Initial REMS Approval 03/2011

NDA 21-321
EXTRANEAL (icodextrin) Peritoneal Dialysis Solution
Baxter Healthcare Corporation
1620 Waukegan Road
McGaw Park IL 60085
847-473-6590

RISK EVALUATION AND MITIGATION STRATEGY (REMS)

I. GOAL(S):

To mitigate the risk of morbidity and mortality associated with the use of non-specific glucose monitors and test strips in patients using Extraneal by:

- Informing the dialysis clinic staff managing the patient's treatment (such as peritoneal dialysis nurses) about the drug-device interaction and the potential for falsely elevated blood glucose readings in patients using Extraneal.
- Informing patients of the drug-device interaction and the need to alert health care providers of this interaction whenever they receive treatment outside of a dialysis clinic.

II. REMS ELEMENTS:

A. Medication Guide

A Medication Guide will be dispensed with each Extraneal prescription in accordance with 21 CFR 208.24.

B. Elements to Assure Safe Use

1. Extraneal will only be dispensed to patients with documentation of safe-use conditions

a. Baxter will ensure that Extraneal is only dispensed to patients if there is documentation that the dialysis clinic staff managing the patient's treatment has completed the training on drug-device interactions involving Extraneal. The "Dialysis Clinic Training" on drug-device interactions consists of the following:

i. Why Extraneal patients have elevated blood levels of maltose;
ii. How maltose interferes with non-specific glucose monitoring systems;
iii. How maltose interference with non-specific glucose monitoring systems may result in falsely elevated blood glucose readings;
iv. What are the consequences of falsely elevated blood glucose readings;
v. The risk of maltose interference with non-specific glucose monitoring systems for up to 14 days following cessation of Extraneal therapy;
vi. How to confirm that patients are using glucose-specific monitors and test strips;
vii. How to use the Baxter tools that are available to assist with training of the dialysis clinic staff, and to assist the dialysis clinic staff with training of Extraneal patients;
viii. The importance of educating patients to alert health care providers of the drug-device interaction whenever they are admitted to the hospital or in other medical care settings;
ix. Information on the Extraneal Patient Kit - how it should be used, what it contains, and how patients will receive it;
x. Contact information for glucose monitor manufacturers; and
xi. Contact information for MedicAlert.

b. Dialysis clinic staff is responsible for training patients at the time Extraneal is added to their prescriptions. The patient training includes:
    i. The importance of verifying that home glucose monitors and test strips are glucose-specific;
    ii. Why only glucose-specific monitors and test strips should be used;
    iii. The potential consequences that can result if glucose-specific monitors and test strips are not used;
    iv. The need to alert health care providers of the potential for glucose monitor interference when admitted to the hospital or in other medical care settings;
    v. The importance of informing caregivers of the potential for falsely elevated glucose readings and the need to communicate this information in an emergency situation on the patient's behalf;
    vi. The risk of glucose monitor interference for up to 14 days after stopping use of Extraneal;
    vii. A review of the Extraneal Patient Kit, which includes the following:

        1) "Dear Patient" Letter;
        2) Extraneal Patient Training Tool;
        3) Wallet Card;
        4) Extraneal Wearable Item (*e.g.,* a bracelet and/or pendant);
        5) Stickers and a magnetic hang tag for patient charts and prominent display in the hospital setting;
        6) Letters to hospital staff, including;
            a. Physicians
            b. Nurses
            c. Pharmacists
            d. Laboratory Services
            e. Admissions Personnel
        7) Extraneal Prescribing Information; and,
        8) Extraneal Medication Guide.
    viii. Informing patients that the Extraneal Patient Kit will be delivered directly to the patient's home in parallel with the first delivery of their Extraneal prescription.

c. If a dialysis clinic's staff has not managed the treatment of a patient using Extraneal within six months of having completed training, Baxter will ensure that the staff is re-trained before Extraneal is dispensed.

The following materials are part of the REMS and are appended:

- Extraneal PD Nurse Training Tool (Attachment 1)
- Extraneal Patient Training Tool (Attachment 2)
- Extraneal Patient Kit (Attachment 3)

C. Implementation System

1. Baxter will maintain a database of all dialysis clinics whose staff has been trained and the date training was completed.
2. Baxter will maintain a database of all patients who are dispensed Extraneal.
3. Baxter will maintain a database of all patients who have received the Extraneal Patient Kit and the date the Patient Kit was received by the patient.
4. Baxter will verify that all patients dispensed Extraneal received a Patient Kit, by tracking the shipment of the Patient Kit and obtaining delivery confirmation.
5. Baxter will monitor compliance with the Extraneal program to help ensure that Extraneal is dispensed to patients who have received training by their dialysis clinic, by conducting surveys of patients.
6. Based on evaluation of the implementation of elements to assure safe use provided for under Sections B1 above, and in the manner described in the REMS supporting document, Baxter will take reasonable steps to improve implementation of these elements to meet the goals of the REMS.

D. Timetable for Submission of Assessments

Baxter will submit REMS Assessments to FDA March 8, 2012 and annually thereafter. To facilitate inclusion of as much information as possible while allowing reasonable time to prepare the submission, the reporting interval covered by each assessment should conclude no earlier than 60 days before the submission date for that assessment. Baxter will submit each assessment so that it will be received by FDA on or before the due date.

Attachment 1

Extraneal PD Nurse Training Tool

(8 pages)

Baxter

EXTRANEAL (icodextrin) Peritoneal Dialysis Solution

Important Risk Information for All Patients
A GUIDE FOR THE PD NURSE

This guide is part of an FDA approved REMS

Important Risk Information for the PD Nurse About **Extraneal** (icodextrin) Peritoneal Dialysis Solution

Dangerous Drug Device Interaction

Only use glucose-specific monitors and test strips to measure blood glucose levels in patients using **Extraneal** (icodextrin) Peritoneal Dialysis Solution. Blood glucose monitoring devices using glucose dehydrogenase pyrroloquinolinequinone (GDH-PQQ) or glucose-dye-oxidoreductase (GDO)-based methods must not be used. In addition, some blood glucose monitoring systems using glucose dehydrogenase flavin-adenine dinucleotide (GDH-FAD)-based methods must not be used. Use of GDH-PQQ, GDO, and GDH-FAD-based glucose monitors and test strips has resulted in falsely elevated glucose readings (due to the presence of maltose, see **PRECAUTIONS/Drug/Laboratory Test Interactions**). Falsely elevated glucose readings have led patients or health care providers to withhold treatment of hypoglycemia or to administer insulin inappropriately. Both of these situations have resulted in unrecognized hypoglycemia, which has led to loss of consciousness, coma, permanent neurological damage, and death. Plasma levels of **Extraneal** (icodextrin) and its metabolites return to baseline within approximately 14 days following cessation of **Extraneal** (icodextrin) administration. Therefore falsely elevated glucose levels may be measured up to two weeks following cessation of **Extraneal** (icodextrin) therapy when GDH-PQQ, GDO, and GDH-FAD-based blood glucose monitors and test strips are used.

Because GDH-PQQ, GDO, and GDH-FAD-based blood glucose monitors may be used in hospital settings, it is important that the health care providers of peritoneal dialysis patients using **Extraneal** (icodextrin) carefully review the product information of the blood glucose testing system, including that of test strips, to determine if the system is appropriate for use with **Extraneal** (icodextrin).

To avoid improper insulin administration, educate patients to alert health care providers of this interaction whenever they are admitted to the hospital.

The manufacturer(s) of the monitor and test strips should be contacted to determine if icodextrin or maltose causes interference or falsely elevated glucose readings. For a list of toll free numbers for glucose monitor and test strip manufacturers, please contact the Baxter Renal Clinical Help Line 1-888-RENAL-HELP or visit www.glucosesafety.com.

Please see additional risk information on page 7 and enclosed prescribing information.

Indications

- **Extraneal** PD solution is indicated for a single daily exchange for the long (8 to 16 hour) dwell during Continuous Ambulatory Peritoneal Dialysis (CAPD) or Automated Peritoneal Dialysis (APD) for the management of End-Stage Renal Disease (ESRD). **Extraneal** PD solution is also indicated to improve (compared to 4.25% dextrose) long-dwell ultrafiltration and clearance of creatinine and urea nitrogen in patients with high-average or greater transport characteristics, as defined using the Peritoneal Equilibration Test (PET)

Contraindications

- **Extraneal** PD solution is contraindicated in patients with a known allergy to cornstarch or icodextrin, in patients with maltose or isomaltose intolerance, in patients with glycogen storage disease, and in patients with pre-existing severe lactic acidosis

Information Regarding the Use of Glucose Monitors and Test Strips

All patients receiving **Extraneal** PD solution may have incorrect blood glucose results when using particular blood glucose monitoring systems.

Use of **Extraneal** PD solution results in elevated blood levels of maltose, a metabolite of icodextrin. Maltose interferes with glucose monitors that utilize certain enzymes on their test strips, specifically glucose dehydrogenase pyrroloquinolinequinone (GDH-PQQ), glucose-dye-oxidoreductase (GDO) and in some cases, glucose dehydrogenase flavin-adenine dinucleotide (GDH-FAD), resulting in falsely elevated glucose monitor readings. This interference may mask true hypoglycemia or lead to the erroneous diagnosis of hyperglycemia.

