



NDA 021290/S-039
NDA 209279/S-005

SUPPLEMENT APPROVAL

Actelion Pharmaceuticals, Ltd.
c/o: Actelion Clinical Research, Inc.
Attention: Lori A. Palmer
Director, US Regulatory Affairs
1820 Chapel Avenue West, Suite 300
Cherry Hill, NJ 08002

Dear Ms. Palmer:

Please refer to your supplemental new drug application (sNDA) dated and received May 10, 2019, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Tracleer (bosentan) 62.5 mg and 125 mg Tablets (NDA 021290) and Tracleer (bosentan) 32 mg Tablets for Oral Suspension (NDA 209279)

This “Changes Being Effected” supplemental new drug application provides for revisions to the approved labeling and Medication Guide as follows (additions are shown as underlined text and deletions are shown as ~~strikethrough~~ text):

1. Under **PATIENT COUNSELING**, the word “certified” replaces the word “specialty” in the 6th paragraph under Embryo-fetal toxicity.

The following change was made to the Medication Guide:

1. Under **How should I take Tracleer?**, the following text was added/deleted to/from the first bullet:
 - Tracleer is only available through certified ~~will be mailed to you by a specialty pharmacy~~ies. You will only receive a 30-day supply of Tracleer at one time.

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 [FDA.gov](http://www.fda.gov).¹ Content of labeling must be identical to the enclosed labeling (text for the Prescribing Information, and Medication Guide), 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. If the content of labeling in SPL format initially submitted with this CBE-0 labeling supplement is identical to the attached approved labeling, an additional submission of content of labeling in SPL format is not required.

¹ <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>

Information on submitting SPL files using eList may be found in the guidance for industry *SPL Standard for Content of Labeling Technical Qs and As*.²

The SPL will be accessible from publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications that include labeling changes 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 Microsoft Word format, that includes the changes approved in this supplemental application, as well as annual reportable changes. To facilitate review of your submission(s), 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:

Lori Anne Wachter, RN, BSN, RAC
Regulatory Project Manager for Safety
301 796-3975

Sincerely,

{See appended electronic signature page}

Mary Ross Southworth, PharmD.
Deputy Director for Safety
Office of Drug Evaluation I
Center for Drug Evaluation and Research

ENCLOSURE(S):

- Content of Labeling
 - Prescribing Information

² We update guidances periodically. For the most recent version of a guidance, check the FDA Guidance Documents Database <https://www.fda.gov/RegulatoryInformation/Guidances/default.htm>.

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

MARY R SOUTHWORTH
05/16/2019 10:35:49 AM