

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*

**022383Orig1s000**

**APPROVAL LETTER**



NDA 022383/Orig-01

**NDA APPROVAL**

Novartis Pharmaceuticals Corporation  
One Health Plaza  
East Hanover, New Jersey 07936-1080

Attention: Ann Shea  
Director, Drug Regulatory Affairs

Dear Ms. Shea:

Please refer to your New Drug Application (NDA) dated December 15, 2008, received December 18, 2008, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Arcapta Neohaler (indacaterol maleate inhalation powder), 75 mcg.

We acknowledge receipt of your amendments dated December 19, 2008, January 15, March 19 and 31, April 2, 3, 8, 15, 17, 28, and 30, May 20, June 1, 9, 18, and 26, July 1 and 15, August 6, October 29, November 5, and December 11 and 15, 2009, January 15, August 17, October 1, November 19, and December 7, 9, 15, and 24, 2010, and January 7, 14, 20, and 31, February 8, 9, 18, 25, and 28, March 10 and 16, April 4 and 22, May 18, 26, and 30, June 9, 10, 16, 21, 23, and 24, and July 1, 2011.

The October 1, 2010, submission constituted a complete response to our October 16, 2009, action letter.

This new drug application provides for the use of Arcapta Neohaler (indacaterol maleate) Inhalation Powder for the long-term, once-daily maintenance bronchodilator treatment of airflow obstruction in patients with chronic obstructive pulmonary disease (COPD), including chronic bronchitis and/or emphysema.

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 enclosed agreed-upon labeling text.

### **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 and text for the

Medication Guide). 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.

We request that the labeling approved today be available on your website within 10 days of receipt of this letter.

### **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 “**Final Printed Carton and Container Labels for approved NDA 022383.**” Approval of this submission by FDA is not required before the labeling is used.

Marketing the product(s) with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

### **MARKET PACKAGE**

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

If sending via USPS, please send to:

Ms. Carol Hill  
Food and Drug Administration  
Center for Drug Evaluation and Research  
White Oak Bldg 22, Room 3324  
10903 New Hampshire Avenue  
Silver Spring, Maryland 20993

If sending via any carrier other than USPS  
(e.g., UPS, DHL), please send to:

Ms. Carol Hill  
Food and Drug Administration  
Center for Drug Evaluation and Research  
White Oak Bldg 22, Room 3324  
10903 New Hampshire Avenue  
Silver Spring, Maryland 20903

### **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 this application because necessary studies are impossible or highly impracticable. This indication does not occur in children; therefore, pediatric studies are not required.

### **RISK EVALUATION AND MITIGATION STRATEGY REQUIREMENTS**

Section 505-1 of the FDCA authorizes FDA to require the submission of a risk evaluation and mitigation strategy (REMS), if FDA determines that such a strategy is necessary to ensure that the benefits of the drug outweigh the risks [section 505-1(a)]. The details of the REMS requirements were outlined in our complete response letter dated October 16, 2009. We also refer to our communication dated March 29, 2011, where we informed you that we have determined that maintaining the Medication Guide as part of the approved labeling is adequate to address the serious and significant public health concern and meets the standard in 21 CFR 208.1; therefore, the Medication Guide will not be included as an element of the approved REMS to ensure that the benefits of Arcapta Neohaler (indacaterol maleate inhalation powder) outweigh its risk of asthma related deaths. That communication also acknowledged that a communication plan is necessary to support implementation of the REMS.

Your proposed REMS, submitted on July 1, 2011, and appended to this letter, is approved. The REMS consists of a communication plan and a timetable for submission of assessments of the REMS.

The REMS assessment plan should include, but is not limited to, the following:

1. An evaluation of the prescriber understanding of the increased risk of asthma related deaths and the safe use of LABAs.
2. A description of specific measures that would be taken to increase awareness if the assessment of the prescribers indicates that the prescribers' awareness is not adequate.

