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IMPORTANT NOTICE

Zinecard[®] (dexrazoxane for injection) Re-introduction and new reconstitution/dilution and administration instructions

June 7, 2011

Dear Health Care Provider,

This letter is to provide you with new information regarding the re-introduction of Zinecard (dexrazoxane for injection), used in conjunction with doxorubicin.

As you know, Zinecard had been in short supply during 2008-2009. The reason for this shortage of Zinecard was due to the previously approved diluent (0.167 Molar Sodium Lactate USP) co-packaged with Zinecard, not meeting particulate matter acceptance criteria, according to USP.

Pfizer undertook additional laboratory development work on Zinecard and is now able to recommend and distribute a new dilution procedure that will provide a satisfactory solution for intravenous infusion using the readily available diluents, Sterile Water for Injection, USP and Lactated Ringer's Solution USP.

In re-introducing Zinecard with this alternative dilution procedure, Pfizer has recommended some restrictions on the handling and administration of reconstituted and diluted solutions of Zinecard using new reconstitution/dilution instructions. These restrictions include storage of solutions under refrigeration only, and elimination of IV push after reconstitution as an administration option.

To control the pH, and thus the tolerability of Zinecard prepared via the new dilution procedure, Pfizer has recommended that following reconstitution with Sterile Water for Injection, USP, further dilution with Lactated Ringer's solution be restricted to concentrations between 1.3 and 3.0 mg/mL in intravenous infusion bags.

Zinecard will continue to be packaged as a single unit of sale. **The US Package Insert has been revised to reflect the new dilution procedure, the details of which are described below.**

To order Zinecard, please contact your wholesaler. If you have any questions regarding your order, please contact Pfizer's Customer Service at (800) 533-4535.

Product Information:

Zinecard is a sterile, pyrogen-free lyophilizate intended for intravenous administration. It is for use in conjunction with doxorubicin. Zinecard is available in 250 mg and 500 mg single-use vials.

- Each 250 mg vial contains dexrazoxane hydrochloride equivalent to 250 mg dexrazoxane. Hydrochloric Acid, NF is added for pH adjustment.
- Each 500 mg vial contains dexrazoxane hydrochloride equivalent to 500 mg dexrazoxane. Hydrochloric Acid, NF is added for pH adjustment.

Instructions for Reconstitution of Zinecard

The reconstitution diluent Sterile Water for Injection, USP, has been studied for compatibility and stability with Zinecard. Zinecard should be reconstituted only with Sterile Water for Injection, USP. No other diluent should be used to reconstitute Zinecard. Any unused diluent should be discarded.

The amount of diluent used for reconstitution will need to be appropriately proportioned according to the US Package Insert for Zinecard, as follows:

- **A 250 mg single-use vial of dexrazoxane should be reconstituted with 25 mL of Sterile Water for Injection, USP. Once reconstituted, the resultant solution contains 10 mg dexrazoxane per mL.**
- **A 500 mg single-use vial of dexrazoxane should be reconstituted with 50 mL of Sterile Water for Injection, USP. Once reconstituted the resultant solution contains 10 mg dexrazoxane per mL.**

The reconstituted ZINECARD solutions **MUST** be further diluted for rapid intravenous drip infusion. **DO NOT ADMINISTER VIA IV PUSH.** As long as the reconstitution instructions for Zinecard are followed as described within this letter, there are no anticipated changes to the safety and efficacy of Zinecard to patients.

- The reconstituted Zinecard solution is intended for further dilution with Lactated Ringer's Injection, USP, to a concentration range of 1.3 to 3.0 mg/mL in intravenous infusion bags. The resultant solutions have a pH of 3.5 to 5.0 and are stable for 4 hours when stored under refrigeration, 2° to 8°C (36° to 46°F). DISCARD UNUSED SOLUTIONS.

NDC Codes

The NDC numbers for the single-unit vials packaged **without** diluent have NOT been changed.

Current NDC #s for Zinecard Vials

Presentation	NDC
Zinecard 250 mg vial	0013-8717-62
Zinecard 500 mg vial	0013-8727-89

Please direct any questions related to the content of this Dear Health Care Provider Letter to Pfizer Medical Information at 1-800-438-1985. For questions related to the distribution of or to order Zinecard, please contact Pfizer Customer Service at (800) 533-4535.

Sincerely,

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