



NDA 21747/S-001

**SUPPLEMENT APPROVAL**

Boehringer Ingelheim Pharmaceutical, Inc.  
900 Ridgebury Rd.  
PO box 368  
Ridgefield, CT 06877-0368

Attention: Amy Van Anandel, DVM, MPH  
Senior Associate Director  
Drug Regulatory Affairs

Dear Dr. Van Anandel:

Please refer to your Supplemental New Drug Application (sNDA) dated February 28, 2012, received February 29, 2012, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Combivent Respimat (ipratropium bromide and albuterol) Inhalation Spray.

We acknowledge receipt of your amendments dated June 15, July 11, August 8, and August 16, 2012.

This "Prior Approval" supplemental new drug application provides for the addition of the term "metabolic acidosis" to the ADVERSE REACTIONS, Postmarketing Experience and the OVERDOSAGE sections of the package insert. This supplement also provides for revisions to the Instructions for Use (IFU) leaflet to align the language with other Boehringer Ingelheim products with similar risk profiles as well as the addition of a language referencing the availability of a video demonstration for patient information.

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

We remind you to incorporate the recommended formatting for the Steps and Figures in the Patient's Instructions for Use that were outlined in our facsimile dated August 1, 2012, when you update the labeling for this application in any future submission.

**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, text for the patient package insert, Instructions For Use), 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 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 and container labels that are identical to the enclosed carton and immediate container labels 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 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 “**Product Correspondence – Final Printed Carton and Container Labels for approved NDA 21747/S-001.**” Approval of this submission by FDA is not required before the labeling is used.

### **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.

Because none of these criteria apply to your application, you are exempt from this requirement.

## **PROMOTIONAL MATERIALS**

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit the following, in triplicate, (1) a cover letter requesting advisory comments, (2) the proposed materials in draft or mock-up form with annotated references, and (3) the package insert(s) to:

Food and Drug Administration  
Center for Drug Evaluation and Research  
Office of Prescription Drug Promotion (OPDP)  
5901-B Ammendale Road  
Beltsville, MD 20705-1266

You must submit final promotional materials and package insert(s), accompanied by a Form FDA 2253, at the time of initial dissemination or publication [21 CFR 314.81(b)(3)(i)]. Form FDA 2253 is available at <http://www.fda.gov/opacom/morechoices/fdaforms/cder.html>; instructions are provided on page 2 of the form. For more information about submission of promotional materials to the Office of Prescription Drug Promotion (OPDP), see <http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm>.

## **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 Wayne Amchin, Senior Regulatory Health Project Manager for Safety, at (301) 796-0421.

Sincerely,

*{See appended electronic signature page}*

Sally M. Seymour, M.D.  
Deputy Director for Safety  
Office of Drug Evaluation II  
Center for Drug Evaluation and Research

ENCLOSURE(S):

Content of Labeling, Carton and Immediate Container label

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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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SALLY M SEYMOUR  
08/29/2012