



NDA 022113

**NDA APPROVAL**

Pfizer Consumer Healthcare  
Attention: Erica Sinclair, MBA  
Senior Manager, Regulatory Affairs  
5 Giralda Farms  
Madison, NJ 07940

Dear Ms. Sinclair:

Please refer to your New Drug Application (NDA) dated September 25, 2007, received September 25, 2007, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for Advil<sup>®</sup> Allergy and Congestion Relief (ibuprofen, 200 mg/phenylephrine HCl, 10 mg/chlorpheniramine maleate, 4 mg) tablets.

We acknowledge receipt of your amendments dated November 19 and December 18, 2007, January 25, 30, and 31, March 5, April 15 and 18, and May 16, 2008, June 21 and 30, August 11, and November 23, 2011.

The June 21, 2011, submission constituted a complete response to our July 25, 2008, action letter.

This new drug application provides for the use of Advil<sup>®</sup> Allergy and Congestion Relief tablets for the temporary relief of symptoms associated with hay fever or other respiratory allergies, and the common cold.

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.

**LABELING**

Submit final printed labeling, as soon as they are available, but no more than 30 days after they are printed. The final printed labeling (FPL) must be identical to the enclosed labeling (10-count immediate container (blister card) and 10-, 20-, and 40- count carton labels submitted on June 21, 2011; and 1-count immediate container (pouch), 50-count (dispenser bin) carton (including piggyback "Drug Facts") label submitted on November 23, 2011), and must be in the "Drug Facts" format (21 CFR 201.66), where applicable.

The final printed labeling should be submitted electronically according to the guidance for industry titled "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 Labeling for approved NDA 022113.**” 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 and in the required format may render the product misbranded and an unapproved new drug.

We remind you that the "New" flag is to be removed from the label after 180 days of marketing.

## **DRUG REGISTRATION AND LISTING**

All drug establishment registration and drug listing information is to be submitted to FDA electronically, via the FDA automated system for processing structured product labeling (SPL) files (eLIST). At the time that you submit your final printed labeling (FPL), the content of labeling (Drug Facts) should be submitted in SPL format as described at <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>. 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>. In addition, representative container or carton labeling, whichever includes Drug Facts, (where differences exist only in the quantity of contents statement) should be submitted as a JPG file.

## **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 those who are less than 2 years of age because there is evidence suggesting that the drug product would be unsafe in this pediatric group. FDA recommends that over-the-counter cough and cold products should not be used in infants and children under 2 years of age because serious side effects can occur in this age group.

We are deferring submission of your pediatric studies for ages 2 years to less than 12 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. These required studies are listed below.

## 1848-1

You must conduct PK trial(s) in children 6 to < 12 who may benefit from the drug (i.e. not in otherwise healthy pediatric volunteers). You should conduct single and multiple dose PK trial(s) that would evaluate the appropriate dosing interval based on pharmacokinetics, safety, and tolerability of phenylephrine in children, and in order to identify whether the dosing interval for phenylephrine can overlap with that of ibuprofen and chlorpheniramine. After you identify the phenylephrine dose, develop and use an age appropriate triple ingredient formulation in the described studies. Any new commercially marketable formulation you develop for use in children must meet FDA standards for marketing approval. You should also provide single and multiple dose PK information for chlorpheniramine in this pediatric age group.

Final Protocol Submission: December 2012

Final Report Submission: December 2013

## 1848-2

You must conduct randomized, double blind, placebo controlled clinical safety and efficacy trial(s) in children 6 to < 12 years of age to evaluate PD response and clinical symptoms response of phenylephrine, chlorpheniramine, and the triple combination for the temporary relief of nasal congestion and other symptoms associated with the common cold. The trial(s) should evaluate clinical efficacy as well as safety of phenylephrine, chlorpheniramine, and the triple combination in this population, obtain data to support the appropriate dosing interval, and allow dosing to cover the expected period of clinical use (for example, up to 7 days). The study(ies) must include adequate representation of these age groups and be conducted in the target population, i.e. children with cough and cold symptoms.

Final Protocol Submission: June 2013

Final Report Submission: June 2015

## 1848-3

You must conduct PK trial(s) in children 2 to < 6 who may benefit from the drug (i.e. not in otherwise healthy pediatric volunteers). You should conduct single and multiple dose, PK trial(s) that would evaluate the appropriate dosing interval based on pharmacokinetics, safety, and tolerability of phenylephrine in children, and in order to identify whether the dosing interval for phenylephrine can overlap with that of ibuprofen and chlorpheniramine. After you identify the phenylephrine dose, develop and use an age appropriate triple ingredient formulation in the described studies. Any new commercially marketable formulation you develop for use in children must meet FDA standards for

marketing approval. You should also provide single and multiple dose PK information for chlorpheniramine in this pediatric age group.

Final Protocol Submission: December 2015

Final Report Submission: December 2016

1848-4

You must conduct randomized, double blind, placebo controlled clinical safety and efficacy trial(s) in children 2 to < 6 years of age to evaluate PD response and clinical symptoms response of phenylephrine, chlorpheniramine, and the triple combination for the temporary relief of nasal congestion and other symptoms associated with the common cold. The trial(s) should evaluate clinical efficacy as well as safety of phenylephrine, chlorpheniramine, and the triple combination in this population, obtain data to support the appropriate dosing interval, and allow dosing to cover the expected period of clinical use (for example, up to 7 days). The study(ies) must include adequate representation of these age groups and be conducted in the target population, i.e. children with cough and cold symptoms.

Final Protocol Submission: May 2017

Final Report Submission: August 2019

This product is appropriately labeled for use in children ages 12 to less than 17 years for these indications. Therefore no additional pediatric studies are needed in this age group.

We note in our administrative record that you never opened a new IND for this drug product. We recommend that you open a PIND if you wish to submit your **draft** protocols for our review and comment. In addition, you will need to open a new IND before you initiate your pediatric studies. IND protocols would be submitted to this IND number, with a cross-reference letter to the NDA.

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.

### **REPORTING REQUIREMENTS**

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

If you have any questions, call Janice Adams-King, Regulatory Project Manager, at (301) 796-3713.

Sincerely,

*{See appended electronic signature page}*

Joel Schiffenbauer, M.D.  
Deputy Director  
Division of Nonprescription Clinical Evaluation  
Office of Drug Evaluation IV  
Center for Drug Evaluation and Research

ENCLOSURE(S):

Carton and Immediate Container Labeling

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**This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.**  
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/s/  
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JOEL SCHIFFENBAUER  
12/21/2011