



NATIONAL PBM BULLETIN

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DEPARTMENT OF VETERANS AFFAIRS (VA) VETERANS HEALTH ADMINISTRATION (VHA)
NATIONAL PHARMACY BENEFITS MANAGEMENT STRATEGIC HEALTHCARE GROUP (PBM),
MEDICAL ADVISORY PANEL (MAP), AND
CENTER FOR MEDICATION SAFETY (VA MedSAFE)

Ceftriaxone (Rocephin®) and Calcium Interaction

I. ISSUE – The combination of ceftriaxone (Rocephin®) and parenteral calcium-containing products may result in fatal precipitates for any patient at any age according to the Food and Drug Administration (FDA) and Roche, the manufacturer of Rocephin® (ceftriaxone).

II. BACKGROUND – In May 2007, Roche revised the product package insert of ceftriaxone (Rocephin®) to include new information on the risk of precipitate formation when ceftriaxone is used with calcium or calcium-containing products/solutions. Per the FDA and Roche:

“...The drug must not be mixed or administered simultaneously with calcium-containing solutions or products, even via different infusion lines. Additionally, calcium-containing solutions or products must not be administered within 48-hours of the last administration of ceftriaxone.”

This is based on cases of fatal reactions in neonates with evidence of calcium-ceftriaxone crystals in the lungs and kidneys. As such, concurrent administration of ceftriaxone and calcium or calcium-containing products/solutions is contraindicated in newborns due to the possibility of ceftriaxone-calcium salt precipitation.

A more recent update from the FDA in September 2007 shows additional changes to the product package insert for ceftriaxone, extending the pediatric warning issued earlier this year to include adults due to the “theoretical possibility...for an interaction between ceftriaxone and IV calcium-containing solutions in patients other than neonates.” The new warning in the prescribing information states:

“Rocephin and calcium-containing solutions, including continuous calcium-containing infusions such as parenteral nutrition, should not be mixed or co-administered to any patient irrespective of age, even via different infusion lines at different sites. ...Rocephin and IV calcium-containing solutions should not be administered within 48 hours of each other in any patient.”

III. DISCUSSION – Ceftriaxone is a cephalosporin antibiotic approved by the FDA in 1984 for use in the treatment of various infections (respiratory, integumentary, skeletal, genito-urinary and gastrointestinal infections, as well as acute bacterial otitis media, uncomplicated gonorrhea, pelvic inflammatory disease, bacterial septicemia, meningitis, and surgical prophylaxis) when caused by susceptible microorganisms. There are no reports of ceftriaxone-calcium interactions or precipitations in patients, other than in neonates. 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.

IV. RECOMMENDATIONS - PBM and VAMedSAFE recommendations mirror that of the FDA:

- Ceftriaxone (Rocephin®) and parenteral calcium-containing solutions including continuous calcium-containing infusions such as parenteral nutrition, should not be mixed or co-administered to any patient irrespective of age, even via different infusion lines at different sites.
- Parenteral calcium-containing solutions or products should not be administered within 48-hours of the last administration of ceftriaxone (Rocephin®) in any patient.
- Diluents containing calcium, such as Ringer’s solution or Hartmann’s solution, should not be used to reconstitute ceftriaxone (Rocephin®). Particulate formation can result.
- Before initiating therapy with ceftriaxone (Rocephin®) or parenteral calcium-containing products, a careful medication history should be performed to review concurrent therapies and those received within 48 hours.
- Report adverse events to VHA’s Adverse Drug Event Reporting Program and/or FDA’s MedWatch program.