- A blood glucose reading that is within the normal range may mask low blood sugar, and a patient who is hypoglycemic may appear to be euglycemic. This could cause a patient or health care professional not to take the appropriate steps to bring the blood sugar into a normal range
- A falsely elevated blood glucose reading may make a patient who is euglycemic to appear hyperglycemic, and could cause the patient to get more insulin than needed
- Both of these situations can lead to life-threatening events, including loss of consciousness, coma, permanent neurological damage, and death
- Falsely elevated glucose levels may be measured up to two weeks following cessation of **Extraneal** PD solution when some, but not all GDH-PQQ, GDO, and GDH-FAD-based blood glucose monitors and test strips are used

Glucose monitors that utilize GDH-PQQ, GDO, and in some cases GDH-FAD MUST NOT be used for patients using **Extraneal** PD solution. Blood glucose measurement must be done with a method that does not cause maltose interference with test results. **ONLY glucose monitors and test strips that are glucose-specific must be used for patients on Extraneal PD solution. Contact the manufacturer of the glucose monitors and test strips to determine the method that is used. For further information, visit www.glucosesafety.com.**

To assist in patient training, Baxter has developed an **Extraneal** PD Solution Patient Training Tool that contains important risk information about **Extraneal** PD solution specifically intended for patients.

Baxter recommends that each patient be given a copy of the **Extraneal** PD Solution Patient Training Tool and that all information in the tool be discussed with the patient in detail.

Recommendations for patient training and follow-up regarding glucose monitors and test strips.

- Train the patient and all caregivers on the importance of using only certain monitors and test strips and about the potential consequences if these guidelines are not followed. Instruct them to ensure that any emergency contacts also be made aware of this information
- Use the **Extraneal** PD Solution Patient Training Tool and **Extraneal** Patient Medication Guide to review the information about glucose monitor and test strip interference, particularly the need to alert health care providers outside the dialysis unit (e.g., emergency room, hospital, outpatient clinic, physician offices)
- Verify the type of glucose monitor and test strips used by the patient; call or instruct the patient to call the manufacturers to verify that the monitor and/or test strips measure only glucose. Monitors and test strips that are subject to maltose interference must not be used
- Your PD unit has received a Demonstration Kit, which contains a sample of all the items included in the **Extraneal** PD Solution Patient Kit. Prior to initiating therapy with **Extraneal** PD Solution, review the contents of the kit with the patient, and inform them that an **Extraneal** patient kit will be delivered to their home shortly. Also assist the patient in completing the information on the Wallet Card included in the **Extraneal** PD Solution Patient Training Tool
- Obtain additional materials, including **Extraneal** PD Solution Demonstration Kit or any of its components, Patient Training Tools, and Guides for the PD Nurse, free of charge from your Baxter Clinical Educator or Account Executive

Recommendations if you suspect hypoglycemia based on the patient's symptoms:

- Treatment must not be delayed since severe hypoglycemia may lead to life-threatening consequences including loss of consciousness, coma, permanent neurological damage and death
- The patient's blood glucose level must be measured immediately with either a laboratory-based method, if available or a glucose-specific monitor and test strips

Additional Information Regarding the Use of Glucose Monitors and Test Strips

Glucose Monitor Manufacturers

The following list provides the names and contact information for manufacturers of today's most commonly used glucose monitors and test strips. It is included for reference only; you need to contact the manufacturer to ensure that your monitor and test strips use a method that does not cause maltose interference with test results. **This list does not indicate that Baxter is recommending these products**. You should call the manufacturer to verify if the monitor and test strips measure only glucose. The list is current as of September 2010.

Manufacturer	Contact Information
Abbott Diabetes Care	888-522-5226 www.abbottdiabetescare.com
Arkray	800-818-8877, Option #5 www.arkrayusa.com
Bayer Healthcare	800-348-8100 www.bayerdiabetes.com
Lifescan, Inc (Division of Johnson & Johnson)	800-524-SCAN 800-227-8862 www.lifescan.com
Roche Diagnostics	800-858-8072 www.roche-diagnostics.com | www.accu-chek.com

Protect your patients. Take these steps below.

- If your patients are not MedicAlert members, be sure to encourage them to enroll in MedicAlert or to wear the **Extraneal** PD solution necklace or bracelet provided by Baxter in the **Extraneal** PD Solution Patient Kit – this could help to save their lives
- MedicAlert can be reached at 1-888-633-4298 or at www.medicalert.org
- If you have any questions please contact your Baxter Account Representative at **1-888-736-2543**
- If any of your patients need a replacement of any of the components in the **Extraneal** PD Solution Patient Kit such as a necklace and/or braclet, please have them contact HomeCare Services at 1-800-284-4060

Additional Important Risk Information

- **Extraneal** PD solution is intended for intraperitoneal administration only. Not for intravenous injection
- Rarely, serious hypersensitivity reactions to **Extraneal** have been reported, such as toxic epidermal necrolysis, angioedema, serum sickness, erythema multiforme and leukocytoclastic vasculitis. If a serious reaction is suspected, discontinue **Extraneal** and institute appropriate treatment as clinically indicated
- Patients with insulin-dependent diabetes may require modification of insulin dosage following initiation of treatment
- A patient's volume status should be carefully monitored to avoid hyper- or hypovolemia and potentially severe consequences including congestive heart failure, volume depletion and hypovolemic shock. An accurate fluid balance record must be kept and the patient's body weight monitored
- In clinical trials, the most frequently reported adverse events occurring in ≥10% of patients, and more common in **Extraneal** PD solution patients than in control patients, were peritonitis, upper respiratory infection, hypertension, and rash. The most common treatment-related adverse event for **Extraneal** PD solution patients was skin rash. Additional adverse reactions have been reported in the post-marketing setting and are detailed in the full prescribing information

General Peritoneal Dialysis-Related

- Encapsulating peritoneal sclerosis (EPS) is a known, rare complication of peritoneal dialysis therapy. EPS has been reported in patients using peritoneal dialysis solutions including **Extraneal** PD solution. Infrequent but fatal outcomes have been reported
- Aseptic technique should be used throughout the peritoneal dialysis procedure to reduce the possibility of infection, such as peritonitis
- Fluid status, hematologic indices, blood chemistry, and electrolyte concentrations, including calcium, potassium, sodium, magnesium and bicarbonate, should be monitored periodically. Abnormalities in any of these parameters should be treated promptly under the care of a physician
- Overinfusion of peritoneal dialysis solution volume into the peritoneal cavity may be characterized by abdominal distention, feeling of fullness and/or shortness of breath. Treatment of overinfusion is to drain the peritoneal dialysis solution from the peritoneal cavity
- Treatment should be initiated and monitored under the supervision of a physician knowledgeable in the management of patients with renal failure

Please see full prescribing information.

For more information, contact your Baxter Account Executive, Clinical Educator or the Renal Clinical HelpLine at 1-888-RENALHELP (1-888-736-2543).

Additional training on glucose monitors and test strips is also available at www.glucosesafety.com.

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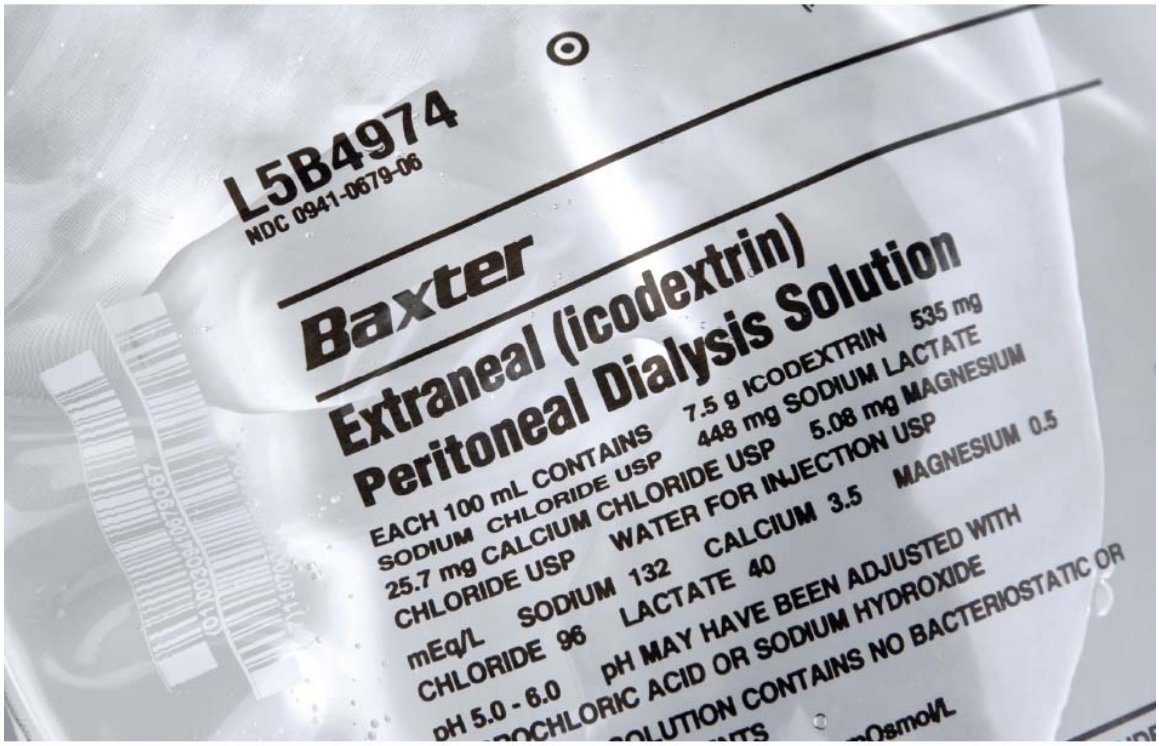
Attachment 2

Extraneal Patient Training Tool

(8 pages)

Baxter

Using EXTRANEAL (icodextrin) Peritoneal Dialysis Solution



Important Risk Information for All Patients
A PATIENT TRAINING TOOL

This Patient Training Tool is part of an FDA approved REMS

Important Risk Information for **Extraneal** (icodextrin) Peritoneal Dialysis Solution Patients Who Measure Blood Sugar (Glucose) Levels

Icodextrin or its by-products, such as maltose, cause some types of glucose monitors and/or test strips to give a **false high glucose reading**.

