URGENT: Important Safety Information

Subject: Notice of New Special Handling Instructions due to Potential for Crystallization, Cracked Needle Hubs and Particulate in Diazepam Injection, USP, CIV 10 mg/2 mL (5 mg/mL) Carpuject™ Luer Lock Glass Syringe

Diazepam Injection, USP, CIV Carpuject™ Luer Lock Glass Syringe

<table>
<thead>
<tr>
<th>Strength</th>
<th>Product Configuration</th>
<th>NDC Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 mg/2 mL (5 mg/mL)</td>
<td>Carpuject™, Single-dose cartridge with Luer Lock for the Carpuject Syringe System; 10 units per carton</td>
<td>0409-1273-32 (unit of sale)</td>
</tr>
<tr>
<td></td>
<td>Carpuject™, Single-dose cartridge with Luer Lock for the Carpuject Syringe System; Single Use unit</td>
<td>0409-1273-03 (single unit)</td>
</tr>
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</table>

Dear Health Care Provider,

Hospira, a Pfizer company (Hospira) is issuing this Important Safety Information Letter to alert Health Care Providers to the potential for crystallization, cracked needle hubs, and/or particulate in Diazepam Injection, USP, CIV 10 mg/2 mL (5 mg/mL) Carpuject™ Luer Lock Glass Syringe.

In order to minimize the potential risk of adverse events with this product, special handling directions described below are required prior to administering the affected product to patients. To help alleviate the critical drug shortage of this product, Hospira has evaluated product lots within its control and, in coordination with FDA, is releasing the impacted lots listed in Appendix 1.

Special handling instructions in this letter only apply to Diazepam Injection, USP, CIV 10 mg/2 mL (5 mg/mL) Carpuject™ Luer Lock Glass Syringe lots described in Appendix 1. All other lots may be administered following routine procedures.

Please ensure your staff and any provider in your institution who may be involved in the administration of the diazepam products listed in Appendix 1 receives a copy of this letter and specifically reviews the special handling directions in the Directions for Health Care Provider section below.
Hospira has determined that there is a potential for Diazepam Injection, USP, CIV, 10 mg/2 mL in the Carpuject™ Syringe System to form small transparent-visible crystals in the cartridge in some lots over time. The crystals have been determined to be Diazepam API (the active pharmaceutical ingredient in the finished product), which is intrinsic to the product.

As a precautionary measure in response to crystalline particulates being observed in Diazepam Injection, USP, CIV, 10 mg/2 mL Carpujects, Health Care Providers are being alerted to ensure that the current label instructions are followed as detailed in the Directions for Health Care Provider section of this letter.

In addition to crystallization (shown in Figure 1), cracked needle hubs (shown in Figure 2) and particulate (shown in Figure 3) were identified either during routine inspection or during routine quality checks of the product in the Carpuject syringe. The probability of crystallization, cracked needle hubs and/or particulate is low.

The process conditions that facilitate crystallization of the active ingredient have been identified and controls are being enhanced to eliminate this effect in future lots. In addition, the root cause of the cracked needle hubs and particulate has been identified, and corrective and preventative actions are now in place.

**Figure 1. Magnification of Potential API Crystallization**
Figure 2. Magnification of Cracked Needle Hubs

Figure 3. Magnification of Potential Particulate
Potential Safety Risk of Adverse Events

For Carpuject product lots impacted, a damaged needle hub assembly has the potential to impact the sterile pathway during product delivery. The potential for patient exposure occurs through the use of the split Luer Lock II hub assembly.

With intravenous injection, injected particulate matter, including API crystals, may result acutely in local inflammation or phlebitis. It may also lead to micro-embolic effects in other tissue, most commonly the lungs. If extensive, this can result in chest pain or respiratory symptoms. Chronically, following sequestration, granuloma formation is possible.

Subcutaneous or intramuscular injection of particulate may result in local inflammation or tissue injury.

Directions for Wholesalers/Distributors

If you have distributed the product listed in this Dear Health Care Provider (DHCP) letter, please notify your impacted accounts of this Important Safety Information notification.

