

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER: 20-837

APPROVAL LETTER

NDA 20-837

Sepracor Inc.
111 Locke Drive
Marlborough, Massachusetts 01752

Attention: James A. Wachholz
Senior Director, Regulatory Affairs

Dear Mr. Wachholz:

Please refer to your new drug application (NDA) dated June 30, 1997, received July 1, 1997, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for Xopenex (levalbuterol HCl) Inhalation Solution, 0.63 mg/3 mL and 1.25 mg/3 mL.

We acknowledge receipt of your submissions dated August 4, September 8 and 17, October 21, November 4 and 20, and December 1, 1997, April 9, May 28, June 16 and 26, August 6, and September 24 and 30, 1998, and January 8, 28, and 29, and March 8, 18, 22, 23, and 24, 1999.

We also refer to your facsimile transmission dated March 25, 1999. Your submission of September 25, 1998, constituted a complete response to our July 1, 1998, action letter.

This new drug application provides for the use of Xopenex (levalbuterol HCl) Inhalation Solution for the treatment or prevention of bronchospasm in adults and adolescents 12 years of age and older with reversible obstructive airway disease.

We have completed the review of this application, as amended, and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the enclosed labeling text. Accordingly, the application is approved effective on the date of this letter.

The final printed labeling (FPL) must be identical to the enclosed labeling text (package insert and patient package insert). The immediate container and carton labels must be identical to the labeling submitted March 18, 1999, with the revision listed below.

- The statement "Once removed from the foil pouch, the individual vials should be used within one week." will be revised to "Once the foil pouch is opened, the vials should be used within two weeks."

The revisions in the enclosed marked-up draft package insert and draft patient package insert, and the revision noted above for the immediate carton and container labels, are terms of the NDA approval. Marketing the product before making the revisions, exactly as requested, in the product's final printed labeling (FPL) may render the product misbranded and an unapproved new drug.

Please submit 20 copies of the FPL as soon as it is available, in no case more than 30 days after it is printed. Please individually mount ten of the copies on heavy-weight paper or similar material. For administrative purposes, this submission should be designated "FPL for approved NDA 20-837." Approval of this submission by FDA is not required before the labeling is used.

We remind you of your Phase 4 commitments specified in your submissions dated May 28, 1998, and March 18, 1999. These commitments, along with any completion dates agreed upon, are listed below.

(b)(4)(TS) _____

In addition, we remind you of the following agreements.

~~3-1~~ As stated in your submission dated January 28, 1999, approximately (b)(4)(CC) _____
(b)(4)(TS)-----

drug product.

~~4-2~~ The expiration dating period of Xopenex (levalbuterol HCl) Inhalation Solution is 15 months for the 0.63 mg/3mL strength and 12 months for the 1.25 mg/3mL strength from their respective dates of manufacture.

~~5-3~~ As stated in your submission dated May 28, 1998, the first three production batches of the drug substance manufactured post-approval, and at least one batch annually thereafter, will be placed into stability studies. The stability data will be submitted in the annual reports.

6.4. As stated in your submission dated March 24, 1999, the expiration date and the lot number will be included directly on the foil pouches of all Xopenex (levalbuterol HCl) Inhalation Solution commercially distributed. A method for printing this information directly on the foil package will be evaluated beginning immediately after approval and will be implemented within 3 months of approval for all commercially distributed product.

7.5. As stated in your submission dated March 24, 1999, the text for recording the "date foil pouch opened" will be added to the foil package within 3 months of approval for all commercially distributed product.

Protocols, data, and final reports should be submitted to your IND for this product and a copy of the cover letter sent to this NDA. If an IND is not required to meet your Phase 4 commitments, please submit protocols, data and final reports to this NDA as correspondence. In addition, under 21 CFR 314.82(b)(2)(vii), we request that you include a status summary of each commitment in your annual report to this NDA. The status summary should include the number of patients entered in each study, expected completion and submission dates, and any changes in plans since the last annual report. For administrative purposes, all submissions, including labeling supplements, relating to these Phase 4 commitments must be clearly designated "Phase 4 Commitments."

Validation of the regulatory methods has not been completed. At the present time, it is the policy of the Center not to withhold approval because the methods are being validated. Nevertheless, we expect your continued cooperation to resolve any problems that may be identified.

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

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, contact Parinda Jani, Project Manager, at (301) 827-1064.

Sincerely yours,

John K. Jenkins, M.D., F.C.C.P.
Director
Division of Pulmonary Drug Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

Enclosure