- A false high glucose reading could cause you or a clinician to give you more insulin than you need
- A false high glucose reading may mask a very low actual glucose reading and cause you to delay in correcting the low blood sugar
- Both of these situations can cause life-threatening event
- Taking too much insulin or waiting too long to treat low blood sugar can cause you to have serious reactions including: loss of consciousness (passing out), coma, permanent neurological problems, and death
- You or your PD nurse must confirm that your glucose monitor(s) and test strip(s) will provide an accurate reading when using **Extraneal** PD solution
- DO NOT use glucose monitors or test strips that utilize glucose dehydrogenase pyrroloquinolinequinone (GDH-PQQ) or glucose-dye-oxidoreductase (GDO)-based methods. In addition, some blood glucose monitors or test strips that utilize glucose dehydrogenase flavin-adenine dinucleotide (GDH-FAD)-based methods must not be used. Blood glucose measurements must be done with a method that does not cause maltose interference with test results. **ONLY glucose monitors and test strips that use glucose-specific methods must be used by patients on Extraneal PD solution**
- Contact the manufacturer of your glucose monitor(s) and glucose test strip(s) and ask, "Does icodextrin or maltose interfere with my glucose monitor or test strip results?"
- **You must notify your PD nurse and dialysis doctor before you change** your home glucose monitor(s) or test strip(s)
- It's important to regularly check the test method of your glucose monitor(s) and test strips(s) while using **Extraneal** PD Solution. Also, if the manufacturer that makes your glucose monitor or test strips changes its methods of glucose measurement, be sure to contact your PD nurse of dialysis doctor to let them know. They can help you make the necessary adjustments

Be sure to discuss this important information about glucose monitors with your family and friends. In an emergency, they will be able to make sure the nurse or doctor knows of the potential for false high glucose readings.

If you receive medical care from doctors or nurses other than those in your PD clinic, be sure to:

- Tell the doctors and nurses that you are using **Extraneal** PD solution, and that some glucose monitors and test strips may give a false high glucose reading
- Take the **Extraneal** PD Solution Patient Kit with you and give it to the doctor or nurse treating you. This kit has additional information related to glucose monitors for doctors and nurses
- Even if you stop using **Extraneal** PD solution, this will not resolve the potential for interference with glucose monitors or test strips. Your blood will have increased levels of icodextrin and maltose for approximately 14 days after stopping the use of **Extraneal** PD solution

Also present your wallet card, which explains that maltose may interfere with some glucose monitors. A wallet card is included here.

If you have any questions concerning glucose monitors and/or glucose test results, call your PD nurse or the Emergency Contact number shown on the reverse side of your wallet card.

See reverse side for warnings

Patient Name

Is using EXTRANEAL (icodextrin) peritoneal dialysis solution

Emergency Contact Information

Nephrologist _____ ( ) _____
PD Nurse/Center _____ ( ) _____
Other Contact _____ ( ) _____

Extraneal (icodextrin) PD Solution Patient Kit

Because you are on **Extraneal** PD solution, you'll soon receive an **Extraneal** PD Solution Patient Kit delivered to your home. This kit will contain tools you need to safely use **Extraneal** PD solution, along with information for clinicians on measuring blood glucose levels. Your PD nurse will also show you a sample of the kit and explain all of the components that are included.

Whenever you receive medical care – whether it's a scheduled appointment, an outpatient procedure or an emergency room visit – be sure to bring your Extraneal PD Solution Patient Kit along with you.

Included in the kit are a bracelet and a necklace that are designed to alert clinicians about the potential for incorrect blood glucose measurements. You should wear one or the other to alert clinicians so they use the right kind of glucose monitor and test strips for you.

Bracelet

The kit also contains important medical information for doctors, nurses and clinicians who provide care to you, other than those at your PD clinic. That's why it's so important to take the kit with you when receiving medical care. Simply give it to the nurse or physician who is seeing you.

Specifically, the "For Clinicians" portion of the kit contains letters to doctors, nurses and other professionals at a hospital or clinic. These letters describe the potential for interference with certain glucose monitors and test strips, and provide information to let them know the appropriate test methods to use. The patient chart sticker and hang tag provided in your kit are tools your clinician may want to use to remind them about your history, and can be attached to your medical chart.

Necklace

Protect Yourself. Take These Steps Below.

If you are a MedicAlert member, inform them that you use **Extraneal** PD solution as soon as possible. **Call 1-888-633-4298 today** to update your records and bracelet, or to become a member.

If you are not a MedicAlert member, enroll today and receive a FREE* stainless steel bracelet or pendant, or be sure to wear the **Extraneal** PD solution bracelet or necklace provided by Baxter in your **Extraneal** PD Solution Patient Kit.

Either action could save your life.

If you require a replacement kit, please order one through your Baxter HomeCare Services Representative (HCSR) Team at 1-800-284-4060.

* Pay only $39.95 for your first year's membership and receive any of the stainless steel bracelets or pendants along with free shipping (a $15.00 savings). To receive this offer, please reference code **5746** when becoming a member.

Glucose Monitor Manufacturers

The following list provides the names and contact information for manufacturers of today's most commonly used glucose monitors and test strips. It is included for reference only; you or your PD nurse need to contact the manufacturer to ensure that your monitor and test strips use a method that does not cause maltose interference with test results. **This list does not indicate that Baxter is recommending these products**. You or your PD nurse should call the manufacturer to verify if the monitor and/or test strip measures only glucose. The list is current as of September 2010.

Manufacturer	Contact Information
Abbott Diabetes Care	888-522-5226 www.abbottdiabetescare.com
Arkray	800-818-8877, Option #5 www.arkrayusa.com
Bayer Healthcare	800-348-8100 www.bayerdiabetes.com
Lifescan, Inc (Division of Johnson & Johnson)	800-227-8862 www.lifescan.com
Roche Diagnostics	800-858-8072 www.roche-diagnostics.com www.accu-chek.com

Important Risk Information for **Extraneal** (icodextrin) PD Solution

Do not use **Extraneal** PD solution if you:

- have a glycogen storage disease
- cannot tolerate maltose or isomaltose
- have severe lactic acidosis
- are allergic to cornstarch or icodextrin

Extraneal may not be right for you. Before using **Extraneal** PD solution, tell your doctor about all your medical conditions, including if you have:

- a condition that affects your nutrition
- low potassium levels in your blood
- low magnesium levels in your blood
- had stomach area:
  - surgery in the past 30 days
  - tumors
  - open wounds or an infection
  - hernia
- a lung or breathing problem
- high calcium levels in your blood
- had recent aortic graft surgery
- have certain bowel conditions including:
  - colostomy or ileostomy
  - frequent episodes of diverticulitis
  - inflammatory bowel disease
- are pregnant or plan to become pregnant. It is not known if **Extraneal** PD solution will harm your unborn baby
- are breast-feeding. It is not known if **Extraneal** PD solution passes into your breast milk

Extraneal can cause serious side effects, including:

- **Serious allergic reactions.** Tell your doctor or get medical help right away if you get any of these symptoms of a serious allergic reaction during treatment with **Extraneal**;
  - swelling of your face, eyes, lips, tongue or mouth
  - trouble swallowing or breathing
  - skin rash, hives, sores in your mouth, on your eyelids, or in your eyes
  - your skin blisters or peels

Common side effects of **Extraneal** PD solution include:

- Peritonitis, an infection in the peritoneal (abdominal) cavity, which is common in people on peritoneal dialysis. Tell your doctor right away if you have any pain, redness, fever, or cloudy drained fluid
- High blood pressure, nausea, headache, swelling, stomach area (abdomen) pain, chest pain, increased cough, upset stomach, flu-like symptoms, high blood sugar

These are not all the possible side effects of **Extraneal** PD solution. For more information, ask your doctor or dialysis center. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088 or at www.fda.gov/medwatch.

For additional information please see the **Extraneal** PD Solution Medication Guide.

