CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

50-805

APPROVAL LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration
Rockville, MD 20857

NDA 50-805

CollaGenex Pharmaceuticals, Inc.
Attention: Christopher Powala
Vice President, Drug Development and Regulatory Affairs
41 University Drive
Newton, PA 18940

Dear Mr. Powala:

Please refer to your new drug application (NDA) dated July 29, 2005, received August 1, 2005, submitted pursuant to section 505(b)(1) of the Federal Food, Drug, and Cosmetic Act for Oracea™ (doxycycline, USP) Capsules, 40 mg.

We acknowledge receipt of your submissions dated September 8, and October 26, 2005; January 5, February 10, March 17 and 24, April 7, 17, and 19, May 11, 15, 16, 22 (two), 25 (electronic mail), and 26 (electronic mail), 2006.

This new drug application provides for the use of Oracea™ (doxycycline, USP) Capsules, 40 mg, for the treatment of inflammatory lesions (papules and pustules) of rosacea in adult patients.

We completed our review of this application, as amended. This application is approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text.

The final printed labeling (FPL) must be identical to the enclosed labeling (text for the package insert, text for the patient package insert, immediate container and container labels). 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 15 of the copies on heavy-weight paper or similar material. For administrative purposes, designate this submission "FPL for approved supplement NDA 50-805." Approval of this submission by FDA is not required before the labeling is used.

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 waived or deferred. We are waiving the pediatric study requirement for ages 0 to 18 years for this application.

In addition, we remind you of your postmarketing study commitments in your letter dated May 26, 2006. These commitments are listed below.

1. Submission of carcinogenicity study protocol and dose finding data: June 2007 Carcinogenicity study start date: August 2007 Submission of final carcinogenicity study report: February 2010.

   Study protocol submission: June 2007
   Study start date: August 2007
   Final report Submission: February 2010

2. Conduct a properly designed human sperm motility and morphology study to evaluate the effects of long-term use of ORACEA™ (doxycycline, USP) 40mg on human sperm in male patients with rosacea. Study report submission within 2 years from date of approval.

   Study protocol submission: September 2006
   Study start date: February 2007
   Final report Submission: June 2008

3. A post-approval Medication Error Monitoring Program for the proprietary name, Oracea™. This program should consist of:

   15-Day reporting of all Medication Errors;
   Root Cause Analysis; and
   Trigger requiring a proprietary name change.

   CollaGenex Pharmaceuticals agrees to a Medication Error Monitoring Program for the proprietary name, Oracea™, consisting of the above three components. Specifically, the sponsor will report as if it were a "15 day report" all medication errors, regardless of patient outcome. The sponsor will conduct a root cause analysis for each reported medication error and submit the analysis as a "follow-up" to the 15 day report.

   Collagenex will promptly (within 30 days of receipt of the approval letter) submit a detailed plan that addresses circumstances that would trigger a name change and also include any other risk management actions and the time frame for implementation of such action.

   In the event that a serious adverse event results from a medication error, CollaGenex will promptly meet with the Division to discuss ways to prevent future errors, including changing the propriety name, Oracea™.

Submit clinical protocols to your IND for this product. Submit nonclinical and chemistry, manufacturing, and controls protocols and all study final reports to this NDA. In addition, under 21 CFR 314.81(b)(2)(vii) and 314.81(b)(2)(viii), you should include a status summary of each commitment in your annual report to this NDA. The status summary should include expected summary completion and final report submission dates, any changes in plans since the last annual report, and, for clinical studies, number of patients entered into each study. All submissions, including supplements, relating to these postmarketing study commitments must be prominently labeled "Postmarketing Study Commitment Protocol", "Postmarketing Study Commitment Final Report", or "Postmarketing Study Commitment Correspondence."

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 Dermatology and Dental Products and two copies of both the promotional materials and the package insert directly to:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Drug Marketing, Advertising, and Communications
Food and Drug Administration
5901-B Ammendale Road
Beltsville, MD 20705-1266

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

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 Shalini Jain, Regulatory Project Manager, at (301) 796-0692.

Sincerely,

{See appended electronic signature page}

Stanka Kukich, M.D.
Acting Division Director
Division of Dermatology & Dental Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

Enclosure

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

/s/

Stanka Kukich
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