</b> , was a waiver or deferral requested before the application was received or in the submission? <b>If requested before application was submitted</b> , what is the status of the request?  <i>If no waiver or deferral, request PLR format in 74-day letter.</i>			x	
All labeling (PI, PPI, MedGuide, IFU, carton and immediate container labels) consulted to DDMAC?	x			
MedGuide, PPI, IFU (plus PI) consulted to OSE/DRISK? <i>(send WORD version if available)</i>			x	Not applicable at this time.
REMS consulted to OSE/DRISK?			x	No REMS planned for this application
Carton and immediate container labels, PI, PPI sent to OSE/DMEPA?	x			
<b>OTC Labeling</b>	<input checked="" type="checkbox"/> <b>Not Applicable</b>			
Check all types of labeling submitted.	<input type="checkbox"/> Outer carton label <input type="checkbox"/> Immediate container label <input type="checkbox"/> Blister card <input type="checkbox"/> Blister backing label <input type="checkbox"/> Consumer Information Leaflet (CIL) <input type="checkbox"/> Physician sample <input type="checkbox"/> Consumer sample <input type="checkbox"/> Other (specify)			
	<b>YES</b>	<b>NO</b>	<b>NA</b>	<b>Comment</b>
Is electronic content of labeling (COL) submitted?  <i>If no, request in 74-day letter.</i>				

Are annotated specifications submitted for all stock keeping units (SKUs)? <i>If no, request in 74-day letter.</i>				
If representative labeling is submitted, are all represented SKUs defined? <i>If no, request in 74-day letter.</i>				
All labeling/packaging, and current approved Rx PI (if switch) sent to OSE/DMEPA?				
<b>Consults</b>	<b>YES</b>	<b>NO</b>	<b>NA</b>	<b>Comment</b>
Are additional consults needed? (e.g., IFU to CDRH; QT study report to QT Interdisciplinary Review Team) <i>If yes, specify consult(s) and date(s) sent:</i>		x		

<b>Meeting Minutes/SPAs</b>	<b>YES</b>	<b>NO</b>	<b>NA</b>	<b>Comment</b>
End-of Phase 2 meeting(s)? <b>Date(s):</b> 07-16-07 <i>If yes, distribute minutes before filing meeting</i>	x			
Pre-NDA/Pre-BLA/Pre-Supplement meeting(s)? <b>Date(s):</b> 10-07-09 <i>If yes, distribute minutes before filing meeting</i>	x			
Any Special Protocol Assessments (SPAs)? <b>Date(s):</b> <i>If yes, distribute letter and/or relevant minutes before filing meeting</i>		x		

<http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm072349.pdf>

ATTACHMENT

**MEMO OF FILING MEETING**

**DATE:** 01-27-2010

**BLA/NDA/Supp #:** 200738

**PROPRIETARY NAME:** Lotemax

**ESTABLISHED/PROPER NAME:** Loteprednol Ophthalmic Ointment

**DOSAGE FORM/STRENGTH:** 0.5%

**APPLICANT:** Bausch & Lomb

**PROPOSED INDICATION(S)/PROPOSED CHANGE(S):** Treatment of post-operative inflammation and pain following ocular surgery.

**BACKGROUND.**

**REVIEW TEAM:**

Discipline/Organization	Names		Present at filing meeting? (Y or N)
Regulatory Project Management	RPM:	Fariba Izadi	Y
	CPMS/TL:	Maureen Dillon-Parker	N
Cross-Discipline Team Leader (CDTL)	William Boyd		Y
Clinical	Reviewer:	Sonal Wadhwa	Y
	TL:	William Boyd	Y
Social Scientist Review ( <i>for OTC products</i> )	Reviewer:		
	TL:		
OTC Labeling Review ( <i>for OTC products</i> )	Reviewer:		
	TL:		
Clinical Microbiology ( <i>for antimicrobial products</i> )	Reviewer:		