What you should know about **Extraneal** (icodextrin) PD Solution

1. It's important to do your dialysis daily as your doctor has prescribed. Use **Extraneal** PD solution for your long dwell (8 to 16 hours).
2. It's equally important to do your PD exchanges just as you were taught, every time.
3. To track your progress, record your weight, blood pressure, and how you feel every day. If there are any changes, be sure to let your PD nurse know right away.
4. Always keep some 1.5% dextrose solution at home. Why?
   - Using both 4.25% dextrose solution and **Extraneal** PD solution may cause you to become dehydrated, and your doctor may direct you to use 1.5% dextrose
   - If you are dehydrated, you may feel dizzy or become weak. Report these symptoms to your PD nurse or doctor immediately
5. Talk to you PD nurse or dialysis doctor about adding any medications to **Extraneal** PD solution.
6. If you're a Continuous Ambulatory Peritoneal Dialysis (CAPD) patient – and you notice a black-blue color in the drain line when switching from dextrose solutions to **Extraneal** PD solution – don't worry. The color appears when **Extraneal** PD soltution mixes with leftover povidone-iodine in the **MiniCap** Disconnect Cap.
7. If you have insulin-dependent diabetes, pay attention to your insulin dose and monitor your blood sugar levels when using **Extraneal** PD Solution. Here are a few guidelines to follow:
   - Only use glucose-specific monitors and test strips to measure blood glucose levels
   - **See Important Risk Information about glucose monitors and test strips on Page 2 and the Extraneal Medication Guide for additional cautionary measures**
   - Be sure to check your blood sugar levels regularly
   - Discuss any changes needed to your current insulin dosage with your PD nurse or dialysis doctor. You may need to alter your insulin dose
8. **Extraneal** PD solution is best stored at room temperature: 68-77°F (20-25°C).
   - Until you use it, keep **Extraneal** PD solution in its moisture barrier overpouch in its carton
   - Avoid high heat (104°F/40°C) and protect from freezing

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Attachment 3

Extraneal Patient Kit

EXTRANEAL PATIENT KIT: DEAR PATIENT LETTER

Attention EXTRANEAL Patient

Important Information About EXTRANEAL (icodextrin) Peritoneal Dialysis (PD) Solution and Measuring Blood Sugar

Dear Patient,

This patient kit has been created to protect you from false blood glucose (sugar) readings while using **EXTRANEAL** (icodextrin) Peritoneal Dialysis (PD) solution. Your PD nurse should have reviewed the contents of this kit, and what you need to do when measuring blood sugar. If your PD nurse has not reviewed this information with you, be sure to talk about this at your next regular visit.

EXTRANEAL PD solution contains maltose, which can react with certain blood glucose monitors and test strips. Using **EXTRANEAL** PD solution may cause a false (incorrect) high blood sugar reading or may hide a blood sugar reading that is actually very low. This can happen if you use a glucose monitor or test strips that use glucose dehydrogenase pyrroloquinolinequinone (GDH-PQQ) or glucose-dye-oxidoreaductase (GDO) methods. In addition, some but not all monitors or test strips that utilize a glucose dehydrogenase flavin-adenine dinucleotide (GDH-FAD) method must not be used. Use of these methods may result in falsely elevated blood glucose readings in patients using **EXTRANEAL** (icodextrin) due to maltose interference at any time during treatment with **EXTRANEAL** PD solution or within approximately 2 weeks (14 days) after you stop treatment with **EXTRANEAL** PD solution. A false reading means that your blood sugar may really be too low even though the test says that it is normal or high. This can lead to dangerous side effects.

So which items are important to use and wear and why?

You should have received a wallet card during training from your PD nurse. If you always keep this card in your wallet, it can help you to share the risk information with other clinicians you are seeing, or if you are hospitalized. Please always carry it with you. In addition, use this card to inform other doctors and nurses treating you about your potentially falsely high blood glucose readings.

Whenever you receive medical care – whether it's a scheduled appointment, an outpatient procedure or an emergency room visit – be sure to bring your **EXTRANEAL** PD Solution Patient Kit along with you. The information contained in your **patient kit** will explain the glucose test issue to the different hospital departments. Please be sure to make family and friends aware of the kit, and tell them to bring it to the hospital in cases where you can't take it yourself.

The kit also contains important medical information for doctors, nurses and clinicians who provide care to you, other than those at your PD clinic. That's why it's so important to take the kit with you when receiving medical care. Simply give it to the nurse or physician who is seeing you.

Also included in the kit are a **bracelet** and a **necklace** that are designed to alert clinicians about the potential for incorrect blood glucose measurements. You should wear one or the other to alert clinicians in an emergency or if you are hospitalized.

Should you lose any of the items or need a replacement, please order these items through your Baxter HomeCare Services Representative (HCSR) Team. Your safety is very important to us. Please use the items as recommended.

We hope this information is helpful to you. If you have additional questions about **EXTRANEAL** PD solution or measuring blood sugar, please contact your PD nurse.

Sincerely,

Your Baxter Support Team

Please see Important Risk Information on reverse side and enclosed Medication Guide.

This letter is part of an FDA approved REMS

INDICATION FOR PATIENTS

EXTRANEAL is indicated for a single daily exchange for the long (8- to 16-hour) dwell during continuous ambulatory peritoneal dialysis (CAPD) or automated peritoneal dialysis (APD) for the management of end-stage renal disease. **EXTRANEAL** is also indicated to improve (compared to 4.25% dextrose) long-dwell ultrafiltration and clearance of creatinine and urea nitrogen in patients with high average or greater transport characteristics, as defined using the peritoneal equilibration test (PET).

IMPORTANT RISK INFORMATION FOR PATIENTS

EXTRANEAL PD solution contains maltose, which can react with certain blood glucose (blood sugar) monitors and test strips.

- Using **EXTRANEAL** PD solution may cause a false (incorrect) high blood sugar reading or may hide a blood sugar reading that is actually very low. This kind of false reading means that your blood sugar may really be too low even though the test says that it is normal or high. This can lead to dangerous side effects
- **Only use a glucose-specific monitor and test strips to monitor your blood glucose when being treated with EXTRANEAL and approximately 2 weeks after stopping EXTRANEAL**
- **If you are hospitalized or go to an emergency room, take your EXTRANEAL PD Solution Patient Kit along with you and tell the hospital staff that you use EXTRANEAL PD solution so that they use the right kind of blood glucose monitor and test strips for you**
- **Taking too much insulin or waiting too long to treat low blood sugar can cause you to have serious reactions including: loss of consciousness (passing out), coma, permanent neurological problems, or death**

Do not use **EXTRANEAL** PD solution if you:

- have a glycogen storage disease
- cannot tolerate maltose or isomaltose
- have severe lactic acidosis
- are allergic to cornstarch or icodextrin

EXTRANEAL may not be right for you. Before using **EXTRANEAL** PD solution, tell your doctor about all your medical conditions, including if you have:

- a condition that affects your nutrition
- low potassium levels in your blood
- low magnesium levels in your blood
- had stomach area:
  - surgery in the past 30 days
  - tumors
  - open wounds or an infection
  - hernia
- a lung or breathing problem
- high calcium levels in your blood
- had recent aortic graft surgery
- have certain bowel conditions including:
  - colostomy or ileostomy
  - frequent episodes of diverticulitis
  - inflammatory bowel disease
- are pregnant or plan to become pregnant. It is not known if **EXTRANEAL** PD solution will harm your unborn baby
- are breast-feeding. It is not known if **EXTRANEAL** PD solution passes into your breast milk

EXTRANEAL can cause serious side effects, including:

Serious allergic reactions. Tell your doctor or get medical help right away if you get any of these symptoms of a serious allergic reaction during treatment with **EXTRANEAL**;

- swelling of your face, eyes, lips, tongue or mouth
- trouble swallowing or breathing
- skin rash, hives, sores in your mouth, on your eyelids, or in your eyes
- your skin blisters and peels

Common side effects of **EXTRANEAL** PD solution include:

- Peritonitis, an infection in the peritoneal (abdominal) cavity, which is common in people on peritoneal dialysis. Tell your doctor right away if you have any pain, redness, fever, or cloudy drained fluid
- High blood pressure, nausea, headache, swelling, stomach area (abdomen) pain, chest pain, increased cough, upset stomach, flu-like symptoms, high blood sugar

These are not all the possible side effects of **EXTRANEAL** PD solution. For more information, ask your doctor or dialysis center. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088 or at www.fda.gov/medwatch.

For additional information please see the **EXTRANEAL** PD Solution Medication Guide.

EXTRANEAL PATIENT KIT: WALLET CARD:

WARNING

Potential for Incorrect Blood Glucose Reading

ONLY use glucose-specific monitors and test strips on this peritoneal dialysis patient. Some glucose monitors are not glucose-specific and cannot tell the difference between glucose and other sugars in the blood (e.g., maltose, a metabolite of icodextrin). Use laboratory-based methods, if available or a glucose-specific monitor and test strips.

