050-804_ORIG_APPROVAL_PKG

CENTER FOR DRUG EVALUATION AND RESEARCH

APPROVAL PACKAGE FOR:

APPLICATION NUMBER(S)

50-804 (formerly 21-675)

Trade Name: Zylet Ophthalmic Suspension 0.5%/0.3%

Generic Name(s): (loteprednol etabonate & tobramycin)

Sponsor: Bausch & Lomb, Inc.
Agent:

Approval Date: December 14, 2004

Indication: Provides for steroid-responsive inflammatory ocular conditions for which a corticosteroid is indicated and where superficial bacterial ocular infection or a risk of bacterial ocular infection exists

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APPLICATION NUMBER:

50-804

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Pharmacology Review(s)	X
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APPROVAL PACKAGE FOR:

APPLICATION NUMBER

50-804 (formerly 21-675)

Approval Letter(s)

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 50-804

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

Dear Ms. Townsend:

Please refer to your new drug application (NDA) dated September 8, 2003, received September 8, 2003, submitted pursuant to section 505 (b)(2) of the Federal Food, Drug, and Cosmetic Act for Zylet (loteprednol etabonate and tobramycin ophthalmic suspension) 0.5%/0.3%. This application is subject to the exemption provisions in section 125(d)(2) of Title I of the FDA Modernization Act of 1997.

We acknowledge receipt of your submissions dated June 14 and 15, October 14, November 1, and December 2, 7, 8, 9, 10 and 13, 2004.

The October 14, 2004, submission constituted a complete response to our July 7, 2004, action letter.

This new drug application provides for the use of Zylet (loteprednol etabonate and tobramycin ophthalmic suspension) 0.5%/0.3% for steroid-responsive inflammatory ocular conditions for which a corticosteroid is indicated and where superficial bacterial ocular infection or a risk of bacterial ocular infection exists.

We have completed our review of this application, as amended, and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the agreed upon labeling text submitted December 13, 2004. Accordingly, the application is approved effective on the date of this letter.

The final printed labeling (FPL) must be identical with the enclosed agreed upon labeling text for the package insert, dated December 13, 2004. Marketing the product with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.
Please submit an electronic version of the FPL according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDA*. Alternatively, you may submit 20 paper copies of the FPL as soon as it is available but no more than 30 days after it is printed. Individually mount ten of the copies on heavy-weight paper or similar material. For administrative purposes, designate this submission "**FPL for approved NDA 50-804**." Approval of this submission by FDA is not required before the labeling is used.

In addition, submit three copies of the introductory promotional materials that you propose to use for this product. Submit all proposed materials in draft or mock-up form, not final print. Send one copy to this Division and two copies of both the promotional materials and the package insert directly to:

Division of Drug Marketing, Advertising
and Communications, HFD-42
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

Please submit one market package of the drug product when it is available.

All applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is deferred. We are deferring submission of your pediatric studies for ages 0 to 6 years until March 31, 2007.

Your deferred pediatric studies required under section 2 of the Pediatric Research Equity Act (PREA) are considered required postmarketing study commitments. The status of this postmarketing study shall be reported annually according to 21 CFR 314.81. This commitment is listed below.

Deferred pediatric study under PREA for steroid-responsive inflammatory ocular conditions for which a corticosteroid is indicated and where superficial bacterial ocular infection or a risk of bacterial ocular infection exists in 60 pediatric patients ages 0 to 6 years.

Final Study Report Submission: March 31, 2007.

Submit final study reports to this NDA. For administrative purposes, all submissions related to this pediatric postmarketing study commitment must be clearly designated "**Required Pediatric Study Commitments**".

We have not completed validation of the regulatory methods. However, we expect your continued cooperation to resolve any problems that may be identified.

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, call Raphael R. Rodriguez, Regulatory Project Manager, at (301) 827-2090.

Sincerely,

{See appended electronic signature page}
Wiley A. Chambers, M.D.
Deputy Director
Division of Anti-Inflammatory, Analgesic and
Ophthalmic Drug Products, HFD-550
Office of Drug Evaluation V
Center for Drug Evaluation and Research

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/s/

Wiley Chambers
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APPROVAL PACKAGE FOR:

APPLICATION NUMBER

50-804 (formerly 21-675)

Approvable Letter (S)

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-675

Bausch & Lomb, Inc.
ATTN: Julie Townsend, MPH
Manager, Regulatory Affairs
8500 Hidden River Parkway
Tampa, FL 33637

Dear Ms. Townsend

Please refer to your new drug application (NDA) dated September 8, 2003, received September 8, 2003, submitted pursuant to section 505 (b)(2) of the Federal Food, Drug, and Cosmetic Act for Zylet (loteprednol etabonate and tobramycin ophthalmic suspension) 0.5%/0.3%.

We acknowledge receipt of your submissions dated September 8 and 26 (two), October 24, and November 17, and 26, 2003; and March 2, April 13, 19, and 21, May 10 and 19, and June 7, 2004.

We also acknowledge receipt of your submissions dated June 14 and 15, 2004. These submissions were not reviewed for this action. You may incorporate these submissions by specific reference as part of your response to the deficiencies cited in this letter. It is not necessary to resubmit any information that has already been received by the Agency.

We completed our review of this application, as amended, and it is approvable. Before the application may be approved, however, it will be necessary for you to respond to the following:

1. Review of the analytical portion of the BLP 358-006 dataset has called into question the integrity and validity of the dataset. The methods and procedures used to correct the deficiencies cited in the inspection report should be submitted. A corrected dataset should be submitted. Any additional analyses of the analytic procedures conducted at the original facility or any alternative facilities should be submitted.

2. Clarification is needed regarding the patent certification. The application includes a Paragraph II Certification covering an ingredient which is not listed in the "Approved Drug Products with Therapeutic Equivalence Evaluations" (Orange Book) as having a listed patent. The application also includes a Paragraph IV Certification covering an NDA which you appear to own. Clarification of these patent certifications should be submitted.

We will continue to work with you on the proposed labeling for this product.

Be advised that all manufacturing facilities must be in compliance with current good manufacturing practice.

Under 21 CFR 314.50(d)(5)(vi)(b), we are requesting that you update your NDA by submitting all safety information you now have regarding your new drug.

In addition, submit three copies of the introductory promotional materials that you propose to use for this product. Submit all proposed materials in draft or mock-up form, not final print. Send one copy to the Division of Anti-Inflammatory, Analgesic, and Ophthalmic Drug Products, HFD-550 and two copies of both the promotional materials and the package insert directly to:

Drug Marketing, Advertising, and Communications, HFD-42
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

Within 10 days after the date of this letter, you are required to amend this application, notify us of your intent to file an amendment, or follow one of your other options under 21 CFR 314.110. If you do not follow one of these options, we will consider your lack of response a request to withdraw the application under 21 CFR 314.65. Any amendment should respond to all the deficiencies listed. We will not process a partial reply as a major amendment nor will the review clock be reactivated until all deficiencies have been addressed.

Under 21 CFR 314.102(d), you may request an informal meeting or telephone conference with the Division to discuss what steps need to be taken before the application may be approved.

The drug product may not be legally marketed until you have been notified in writing that the application is approved.

If you have any questions, call Raphael R. Rodriguez, Regulatory Project Manager, at (301) 827-2090.

Sincerely,

{See appended electronic signature page}

Wiley A. Chambers, M.D.
Deputy Director
Division of Anti-Inflammatory, Analgesic, and
Ophthalmic Drug Products, HFD-550
Office of Drug Evaluation V
Center for Drug Evaluation and Research

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/s/

Wiley Chambers
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