



NDA 020725/S-003

**SUPPLEMENT APPROVAL**

Abbott Products, Inc.  
Attention: Adam E. Allgood, PharmD., RPh.  
Assistant Director & Regulatory Liaison, Global Pharmaceutical Regulatory Affairs  
901 Sawyer Road  
Marietta, GA 30062

Dear Dr. Allgood:

Please refer to your Supplemental New Drug Application (sNDA) dated June 30, 2009, received July 1, 2009, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Creon (pancrelipase) Delayed-Release Capsules.

We acknowledge receipt of your submissions dated October 20, 2009, November 11, 2009, November 13, 2009, January 11, 2010, January 22, 2010, April 5, 2010, April 23, 2010, and April 30, 2010.

This "Prior Approval" supplemental new drug application provides for the use of Creon (pancrelipase) Delayed-Release Capsules for the treatment of exocrine pancreatic insufficiency due to chronic pancreatitis or pancreatectomy.

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, using the FDA automated drug registration and listing system (eLIST), the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format, as described at <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>, that is identical to the enclosed labeling (text for the package insert and Medication Guide) and include the labeling changes proposed in any pending "Changes Being Effected" (CBE) supplements. 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 pending “Changes Being Effected” (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.

### **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 this application because necessary studies are impossible or highly impracticable. This is because there are too few children with exocrine pancreatic insufficiency due to chronic pancreatitis or pancreatectomy to study.

### **POSTMARKETING REQUIREMENTS UNDER 505(o)**

Section 505(o) of the 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 (section 505(o)(3)(A)).

Since Creon (pancrelipase) Delayed-Release Capsules was approved on April 30, 2009, we have received a new supplemental NDA (S-003) that expands the population of patients expected to use the drug to include patients being treated for “exocrine pancreatic insufficiency due to chronic pancreatitis or pancreatectomy.” This changes the risk-benefit profile of Creon (pancrelipase) Delayed-Release Capsules because the magnitude of the risk of fibrosing colonopathy in patients with chronic pancreatitis is unknown. Therefore, we consider this information to be “new safety information” as defined in FDAAA.

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 identify an unexpected serious risk of fibrosing colonopathy associated with Creon (pancrelipase) Delayed-Release Capsules.

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

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

- 1631-1. A 10-year observational study to prospectively evaluate the incidence of fibrosing colonopathy in patients with chronic pancreatitis or pancreatectomy treated with Creon (pancrelipase) Delayed-Release Capsules in the U.S. and to assess potential risk factors for the event.

The timetable you submitted on April 5, 2010 states that you will conduct this study according to the following timetable:

<b>Final Protocol Submission:</b>	<b>July 31, 2011</b>
<b>Study Completion Date:</b>	<b>February 28, 2022</b>
<b>Final Report Submission:</b>	<b>July 31, 2022</b>

Submit the protocol to your IND 047546, with a cross-reference letter to this NDA 020725. Submit all final reports to this 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(s) to:

Food and Drug Administration  
Center for Drug Evaluation and Research  
Division of Drug Marketing, Advertising, and Communications  
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(s), 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 Division of Drug Marketing, Advertising, and Communications (DDMAC), see <http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm>.

### **LETTERS TO HEALTH CARE PROFESSIONALS**

If you decide to issue a letter communicating important safety-related information about this drug product (i.e., a “Dear Health Care Professional” letter), we request that you submit, at least 24 hours prior to issuing the letter, an electronic copy of the letter to this NDA, to CDERMedWatchSafetyAlerts@fda.hhs.gov, and to the following address:

MedWatch  
Food and Drug Administration  
Suite 12B-05  
5600 Fishers Lane  
Rockville, MD 20857

### **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 Jagjit Grewal, Regulatory Project Manager, at (301) 796-0846.

Sincerely,

*{See appended electronic signature page}*

Donna Griebel, M.D.  
Director  
Division of Gastroenterology Products  
Office of Drug Evaluation III  
Center for Drug Evaluation and Research

Enclosures: Package Insert Label, Medication Guide

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-20725	SUPPL-3	ABBOTT PRODUCTS INC	CREON/MINIMICROSPHERE)PA NCRELIPASE D-R C

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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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DONNA J GRIEBEL  
04/30/2010