	TL:		
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Clinical Pharmacology	Reviewer:	Kimberly Bergman	Y
	TL:	Charles Bonapace	Y
Biostatistics	Reviewer:	Mushfiqur Rashid	Y
	TL:	Yan Wang	Y
Nonclinical (Pharmacology/Toxicology)	Reviewer:	Conrad Chen	Y
	TL:	Wendy Schmidt	Y
Statistics (carcinogenicity)	Reviewer:		
	TL:		
Immunogenicity (assay/assay validation) ( <i>for BLAs/BLA efficacy supplements</i> )	Reviewer:		
	TL:		
Product Quality (CMC)	Reviewer:	Lin Qi	Y
	TL:	Steven Miller Linda Ng	N Y
Quality Microbiology ( <i>for sterile products</i> )	Reviewer:	Bryan Riley	Y
	TL:		
CMC Labeling Review ( <i>for BLAs/BLA supplements</i> )	Reviewer:		
	TL:		
Facility Review/Inspection	Reviewer:		
	TL:		
OSE/DMEPA (proprietary name)	Reviewer:	Brantley Dorch	Y
	TL:	Tsaline Jones-Smith Kristina Toliver	Y Y
OSE/DRISK (REMS)	Reviewer:		
	TL:		
Bioresearch Monitoring (DSI)	Reviewer:	Kassa Ayalew	Y
	TL:	Teshani Purohit-sheth	N

Other reviewers		
Other attendees		

**FILING MEETING DISCUSSION:**

<b>GENERAL</b>	
<ul style="list-style-type: none"> <li>505(b)(2) filing issues?</li> </ul> <p><b>If yes, list issues:</b></p>	<input checked="" type="checkbox"/> Not Applicable <input type="checkbox"/> YES <input type="checkbox"/> NO
<ul style="list-style-type: none"> <li>Per reviewers, are all parts in English or English translation?</li> </ul> <p><b>If no, explain:</b></p>	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO
<ul style="list-style-type: none"> <li>Electronic Submission comments</li> </ul> <p><b>List comments:</b> No Comments</p>	<input type="checkbox"/> Not Applicable
<b>CLINICAL</b>	<input type="checkbox"/> Not Applicable <input checked="" type="checkbox"/> FILE <input type="checkbox"/> REFUSE TO FILE  <input type="checkbox"/> Review issues for 74-day letter
<ul style="list-style-type: none"> <li>Clinical study site(s) inspections(s) needed?</li> </ul> <p><b>If no, explain:</b></p>	<input checked="" type="checkbox"/> YES <input type="checkbox"/> NO
<ul style="list-style-type: none"> <li>Advisory Committee Meeting needed?</li> </ul> <p><b>Comments:</b></p> <p><i>If no, for an original NME or BLA application, include the reason. For example:</i></p> <ul style="list-style-type: none"> <li><i>this drug/biologic is not the first in its class</i></li> <li><i>the clinical study design was acceptable</i></li> <li><i>the application did not raise significant safety or efficacy issues</i></li> <li><i>the application did not raise significant public health questions on the role of the drug/biologic in the diagnosis, cure, mitigation, treatment or prevention of a disease</i></li> </ul>	<input type="checkbox"/> YES Date if known: <input checked="" type="checkbox"/> NO <input type="checkbox"/> To be determined  Reason:

<ul style="list-style-type: none"> <li>If the application is affected by the AIP, has the division made a recommendation regarding whether or not an exception to the AIP should be granted to permit review based on medical necessity or public health significance?</li> </ul> <p><b>Comments:</b></p>	<input checked="" type="checkbox"/> Not Applicable <input type="checkbox"/> YES <input type="checkbox"/> NO
<p><b>CLINICAL MICROBIOLOGY</b></p> <p><b>Comments:</b> No Clinical Micro review is required</p>	<input checked="" type="checkbox"/> Not Applicable <input type="checkbox"/> FILE <input type="checkbox"/> REFUSE TO FILE <input type="checkbox"/> Review issues for 74-day letter
<p><b>CLINICAL PHARMACOLOGY</b></p> <p><b>Comments:</b></p>	<input type="checkbox"/> Not Applicable <input checked="" type="checkbox"/> FILE <input type="checkbox"/> REFUSE TO FILE <input type="checkbox"/> Review issues for 74-day letter
<ul style="list-style-type: none"> <li>Clinical pharmacology study site(s) inspections(s) needed?</li> </ul>	<input type="checkbox"/> YES <input checked="" type="checkbox"/> NO
<p><b>BIOSTATISTICS</b></p> <p><b>Comments:</b> IR and comments to be sent</p>	<input type="checkbox"/> Not Applicable <input checked="" type="checkbox"/> FILE <input type="checkbox"/> REFUSE TO FILE <input type="checkbox"/> Review issues for 74-day letter
<p><b>NONCLINICAL (PHARMACOLOGY/TOXICOLOGY)</b></p> <p><b>Comments:</b> IR and comments to be sent.</p>	<input type="checkbox"/> Not Applicable <input checked="" type="checkbox"/> FILE <input type="checkbox"/> REFUSE TO FILE <input type="checkbox"/> Review issues for 74-day letter
<p><b>IMMUNOGENICITY (BLAs/BLA efficacy supplements only)</b></p> <p><b>Comments:</b></p>	<input checked="" type="checkbox"/> Not Applicable <input type="checkbox"/> FILE <input type="checkbox"/> REFUSE TO FILE <input type="checkbox"/> Review issues for 74-day letter
<p><b>PRODUCT QUALITY (CMC)</b></p> <p><b>Comments:</b> IR and comments to be sent.</p>	<input type="checkbox"/> Not Applicable <input checked="" type="checkbox"/> FILE <input type="checkbox"/> REFUSE TO FILE <input type="checkbox"/> Review issues for 74-day letter

<p><b><u>Environmental Assessment</u></b></p> <ul style="list-style-type: none"> <li>• Categorical exclusion for environmental assessment (EA) requested?</li> </ul> <p><b>If no</b>, was a complete EA submitted?</p> <p><b>If EA submitted</b>, consulted to EA officer (OPS)?</p> <p><b>Comments:</b></p>	<p><input type="checkbox"/> Not Applicable</p> <p><input checked="" type="checkbox"/> YES <input type="checkbox"/> NO</p> <p><input type="checkbox"/> YES <input type="checkbox"/> NO</p> <p><input type="checkbox"/> YES <input type="checkbox"/> NO</p>
<p><b><u>Quality Microbiology (for sterile products)</u></b></p> <ul style="list-style-type: none"> <li>• Was the Microbiology Team consulted for validation of sterilization? (<b>NDAs/NDA supplements only</b>)</li> </ul> <p><b>Comments:</b></p>	<p><input type="checkbox"/> Not Applicable</p> <p><input checked="" type="checkbox"/> YES <input type="checkbox"/> NO</p>
<p><b><u>Facility Inspection</u></b></p> <ul style="list-style-type: none"> <li>• Establishment(s) ready for inspection?</li> <li>▪ Establishment Evaluation Request (EER/TBP-EER) submitted to DMPQ?</li> </ul> <p><b>Comments:</b></p>	<p><input type="checkbox"/> Not Applicable</p> <p><input checked="" type="checkbox"/> YES <input type="checkbox"/> NO</p> <p><input checked="" type="checkbox"/> YES <input type="checkbox"/> NO</p>
<p><b><u>Facility/Microbiology Review (BLAs only)</u></b></p> <p><b>Comments:</b></p>	<p><input checked="" type="checkbox"/> Not Applicable <input type="checkbox"/> FILE <input type="checkbox"/> REFUSE TO FILE</p> <p><input type="checkbox"/> Review issues for 74-day letter</p>
<p><b><u>CMC Labeling Review (BLAs/BLA supplements only)</u></b></p> <p><b>Comments:</b></p>	<p><input type="checkbox"/> Review issues for 74-day letter</p>

