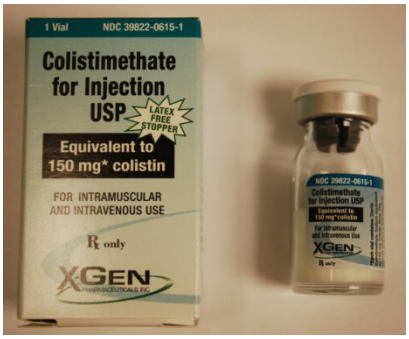
NAN ALERT
RISK OF SERIOUS OR FATAL MEDICATION ERROR
June 29, 2011

The following alert about the risk of a serious medication error is based on information from the National Medication Error Reporting Program operated by the Institute for Safe Medication Practices [ISMP MERP].



Warning! Dosing confusion with colistimethate for injection.

Colistimethate for injection, USP, is a prodrug of colistin, a polymyxin E antibiotic, available for several decades for the treatment of gram-negative infections. While vials are labeled colistimethate for injection, FDA officially lists it on the FDA website as the sodium salt, colistimethate sodium. Although its popularity has diminished over the years due to its potential for nephrotoxicity and neurotoxicity, its use has been increasing lately as a last resort treatment for multidrug-resistant organisms such as *Pseudomonas aeruginosa* and *Acinetobacter* species.

Risk for error

In the United States, the strength of all FDA-approved injectable colistimethate for injection products is labeled in terms of the colistin base, colistin, not the prodrug. Thus, the label expresses product strength as 150 mg of colistin base per vial (http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm). Dosing is also expressed in terms of the colistin base. By weight, the dose is between 2.5 to 5 mg/kg/day for patients with normal renal function. The usual maximum dose of colistin as the base is not more than 5 mg/kg/day. However, pharmacokinetic studies are still needed to properly determine maximum dose under certain circumstances such as extremely large patients and patients with cystic fibrosis. Data suggest that using a measure of lean body mass, such as ideal body weight, for dosing may be less nephrotoxic (1).

Unfortunately, some ambiguity exists in terms of product nomenclature and dose. Although the US product is labeled in terms of colistin base, listings in various references also refer to the dose in terms of international units or mg of the prodrug, colistimethate sodium (2). Dosing in terms of the prodrug when a dose of colistin base is intended will yield a dose that is approximately 2.5 times higher than if calculated as the base.

We are aware of a recent case where the prescribing physician ordered a dose as mg of the prodrug instead of the base. This went unrecognized by pharmacists and nurses and resulted in a dose approximately 2.5 times greater than it should have been. The patient received higher than intended doses, developed acute renal failure and other complications and later expired.

Error prevention

The following recommendations should be considered for safety reasons:

1. In the US, colistimethate for injection must ONLY be prescribed as colistin in terms of base activity with dose range of 2.5 to 5 mg/kg/day in patients with normal renal function. As per package insert, use ideal body weight for obese patients. This total daily dose should be given in 2 to 4 divided doses.

What is the NAN alert?
The National Alert Network is a coalition of members of the National Coordinating Council on Medication Error Reporting and Prevention (NCCMERP). The network distributes NAN alerts to warn healthcare providers of the risk for medication errors that have caused or may cause serious harm or death. NCC MERP encourages sharing and reporting of medication errors both nationally and locally, so that lessons learned can be used to increase the safety of the medication use system.

2. Dosage reduction in the setting of renal insufficiency is recommended (see product labeling for suggested modification of dosage schedules).
3. If the drug is ordered as “colistimethate” or “colistimethate sodium,” the prescriber should be contacted to verify the dose in terms of colistin base.
4. Consider restricting ordering to infectious disease specialists or intensivists.
5. To prevent errors, pre-approved printed guidelines or computer order sets should be made available with dosing only as colistin base. Include adjustments for renal dysfunction.
6. Dose limits should be established with immediate investigation required for doses outside hospital guidelines. Guidelines should define any circumstances where dosing outside the 2.5 to 5 mg/kg/day range may be appropriate. Testing of CPOE and pharmacy computer systems should be accomplished to assure proper function of alerts.
7. Monitoring of renal function while receiving colistin is important to detect signs of renal toxicity associated with colistin and the appropriateness of dosage should be re-evaluated periodically while on treatment.

Reference:

1. DeRyke CA, Crawford AJ, Uddin N, Wallace MR. Colistin dosing and nephrotoxicity in a large community teaching hospital. Antimicrob. Agents Chemother. 2010;54: 4503–4505
2. Lim LM, Ly N, Anderson D, et al. Resurgence of colistin: A review of resistance, toxicity, pharmacodynamics, and dosing. Pharmacotherapy 2010;30:1279–1291

Please report medication errors with this product in confidence to both the ISMP National Medication Error Reporting Program and the FDA MedWatch Program via this single portal: https://www.ismp.org/orderforms/reporterrortoismp.asp. **ISMP is federally-certified Patient Safety Organization (PSO).**