DO NOT use glucose monitors or test strips that utilize glucose dehydrogenase pyrroloquinolinequinone (GDH-PQQ) or glucose-dye-oxidoreductase methods. In addition, some but not all monitors or test strips that utilize a glucose dehydrogenase flavin-adenine dinucleotide (GDH-FAD) method must not be used. Use of these methods may result in falsely elevated blood glucose readings in patients using **Extraneal** (icodextrin) Peritoneal Dialysis Solution due to maltose interference. Falsely elevated blood glucose readings may mask true hypoglycemia or lead to the erroneous diagnosis of hyperglycemia. Treatment decisions based on incorrect blood glucose readings may lead to life-threatening events.

Visit www.glucosesafety.com for additional information, including a glucose monitor compatibility list.

Baxter

See reverse side for warnings

Patient Name

Is using EXTRANEAL (icodextrin) peritoneal dialysis solution

Emergency Contact Information

Nephrologist _____ ( ) _____

PD Nurse/Center _____ ( ) _____

Other Contact _____ ( ) _____

EXTRANEAL PATIENT KIT: WEARABLE ITEMS:

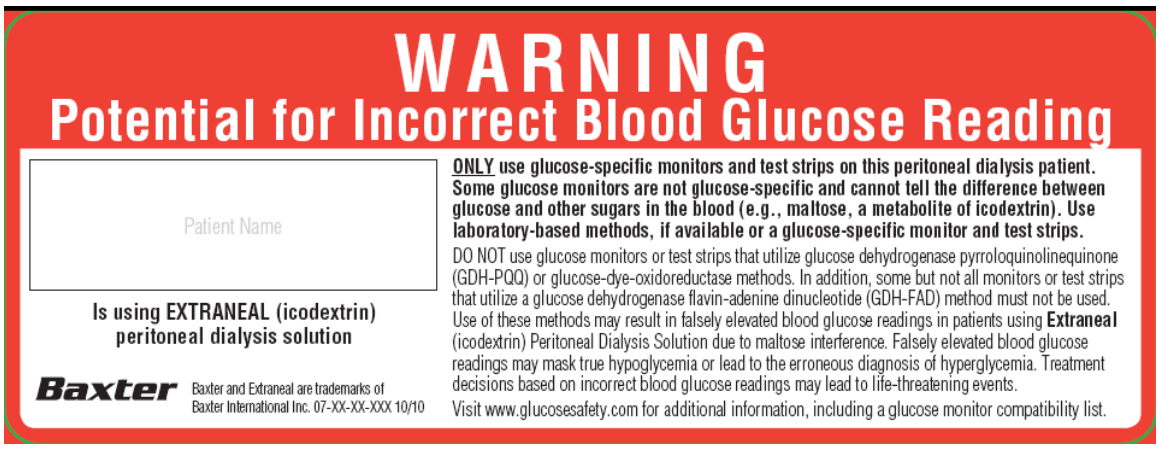
Bracelet

EXTRANEAL PATIENT KIT: WEARABLE ITEMS (continued):

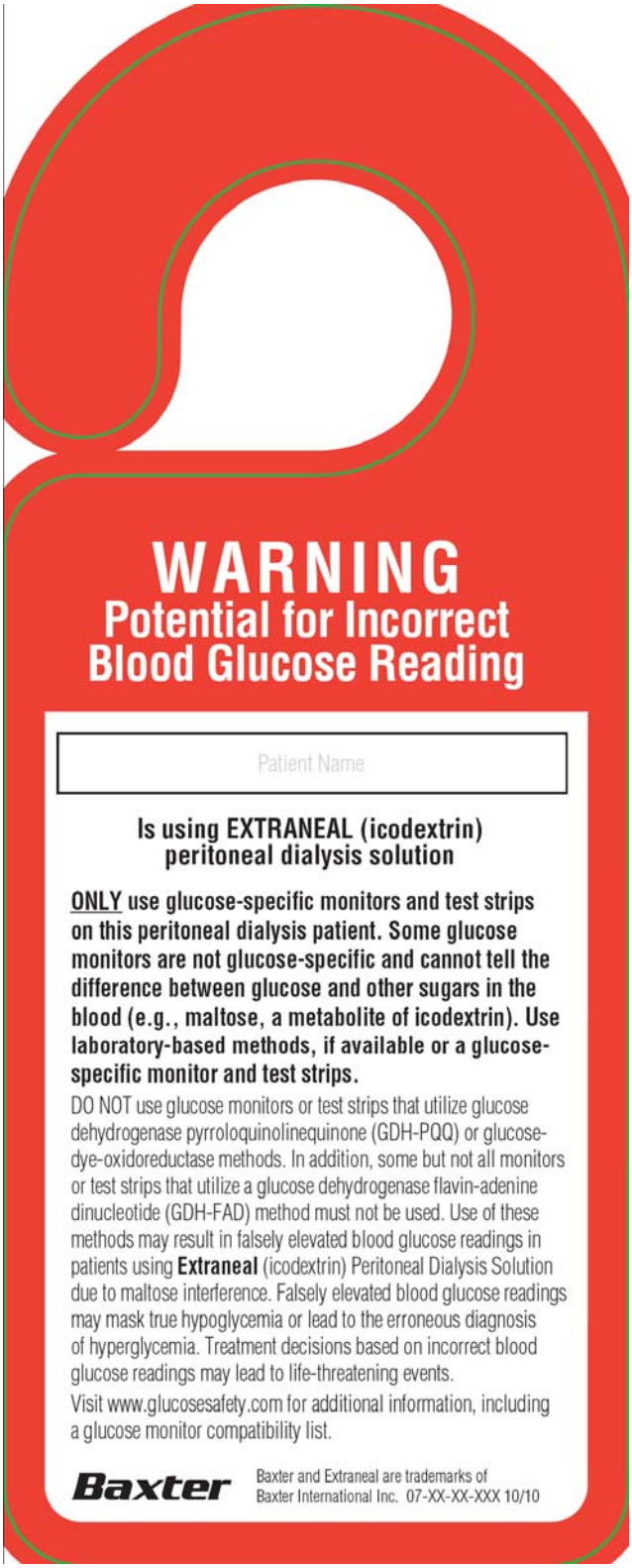
Pendant

FRONT **BACK**

EXTRANEAL PATIENT KIT: CHART STICKER



EXTRANEAL PATIENT KIT: MAGNETIC HANG TAG



Attention Hospital Physician

WARNING

Potential For Incorrect Blood Glucose Reading

November 2010

Dear Hospital Physician,

Baxter Healthcare Corporation would like to notify you of Important Safety Information involving all patients who use **EXTRANEAL** (icodextrin) Peritoneal Dialysis (PD) solution and who may require the use of blood glucose monitors and test strips.

Patients using EXTRANEAL (icodextrin) peritoneal dialysis solution may have incorrect blood glucose results when using particular blood glucose monitors and test strips.

ONLY use glucose monitors and test strips that are glucose-specific. Some glucose monitors are not glucose-specific and cannot tell the difference between glucose and other sugars in the blood (e.g., maltose, a metabolite of icodextrin). Use laboratory-based methods, if available or a glucose-specific monitor and test strips. Contact the manufacturer of the glucose monitors and test strips to determine the method that is used. Visit www.glucosesafety.com for additional information including a glucose monitor compatibility list.

The term "glucose-specific" applies to monitors or test strips that are not affected by the presence of maltose or certain other sugars. Because **EXTRANEAL** (icodextrin) PD solution results in elevated blood levels of maltose, only glucose-specific monitors and test strips should be used.

DO NOT use glucose monitors or test strips that utilize glucose dehydrogenase pyrroloquinolinequinone (GDH-PQQ) or glucose-dye-oxidoreductase (GDO) methods. In addition, some but not all monitors or test strips that utilize a glucose dehydrogenase flavin-adenine dinucleotide (GDH-FAD) method must not be used. Use of these methods may result in falsely elevated blood glucose readings in patients using **EXTRANEAL** (icodextrin) due to maltose interference. A blood glucose reading with these monitors that appears to be within the normal range in a patient on **EXTRANEAL** (icodextrin) may mask true hypoglycemia (low blood sugar). This would cause a patient or health care professional not to take the appropriate steps to bring the blood sugar into a normal range. A falsely elevated blood glucose reading could cause a patient to get more insulin than needed. Both of these situations can lead to life-threatening events, including loss of consciousness, coma, permanent neurological damage or death.

Additional considerations for patients who use **EXTRANEAL** (icodextrin) PD solution:

1. Discontinuing **EXTRANEAL** (icodextrin) PD solution use will not immediately address the risk for the potential interference with glucose monitors. Falsely elevated glucose levels may result up to two weeks following cessation of **EXTRANEAL** (icodextrin).
2. To determine what type of method is used for monitoring glucose levels, review the labeling for BOTH the glucose monitor and the test strips used. If in doubt, contact the manufacturer of the glucose monitors and test strips to determine the method that is used.
3. If your hospital uses electronic medical records, the above information describing the potential for interference with blood glucose monitors or test strips needs to be entered in a suitable field that is readily apparent to all users.

For further information, refer to **EXTRANEAL** (icodextrin) PD solution prescribing information enclosed or visit www.glucosesafety.com.

I hope this information is helpful to you. If you have additional questions about **EXTRANEAL** (icodextrin) PD solution, please contact your Baxter Renal Representative.

Sincerely,

James A. Sloand, MD
Senior Medical Director, Medical Affairs
Baxter Healthcare Corporation

Please see Important Risk Information on reverse side and enclosed Full Prescribing Information.