3. A narrative summary with analysis of all reported asthma-related deaths during the reporting period.
4. An annual assessment and conclusions regarding the success of the REMS in meeting the stated goals.
5. Drug use patterns (reasons for use, patient demographics, length of therapy, prescribing medical specialties)
6. An assessment of the communication plan including:
  - i. The date of launch of the communication plan (DHCPL, website, and communication to professional societies)
  - ii. The number of recipients of the DCHP letter distribution
  - iii. Date(s) of distribution of the DHCP letter
  - iv. A copy of all documents included in each distribution
  - v. The professional societies that you communicated with
  - vi. The information that the professional societies disseminated to their members and the timing of the dissemination
7. As required under section 505-1(g)(3)(B) and (C), information on the status of any postapproval study or clinical trial required under section 505(o) or otherwise undertaken to investigate a safety issue. With respect to any such postapproval study, you must include the status of such study, including whether any difficulties completing the study have been encountered. With respect to any such postapproval clinical trial, you must include the status of such clinical trial, including whether enrollment has begun, the number of participants enrolled, the expected completion date, whether any difficulties completing the clinical trial have been encountered, and registration information with respect to requirements under subsections (i) and (j) of section 402 of the Public Health Service Act. You can satisfy these requirements in your REMS assessments by referring to relevant information included in the most recent annual report required under section 506B and 21 CFR 314.81(b)(2)(vii) and including any material or significant updates to the status information since the annual report was prepared. Failure to comply with the REMS assessments provisions in section 505-1(g) could result in enforcement action.

We remind you that in addition to the assessments submitted according to the timetable included in the approved REMS, you must submit a REMS assessment and may propose a modification to the approved REMS when you submit a supplemental application for a new indication for use as described in section 505-1(g)(2)(A) of the FDCA.

If you plan to distribute an authorized generic product under this NDA, you must submit a complete proposed REMS that relates only to the authorized generic product. Submit a proposed REMS, REMS supporting document, and any required appended documents as a prior approval supplement. Approval of the proposed REMS is required before you may market your authorized generic product.

Prominently identify the submission containing the REMS assessments or proposed modifications with the following wording in bold capital letters at the top of the first page of the submission:

**NDA 22-383 REMS ASSESSMENT**

**NEW SUPPLEMENT FOR NDA22-383  
PROPOSED REMS MODIFICATION  
REMS ASSESSMENT**

**NEW SUPPLEMENT (NEW INDICATION FOR USE)  
FOR NDA 22-383  
REMS ASSESSMENT  
PROPOSED REMS MODIFICATION *(if included)***

If you do not submit electronically, please send five copies of REMS-related submissions.

**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>.

**REPORTING REQUIREMENTS**

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

**MEDWATCH-TO-MANUFACTURER PROGRAM**

The MedWatch-to-Manufacturer Program provides manufacturers with copies of serious adverse event reports that are received directly by the FDA. New molecular entities and important new

biologics qualify for inclusion for three years after approval. Your firm is eligible to receive copies of reports for this product. To participate in the program, please see the enrollment instructions and program description details at <http://www.fda.gov/Safety/MedWatch/HowToReport/ucm166910.htm>.

**POST-ACTION FEEDBACK MEETING**

New molecular entities and new biologics qualify for a post-action feedback meeting. Such meetings are used to discuss the quality of the application and to evaluate the communication process during drug development and marketing application review. The purpose is to learn from successful aspects of the review process and to identify areas that could benefit from improvement. If you would like to have such a meeting with us, call Ms. Carol Hill, the Regulatory Project Manager for this application.

If you have any questions, call Carol F. Hill, Senior Regulatory Health Project Manager, at (301) 796-1226.

Sincerely,

*{See appended electronic signature page}*

Curtis J. Rosebraugh, M.D., M.P.H.  
Director  
Office of Drug Evaluation II  
Center for Drug Evaluation and Research

Enclosures:

Content of Labeling  
Carton and Container Labeling  
REMS

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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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CAROL F HILL  
07/01/2011

CURTIS J ROSEBRAUGH  
07/01/2011