NATIONAL PBM COMMUNICATION · April 29, 2009

Rocephin (ceftriaxone) and Calcium Interaction: UPDATED SAFETY INFORMATION

- In May 2007, the prescribing information for Rocephin® (ceftriaxone) added new information about the interaction between ceftriaxone and calcium-containing products based on post-marketing reports in neonates. In August 2007, the full prescribing information extended the pediatric warning to adults as well. In September 2007, the PBM issued a NATIONAL PBM Bulletin highlighting the issue. [1]
- On April 14, 2009, the Food and Drug Administration (FDA) released Information for Healthcare Professionals addressing revisions to the product package insert regarding the potential for precipitation when Rocephin® (ceftriaxone) is administered concomitantly with calcium-containing products. [2]
- Roche, the manufacturer of Rocephin® (ceftriaxone), conducted two studies (in vitro) to evaluate precipitation formation when Rocephin® (ceftriaxone) and calcium-containing products are mixed in vials and infusion lines. [2]
    - The studies used neonatal and adult plasma.
    - The studies used varying ceftriaxone and calcium concentrations.
- Based on the results of these studies, FDA has UPDATED its original recommendations to those listed below[2]:
    - *Ceftriaxone and calcium-containing products may be used concomitantly in patients >28 days of age 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.*
    - *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.*
    - *Concomitant use of ceftriaxone and intravenous calcium-containing products is contraindicated in neonates (≤28 days of age). Ceftriaxone should not be used in neonates (≤28 days of age) if they are receiving (or are expected to receive) calcium-containing intravenous products.*
- The following recommendations from the FDA remain the same[2]:
    - Diluents containing calcium, such as Ringer's solution or Hartmann's solution, should not be used to reconstitute Rocephin® (ceftriaxone). Particulate formation can result.
    - There are no data available on the potential interaction of ceftriaxone with oral calcium-containing products.
    - There are no data available on the potential interaction of intramuscular ceftriaxone with oral or intravenous calcium-containing products.

REFERENCES
1. PBM. http://www.pbm.va.gov/vamedsafe/Ceftriaxone%20National%20PBM%20Bulletin.pdf. (Accessed April 14, 2009)
2. FDA. http://www.fda.gov/cder/drug/InfoSheets/HCP/ceftriaxone042009HCP.htm. (Accessed April 14, 2009)

ACTIONS:

- ***Facility COS:*** *Forward this document to all appropriate providers who prescribe this agent (e.g.,* ***primary care providers and infectious disease specialists,*** *including contract providers, etc.). In addition, forward to the Associate Chief of Staff (ACOS) for Research and Development (R&D). Forward to other VA employees as deemed appropriate.*
- ***ACOS for R&D:*** *Forward this document to Principal Investigators (PIs) who have authority to practice at the facility and to your respective Institutional Review Board (IRB).*