



INFECTIOUS DISEASE UPDATE

FDA eases restrictions on use of ceftriaxone in infants

by **John S. Bradley, M.D., FAAP**, and **Joseph A. Bocchini Jr., M.D., FAAP**

The Food and Drug Administration (FDA) has modified its restrictions on the concomitant use of ceftriaxone and calcium-containing intravenous solutions in infants and children (www.fda.gov/Cder/drug/infopage/ceftriaxone/default.htm).

The recommendations ease restrictions issued in 2007 and are more focused on infants who appear to be at highest risk:

- Concomitant use of ceftriaxone and intravenous calcium-containing products still is contraindicated in neonates (28 days of age or younger). Ceftriaxone should not be used in neonates (28 days of age and younger) receiving (or expected to receive) calcium-containing intravenous products.
- Ceftriaxone and calcium-containing products may be used concomitantly in patients older than 28 days, using the following precautionary steps:
 - Ceftriaxone and calcium-containing intravenous products are 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.

Due to the long half-life of ceftriaxone, the 2007 FDA recommendation stated that ceftriaxone and calcium-containing products should not be administered within 48 hours of one another. This recommendation was rescinded in the new guidance, which is based on additional *in vitro* data on ceftriaxone/calcium interactions in serum, ongoing analysis of reported cases and ongoing review of safety data on ceftriaxone from the FDA MedWatch Safety Information and Adverse Event Reporting Program.

With reports of neonatal deaths associated with precipitation of a ceftriaxone-calcium salt in the lung and/or kidneys, the FDA acted quickly to prevent morbidity and mortality in U.S. neonates and infants (www.fda.gov/medwatch/safety/2007/Rocephin_HCP_

[august2007.pdf](#)). The agency issued a warning in 2007 indicating that concomitant administration of ceftriaxone and a calcium-containing intravenous solution was contraindicated in infants and children. With more detailed information subsequently available on the reported neonatal cases (Bradley JS, Wassel RT, Lee L, Nambiar S. *Pediatrics*. 2009;123:e609-613) and a recognition of the risks and benefits of ceftriaxone and alternative antibiotics in pediatric practice, the FDA issued the new recommendations.

Other potential interactions

According to the FDA, there still are no data on interactions between intravenous ceftriaxone and the oral calcium-containing products commonly prescribed for neonates and infants. There also are no new data to define the risk of intramuscular ceftriaxone and intravenous or oral calcium-containing products. The FDA is neither recommending against these uses nor is it saying they are safe.

However, in all of the reported cases of infant death, *intravenous* calcium and intravenous ceftriaxone were given. Therefore, practitioners should be aware of the potential interactions with oral calcium in young infants receiving *intravenous* ceftriaxone, and the potential side effects of *intravenous* or oral calcium in infants receiving *intramuscular* ceftriaxone. However, if the benefits of ceftriaxone therapy in these situations are felt to be greater than a small but yet-to-be-defined risk of concomitant therapy, then ceftriaxone can be used cautiously in these settings.

To help in the ongoing assessment of the adverse event profile of ceftriaxone, health care providers should report possible adverse events to MedWatch at www.fda.gov/medwatch/report/hcp.htm.

Dr. Bradley is a member of the AAP Committee on Infectious Diseases, and Dr. Bocchini is chair of the committee.