<b>REGULATORY PROJECT MANAGEMENT</b>	
<b>Signatory Authority: Wiley A. Chambers</b>	
<b>21<sup>st</sup> Century Review Milestones (see attached):</b>	
<b>Comments:</b> None	
<b>REGULATORY CONCLUSIONS/DEFICIENCIES</b>	
<input type="checkbox"/>	The application is unsuitable for filing. Explain why:
<input checked="" type="checkbox"/>	<p>The application, on its face, appears to be suitable for filing.</p> <p><u>Review Issues:</u></p> <p><input checked="" type="checkbox"/> No review issues have been identified for the 74-day letter.</p> <p><input type="checkbox"/> Review issues have been identified for the 74-day letter. List (optional):</p> <p><u>Review Classification:</u></p> <p><input checked="" type="checkbox"/> Standard Review</p> <p><input type="checkbox"/> Priority Review</p>
<b>ACTIONS ITEMS</b>	
<input checked="" type="checkbox"/>	Ensure that the review and chemical classification properties, as well as any other pertinent properties (e.g., orphan, OTC) are correctly entered into tracking system.
<input type="checkbox"/>	If RTF, notify everybody who already received a consult request, OSE PM, and Product Quality PM (to cancel EER/TBP-EER).
<input type="checkbox"/>	If filed, and the application is under AIP, prepare a letter either granting (for signature by Center Director) or denying (for signature by ODE Director) an exception for review.
<input type="checkbox"/>	BLA/BLA supplements: If filed, send 60-day filing letter
<input type="checkbox"/>	<p>If priority review:</p> <ul style="list-style-type: none"> <li>• notify sponsor in writing by day 60 (For BLAs/BLA supplements: include in 60-day filing letter; For NDAs/NDA supplements: see CST for choices)</li> <li>• notify DMPQ (so facility inspections can be scheduled earlier)</li> </ul>
<input checked="" type="checkbox"/>	Send review issues/no review issues by day 74
<input type="checkbox"/>	Other

APPEARS THIS WAY ON ORIGINAL

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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**This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.**  
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/s/  
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FARIBA IZADI  
05/06/2010

## **DSI CONSULT: Request for Clinical Inspections**

**Date:** January 22, 2010

**To:** Leslie Ball, M.D., Branch Chief, GCP2  
Constance Lewin, M.D., M.P.H, Branch Chief, GCP1  
Teshari Purohit-Sheth, M.D., Branch Chief  
Jean Mulinde, M.D., Team Leader  
Kassa Ayalew, M.D., Medical Officer  
Joseph Peacock, Program Analyst  
Division of Scientific Investigations, HFD-45  
Office of Compliance/CDER

**Through:** Sonal D. Wadhwa, MD, Medical Officer  
Division of Anti-Infective and Ophthalmology Products

**From:** Fariba Izadi, Regulatory Health Project Manager  
Division of Anti-Infective and Ophthalmology Products

**Subject:** **Request for Clinical Site Inspections**

### **General Information**

Application#: NDA 200738

Sponsor/Sponsor contact information: Bausch and Lomb  
Julie Townsend, MPH  
813-866-2299

Drug: loteprednol etabonate ophthalmic ointment 0.5%

Trade Name: Lotemax

NME: No

Standard or Priority: Standard

Proposed indication: Treatment of post-operative inflammation and pain following ocular surgery

**PDUFA:** **October 23, 2010**  
**Action Goal Date:** **August 23, 2010**  
**Inspection Summary Goal Date:** **July 5, 2010**

**Protocol/Site Identification**

<b>Site # (Name,Address, Phone number, email, fax#)</b>	<b>Protocol #</b>	<b>Number of Subjects</b>	<b>Indication</b>
DSI choice	Study 525	400	Treatment of post-operative inflammation and pain following ocular surgery
	Study 526	405	

An inspection is requested for at least one site for each of these clinical trials as your resources permit.

