DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 22439

NDA APPROVAL

Cypress Pharmaceutical, Inc.
135 Industrial Blvd
Madison, MS 39110

Attention: Janet DeLeon
Director, Product Development

Dear Ms. DeLeon:

Please refer to your New Drug Application (NDA) dated November 6, 2008, received November 7, 2008, submitted under 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for Zutripro® (hydrocodone, chlorpheniramine, and pseudoephedrine) Oral Solution.

We acknowledge receipt of your amendments dated November 24, 2008, January 26, 28, and 29, March 4, April 8, May 19, July 10, November 20, and December 10, 2009, February 3 and 17, April 9, 20, 27, and 30, May 6, 17, and 19, September 15, and December 8, 10, and 28, 2010, and February 8, March 31, April 20, and May 3, 17, 24, and 27, and June 1, 2011.

The December 8, 2010, submission constituted a complete response to our June 11, 2010, action letter.

This new drug application provides for the use of Zutripro® Oral Solution for relief of cough and nasal congestion associated with common cold; and relief of symptoms including nasal congestion associated with upper respiratory allergies.

We have 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 revisions indicated in the enclosed labeling. The approved shelf life for the drug product is 24 months when stored under the labeled conditions.

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, except with the revisions indicated, the enclosed labeling (text for the package insert). 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/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf.

The SPL will be accessible via publicly available labeling repositories.

CARTON AND IMMEDIATE CONTAINER LABELS

We acknowledge your May 27, 2011, submission containing final printed carton and container labels.

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We are waiving the pediatric study requirement for ages 0 to 5 years based on the fact that the your combination product, Zutripro, contains hydrocodone which, because of the risk of fatal respiratory depression, is not recommended for use as an antitussive in children less than 6 years of age.

We are deferring submission of your pediatric study for ages 6 to 17 years for this application because this product is ready for approval for use in adults and the pediatric studies have not been completed.

Your deferred pediatric studies required by section 505B(a) of the Federal Food, Drug, and Cosmetic Act are required postmarketing studies. The status of these postmarketing studies must be reported annually according to 21 CFR 314.81 and section 505B(a)(3)(B) of the Federal Food, Drug, and Cosmetic Act. The required pediatric studies are listed below.

1777-1 Conduct a study to assess the pharmacokinetics of each Zutripro drug component (hydrocodone, chlorpheniramine, and pseudoephedrine oral) in approximately 25-35 children ages 6-17 years with symptoms of the common cold. The results of this study will be used to determine the appropriate dose of the combination product to evaluate in a safety study in children ages 6-17 years.

Final Protocol Submission:	September 30, 2011
Study Completion:	December 31, 2013
Final Report Submission:	June 30, 2014

1777-2 Conduct a study to assess the safety of Zutripro (hydrocodone, chlorpheniramine, and pseudoephedrine combination product oral solution) in approximately 400-450 children 6-17 years of age with symptoms of the common cold. The dose used in this study will be based upon the results of the pharmacokinetic study in children ages 6-17 years.

Final Protocol Submission:	September 30, 2014
Study Completion:	December 31, 2015
Final Report Submission:	September 30, 2016

Reports of these required pediatric postmarketing studies must be submitted as a new drug application (NDA) or as a supplement to your approved NDA with the proposed labeling changes you believe are warranted based on the data derived from these studies. When submitting the reports, please clearly mark your submission "**SUBMISSION OF REQUIRED PEDIATRIC ASSESSMENTS**" in large font, bolded type at the beginning of the cover letter of the submission.

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit, in triplicate, a cover letter requesting advisory comments, the proposed materials in draft or mock-up form with annotated references, and the package insert to:

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

As required under 21 CFR 314.81(b)(3)(i), you must submit final promotional materials, and the package insert, at the time of initial dissemination or publication, accompanied by a Form FDA 2253. For instruction on completing the Form FDA 2253, see page 2 of the Form. For more information about submission of promotional materials to the Division of Drug Marketing,

Advertising, and Communications (DDMAC), see
http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm.

METHODS VALIDATION

Method validation by the Agency laboratory was not requested. The NDA provided adequate information for the analytical methods used for product quality control. However, we expect your continued cooperation to resolve any problems should they be identified in the future.

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 Philantha Montgomery Bowen, Senior Regulatory Project Management Officer, at (301) 796-2466.

Sincerely,

{See appended electronic signature page}

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

ENCLOSURE(S):
Content of Labeling
Carton and Container Labeling

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

/s/

LYDIA I GILBERT MCCLAIN
06/08/2011
Deputy Division Director