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# NATIONAL PBM BULLETIN

JULY 8, 2011

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VETERANS HEALTH ADMINISTRATION PHARMACY BENEFITS MANAGEMENT SERVICES (PBM),  
MEDICAL ADVISORY PANEL (MAP), & CENTER FOR MEDICATION SAFETY (VA MEDSAFE)

## COLISTIMETHATE FOR INJECTION AND DOSING CONFUSION

### I. ISSUE<sup>1</sup>

A National Alert Network (NAN) Alert has been issued by the National Coordinating Council on Medication Error Reporting and Prevention (NCCMERP) regarding the potential for confusion that exists in the nomenclature and dose of colistimethate for injection, USP, a prodrug of colistin, used for the treatment of gram-negative infections. This polymyxin E antibiotic is typically reserved as a last resort for infections caused by multiple drug resistant organisms due to neurotoxic and nephrotoxic tendencies.

### II. BACKGROUND<sup>1</sup>

Confusion regarding colistimethate for injection, USP, can be attributed to:

- Variances in the European and US dosage measures (i.e., units versus milligrams);
- Differences between dosing of the colistimethate conjugate and the base product colistin; and
- Potential sound-alike confusion when giving colistin (polymyxin E) as opposed to polymyxin B.

FDA-approved dosing of injectable colistimethate lists the strength in terms of the colistin base (150 mg of colistin base per vial). However, other references express the dosing based on international units or milligrams of the prodrug, colistimethate sodium, which may lead to a dose almost three times higher than if calculated as the base. This became the case in a reported error that led to a patient death, where a physician prescribed colistimethate as milligrams of the prodrug instead of the base. Because other healthcare staff did not recognize the error prior to administration, the patient received higher doses than intended, developed complications including acute renal failure, and expired.

### III. PROVIDER RECOMMENDATIONS<sup>1</sup>

Considerations as per the NAN Alert:

1. Prescribe colistimethate for injection ONLY as colistin base with dose ranging from 2.5 to 5 mg/kg/day (given in 2 to 4 divided doses) in patients with normal renal function, using ideal body weight for calculating doses in obese patients.
2. Reduce dose in patients with renal impairment as per product labeling.
3. Contact prescribing physician to verify dose of colistin base if provider orders "colistimethate" or "colistimethate sodium".
4. Consider restricting ordering of colistin (polymyxin E) and parenteral polymyxin B to infectious disease specialists and/or intensivists.
5. Consider providing guidelines addressing colistimethate dosing:
  - a. Only as colistin base;
  - b. Adjustments for renal dysfunction;
  - c. Maximum limits;
  - d. Circumstances where greater than the 2.5 to 5 mg/kg/day range may be appropriate.
6. Monitor renal function during colistin use for signs/symptoms of renal toxicity, and if present, evaluate for dose adjustment.

Providers should continue to report any adverse events with colistimethate for injection by entering the information into CPRS' Allergies/Adverse Reactions field and/or via local reporting mechanisms. Facilities should continue to report adverse events into VA ADERS and to the FDA (as appropriate).

### IV. REFERENCES

1. ASHP NAN ALERT: Dosing Confusion with Colistimethate for Injection.  
<http://www.ashp.org/DocLibrary/Policy/PatientSafety/NANAlert-Colistimethatesodium.aspx> . (Accessed 07/07/2011).

#### **ACTIONS**

- **Facility Director** (or physician designee): Forward this document to the Facility Chief of Staff (COS).
- **Facility COS and Chief Nurse Executives**: Forward this document to all appropriate providers who handle these medications (e.g., **infectious disease providers, critical care providers, inpatient pharmacy staff**, 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).