

## Drugs in the News 4/17/09 – Update to the Ceftriaxone-Calcium Interaction

In May of 2007, the Rocephin<sup>®</sup> package insert was updated to reflect a new interaction between ceftriaxone and concurrently administered IV calcium products. Roche provided the FDA with five post marketing reports of neonatal deaths related to the interaction. Since, four additional post-marketing reports of the interaction have occurred in patients up to 1 year of age. In September of 2007, an FDA alert was distributed to healthcare professionals to update them on the revisions in the package insert concerning the interaction. At this time the FDA provided a recommendation to not mix or infuse calcium-containing products concurrently with ceftriaxone, along with not administering either product in the same or different infusion lines or sites in **any patient** within 48 hours of each product being given. A theoretical recommendation based on 5 elimination half-lives of the medications. Tuesday April 14, 2009, the FDA retracted their statement on the ceftriaxone and calcium interaction after Roche provided results on two in vitro studies on the interaction in neonatal and adult plasma. Based on the results of these studies the FDA has recommended the following:

“Concomitant use of ceftriaxone and intravenous calcium-containing products is contraindicated in neonates ( $\leq 28$  days of age). Ceftriaxone should not be used in neonates ( $\leq 28$  days of age) if they are receiving (or are expected to receive) calcium-containing intravenous products.”

“In patients  $>28$  days of age, ceftriaxone and calcium-containing products may be administered sequentially, provided the infusion lines are thoroughly flushed between infusions with a compatible fluid.”

“Ceftriaxone must not be administered simultaneously with intravenous calcium-containing solutions via a Y-site in any age group.”

“FDA now recommends that **ceftriaxone and calcium-containing products may be used concomitantly in patients  $>28$  days of age, using the precautionary steps above because the risk of precipitation is low in this population.** FDA had previously recommended, but no longer recommends, that in all age groups ceftriaxone and calcium-containing products should not be administered within 48 hours of one another.”

Despite the FDA’s recommendations, the combination of these medications should also be avoided in patients up to 1 year of age due to the documented post-marketing deaths. Additionally, using ceftriaxone 28 days and under is already contraindicated due to bilirubin displacement from its binding to serum albumin leading to bilirubin encephalopathy and eventually mental retardation.

<p><b>Warning to Pharmacists: Do not dispense ceftriaxone to any patient <math>\leq 28</math> days old or patients <math>&lt; 1</math> year of age currently receiving calcium containing products including total parenteral nutrition containing calcium.</b></p>
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See the FDA alert for more information at <http://www.fda.gov/cder/drug/InfoSheets/HCP/ceftriaxone042009HCP.htm> and dailymed at <http://dailymed.nlm.nih.gov/dailymed/about.cfm> for more information on ceftriaxone.

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