DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville MD 20857

MAR 23 2000

TRANSMITTED VIA FACSIMILE

Mr. James Allen Wachholz
Senior Director, Regulatory Affairs
Sepracor Inc.
111 Locke Drive
Marlborough, MA 01752

RE: NDA# 20-837
Xopenex (levalbuterol HCl) Inhalation Solution
MACMIS ID#: 8815

Dear Mr. Wachholz:

The Division of Drug Marketing, Advertising, and Communications (DDMAC) has received reports from several health care professionals that a Sepracor Inc. (Sepracor) sales representative in the Dallas, Texas area recently made oral statements promoting Xopenex 0.63 mg (levalbuterol HCl) Inhalation Solution for an unapproved dosage regimen ("every four hours, similarly to albuterol"). These unapproved dosage regimen statements violate the Federal Food, Drug, and Cosmetic Act and its implementing regulations and should be immediately discontinued.

Discussion

The approved product labeling recommends dosing Xopenex 0.63 mg or 1.25 mg three times a day (every 6 to 8 hours). A Sepracor sales representative orally promoted a dosage regimen for "every 4 hours, similarly to albuterol." Such unapproved dosage statements are inconsistent with the Xopenex approved product labeling. Furthermore, Sepracor has not demonstrated this regimen to be a safe and effective dosage schedule.

Pertinent Excerpts of Xopenex Approved Product Labeling

The Warnings Section "Do Not Exceed Recommended Doses" states: "Fatalities have been reported in association with excessive use of inhaled sympathomimetic drugs in patients with asthma. The exact cause of death is unknown, but cardiac arrest following an unexpected development of a severe acute asthmatic crisis and subsequent hypoxia is suspected."

The Precautions Section "Information for Patients" warns: "The action of Xopenex ... may last up to 8 hours. Xopenex Inhalation Solution should not be used more frequently than recommended. Do not increase the dose or frequency of dosing of Xopenex Inhalation Solution without consulting your physician....Common adverse events include palpitations, chest pain, rapid heart rate, headache, dizziness, and tremor or nervousness...."

The Dosage and Administration Section states: The usual starting dosage of Xopenex is 0.63 mg administered three times a day, every 6 to 8 hours. Patients ... with more severe asthma or patients who do not respond adequately to a dose of 0.63 mg of Xopenex may benefit from a dosage of 1.25 mg three times a day. Patients receiving the higher dose of Xopenex should be monitored closely for adverse systemic effects, and the risks of such effects should be balanced against the potential for improved efficacy."

Conclusion

Sepracor's oral statements promoting an unapproved dosage regimen are false or misleading. The dosage regimen being promoted is more frequent than that recommended in the Xopenex approved product labeling.

This Sepracor sales representative, and any other Sepracor sales representative or agent, should immediately cease making such violative oral statements and should cease the distribution and use of any Xopenex promotional materials that contain this or similar violative statements. Your written response should be received no later than April 6, 2000, and should describe your method to discontinue such verbal or written statements.

Your response should be directed to the undersigned at (301) 594-6771, or at the Food and Drug Administration, Division of Drug Marketing, Advertising and Communications, HFD-42, Rm 17-B-20, 5600 Fishers Lane, Rockville, MD 20857. We remind Sepracor that only written communications are considered official.

In all future correspondence regarding this particular matter, please refer to MACMIS ID# 8815 in addition to the NDA number.

Sincerely,

/S/

Joan Hankin, JD
Regulatory Review Officer
Division of Drug Marketing,
Advertising, and Communications