DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 21779/S-013

SUPPLEMENT APPROVAL

Actelion Clinical Research, Inc.
Attention: Patricia H. Palumbo, BSN, JD
Director, Drug Regulatory Affairs
1820 Chapel Avenue West, Suite 300
Cherry Hill, NJ 08002

Dear Ms. Palumbo:

Please refer to your Supplemental New Drug Application (sNDA) dated December 22, 2011, received December 22, 2011, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Ventavis (iloprost) Inhalation Solution, 10 mcg/mL and 20 mcg/mL.

We also acknowledge receipt of your amendments dated January 10, 17, and 25, 2012.

This "Changes Being Effected" supplemental new drug application provides for the following revisions to the labeling.

1. In **ADVERSE REACTIONS/Postmarketing Experience**, revise the following text

   FROM
   Cases of epistaxis and gingival bleeding have been reported within one month of starting Ventavis treatment. Cases of dizziness, diarrhea, mouth and tongue irritation, dysgeusia, hypersensitivity, and rash have also been reported with the use of Ventavis.

   TO
   Bleeding events most commonly reported as epistaxis and hemoptysis were observed on Ventavis treatment *[see Drug Interactions (7.3)]*. Cases of thrombocytopenia, dizziness, diarrhea, mouth and tongue irritation, dysgeusia, hypersensitivity, and rash have also been reported with the use of Ventavis.

2. In **USE IN SPECIFIC POPULATIONS/Nursing Mothers**

   Delete
   It is not known whether iloprost is excreted in human milk.

   Add

In rats a passage of low levels of iloprost or metabolites in to the milk was observed (less than 1% of iloprost dose given intravenously). No disturbance of post-natal development and reproductive performance was seen in animals exposed during lactation.

3. In **PATIENT INFORMATION/What are the ingredients in Ventavis?**

   Add
   Ventavis is a clear, colorless solution.

We have completed our review of this supplemental 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, text for the patient package insert), with the addition of any labeling changes in pending "Changes Being Effected" (CBE) supplements, as well as annual reportable changes not included in the enclosed labeling.

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/DrugsGuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf.

The SPL will be accessible from publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications for this NDA, including CBE supplements for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 314.50(l)(1)(i)] in MS Word format, that includes the changes approved in this supplemental application, as well as annual reportable changes and annotate each change. To facilitate review of your submission, provide a highlighted or marked-up copy that shows all changes, as well as a clean Microsoft Word version. The marked-up copy should provide appropriate annotations, including supplement number(s) and annual report date(s).

REPORTING REQUIREMENTS

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, PharmD, BCPS, RAC, Regulatory Project Manager, at (301)796-0578.

Sincerely,

{See appended electronic signature page}

Mary Ross Southworth, Pharm.D.
Deputy Director for Safety
Division of Cardiovascular and Renal Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

ENCLOSURE:
Content of Labeling

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

/s/

MARY R SOUTHWORTH
04/26/2012