DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 202514/S003
NDA 202514/S004

SUPPLEMENT APPROVAL

Oak Pharmaceuticals, Inc.
Attention: Sam Boddapati, PhD
Vice President, Regulatory Affairs
1925 West Field Court, Suite 300
Lake Forest, OL 60045

Dear Dr. Boddapati:

Please refer to your Supplemental New Drug Applications (sNDAs) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for ZIOPTAN (tafluprost ophthalmic solution), 0.0015% as follows:

Supplement #	Submission date	Receipt date	Provides for
S-003 (Prior Approval)	July 18, 2013	July 19, 2013	Revisions to the How Supplied/Storage and Handling, Patient Counseling Information, Patient Package Insert, and Carton to reflect shipping instructions, as well as for assay release specification
S-004 (Changes being effected)	July 30, 2013	July 30, 2013	Revisions to the Adverse Reactions of the Package Insert and corresponding sections of the Patient Package Insert

We also acknowledge receipt of your amendment dated March 4, 2015. This submission constituted a complete response to our Complete Response letter issued on February 21, 2015.

In addition to numerous editorial changes, specific revisions to the Package Insert, Patient Package Insert and Carton Labels are described below (additions are in underlined text and deletions are ~~strikethrough~~ text).

S003:

1. **16 HOW SUPPLIED/STORAGE AND HANDLING/Storage** subsection is revised as follows:

   Storage
   Store refrigerated at 2 to 8°C (36 to 46°F). During shipment, ZIOPTAN may be maintained at temperatures up to 40°C (104°F) for a period not exceeding 2 days. Mail-order prescriptions received after two days of the dispensing date noted in the prescribing label should not be used. Store in the original pouch. After the pouch is opened, the single-use containers may be stored in the opened foil pouch for up to ~~28~~ 30 days at room temperature: 20 to 25°C (68 to 77°F). Protect from moisture. Write down the date you open the foil pouch in the space provided on the pouch. Discard any unused containers ~~28~~30 days after first opening the pouch.

2. **17 PATIENT COUNSELING INFORMATION/17.1 Storage Information** subsection is revised as follows:

   17.7 Storage Information
   Instruct patients on proper storage of cartons, unopened foil pouches, and opened foil pouches *[see How Supplied/Storage and Handling (16)]*. Recommended storage for cartons and unopened foil pouches is to store refrigerated at 2 to 8°C (36 to 46°F). After the pouch is opened, the single-use containers may be stored in the opened foil pouch for up to ~~28~~30 days at room temperature: 20 to 25°C (68 to 77°F). Protect from moisture.

3. PATIENT PACKAGE INSERT/How should I store ZIOPTAN? subsection is revised as follows:

   Important information for Mail-Order Patients:
   Do not use if prescription is not received within two days of dispensing date.
   (b) (4)
   [redacted]

4. In the PATIENT PACKAGE INSERT/After opening the foil pouch subsection has been revised as follows:

   After opening the foil pouch:
   - Store the opened foil pouch at room temperature, between 68°F to 77°F (20°C to 25°C), for up to ~~28~~30 days.

   - Throw away all unused ZIOPTAN single-use containers in the opened foil pouch after ~~28~~30 days.

5. CARTON LABELS for the 30 and 90 count

   a. Moved the information for mail order patients statement under the shipping instructions

   b. Added statement advising patients to not use product if received beyond two days from dispensing date

S-004

6. In the 6 ADVERSE REACTIONS/6.2 Postmarketing Experience, a new subsection, titled "Respiratory disorders" is added as follows:

   Respiratory disorders: exacerbation of asthma, dyspnea

7. In the PATIENT INFORMATION/What are the possible side effects of ZIOPTAN, the following information is added

   Additionally, the following side effects have been reported in general use:
   - worsening of asthma
   - shortness of breath

APPROVAL & LABELING

We have completed our review of these supplemental applications, as amended. They are approved, effective on the date of this letter, for use as recommended in the enclosed, agreed-upon labeling text for the Package Insert, Patient Package Insert and Cartons, which are identical to the labeling submitted on March 4, 2015.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using the FDA automated drug registration and listing system (eLIST), as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm. Content of labeling must be identical to the enclosed labeling text for the Package Insert and Patient Package Insert, with the addition of any labeling changes in pending "Changes Being Effected" (CBE) supplements, as well as annual reportable changes not included in the enclosed labeling.

Information on submitting SPL files using eList may be found in the guidance for industry titled "SPL Standard for Content of Labeling Technical Qs and As at http://www.fda.gov/downloads/DrugsGuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf
The SPL will be accessible from publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications that includes labeling changes for this NDA, including CBE supplements for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 314.50(l)(1)(i)] in MS Word format, that includes the changes approved in this supplemental application, as well as annual reportable changes and annotate each change. To facilitate review of your submission, provide a highlighted or marked-up copy that shows all changes, as well as a clean Microsoft Word version. The marked-up copy should provide appropriate annotations, including supplement number(s) and annual report date(s).

CARTON AND IMMEDIATE CONTAINER LABELS

Submit final printed carton labels that are identical to the ones submitted on March 4, 2015, as soon as they are available, but no more than 30 days after they are printed. Please submit these labels electronically according to the guidance for industry *Providing Regulatory Submissions in Electronic Format – Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications (June 2008)*. Alternatively, you may submit 12 paper copies, with 6 of the copies individually mounted on heavy-weight paper or similar material. For administrative purposes, designate this submission "**Final Printed Carton and Container Labels for approved NDA 202514/S003.** Approval of this submission by FDA is not required before the labeling is used.

Marketing the product with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

REPORTING REQUIREMENTS

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 Judit Milstein, Chief, Project Management Staff, at 301-796-0763.

Sincerely,
{See appended electronic signature page}

Wiley A. Chambers, MD
Deputy Director
Division of Transplant and Ophthalmology Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

ENCLOSURE(S): Package Insert
Patient Package Insert

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