



NDA 21-369

Celltech Pharmaceuticals, Inc.
755 Jefferson Road
P.O. Box 31710
Rochester, NY 14603-1710

Attention: Norman D. LaFrance, M.D.
Sr. Vice President, Medical and Regulatory Affairs

Dear Dr. LaFrance:

Please refer to your new drug application (NDA) dated and received April 13, 2001, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for Codeprex (codeine polistirex and chlorpheniramine polistirex) Extended-Release Suspension.

We acknowledge receipt of your submissions dated June 19, July 13, August 3 and 24, October 12, November 8, and December 5, 2001, January 3, February 21 and 25, May 10, June 26, August 22 and 23, and September 2 and 27, 2002, April 25, June 9 and 16, August 11 and 18, September 25, and December 19, 2003, and June 4, 7 and 14, 2004.

The December 19, 2003, submission constituted a complete response to our February 13, 2002, action letter.

This new drug application provides for the use of Codeprex (codeine polistirex and chlorpheniramine polistirex) Extended-Release Suspension for the temporary relief of cough, as may occur with the common cold or inhaled irritants, and for the temporary relief of runny nose, sneezing, itching of the nose or throat, and itchy watery eyes due to hay fever, other upper respiratory allergies, or allergic rhinitis.

We completed our review of this application, as amended. It is approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text and with the minor editorial revision indicated in the enclosed labeling.

The final printed labeling (FPL) must be identical to, except for including the revisions indicated, the enclosed labeling (text for the package insert) and submitted labeling (immediate container label submitted June 14, 2004). These revisions are terms of the NDA approval. Marketing the product(s) before making the revisions, exactly as stated, in the product's labeling may render the product misbranded and an unapproved new drug.

The electronic labeling rule published December 11, 2003, (68 FR 69009) requires submission of labeling content in electronic format (pdf) effective June 8, 2004. For additional information, consult the following guidances for industry regarding electronic submissions: *Providing Regulatory Submissions in Electronic Format - NDAs* (January 1999) and *Providing Regulatory Submissions in Electronic Format - Content of Labeling* (February 2004). The guidances specify that the labeling

content must be submitted in *pdf* format. To assist in our review, we request that labeling also be submitted in MS Word format. If formatted copies of all labeling pieces (i.e., package insert, patient package insert, container labels, and carton labels) are submitted electronically, labeling does not need to be submitted in paper. 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 deferring submission of your pediatric studies for children under 6 years of age until June 22, 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.

1. Deferred pediatric study under PREA for the treatment of temporary relief of cough, as may occur with the common cold or inhaled irritants, and for the temporary relief of runny nose, sneezing, itching of the nose or throat, and itchy watery eyes due to hay fever, other upper respiratory allergies, or allergic rhinitis in pediatric patients under 6 years of age.

Final Report Submission: June 22, 2007.

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

We remind you of your postmarketing study commitment in your submission dated June 4, 2004. This commitment is listed below.

2. Conduct two in vitro genetic toxicity tests (ICH Q3A) to assess the genotoxic potential of (b)(4)-----

- If genotoxicity tests are negative, a new specification for (b)(4)----- could be qualified by a 28-day toxicology study in the most appropriate species.
- If (b)(4)----- is genotoxic, levels of (b)(4)----- in the drug product should be (b)(4)----- This may require the development of a more sensitive method for (b)(4)----- within this same time frame. Alternatively, additional testing could be performed in consultation with the Division to permit a higher level.

Protocol Submission: received June 4, 2004

Study Start: Upon receipt of Agency comments on proposed protocol

Final Report Submission: by December 22, 2004

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 Protocol**”, “**Postmarketing Study Final Report**”, or “**Postmarketing Study Correspondence.**”

We also remind you of Chemistry, Manufacturing and Controls (CMC) agreements submitted June 4, 2004, and as listed below.

3. (b)(4)-----

4. -----

5. (b)(4)-----

6. -----

7. -----

8. -----

In your December 19, 2003, submission, you also agreed to perform the following.

9. (b)(4)-----

10. -----

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 Pulmonary & Allergy Drug Products and two copies of both the promotional materials and the package insert directly to:

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

We have not completed validation of the regulatory methods. However, we expect your continued cooperation to resolve any problems that may be identified. Resubmit the updated methods validation package in duplicate, incorporating the agreed upon changes to drug substance and drug product specifications (acceptance criteria and test methods).

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 Ms. Christine Yu, R.Ph., Regulatory Project Manager, at (301) 827-1051.

Sincerely,

{See appended electronic signature page}

Badrul A. Chowdhury, M.D., Ph.D.
Director
Division of Pulmonary and Allergy Drug Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

Enclosure: Package Insert with minor edit

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

/s/

Badrul Chowdhury
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