Directions for Health Care Provider

After opening the carton or box, visually inspect the Carpuject cartridge to confirm there are no cracks or damage to the needle hub and that there is no visible particulate matter. Per the package insert, parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution or container permits. Do not use if the solution is darker than slightly yellow or contains a precipitate. These requirements are specifically stated in the package insert for Diazepam Injection, USP in the Carpuject syringe system.

Please note that the instructions described below to use the Carpuject cartridge as a vial is not routine and is advised because of the critical drug shortage.
As a precaution, use a 5 micron filter needle (BD REF 305200 or equivalent) to prepare the drugs listed in this letter for administration. The following steps are recommended to remove the Carpuject cartridge from the Carpuject Hub assembly and prepare the drug solution for administration using a filter needle with the product:

1. Remove Carpuject cartridge from packaging
2. Perform a visual inspection of the Carpuject cartridge prior to use.
   • DO NOT USE IF CRYSTALS OR PARTICULATES ARE VISIBLE, AND DISCARD CARTRIDGE PER YOUR INSTITUTION’S POLICY. USE A NEW CARPUJECT CARTRIDGE.
   • DO NOT USE IF CRACKS OR DAMAGE TO THE NEEDLE HUB ARE VISIBLE, AND DISCARD CARTRIDGE PER YOUR INSTITUTION’S POLICY. USE A NEW CARPUJECT CARTRIDGE.
3. If no crystals or particulates are visible and no damage to the needle hub is present, as a precaution, attach a filter needle with 5 micron filter to a sterile empty syringe.
4. Remove white needle hub from Carpuject cartridge and discard per hospital procedure

5. Swab the septum of the Carpuject cartridge with sterile alcohol pad
6. Insert syringe needle into Carpuject cartridge septum.

7. Withdraw intended dose from Carpuject cartridge purging air from filter to help maximize amount withdrawn.
8. Remove 5 micron filter needle and discard per hospital procedure.
9. Attach needle if applicable and administer drug or connect syringe to a port that does not require needle access and administer drug.

This letter is not intended as a complete description of the benefits and risks related to the use of Diazepam Injection, USP. Full Prescribing Information including BOXED WARNING is available at www.pfizerinjectables.com/products/Diazepam

Please contact Hospira customer Service at 1-844-646-4398 (Mon.-Fri. 8am-7pm ET) or your Hospira representative for any questions you may have regarding this notification.

To report adverse reactions or quality issues, contact Hospira at 1-800-438-1985.

Adverse events or quality problems experienced with the use of this product may be reported to the FDA’s MedWatch Adverse Event Reporting Program either online, by regular mail, or by fax:

- Complete and submit the report Online: www.fda.gov/medwatch/report.htm
- Regular mail or Fax: download form www.fda.gov/MedWatch/getforms.htm or call 1-800-332-1088 to request a reporting form, then complete and return to the address on the pre-addressed form, or submit by fax to 1-800-FDA-0178 (1-800-332-0178)
This letter is being issued with the knowledge of the U.S. Food and Drug Administration. We thank you for your attention to this important matter.

Sincerely,

Eddie G.M. Power PhD MBA  
Vice President, US Medical Affairs, Chief Medical Officer  
Pfizer Essential Health
Appendix 1. Impacted Diazepam Injection, USP, CIV Carpuject™ Luer Lock Glass Syringe Product Lot Numbers with Potential Crystallization, Cracked Needle Hub and/or Particulate Matter

<table>
<thead>
<tr>
<th>NDC Number</th>
<th>Product Description</th>
<th>Lot Numbers</th>
<th>Expiration Date</th>
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<tbody>
<tr>
<td>0409-1273-32</td>
<td>Diazepam Injection, USP, CIV Carpuject™ Luer Lock Glass Syringe 10 mg/2 mL (5 mg/mL)</td>
<td>79505LL</td>
<td>01 Jan 2019</td>
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<tr>
<td></td>
<td></td>
<td>80760LL</td>
<td>01 Feb 2019</td>
</tr>
<tr>
<td></td>
<td></td>
<td>81535LL</td>
<td>01 Mar 2019</td>
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