This letter is part of an FDA approved REMS

IMPORTANT RISK INFORMATION
EXTRANEAL (icodextrin) Peritoneal Dialysis (PD) Solution

Dangerous Drug-Device Interaction
Only use glucose-specific monitors and test strips to measure blood glucose levels in patients using EXTRANEAL (icodextrin) Peritoneal Dialysis Solution. Blood glucose monitoring devices using glucose dehydrogenase pyrroloquinolinequinone (GDH-PQQ) or glucose-dye-oxidoreductase (GDO)-based methods must not be used. In addition, some blood glucose monitoring systems using glucose dehydrogenase flavin-adenine dinucleotide (GDH-FAD)-based methods must not be used. Use of GDH-PQQ, GDO, and GDH-FAD-based glucose monitors and test strips has resulted in falsely elevated glucose readings (due to the presence of maltose, see **PRECAUTIONS/Drug/Laboratory Test Interactions**). Falsely elevated glucose readings have led patients or health care providers to withhold treatment of hypoglycemia or to administer insulin inappropriately. Both of these situations have resulted in unrecognized hypoglycemia, which has led to loss of consciousness, coma, permanent neurological damage, and death. Plasma levels of EXTRANEAL (icodextrin) and its metabolites return to baseline within approximately 14 days following cessation of EXTRANEAL (icodextrin) administration. Therefore falsely elevated glucose levels may be measured up to two weeks following cessation of EXTRANEAL (icodextrin) therapy when GDH-PQQ, GDO, and GDH-FAD based blood glucose monitors and test strips are used.

Because GDH-PQQ, GDO, and GDH-FAD-based blood glucose monitors may be used in hospital settings, it is important that the health care providers of peritoneal dialysis patients using EXTRANEAL (icodextrin) carefully review the product information of the blood glucose testing system, including that of test strips, to determine if the system is appropriate for use with EXTRANEAL (icodextrin).

To avoid improper insulin administration, educate patients to alert health care providers of this interaction whenever they are admitted to the hospital.

The manufacturer(s) of the monitor and test strips should be contacted to determine if icodextrin or maltose causes interference or falsely elevated glucose readings. For a list of toll free numbers for glucose monitor and test strip manufacturers, please contact the Baxter Renal Clinical HelpLine 1-888-RENAL-HELP or visit www.glucosesafety.com.

EXTRANEAL PD solution is contraindicated in patients with a known allergy to cornstarch or icodextrin, in patients with maltose or isomaltose intolerance, in patients with pre-existing severe lactic acidosis, and in patients with glycogen storage disease.

EXTRANEAL PD solution is intended for intraperitoneal administration only. Not for intravenous injection.

Rarely, serious hypersensitivity reactions to EXTRANEAL have been reported, such as toxic epidermal necrolysis, angioedema, serum sickness, erythema multiforme, and leukocytoclastic vasculitis. If a serious reaction is suspected, discontinue EXTRANEAL and institute appropriate treatment as clinically indicated.

Patients with insulin-dependent diabetes may require modification of insulin dosage following initiation of treatment.

A patient's volume status should be carefully monitored to avoid hyper- or hypovolemia and potentially severe consequences including congestive heart failure, volume depletion and hypovolemic shock. An accurate fluid balance record must be kept and the patient's body weight monitored.

In clinical trials, the most frequently reported adverse events occurring in ≥ 10% of patients, and more common in EXTRANEAL PD solution patients than in control patients, were peritonitis, upper respiratory infection, hypertension, and rash. The most common treatment-related adverse event for EXTRANEAL PD solution patients was skin rash. Additional adverse reactions have been reported in the post-marketing setting and are detailed in the full prescribing information.

General Peritoneal Dialysis-Related
Encapsulating Peritoneal Sclerosis (EPS) is a known, rare complication of peritoneal dialysis therapy. EPS has been reported in patients using peritoneal dialysis solutions including EXTRANEAL PD solution. Infrequent but fatal outcomes have been reported.

Aseptic technique should be used throughout the peritoneal dialysis procedure to reduce the possibility of infection, such as peritonitis.

Fluid status, hematologic indices, blood chemistry, and electrolyte concentrations, including calcium, potassium, sodium, magnesium and bicarbonate, should be monitored periodically. Abnormalities in any of these parameters should be treated promptly under the care of a physician.

Overinfusion of peritoneal dialysis solution volume into the peritoneal cavity may be characterized by abdominal distention, feeling of fullness and/or shortness of breath. Treatment of overinfusion is to drain the peritoneal dialysis solution from the peritoneal cavity.

Treatment should be initiated and monitored under the supervision of a physician knowledgeable in the management of patients with renal failure.

Please see full prescribing information.

Attention Hospital Nurse

WARNING

Potential For Incorrect Blood Glucose Reading

November 2010

Dear Hospital Nurse,

Baxter Healthcare Corporation would like to notify you of Important Safety Information involving all patients who use **EXTRANEAL** (icodextrin) Peritoneal Dialysis (PD) solution and who may require the use of blood glucose monitors and test strips.

Patients using EXTRANEAL (icodextrin) peritoneal dialysis solution may have incorrect blood glucose results when using particular blood glucose monitors and test strips.

ONLY use glucose monitors and test strips that are glucose-specific. Some glucose monitors are not glucose-specific and cannot tell the difference between glucose and other sugars in the blood (e.g., maltose, a metabolite of icodextrin). Use laboratory-based methods, if available or a glucose-specific monitor and test strips. Contact the manufacturer of the glucose monitors and test strips to determine the method that is used. Visit www.glucosesafety.com for additional information including a glucose monitor compatibility list.

The term "glucose-specific" applies to monitors or test strips that are not affected by the presence of maltose or certain other sugars. Because **EXTRANEAL** (icodextrin) PD solution results in elevated blood levels of maltose, only glucose-specific monitors and test strips should be used.

DO NOT use glucose monitors or test strips that utilize glucose dehydrogenase pyrroloquinolinequinone (GDH-PQQ) or glucose-dye-oxidoreductase (GDO) methods. In addition, some but not all monitors or test strips that utilize a glucose dehydrogenase flavin-adenine dinucleotide (GDH-FAD) method must not be used. Use of these methods may result in falsely elevated blood glucose readings in patients using **EXTRANEAL** (icodextrin) due to maltose interference. A blood glucose reading with these monitors that appears to be within the normal range in a patient on **EXTRANEAL** (icodextrin) may mask true hypoglycemia (low blood sugar). This would cause a patient or health care professional not to take the appropriate steps to bring the blood sugar into a normal range. A falsely elevated blood glucose reading could cause a patient to get more insulin than needed. Both of these situations can lead to life-threatening events, including loss of consciousness, coma, permanent neurological damage or death.

Additional considerations for patients who use **EXTRANEAL** (icodextrin) PD solution:

1. Discontinuing **EXTRANEAL** (icodextrin) PD solution use will not immediately address the risk for the potential interference with glucose monitors. Falsely elevated glucose levels may result up to two weeks following cessation of **EXTRANEAL** (icodextrin).
2. To determine what type of method is used for monitoring glucose levels, review the labeling for BOTH the glucose monitor and the test strips used. If in doubt, contact the manufacturer of the glucose monitors and test strips to determine the method that is used.
3. If your hospital uses electronic medical records, the above information describing the potential for interference with blood glucose monitors or test strips needs to be entered in a suitable field that is readily apparent to all users.

For further information, refer to **EXTRANEAL** (icodextrin) PD solution prescribing information enclosed or visit www.glucosesafety.com.

I hope this information is helpful to you. If you have additional questions about **EXTRANEAL** (icodextrin) PD solution, please contact your Baxter Renal Representative.

Sincerely,

James A. Sloand, MD
Senior Medical Director, Medical Affairs
Baxter Healthcare Corporation

Please see Important Risk Information on reverse side and enclosed Full Prescribing Information.

This letter is part of an FDA approved REMS

IMPORTANT RISK INFORMATION
EXTRANEAL (icodextrin) Peritoneal Dialysis (PD) Solution

Dangerous Drug-Device Interaction
Only use glucose-specific monitors and test strips to measure blood glucose levels in patients using EXTRANEAL (icodextrin) Peritoneal Dialysis Solution. Blood glucose monitoring devices using glucose dehydrogenase pyrroloquinolinequinone (GDH-PQQ) or glucose-dye-oxidoreductase (GDO)-based methods must not be used. In addition, some blood glucose monitoring systems using glucose dehydrogenase flavin-adenine dinucleotide (GDH-FAD)-based methods must not be used. Use of GDH-PQQ, GDO, and GDH-FAD-based glucose monitors and test strips has resulted in falsely elevated glucose readings (due to the presence of maltose, see **PRECAUTIONS/Drug/Laboratory Test Interactions**). Falsely elevated glucose readings have led patients or health care providers to withhold treatment of hypoglycemia or to administer insulin inappropriately. Both of these situations have resulted in unrecognized hypoglycemia, which has led to loss of consciousness, coma, permanent neurological damage, and death. Plasma levels of EXTRANEAL (icodextrin) and its metabolites return to baseline within approximately 14 days following cessation of EXTRANEAL (icodextrin) administration. Therefore falsely elevated glucose levels may be measured up to two weeks following cessation of EXTRANEAL (icodextrin) therapy when GDH-PQQ, GDO, and GDH-FAD based blood glucose monitors and test strips are used.

