Acute Care ISMP Medication Safety Alert!®
Educating the Healthcare Community About Safe Medication Practices

FDA Advise-ERR: Medication errors associated with Cerebyx

From the April 10, 2008 issue

Problem: **CEREBYX** (fosphenytoin) has been associated with medication errors dating back to the drug's approval in 1996, and ISMP has been publishing warnings about these errors for close to a decade (*ISMP Medication Safety Alert!* January 27, 1999, available at: www.ismp.org/Newsletters/acutecare/articles/19990127.asp). Confusion between the per mL concentration of Cerebyx (50 mg PE/mL) and total drug content (either 100 mg PE/2 mL vial or 500 mg PE/10 mL vial) is one type of error quickly identified with the product following its approval. When first marketed, the container labels prominently displayed only the concentration (50 mg PE/mL). After conducting root cause analyses of these errors, FDA, ISMP, and other medication safety advocates determined that practitioners were misinterpreting the concentration on the label as the total drug content in the vial, which then led to 2-fold or 10-fold overdoses of Cerebyx.

In order to remedy this source of confusion and error, Pfizer changed the labels in January 1999 to prominently display the total container contents (100 mg PE in 2 mL, and 500 mg PE in 10 mL) and to eliminate the per mL concentration expression (see Figure 1 in the PDF version of the newsletter). Pfizer also distributed "Dear Healthcare Professional" letters to alert practitioners to the risk of confusion.

Prior to the container label changes, the FDA MedWatch program identified five deaths involving 10-fold overdoses with Cerebyx, as well as additional cases of non-fatal overdoses. Unfortunately, despite the label changes, the MedWatch program has recently identified seven additional cases of fatal medication errors in which pediatric patients 3 year of age or younger received 10 times more than the intended Cerebyx dose. Four of the seven fatalities occurred in the emergency department (ED) of a hospital. In six cases, 200 mg PE was the intended dose but 2,000 mg PE of Cerebyx was administered; in one case, 150 mg PE was the intended dose but 1,500 mg PE of Cerebyx was administered. Two cases specified that the 10 mL vials were involved in the errors; the remaining cases did not specify the package size. However, the magnitude of the overdoses (10-fold) suggests that the 10 mL vials were used in error in all the fatal cases.

Root cause analyses of the most recently identified errors suggests that the per mL concentration of the product (50 mg PE/mL) continues to be misinterpreted as the total amount of drug in the vial, despite the prominent display of total drug content on the vial label and carton labeling. The 50 mg PE/mL concentration of Cerebyx also continues to be communicated as the primary identifier in many healthcare inventory listings in electronic databases such as automated dispensing cabinet (ADC) displays. Four of the seven cases noted that the drug was obtained from an ADC. Two cases explicitly noted that the drug strength was displayed on the ADC screen as 50 mg PE/mL,10 mL, instead of the total drug content of 500 mg PE/10 mL.

Safe Practice Recommendations: If you stock Cerebyx in your organization, check your ADC screen display, shelf labels, and printed requisitions to ensure the total drug content per container is identified instead of the concentration per mL. The information communicated should be consistent with the manufacturer's label (100 mg PE /2 mL, or 500 mg PE/10 mL) to lessen the potential for confusion. Remove any auxiliary or computer-generated labels that state 50 mg PE/mL from bins in the ADCs, as practitioners may rely on those labels, instead of the manufacturer's label, to identify the amount in the vial.

Because the 10 mL vial appears to be most frequently involved in massive overdoses, pediatric facilities should consider stocking only the 2 mL vials of Cerebyx in the ED. The need to retrieve many vials in order to prepare a single dose (i.e., ten 2 mL vials would be needed to prepare a 1,000 mg PE dose versus just two 10 mL vials) may serve to

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alert practitioners that a dosing error has been made before the error reaches the patient.

Sources of fatal cases: *USP MEDMARX (n=1); MedWatch, FDA's Adverse Events Reporting System (AERS) (n=6). Cases from FDA's AERS database can be obtained through a FOI request.*

Editor's note: *ISMP has alerted major drug information vendors to the risk of errors with Cerebyx and requested modification of drug information files to primarily express the 100 mg PE/2 mL or 500 mg PE/10 mL content. ADC cabinet inventory screens that can be modified by the facility should likewise include the total vial content. ISMP also recommends limiting par levels to reduce the number of vials available in ADCs, as well as limiting locations where the drug is stored.*

FDA Advise-ERR is provided by the U.S. Food and Drug Administration.

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