RISK OF EOSINOPHILIC PNEUMONIA ASSOCIATED WITH DAPTOMYCN (CUBICIN)

This issue of *New Drug FAX Sheet* provides information from the FDA regarding the association of eosinophilic pneumonia with daptomycin use. The verbatim FDA drug safety communication is provided below. If you need further information please contact the Samford University Global Drug Information Service at (205) 726-2659.

The U.S. Food and Drug Administration (FDA) is informing patients and healthcare professionals about the potential for developing eosinophilic pneumonia during treatment with Cubicin (daptomycin), an intravenous antibacterial drug. Cubicin was first approved in September 2003 to treat serious skin infections. In 2006, it was approved to treat bloodstream infections.

Eosinophilic pneumonia is a rare, but serious condition where a type of white blood cell (eosinophil) fills the lungs. Symptoms of eosinophilic pneumonia include fever, cough, shortness of breath, and difficulty breathing. Healthcare professionals should closely monitor patients being treated with Cubicin for eosinophilic pneumonia (see Additional Information for Healthcare Professionals). Patients receiving Cubicin should immediately contact their healthcare professional if they develop a new or worsening fever, cough, shortness of breath, or difficulty breathing. In 2007, pulmonary eosinophilia was added to the Adverse Reactions, Post-Marketing Experience section of the Cubicin product label. Since then, the Agency has reviewed published case reports of Cubicin-associated eosinophilic pneumonia, and conducted a review of post-marketing adverse event reports from the FDA's Adverse Event Reporting System (AERS). FDA's review identified 7 cases of eosinophilic pneumonia between 2004 and 2010 that were most likely associated with Cubicin (see Data Summary below).

Based on these reviews, FDA determined that eosinophilic pneumonia can be associated with Cubicin use and requested that the manufacturer of Cubicin include this information in the Warnings and Precautions and Adverse Reactions, Post-Marketing Experience sections of the drug label.

Additional Information for Patients
- Be aware that eosinophilic pneumonia has been reported in patients receiving Cubicin.
- If you experience a new or worsening fever, cough, shortness of breath, or have difficulty breathing while receiving Cubicin, contact your healthcare professional immediately.
- Talk to your healthcare professional about any concerns with Cubicin.
- Report any side effects from the use of Cubicin to the FDA MedWatch program, using the information in the "Contact Us" box at the bottom of the page.

Additional Information for Healthcare Professionals
- Be aware that eosinophilic pneumonia has been reported in patients receiving Cubicin.
- Discuss with patients the clinical benefits and potential risks of Cubicin, including the risk of eosinophilic pneumonia, prior to beginning treatment.
- Monitor patients for signs and symptoms of eosinophilic pneumonia, including new onset or worsening fever, dyspnea, difficulty breathing, and new infiltrates on chest imaging studies.
- In patients exhibiting signs and symptoms of eosinophilic pneumonia, discontinue Cubicin and consider treating as clinically indicated.
- Report adverse events involving Cubicin to the FDA MedWatch program using the information in the "Contact Us" box at the bottom of this page.

Data Summary
FDA identified six cases of eosinophilic pneumonia reported to AERS between 2004 and 2010 that were most likely associated with Cubicin. One additional case of eosinophilic pneumonia most likely associated with Cubicin was identified in the medical literature.

For FDA’s review, a case of eosinophilic pneumonia most likely associated with Cubicin was defined as meeting all of the following criteria:

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Concurrent exposure to Cubicin
- Fever
- Dyspnea with increased oxygen requirement or requiring mechanical ventilation
- New infiltrates on chest x-ray or computed tomography scan
- Bronchoalveolar lavage with > 25% eosinophils
- Clinical improvement following Cubicin withdrawal

Of the seven cases identified using the above definition:
- Cubicin was prescribed for non-FDA approved indications, including osteomyelitis (n=4), prosthetic hip infection (n=1), enterococcal endocarditis (n=1), and aortic valve endocarditis (n=1).
- The ages of patients ranged from 60 to 87 years.
- Eosinophilic pneumonia developed 2-4 weeks after initiating Cubicin treatment.
- All seven cases reported improvement or resolution of symptoms after Cubicin was discontinued. Five of the seven cases were also treated with systemic corticosteroids.
- Two cases reported recurrence of eosinophilic pneumonia after Cubicin was restarted.

FDA also identified 36 possible cases of eosinophilic pneumonia associated with Cubicin use. Although these cases did not meet the full criteria for a likely case of eosinophilic pneumonia associated with Cubicin, they do provide additional support for an association between use of Cubicin and development of eosinophilic pneumonia. Based on FDA's review, there appears to be a temporal association between Cubicin administration and the development of eosinophilic pneumonia. Eosinophilic pneumonia may lead to progressive respiratory failure and is potentially fatal if not quickly recognized and appropriately managed. FDA requested that Cubist, the manufacturer of the product, revise the Warnings and Precautions and Adverse Reactions, Post-Marketing Experience sections of the Cubicin product label to further inform healthcare professionals of this association.

References: