DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 21321/S-020/S-021

SUPPLEMENT APPROVAL

Baxter Healthcare Corporation
Attention: Linda Coleman, R.A.C.
Associate Director, Global Regulatory Affairs
1620 Waukegan Road
McGaw Park, IL 60085

Dear Ms. Coleman:

Please refer to your supplemental new drug applications (sNDAs) dated April 3, 2009 (S-020 for risk evaluation and mitigation strategy [REMS]) and May 21, 2010 (S-021 for labeling), submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Extraneal (icodextrin) 7.5% w/v peritoneal dialysis solution.

We acknowledge receipt of your amendments to S-020 dated September 11, November 20, 2009, and March 10, March 30, May 21, November 15, 2010 and February 7, 2011. We also acknowledge your amendments to S-021 dated June 11, July 30, and November 15, 2010.

These "prior approval" supplemental new drug applications provide for revisions to the package insert, medication guide and a proposed risk evaluation and mitigation strategy (REMS).

We have completed our review of these supplemental applications, as amended. They are approved, effective on the date of this letter, for use as recommended in the enclosed, agreed-upon labeling text.

We request that the labeling approved today be available on your website within 10 days of receipt of this letter.

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, except with the revisions indicated, 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 and any 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 via 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 with the revisions listed approved in this supplemental application.

RISK EVALUATION AND MITIGATION STRATEGY REQUIREMENTS

Section 505-1 of the FDCA authorizes FDA to require the submission of a REMS, if FDA becomes aware of new safety information and makes a determination that such a strategy is necessary to ensure that the benefits of the drug outweigh the risks [section 505-1(a)]. The details of the REMS requirements were outlined in our complete response letter dated December 9, 2008, our REMS notification letter dated November 4, 2010, and our REMS Information Request letters dated July, 2010 and October, 2010.

Since Extraneal (icodextrin) was approved on December 20, 2002, we have become aware of cases of hypoglycemia when patients receiving Extraneal therapy received inappropriate insulin therapy based on falsely elevated blood glucose levels (due to the drug-device interaction with some non-glucose-specific glucometers). We consider this information to be "new safety information" as defined in section 505-1(b) of the FDCA.

Pursuant to 505-1(f)(1), we have determined that to ensure the benefits of the drug outweigh the risks of hypoglycemia resulting from inappropriate insulin therapy, elements necessary to assure safe use are required as part of a REMS to mitigate these risks. The elements to assure safe use are intended to ensure that Extraneal (icodextrin) will be dispensed with evidence of safe-use conditions and that dialysis clinic personnel have received training.

We remind you that section 505-1(f)(8) of the FDCA prohibits holders of an approved covered application with elements to assure safe use from using any element to block or delay approval of an application under section 505(b)(2) or (j). A violation of this provision in 505-1(f) could result in enforcement action.

Your proposed REMS, submitted on November 15, 2010, and appended to this letter, is approved. The REMS consists of a Medication Guide, elements to assure safe use, implementation system, and a timetable for submission of assessments of the REMS.

The REMS assessment plan should include, but is not limited to, the following:

a. Number of Extraneal units sold in the US during the reporting period;
b. Number of new patients in the US dispensed Extraneal during the reporting period;
c. Number of and percentage of new patients who have received an Extraneal Patient Kit during the reporting period;
d. Number of US dialysis clinics that have been trained during the reporting period;
e. The number and percentage of patients receiving Extraneal who attend dialysis clinics were not previously trained;
f. An evaluation of patients' understanding of the safe use of Extraneal, and receipt and understanding of the Medication Guide;
g. An evaluation of the understanding of the safe use of Extraneal by dialysis clinic staff managing the patient's treatment (such as peritoneal dialysis nurses), in particular, the drug-device interaction and the potential for falsely elevated blood glucose readings in patients using Extraneal;

h. Status of safety data exchange agreements between Baxter and manufacturers of nonspecific glucose monitoring systems;
i. A summary of adverse event reports for hypoglycemia related to drug-device interaction, including those resulting in hypoglycemic complications, and the root cause analysis. The root cause analysis will include: the case narrative, the device involved (if known), and information about the use and knowledge of communication tools by the patient involved in the adverse event and the responsible healthcare provider (if known);
j. A summary of any packaging process exceptions related to Extraneal Medication Guide dispensing, including corrective actions taken to address non-compliance;
k. A description of the specific measures that will be taken to increase awareness, if we were to conclude during our Extraneal safety review that dialysis clinic and patient awareness of the drug-device interaction is not adequate;
l. A conclusion about whether the REMS is meeting its goal and whether modifications to the REMS are needed.

The requirements for assessments of an approved REMS under section 505-1(g)(3) include, in section 505-1(g)(3)(A), an assessment of the extent to which the elements to assure safe use are meeting the goal or goals to mitigate a specific serious risk listed in the labeling of the drug, or whether the goal or goals or such elements should be modified.

Assessments of an approved REMS must include, under section 505-1(g)(3)(B) and (C), information on the status of any postapproval study or clinical trial required under section 505(o) or otherwise undertaken to investigate a safety issue. With respect to any such postapproval study, you must include the status of such study, including whether any difficulties completing the study have been encountered. With respect to any such postapproval clinical trial, you must include the status of such clinical trial, including whether enrollment has begun, the number of participants enrolled, the expected completion date, whether any difficulties completing the clinical trial have been encountered, and registration information with respect to requirements under subsections (i) and (j) of section 402 of the Public Health Service Act. You can satisfy these requirements in your REMS assessments by referring to relevant information included in the most recent annual report required under section 506B and 21 CFR 314.81(b)(2)(vii) and including any material or significant updates to the status information since the annual report was prepared. Failure to comply with the REMS assessments provisions in section 505-1(g) could result in enforcement action.

We remind you that in addition to the assessments submitted according to the timetable included in the approved REMS, you must submit a REMS assessment and may propose a modification to the approved REMS when you submit a supplemental application for a new indication for use as described in section 505-1(g)(2)(A) of FDCA.

If you currently distribute or plan to distribute an authorized generic product under this NDA, you will also need to submit a REMS, REMS supporting document, and any required appended documents for that authorized generic, to this NDA. In other words, you must submit a complete proposed REMS that relates only to the authorized generic product. Review and approval of the REMS is required before you may market your product.

Prominently identify the submission containing the REMS assessments or proposed modifications with the following wording in bold capital letters at the top of the first page of the submission as appropriate:

NDA 021321 REMS ASSESSMENT

NEW SUPPLEMENT FOR NDA 021321
PROPOSED REMS MODIFICATION
REMS ASSESSMENT

NEW SUPPLEMENT (NEW INDICATION FOR USE)
FOR NDA 021321
REMS ASSESSMENT
PROPOSED REMS MODIFICATION (if included)

If you do not submit electronically, please send 5 copies of REMS-related submissions.

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit the following, in triplicate, (1) a cover letter requesting advisory comments, (2) the proposed materials in draft or mock-up form with annotated references, and (3) 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

You must submit final promotional materials and package insert(s), accompanied by a Form FDA 2253, at the time of initial dissemination or publication [21 CFR 314.81(b)(3)(i)]. Form FDA 2253 is available at http://www.fda.gov/opacom/morechoices/fdaforms/cder.html; instructions are provided on 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.

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.

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 the following address:

MedWatch Program
Office of Special Health Issues
Food and Drug Administration
10903 New Hampshire Ave
Building 32, Mail Stop 5353
Silver Spring, MD 20993

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:

Anna Park-Hong
Project Manager
301-796-1129

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

Enclosures:
Agreed-upon labeling text
Medication Guide
REMS

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
03/09/2011