DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 202535

NDA APPROVAL

Ferring Pharmaceuticals, Inc.
Attention: Brenda Marczi
Vice President, Regulatory Affairs US
4 Gatehall Drive, 3rd Floor
Parsippany, NJ 07054

Dear Ms. Marczi:

Please refer to your New Drug Application (NDA) dated September 16, 2011, received, September 16, 2011, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for Prepopik (sodium picosulfate, magnesium oxide and citric acid) for Oral Solution, 10 mg sodium picosulfate/sachet.

We acknowledge receipt of your amendments dated November 7, 2011; December 15, 2011; January 20 & 31, 2012; February 17 & 21, 2012; March 12 & 29, 2012; April 13, 2012; May 9, 21, & 23, 2012; June 19 & 26, 2012; July 3, 5, 10, & 16, 2012.

This new drug application provides for the use Prepopik (sodium picosulfate, magnesium oxide and citric acid) for Oral Solution, 10 mg sodium picosulfate/sachet, for cleansing of the colon as a preparation for colonoscopy in adults.

We have completed our review of this 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 and Medication Guide). 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/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf.

The SPL will be accessible via publicly available labeling repositories.

CARTON AND IMMEDIATE CONTAINER LABELS

We acknowledge your July 16, 2012, submission containing final printed carton and container labels.

Your application for Prepopik was not referred to an FDA advisory committee because

a) this drug is not the first in its class

b) the safety profile is similar to that of other drugs approved for this indication

c) the clinical study design is similar to previously approved products in the class

d) evaluation of the safety data [when used for cleansing of the colon as a preparation for colonoscopy in adults] did not raise significant safety or efficacy issues that were unexpected for a drug of this class

e) the application did not raise significant public health questions on the role of the drug in the diagnosis, cure, mitigation, treatment, or prevention of a disease

f) outside expertise was not necessary; there were no controversial issues that would benefit from advisory committee discussion.

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We are waiving the pediatric study requirement for patients less than 1 year of age because the product does not represent a meaningful therapeutic benefit over existing therapies for pediatric patients in this age group and is not likely to be used in a substantial number of pediatric patients in this group. Based on review of the literature and expert opinion, colonoscopies are not performed in a substantial number of pediatric patients under the age of one year, and therefore do not warrant studies. Also, bowel preparation can be achieved with the administration of clear liquids with or without suppositories or enemas in young pediatric patients

We are deferring submission of your pediatric studies for patients greater than or equal to 1 year of age for this application because this product is ready for approval for use in adults and the pediatric studies have not been completed.

Your deferred pediatric studies required by section 505B(a) of the Federal Food, Drug, and Cosmetic Act are required postmarketing studies. The status of these postmarketing studies must be reported annually according to 21 CFR 314.81 and section 505B(a)(3)(B) of the Federal Food, Drug, and Cosmetic Act. These required studies are listed below.

1902-1 Conduct a randomized, single-blind, multicenter dose-ranging study comparing the safety and efficacy of Prepopik to community standard of care in children (ages 9 years to 16 years). This study will include PK assessments.

Final Protocol Submission: February 2013
Study Completion: February 2016
Final Report Submission: August 2016

1902-2 Conduct a randomized, single-blind, multicenter dose-ranging study comparing the safety and efficacy of Prepopik to community standard of care in children (ages 2 years to <9 years). This study will include PK assessments.

Final Protocol Submission: February 2016
Study Completion: February 2019
Final Report Submission: August 2019

1902-3 Conduct a randomized, single-blind, multicenter dose-ranging study comparing the safety and efficacy of Prepopik to community standard of care in children (ages 12 months to <2 years). This study will include PK assessments.

Final Protocol Submission: February 2018
Study Completion: August 2019
Final Report Submission: February 2020

Submit the protocols to your IND 101738, with a cross-reference letter to this NDA.

Reports of these required pediatric postmarketing studies must be submitted as a new drug application (NDA) or as a supplement to your approved NDA with the proposed labeling changes you believe are warranted based on the data derived from these studies. When submitting the reports, please clearly mark your submission "**SUBMISSION OF REQUIRED PEDIATRIC ASSESSMENTS**" in large font, bolded type at the beginning of the cover letter of the submission.

POSTMARKETING REQUIREMENTS UNDER 505(o)

Section 505(o)(3) of the Federal Food, Drug, and Cosmetic Act (FDCA) authorizes FDA to require holders of approved drug and biological product applications to conduct postmarketing studies and clinical trials for certain purposes, if FDA makes certain findings required by the statute.

We have determined that an analysis of spontaneous postmarketing adverse events reported under subsection 505(k)(1) of the FDCA will not be sufficient to assess a signal of a serious risk

of renal insufficiency associated with the use of Prepopik (sodium picosulfate, magnesium oxide and citric acid) for Oral Solution, 10 mg sodium picosulfate/sachet.

Furthermore, the new pharmacovigilance system that FDA is required to establish under section 505(k)(3) of the FDCA will not be sufficient to assess this serious risk.

Therefore, based on appropriate scientific data, FDA has determined that you are required to conduct the following:

1902-4 Conduct a retrospective study to identify the risk factors associated with development of persistent deterioration of renal function in patients undergoing colon cleansing with Prepopik in preparation for colonoscopy.

This study should evaluate all available data for all patients at any point during studies FE2009-01 and FE2009-02, including relevant clinical data not recorded in the CRF such as volume of fluid administered during the colonoscopy and vital signs recorded during the colonoscopy. Identify those patients with a decrease in renal function and compare any difference in risk factors or clinical status with those patients who did not have renal dysfunction.

Evaluate any patient who had a decline in renal function as measured by a decline in eGFR at the Day 30 assessment by collecting additional information with regard to renal function beyond the Day 30 assessment including concomitant medication use, additional procedures, and inter-current illness.

The timetable you submitted on July 12, 2012 states that you will conduct this study according to the following schedule:

Final Protocol Submission:	March 2013
Study Completion:	June 2014
Final Report Submission:	December 2014

Submit the protocol to your IND 101738, with a cross-reference letter to this NDA. Submit the final report to your NDA. Prominently identify the submission with the following wording in bold capital letters at the top of the first page of the submission, as appropriate: **"Required Postmarketing Protocol Under 505(o)", "Required Postmarketing Final Report Under 505(o)", "Required Postmarketing Correspondence Under 505(o)"**.

Section 505(o)(3)(E)(ii) of the FDCA requires you to report periodically on the status of any study or clinical trial required under this section. This section also requires you to periodically report to FDA on the status of any study or clinical trial otherwise undertaken to investigate a safety issue. Section 506B of the FDCA, as well as 21 CFR 314.81(b)(2)(vii) requires you to report annually on the status of any postmarketing commitments or required studies or clinical trials.

FDA will consider the submission of your annual report under section 506B and

21 CFR 314.81(b)(2)(vii) to satisfy the periodic reporting requirement under section 505(o)(3)(E)(ii) provided that you include the elements listed in 505(o) and 21 CFR 314.81(b)(2)(vii). We remind you that to comply with 505(o), your annual report must also include a report on the status of any study or clinical trial otherwise undertaken to investigate a safety issue. Failure to submit an annual report for studies or clinical trials required under 505(o) on the date required will be considered a violation of FDCA section 505(o)(3)(E)(ii) and could result in enforcement action.

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit, in triplicate, a cover letter requesting advisory comments, the proposed materials in draft or mock-up form with annotated references, and the package insert to:

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion
5901-B Ammendale Road
Beltsville, MD 20705-1266

As required under 21 CFR 314.81(b)(3)(i), you must submit final promotional materials, and the package insert, at the time of initial dissemination or publication, accompanied by a Form FDA 2253. For instruction on completing the Form FDA 2253, see page 2 of the Form. For more information about submission of promotional materials to the Office of Prescription Drug Promotion (OPDP), see http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm.

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

MEDWATCH-TO-MANUFACTURER PROGRAM

The MedWatch-to-Manufacturer Program provides manufacturers with copies of serious adverse event reports that are received directly by the FDA. New molecular entities and important new biologics qualify for inclusion for three years after approval. Your firm is eligible to receive copies of reports for this product. To participate in the program, please see the enrollment instructions and program description details at http://www.fda.gov/Safety/MedWatch/HowToReport/ucm166910.htm.

If you have any questions, call Maureen Dewey, Regulatory Health Project Manager, at (301) 796-0845.

Sincerely,

{See appended electronic signature page}

Victoria Kusiak, M.D.
Deputy Director
Office of Drug Evaluation III
Center for Drug Research and Evaluation

ENCLOSURES:
Content of Labeling
Carton and Container Labeling

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

/s/

VICTORIA KUSIAK
07/16/2012