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IMPORTANT SAFETY INFORMATION

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**Dianeal, Extraneal, Nutrineal – presence of endotoxin and risk of aseptic peritonitis**

- Dianeal PD1 Glucose 1.36% w/v 13.6 mg/ml, Solution for peritoneal dialysis
- Dianeal PD1 Glucose 2.27% w/v 22.7 mg/ml, Solution for peritoneal dialysis
- Dianeal PD1 Glucose 3.86% w/v 38.6 mg/ml, Solution for peritoneal dialysis
- Dianeal PD4 Glucose 1.36% w/v 13.6 mg/ml, Solution for peritoneal dialysis
- Dianeal PD4 Glucose 2.27% w/v 22.7 mg/ml, Solution for peritoneal dialysis
- Dianeal PD4 Glucose 3.86% w/v 38.6 mg/ml, Solution for peritoneal dialysis
- EXTRANEAL (Icodextrin 7.5%), Solution for peritoneal dialysis
- Nutrineal PD4 with 1.1% amino acids, Solution for peritoneal dialysis

Dear Mr O'Donnell,

**Summary**

**Baxter has identified that batches of the Peritoneal Dialysis Solutions, Dianeal, Extraneal and Nutrineal have elevated levels of endotoxin. Only a small proportion of bags are likely to be affected, however it is not possible to identify the affected bags.**

**All affected batches of PD solutions will be withdrawn over time as soon as replacement batches are available to meet supply needs (full replacement expected by March 2011).**

**Until replacement stock becomes available, physicians should weigh the risks and benefits of continuing the use of PD solutions that are potentially affected by this issue.**

**Supplies of new unaffected PD solutions (see further information below) should be prioritised for vulnerable populations exclusively dependent on affected PD solutions, including Extraneal patients with fluid overload.**

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**Physicians need to be vigilant for potential adverse reactions relating to aseptic peritonitis, and should report any suspected cases to Baxter UK Pharmacovigilance at Baxter Healthcare Ltd, Wallingford Road, Compton, Newbury RG20 7QW, by email to vigilanceuk@baxter.com or by fax to +44 1635 206281 or to Surecall Baxter Medical Information on telephone +44 1635 206345.**

**Options for use of PD solutions**

Supplies of new unaffected PD solutions should be prioritised for vulnerable populations exclusively dependent on affected PD solutions, including Extraneal patients which may include those with otherwise uncontrollable fluid overload.

For other PD patients, clinicians should determine if alternative PD therapies, solutions or dialysis methods should be pursued based on risk of exposure of patients to endotoxin. Consideration should be given to the following:

(1) In Continuous Ambulatory PD (CAPD) patients, replace Dianeal or Nutrineal with Physioneal for the short dwell since Physioneal is not affected by this problem.
(2) In Automated PD (APD) patients using Dianeal, ensure that only 5L bags are used for the short dwell
(3) For patients using Extraneal for the long dwell in CAPD or APD, assess fluid balance and continue Extraneal specifically in patients with low urine output/fluid balance challenges in whom a different PD therapy prescription change will not be sufficient
(4) Switch CAPD patients to APD using Physioneal or Dianeal (5L bags only) if this is feasible
(5) Use PD solutions from alternative manufacturers

When evaluating potential mitigations or PD therapy changes, physicians should weigh the risk of exposure to endotoxin and the long term consequences of aseptic peritonitis and its management (primarily peritoneal damages and overexposure to antibiotic therapy) and the clinical needs of patients (eg uncontrolled fluid balance, diabetes) with other risks such as a heightened risk of bacterial peritonitis related to changes in type of connector for different PD solutions, patient training and use of alternative PD systems.

New PD patients commencing PD therapy should preferably receive product known to be unaffected.

**Clinical management of suspected aseptic peritonitis**

Aseptic peritonitis is a known rare event in patients undergoing peritoneal dialysis, and the risk is increased in the presence of endotoxin.

Patients using affected PD solutions could present with cloudy effluent suggesting peritonitis with or without symptoms such as abdominal pain, nausea, vomiting or become febrile. Increased peritoneal fluid white cell count (with a majority of monocytes) and a negative microbiological culture would strongly suggest a sterile aseptic peritonitis.

Physicians should take microbiological cultures and white cell count and then commence empirical intraperitoneal antibiotic therapy for gram positive and gram negative organisms according to their standard protocol (ISPD Guidelines PD1 2010). If other possible reasons for cloudy fluid especially

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bacterial peritonitis have been excluded, the suspected PD fluid should be stopped and the result of this action evaluated.

**Further information about the issue**

Batches of Dianeal, Extraneal and Nutrineal have been identified with elevated levels of endotoxin. Investigations indicate that a small proportion of the bags are affected.

At this stage, it is not possible to establish when this problem commenced and as a worst case scenario Baxter has concluded that all batches within expiry date (including products still on the market) are potentially affected by this issue.

Baxter is consulting with the European Medicines Agency (www.ema.europa.eu) on this issue, and will conduct a recall of the affected released batches of PD solutions from the market when replacement batches are available. Baxter will make every effort to increase supply of newly produced Dianeal, Extraneal and Nutrineal solutions to meet clinical needs.

To identify **new unaffected batches** for prioritisation for vulnerable patients, each user should check the first three digits/letter combination in the product batch number. If the digits/letter combination starts with **10L** the product is unaffected. All subsequent unaffected batches will be produced in subsequent order starting with **11A**, e.g. 11B, 11C... 11F,...11L.

**Call for reporting**

If you observe suspected adverse events in association to treatment with Dianeal, Extraneal and Nutrineal you are asked to use the attached adverse event reporting form and send this marked for the attention of Baxter UK Pharmacovigilance at Baxter Healthcare Ltd, Wallingford Road, Compton, Newbury RG20 7QW, by email to vigilanceuk@baxter.com or by fax to +44 1635 206281 or to Surecall Baxter Medical Information on telephone +44 1635 206345.

**Note:** It is very important that you provide the batch number for the product used by the patient when completing the form.

**Communication information**

For further information please contact the Baxter Clinical Nurse Specialist (primary contact) or Surecall Baxter Medical Information on +44 1635 206345.

Sincerely,

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