

### **Azithromycin May Increase Risk of Cardiovascular Death**

A new study published by the New England Journal of Medicine, raises concerns about an increased risk of cardiovascular death in patients taking azithromycin. This study reported a small increase in cardiovascular deaths in patients being treated with a 5 day course of azithromycin (Zithromax, "Z-pack") compared to amoxicillin, ciprofloxacin, or no antibiotic. Azithromycin is a broad spectrum antibiotic used to treat a variety of bacterial infections. The closely related antibiotics, erythromycin and clarithromycin, are known to increase the risk of serious ventricular arrhythmias resulting in sudden cardiac death. Until recently, it was thought that azithromycin was relatively free of cardiotoxic effects. However, there are at least 7 published reports of patients taking azithromycin who had normal baseline QT intervals in which QT-interval prolongation, torsades de points, and polymorphic ventricular tachycardia in the absence of QT-interval prolongation, have occurred. The FDA's Adverse Event Reporting System also includes at least 20 reports of torsades de points associated with azithromycin.

On May 17, 2012, the FDA released a statement advising health care professionals to be aware of the potential for QT prolongation and heart arrhythmias when prescribing certain antibiotics. The FDA is instructing patients not to stop taking azithromycin without talking to their healthcare professional first. In March 2012, the FDA required the manufacturer of Zmax (azithromycin extended release) oral suspension to include warnings and precautions about torsades de points in its product labeling. The new labeling suggests azithromycin should be avoided in patients with known prolongation of the QT interval, those with proarrhythmic conditions, such as hypokalemia, hypomagnesemia, bradycardia, and those taking Class IA (quinidine, procainamide) or Class III (dofetilide, amiodarone, sotalol) antiarrhythmic agents.

The FDA is currently reviewing the results of the study recently published by the New England Journal of Medicine and will release further recommendations regarding the use of azithromycin at a later date. Until then, it is recommended that health care providers use caution when prescribing azithromycin, especially in patients who are at high risk for developing cardiac arrhythmias. Alternative antibiotics that are not likely to cause cardiac arrhythmias, such as amoxicillin, might be a better option in these patients.

#### References:

1. Azithromycin (Zithromax) and the Risk of Cardiovascular Death. Pharmacist's Letter 2012; 28(6):280603
2. Zmax (azithromycin extended release) for oral suspension. Medwatch Safety Information [Updated 04/12/2012]. US Food and Drug Administration. Available at: <http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm262866.htm>. Accessed June 18, 2012.
3. FDA Statement regarding azithromycin (Zithromax) and the risk of cardiovascular death. Medwatch Safety Information [Updated 05/17/2012]. US Food and Drug Administration. Available at [http://www.fda.gov/Drugs/DrugSafety/ucm304372.htm?utm\\_campaign=Google2&utm\\_source=fdaSearch&utm\\_medium=website&utm\\_term=azithromycin&utm\\_content=1](http://www.fda.gov/Drugs/DrugSafety/ucm304372.htm?utm_campaign=Google2&utm_source=fdaSearch&utm_medium=website&utm_term=azithromycin&utm_content=1). Accessed June 18, 2012.