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*APPLICATION NUMBER:*

**21-912**

**APPROVAL LETTER**



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration  
Rockville, MD 20857

NDA 21-912

Sepracor Inc.  
84 Waterford Drive  
Marlborough, MA 01752-7010

Attention: Renee M. Carroll, M.S., RAC  
Associate Director, Regulatory Affairs

Dear Ms. Carroll:

Please refer to your new drug application (NDA) dated December 8, 2005, received December 12, 2005, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Brovana (arformoterol tartrate) Inhalation Solution.

We acknowledge receipt of your submissions dated December 20, 2005, and January 3, and 6, February 14, 16, and 22, March 23, 29, and 31, April 11, 18, and 27, May 15, June 7, 15, 16, and 23, July 12, 13, and 21, August 3, 24, 28, and 29, September 6, 12, 19, 20, 27, and 28, and October 2, 4, and 5, 2006.

This new drug application provides for the use of Brovana (arformoterol tartrate) Inhalation Solution for the treatment of bronchoconstriction associated with chronic obstructive pulmonary disease.

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.

The final printed labeling (FPL) must be identical to the enclosed labeling (text for the package insert, Medication Guide) submitted on October 5, 2006, (immediate container and carton labels) submitted on October 4, 2006. 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.

Please submit an electronic version of the FPL according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDA*. Alternatively, you may submit 20 paper copies of the FPL as soon as it is available but no more than 30 days after it is printed. Individually mount 15 of the copies on heavy-weight paper or similar material. For administrative purposes, designate this submission "**FPL for approved NDA 21-912.**" Approval of this submission by FDA is not required before the labeling is used.

Within 30 days of the date of this letter, submit the content of labeling [21 CFR 601.14(b)] in structured product labeling (SPL) format, as described at <http://www.fda.gov/oc/datacouncil/spl.html>, that is identical in content to the labeling text submitted on October 5, 2006. Upon receipt and verification, we will transmit that version to the National Library of Medicine for posting on the DailyMed website.

We remind you of your postmarketing study commitment(s) in your submission dated October 4, 2006. These commitments are listed below.

1. Conduct a multicenter, randomized, placebo-controlled, large, simple safety trial to evaluate the effects of long term use of BROVANA (arformoterol tartrate) Inhalation Solution in patients with COPD. The objective of this trial is to determine the risk of fatal and life-threatening respiratory events associated with the long term use of BROVANA in patients with COPD. The trial will be of adequate size and duration to meet the objective. The final study report will be submitted as a supplement.

Protocol Submission Date: August 2007

Study Start Date: December 2007

Final Report Submission Date: December 2012

2. Conduct a safety and tolerability study with one or more doses and one or more dose levels of BROVANA (arformoterol tartrate) Inhalation Solution in children with asthma and/or obstructive airway disease. The objective of this study is to assess the safety and tolerability of BROVANA in children 12 years of age and younger with asthma. The study will include a placebo or active control treatment group, as appropriate. The study will also include children age 12 years and younger so that the lower age limit is based upon the age at which asthma/obstructive airway disease exists. The trial will be of adequate size and duration to meet the objective. The final study report will be submitted as a supplement.

Protocol Submission Date: June 2007

Study Start Date: September 2007

Final Report Submission Date: December 2008

3. Conduct a safety and efficacy study with one or more doses and one or more dose levels of BROVANA (arformoterol tartrate) Inhalation Solution in children with asthma and/or obstructive airway disease presenting with an acute exacerbation. The objective of this study is to establish the safety and efficacy of BROVANA in children 12 years of age and younger with an acute exacerbation of asthma. The study will include a placebo or active control treatment group, as appropriate. The study will also include children age 12 years and younger so that the lower age limit is based upon the age at which asthma/obstructive airway disease exists. The trial will be of adequate size and duration to meet the objective. The final study report will be submitted as a supplement.

Protocol Submission Date: September 2008

Study Start Date: January 2009

Final Report Submission Date: May 2011

Submit clinical protocols to your IND for this product. 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 Commitment Protocol”, “Postmarketing Study Commitment Final Report”, or “Postmarketing Study Commitment Correspondence.”**

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 and Allergy Products, and two copies of both the promotional materials and the package insert(s) directly 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

We also remind you of the following Chemistry, Manufacturing, and Controls (CMC) agreements listed in your submission dated September 12, 2006.

1. Submit the validation report for method **(b) (4)** to the Agency upon completion and prior to commercialization of Brovana Inhalation Solution.
2. Conduct further extractable studies of the foil and submit the data to the NDA.

We have not completed validation of the regulatory methods. However, we expect your continued cooperation to resolve any problems that may be identified.

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. Ladan Jafari, Regulatory Project Manager, at (301) 301-796-1231.

Sincerely,

*{See appended electronic signature page}*

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

Enclosure: PKG Insert, Medguide

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**This is a representation of an electronic record that was signed electronically and  
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/s/

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Badrul Chowdhury  
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