Note that the highest enrollers in Study 525 are: Michael P. Graham, MD (47 patients), Michael S. Korenfeld, MD (43 patients), and N. Timothy Peters, MD (48 patients). Note that the highest enrollers in Study 526 are: Douglas Lorenz, MD (40 patients), Stephen Smith, MD (44 patients), and Arthur M. Fishman, MD (47 patients).

**Domestic Inspections:**

Reasons for inspections (please check all that apply):

- Enrollment of large numbers of study subjects
- High treatment responders (specify):
- Significant primary efficacy results pertinent to decision-making
- There is a serious issue to resolve, e.g., suspicion of fraud, scientific misconduct, significant human subject protection violations or adverse event profiles.
- Other (specify): Routine Inspections

**Goal Date for Completion:**

We request that the inspections be performed and that the Inspection Summary Results be provided by July 5, 2010. We intend to issue an action letter on this application by October 23, 2010. The PDUFA due date for this application is **October 23, 2010**.

Should you require any additional information, please contact Fariba Izadi, Project Manager at (301) 796-0563 or Sonal Wadhwa, MD at (301) 796-2446.

**Additional Information:**

This is an eCTD NDA submission. The List and Description of Investigators for both studies are below.

**Study 525: Table of Investigators**

<b>Principal Investigator</b>	<b>Number of Patients Enrolled</b>
David Brown, MD Ft. Myers, FL	9
Raymond DeBarge, MD Ft. Oglethrope, GA	32
William Flynn, MD, OD San Antonio, TX	21
Joseph P. Gira, MD Des Peres, MO	34
Michael Graham, MD Orlando, FL	47
Paul Hartman, MD Rochester, NY	23
John Hunkeler, MD Overland Park, KS	18
Kashyap Kansupada, MD Belmont, NC	16
Michael Korenfeld, MD Washington, MO	43
Stephen Lane, MD Stillwater, MN	8
Thomas Macejko, MD Fairfield, OH	9
Jonathan I. Macy, MD Los Angeles, CA	0
James McDonald, II, MD Fayetteville, AK	0
James Peace, MD Inglewood, CA	17
Timothy Peters, MD Portsmouth, NH	48
Michael Rotberg, MD Charlotte, MC	9
Kenneth Sall, MD Artesia, Ca	36
Stefan Trocme, MD Cleveland, OH	11
Farrell C. Tyson, II, MD Cape Coral , FL	19
Stephen A. Updegraff, MD St. Petersburg, FL	0
<b>TOTAL</b>	<b>400</b>

**Study 526: Table of Investigators**

<b>Principal Investigator</b>	<b>Number of Patients Enrolled</b>
Robert Arleo, MD Ithaca, NY	0
Patrick Arnold, MD Fort Collins, CO	16
Ralph Chu, MD Bloomington, MN	0
Lisa Cibik, MD Monroe ville, PA	0
Andrew J. Cottingham, MD San Antonia, TX	21
Thomas Croley, MD Ocala, FL	23
Arthur M. Fishman, MD Pembroke Pines, FL	47
Walter Fried, MD Gurnee, IL	24
Gregory L. Henderson, MD Brandon, FL	9
Douglas Lorenz, MD Henderson, NV	40
Satish S. Modi, MD Poughkeepsie, NY	20
Bernard R. Perez, MD Tampa, FL	38
Harvey Reiser, MD Kingston, PA	33
Stephen Smith, MD Ft. Meyers, FL	44
Robert Smyth-Medina, MD Mission Hills, CA	2
William Colby Stewart, MD Houston, TX	10
Lloyd R. Taustine, MD Louisville, KY	27
Michael Tepedino, MD High Point, NC	39
Thomas Walters, MD Austin, TX	12
<b>TOTAL</b>	<b>405</b>

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

**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  
01/28/2010