DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-779/S-006

Actelion Clinical Research, Inc.
Attention: Frances Duffy-Warren, Ph.D.
1820 Chapel Avenue West, Suite 300
Cherry Hill, NJ 08002

SUPPLEMENT APPROVAL

Dear Dr. Duffy-Warren:

Please refer to your supplemental new drug application (NDA) dated January 31, 2008, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Ventavis (iloprost) Inhalation Solution.

We also refer to our supplement request letter dated July 6, 2007.

This supplemental new drug application provides for the following revisions to the package insert:

1. To add a subsection heading entitled "**Pre-marketing experiences**" to the **ADVERSE REACTIONS** section and change the first sentence in the first and third paragraphs

   FROM

   ADVERSE REACTIONS
   Safety data on Ventavis were obtained from 215 patients with pulmonary arterial hypertension receiving iloprost in two 12-week clinical trials and two long-term extensions.

   Serious adverse events reported with the use of inhaled iloprost and not shown in Table 3 include congestive heart failure, chest pain, supraventricular tachycardia, dyspnea, peripheral edema, and kidney failure.

   TO

   ADVERSE REACTIONS

   Pre-marketing experiences

   Pre-marketing safety data on Ventavis were obtained from 215 patients with pulmonary arterial hypertension receiving iloprost in two 12-week clinical trials and two long-term extensions.

   Pre-marketing serious adverse events reported with the use of inhaled iloprost and not shown in Table 3 include congestive heart failure, chest pain, supraventricular tachycardia, dyspnea, peripheral edema, and kidney failure.

2. In the **ADVERSE REACTIONS** section, to add the following new subsection header and statements:

   POSTMARKETING EXPERIENCE

   The following adverse reactions have been identified during the postapproval use of Ventavis. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

   Cases of epistaxis and gingival bleeding have been reported within one month of starting iloprost treatment.

3. You made other minor grammatical changes to the 1) **HOW SUPPLIED** section (deleted the word "the"), 2) the **PATIENT INFORMATION/WHAT ARE THE INGREDIENTS IN VENTAVIS** (deleted the letter "s" after the word "contains"), 3) updated the "**Distributed by**" section of the prescribing information and patient information leaflet, and 4) changed a comma to a semicolon in the third sentence of the first paragraph in the **DOSAGE AND ADMINISTRATION** section. Finally, the sponsor added the text "Call your doctor for medical advice about side effects. You may report side effects to the FDA at **1-800-FDA 1088**." to the **PATIENT INFORMATION/WHAT ARE THE SIDE EFFECTS WITH VENTAVIS** section of the labeling.

We have completed our review of this application, and it is approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon electronic labeling text. We will transmit the SPL version of the labeling (with one minor edit) submitted on January 31, 2008 to the National Library of Medicine for public dissemination.

If you issue a letter communicating important information about this drug product (i.e., a "Dear Health Care Professional" letter), we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH
Food and Drug Administration
5515 Security Lane
HFD-001, Suite 5100
Rockville, MD 20852

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

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, please call Dan Brum, Pharm.D., Regulatory Project Manager, at (301)796-0578.

Sincerely,

{See appended electronic signature page}

Norman Stockbridge, M.D., Ph.D.
Director
Division of Cardiovascular and Renal Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

cc: Enclosed Labeling Text

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Norman Stockbridge

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