



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration  
Silver Spring MD 20993

NDA 202811/S-004

**SUPPLEMENT APPROVAL**

Forest Laboratories, Inc.  
Attention: Linda Kunka  
Associate Director, Regulatory Affairs  
Harborside Financial Center  
Plaza V Suite 1900  
Jersey City, NJ 07311

Dear Ms. Kunka:

Please refer to your Supplemental New Drug Application (sNDA) dated July 31, 2013, received August 1, 2013, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for LINZESS (linaclotide) capsules, 145 mcg and 290 mcg.

We acknowledge receipt of your amendments dated August 16, 2013, and January 21, April 14, and July 1, 2014.

This "Prior Approval" supplemental new drug application updates the following sections of the Package Insert with new data from recently completed nonclinical studies that elucidate the mechanism of death in neonatal and juvenile mice and the effects of linaclotide in older juvenile mice:

- Boxed Warning
- Contraindications (4)
- Warnings and Precautions, Pediatric Risk (5.1)
- Warnings and Precautions, Diarrhea (5.2)
- Use in Specific Populations, Pediatric Use (8.4)
- Nonclinical, Animal Toxicology and/or Pharmacology (13.2)
- Patient Counseling Information (17)

**APPROVAL & LABELING**

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 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 that includes 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 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).

All promotional materials that include representations about your drug product must be promptly revised to be consistent with the labeling changes approved in this supplement, including any new safety information [21 CFR 314.70(a)(4)]. The revisions in your promotional materials should include prominent disclosure of the important new safety information that appears in the revised package labeling. Within 7 days of receipt of this letter, submit your statement of intent to comply with 21 CFR 314.70(a)(4) to the address above or by fax to 301-847-8444.

## **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, call Heather Buck, Regulatory Project Manager, at (301) 796-1413.

Sincerely,

*{See appended electronic signature page}*

Joyce Korvick, M.D., M.P.H.  
Deputy Director for Safety  
Division of Gastroenterology and Inborn Errors Products  
Office of Drug Evaluation III  
Center for Drug Evaluation and Research

ENCLOSURE: Content of Labeling

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**This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.**  
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/s/  
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JOYCE A KORVICK  
07/09/2014