Because GDH-PQQ, GDO, and GDH-FAD-based blood glucose monitors may be used in hospital settings, it is important that the health care providers of peritoneal dialysis patients using EXTRANEAL (icodextrin) carefully review the product information of the blood glucose testing system, including that of test strips, to determine if the system is appropriate for use with EXTRANEAL (icodextrin).

To avoid improper insulin administration, educate patients to alert health care providers of this interaction whenever they are admitted to the hospital.

The manufacturer(s) of the monitor and test strips should be contacted to determine if icodextrin or maltose causes interference or falsely elevated glucose readings. For a list of toll free numbers for glucose monitor and test strip manufacturers, please contact the Baxter Renal Clinical HelpLine 1-888-RENAL-HELP or visit www.glucosesafety.com.

EXTRANEAL PD solution is contraindicated in patients with a known allergy to cornstarch or icodextrin, in patients with maltose or isomaltose intolerance, in patients with pre-existing severe lactic acidosis, and in patients with glycogen storage disease.

EXTRANEAL PD solution is intended for intraperitoneal administration only. Not for intravenous injection.

Rarely, serious hypersensitivity reactions to EXTRANEAL have been reported, such as toxic epidermal necrolysis, angioedema, serum sickness, erythema multiforme, and leukocytoclastic vasculitis. If a serious reaction is suspected, discontinue EXTRANEAL and institute appropriate treatment as clinically indicated.

Patients with insulin-dependent diabetes may require modification of insulin dosage following initiation of treatment.

A patient's volume status should be carefully monitored to avoid hyper- or hypovolemia and potentially severe consequences including congestive heart failure, volume depletion and hypovolemic shock. An accurate fluid balance record must be kept and the patient's body weight monitored.

In clinical trials, the most frequently reported adverse events occurring in ≥ 10% of patients, and more common in EXTRANEAL PD solution patients than in control patients, were peritonitis, upper respiratory infection, hypertension, and rash. The most common treatment-related adverse event for EXTRANEAL PD solution patients was skin rash. Additional adverse reactions have been reported in the post-marketing setting and are detailed in the full prescribing information.

General Peritoneal Dialysis-Related
Encapsulating Peritoneal Sclerosis (EPS) is a known, rare complication of peritoneal dialysis therapy. EPS has been reported in patients using peritoneal dialysis solutions including EXTRANEAL PD solution. Infrequent but fatal outcomes have been reported.

Aseptic technique should be used throughout the peritoneal dialysis procedure to reduce the possibility of infection, such as peritonitis.

Fluid status, hematologic indices, blood chemistry, and electrolyte concentrations, including calcium, potassium, sodium, magnesium and bicarbonate, should be monitored periodically. Abnormalities in any of these parameters should be treated promptly under the care of a physician.

Overinfusion of peritoneal dialysis solution volume into the peritoneal cavity may be characterized by abdominal distention, feeling of fullness and/or shortness of breath. Treatment of overinfusion is to drain the peritoneal dialysis solution from the peritoneal cavity.

Treatment should be initiated and monitored under the supervision of a physician knowledgeable in the management of patients with renal failure.

Please see full prescribing information.

Attention Hospital Pharmacy

WARNING

Potential For Incorrect Blood Glucose Reading

November 2010

Dear Director of Pharmacy,

Baxter Healthcare Corporation would like to notify you of Important Safety Information involving all patients who use **EXTRANEAL** (icodextrin) Peritoneal Dialysis (PD) solution and who may require the use of blood glucose monitors and test strips.

Patients using EXTRANEAL (icodextrin) peritoneal dialysis solution may have incorrect blood glucose results when using particular blood glucose monitors and test strips.

ONLY use glucose monitors and test strips that are glucose-specific. Some glucose monitors are not glucose-specific and cannot tell the difference between glucose and other sugars in the blood (e.g., maltose, a metabolite of icodextrin). Use laboratory-based methods, if available or a glucose-specific monitor and test strips. Contact the manufacturer of the glucose monitors and test strips to determine the method that is used. Visit www.glucosesafety.com for additional information including a glucose monitor compatibility list.

The term "glucose-specific" applies to monitors or test strips that are not affected by the presence of maltose or certain other sugars. Because **EXTRANEAL** (icodextrin) PD solution results in elevated blood levels of maltose, only glucose-specific monitors and test strips should be used.

DO NOT use glucose monitors or test strips that utilize glucose dehydrogenase pyrroloquinolinequinone (GDH-PQQ) or glucose-dye-oxidoreductase (GDO) methods. In addition, some but not all monitors or test strips that utilize a glucose dehydrogenase flavin-adenine dinucleotide (GDH-FAD) method should not be used. Use of these methods may result in falsely elevated blood glucose readings in patients using **EXTRANEAL** (icodextrin) due to maltose interference. A blood glucose reading with these monitors that appears to be within the normal range in a patient on **EXTRANEAL** (icodextrin) may mask true hypoglycemia (low blood sugar). This would cause a patient or health care professional not to take the appropriate steps to bring the blood sugar into a normal range. A falsely elevated blood glucose reading could cause a patient to get more insulin than needed. Both of these situations can lead to life-threatening events, including loss of consciousness, coma, permanent neurological damage or death.

Additional considerations for patients who use **EXTRANEAL** (icodextrin) PD solution:

1. Discontinuing **EXTRANEAL** (icodextrin) PD solution use will not immediately address the risk for the potential interference with glucose monitors. Falsely elevated glucose levels may result up to two weeks following cessation of **EXTRANEAL** (icodextrin).
2. To determine what type of method is used for monitoring glucose levels, review the labeling for BOTH the glucose monitor and the test strips used. If in doubt, contact the manufacturer of the glucose monitors and test strips to determine the method that is used.
3. If your hospital uses electronic medical records, the above information describing the potential for interference with blood glucose monitors or test strips needs to be entered in a suitable field that is readily apparent to all users.

For further information, refer to **EXTRANEAL** (icodextrin) PD solution prescribing information enclosed or visit www.glucosesafety.com.

I hope this information is helpful to you. If you have additional questions about **EXTRANEAL** (icodextrin) PD solution, please contact your Baxter Renal Representative.

Sincerely,

James A. Sloand, MD
Senior Medical Director, Medical Affairs
Baxter Healthcare Corporation

Please see Important Risk Information on reverse side and enclosed Full Prescribing Information.

This letter is part of an FDA approved REMS

IMPORTANT RISK INFORMATION
EXTRANEAL (icodextrin) Peritoneal Dialysis (PD) Solution

Dangerous Drug-Device Interaction
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Because GDH-PQQ, GDO, and GDH-FAD-based blood glucose monitors may be used in hospital settings, it is important that the health care providers of peritoneal dialysis patients using EXTRANEAL (icodextrin) carefully review the product information of the blood glucose testing system, including that of test strips, to determine if the system is appropriate for use with EXTRANEAL (icodextrin).

To avoid improper insulin administration, educate patients to alert health care providers of this interaction whenever they are admitted to the hospital.

The manufacturer(s) of the monitor and test strips should be contacted to determine if icodextrin or maltose causes interference or falsely elevated glucose readings. For a list of toll free numbers for glucose monitor and test strip manufacturers, please contact the Baxter Renal Clinical HelpLine 1-888-RENAL-HELP or visit www.glucosesafety.com.

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General Peritoneal Dialysis-Related
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Aseptic technique should be used throughout the peritoneal dialysis procedure to reduce the possibility of infection, such as peritonitis.

Fluid status, hematologic indices, blood chemistry, and electrolyte concentrations, including calcium, potassium, sodium, magnesium and bicarbonate, should be monitored periodically. Abnormalities in any of these parameters should be treated promptly under the care of a physician.

Overinfusion of peritoneal dialysis solution volume into the peritoneal cavity may be characterized by abdominal distention, feeling of fullness and/or shortness of breath. Treatment of overinfusion is to drain the peritoneal dialysis solution from the peritoneal cavity.

Treatment should be initiated and monitored under the supervision of a physician knowledgeable in the management of patients with renal failure.

Please see full prescribing information.

Attention Laboratory Services
WARNING
Potential For Incorrect Blood Glucose Reading

November 2010

Dear Director of Laboratory Services,

Baxter Healthcare Corporation would like to notify you of Important Safety Information involving all patients who use **EXTRANEAL** (icodextrin) Peritoneal Dialysis (PD) solution and who may require the use of blood glucose monitors and test strips.

Patients using EXTRANEAL (icodextrin) peritoneal dialysis solution may have incorrect blood glucose results when using particular blood glucose monitors and test strips.

ONLY use glucose monitors and test strips that are glucose-specific. Some glucose monitors are not glucose-specific and cannot tell the difference between glucose and other sugars in the blood (e.g., maltose, a metabolite of icodextrin). Use laboratory-based methods, if available or a glucose-specific monitor and test strips. Contact the manufacturer of the glucose monitors and test strips to determine the method that is used. Visit www.glucosesafety.com for additional information including a glucose monitor compatibility list.

The term "glucose-specific" applies to monitors or test strips that are not affected by the presence of maltose or certain other sugars. Because **EXTRANEAL** (icodextrin) PD solution results in elevated blood levels of maltose, only glucose-specific monitors and test strips should be used.

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Additional considerations for patients who use **EXTRANEAL** (icodextrin) PD solution:

1. Discontinuing **EXTRANEAL** (icodextrin) PD solution use will not immediately address the risk for the potential interference with glucose monitors. Falsely elevated glucose levels may result up to two weeks following cessation of **EXTRANEAL** (icodextrin).
2. To determine what type of method is used for monitoring glucose levels, review the labeling for BOTH the glucose monitor and the test strips used. If in doubt, contact the manufacturer of the glucose monitors and test strips to determine the method that is used.
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For further information, refer to **EXTRANEAL** (icodextrin) PD solution prescribing information enclosed or visit www.glucosesafety.com.

I hope this information is helpful to you. If you have additional questions about **EXTRANEAL** (icodextrin) PD solution, please contact your Baxter Renal Representative.

Sincerely,

James A. Sloand, MD
Senior Medical Director, Medical Affairs
Baxter Healthcare Corporation

Please see Important Risk Information on reverse side and enclosed Full Prescribing Information.

This letter is part of an FDA approved REMS

IMPORTANT RISK INFORMATION
EXTRANEAL (icodextrin) Peritoneal Dialysis (PD) Solution

Dangerous Drug-Device Interaction
Only use glucose-specific monitors and test strips to measure blood glucose levels in patients using EXTRANEAL (icodextrin) Peritoneal Dialysis Solution. Blood glucose monitoring devices using glucose dehydrogenase pyrroloquinolinequinone (GDH-PQQ) or glucose-dye-oxidoreductase (GDO)-based methods must not be used. In addition, some blood glucose monitoring systems using glucose dehydrogenase flavin-adenine dinucleotide (GDH-FAD)-based methods must not be used. Use of GDH-PQQ, GDO, and GDH-FAD-based glucose monitors and test strips has resulted in falsely elevated glucose readings (due to the presence of maltose, see **PRECAUTIONS/Drug/Laboratory Test Interactions**). Falsely elevated glucose readings have led patients or health care providers to withhold treatment of hypoglycemia or to administer insulin inappropriately. Both of these situations have resulted in unrecognized hypoglycemia, which has led to loss of consciousness, coma, permanent neurological damage, and death. Plasma levels of EXTRANEAL (icodextrin) and its metabolites return to baseline within approximately 14 days following cessation of EXTRANEAL (icodextrin) administration. Therefore falsely elevated glucose levels may be measured up to two weeks following cessation of EXTRANEAL (icodextrin) therapy when GDH-PQQ, GDO, and GDH-FAD based blood glucose monitors and test strips are used.

Because GDH-PQQ, GDO, and GDH-FAD-based blood glucose monitors may be used in hospital settings, it is important that the health care providers of peritoneal dialysis patients using EXTRANEAL (icodextrin) carefully review the product information of the blood glucose testing system, including that of test strips, to determine if the system is appropriate for use with EXTRANEAL (icodextrin).

To avoid improper insulin administration, educate patients to alert health care providers of this interaction whenever they are admitted to the hospital.

The manufacturer(s) of the monitor and test strips should be contacted to determine if icodextrin or maltose causes interference or falsely elevated glucose readings. For a list of toll free numbers for glucose monitor and test strip manufacturers, please contact the Baxter Renal Clinical HelpLine 1-888-RENAL-HELP or visit www.glucosesafety.com.

EXTRANEAL PD solution is contraindicated in patients with a known allergy to cornstarch or icodextrin, in patients with maltose or isomaltose intolerance, in patients with pre-existing severe lactic acidosis, and in patients with glycogen storage disease.

EXTRANEAL PD solution is intended for intraperitoneal administration only. Not for intravenous injection.

Rarely, serious hypersensitivity reactions to EXTRANEAL have been reported, such as toxic epidermal necrolysis, angioedema, serum sickness, erythema multiforme, and leukocytoclastic vasculitis. If a serious reaction is suspected, discontinue EXTRANEAL and institute appropriate treatment as clinically indicated.

Patients with insulin-dependent diabetes may require modification of insulin dosage following initiation of treatment.

A patient's volume status should be carefully monitored to avoid hyper- or hypovolemia and potentially severe consequences including congestive heart failure, volume depletion and hypovolemic shock. An accurate fluid balance record must be kept and the patient's body weight monitored.

In clinical trials, the most frequently reported adverse events occurring in ≥ 10% of patients, and more common in EXTRANEAL PD solution patients than in control patients, were peritonitis, upper respiratory infection, hypertension, and rash. The most common treatment-related adverse event for EXTRANEAL PD solution patients was skin rash. Additional adverse reactions have been reported in the post-marketing setting and are detailed in the full prescribing information.

General Peritoneal Dialysis-Related
Encapsulating Peritoneal Sclerosis (EPS) is a known, rare complication of peritoneal dialysis therapy. EPS has been reported in patients using peritoneal dialysis solutions including EXTRANEAL PD solution. Infrequent but fatal outcomes have been reported.

Aseptic technique should be used throughout the peritoneal dialysis procedure to reduce the possibility of infection, such as peritonitis.

Fluid status, hematologic indices, blood chemistry, and electrolyte concentrations, including calcium, potassium, sodium, magnesium and bicarbonate, should be monitored periodically. Abnormalities in any of these parameters should be treated promptly under the care of a physician.

Overinfusion of peritoneal dialysis solution volume into the peritoneal cavity may be characterized by abdominal distention, feeling of fullness and/or shortness of breath. Treatment of overinfusion is to drain the peritoneal dialysis solution from the peritoneal cavity.

Treatment should be initiated and monitored under the supervision of a physician knowledgeable in the management of patients with renal failure.

Please see full prescribing information.

Attention Hospital Admissions Staff

WARNING

Potential For Incorrect Blood Glucose Reading

November 2010

Dear Hospital Admissions Staff,

Baxter Healthcare Corporation would like to notify you of Important Safety Information involving all patients who use **EXTRANEAL** (icodextrin) Peritoneal Dialysis (PD) solution and who may require the use of blood glucose monitors and test strips.

Patients using EXTRANEAL (icodextrin) peritoneal dialysis solution may have incorrect blood glucose results when using particular blood glucose monitors and test strips.

ONLY use glucose monitors and test strips that are glucose-specific. Some glucose monitors are not glucose-specific and cannot tell the difference between glucose and other sugars in the blood (e.g., maltose, a metabolite of icodextrin). Use laboratory-based methods, if available or a glucose-specific monitor and test strips. Contact the manufacturer of the glucose monitors and test strips to determine the method that is used. Visit www.glucosesafety.com for additional information including a glucose monitor compatibility list.

The term "glucose-specific" applies to monitors or test strips that are not affected by the presence of maltose or certain other sugars. Because **EXTRANEAL** (icodextrin) PD solution results in elevated blood levels of maltose, only glucose-specific monitors and test strips should be used.

DO NOT use glucose monitors or test strips that utilize glucose dehydrogenase pyrroloquinolinequinone (GDH-PQQ) or glucose-dye-oxidoreductase (GDO) methods. In addition, some but not all monitors or test strips that utilize a glucose dehydrogenase flavin-adenine dinucleotide (GDH-FAD) method must not be used. Use of these methods may result in falsely elevated blood glucose readings in patients using **EXTRANEAL** (icodextrin) due to maltose interference. A blood glucose reading with these monitors that appears to be within the normal range in a patient on **EXTRANEAL** (icodextrin) may mask true hypoglycemia (low blood sugar). This would cause a patient or health care professional not to take the appropriate steps to bring the blood sugar into a normal range. A falsely elevated blood glucose reading could cause a patient to get more insulin than needed. Both of these situations can lead to life-threatening events, including loss of consciousness, coma, permanent neurological damage or death.

Additional considerations for patients who use **EXTRANEAL** (icodextrin) PD solution:

1. Discontinuing **EXTRANEAL** (icodextrin) PD solution use will not immediately address the risk for the potential interference with glucose monitors. Falsely elevated glucose levels may result up to two weeks following cessation of **EXTRANEAL** (icodextrin).
2. To determine what type of method is used for monitoring glucose levels, review the labeling for BOTH the glucose monitor and the test strips used. If in doubt, contact the manufacturer of the glucose monitors and test strips to determine the method that is used.
3. If your hospital uses electronic medical records, the above information describing the potential for interference with blood glucose monitors or test strips needs to be entered in a suitable field that is readily apparent to all users.

For further information, refer to **EXTRANEAL** (icodextrin) PD solution prescribing information enclosed or visit www.glucosesafety.com.

I hope this information is helpful to you. If you have additional questions about **EXTRANEAL** (icodextrin) PD solution, please contact your Baxter Renal Representative.

Sincerely,

James A. Sloand, MD
Senior Medical Director, Medical Affairs
Baxter Healthcare Corporation

Please see Important Risk Information on reverse side and enclosed Full Prescribing Information.

This letter is part of an FDA approved REMS

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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.

/s/

MARY R SOUTHWORTH
03/08/2011