

### FDA Drug Safety Communication

FDA review finds additional data supports the potential for increased long-term risks with antibiotic clarithromycin (Biaxin) in patients with heart disease

#### Safety Announcement

**[02-22-2018]** The U.S. Food and Drug Administration (FDA) is advising caution before prescribing the antibiotic clarithromycin (Biaxin) to patients with heart disease because of a potential increased risk of heart problems or death that can occur years later. Our recommendation is based on our review of the results of a 10-year follow-up study<sup>1</sup> of patients with coronary heart disease from a large clinical trial<sup>2</sup> that first observed this safety issue.

As a result, we have added a new warning about this increased risk of death in patients with heart disease, and advised prescribers to consider using other antibiotics in such patients. We have also added the study results to the clarithromycin drug labels. As part of FDA's usual ongoing safety monitoring of drugs, we are continuing to monitor safety reports in patients taking clarithromycin.

**Health care professionals** should be aware of these significant risks and weigh the benefits and risks of clarithromycin before prescribing it to any patient, particularly in patients with heart disease and even for short periods, and consider using other available antibiotics. Advise patients with heart disease of the signs and symptoms of cardiovascular problems, regardless of the medical condition for which you are treating them with clarithromycin.

**Patients** should tell your health care professionals if you have heart disease, especially when you are being prescribed an antibiotic to treat an infection. Talk to them about the benefits and risks of clarithromycin and any alternative treatments. Do not stop taking your heart disease medicine or antibiotic without first talking to your health care professionals. Doing so could be harmful without your health care professionals' direct supervision. Seek medical attention immediately if you experience symptoms of a heart attack or stroke, such as chest pain, shortness of breath or trouble breathing, pain or weakness in one part or side of your body, or slurred speech.

Like other antibiotics, clarithromycin is used to treat many types of infections affecting the skin, ears, sinuses, lungs, and other parts of the body, including Mycobacterium avium complex (MAC) infection, a type of lung infection that often affects people with human immunodeficiency virus (HIV). Clarithromycin is not approved to treat heart disease. The drug has been used for more than 25 years, and is sold under the brand name Biaxin and as generics by many different drug companies. It works by stopping the growth of bacteria. Without treatment, some infections can spread and lead to serious health problems.

The large clinical trial, called the CLARICOR trial<sup>2</sup>, observed an unexpected increase in deaths among patients with coronary heart disease who received a two-week course of clarithromycin that became apparent after patients had been followed for one year or longer. There is no clear explanation for how clarithromycin would lead to more deaths than placebo. Some observational studies also found an increase in deaths or other serious heart-related problems, while others did not. All the studies had limitations in how they were designed. Of the six observational studies published to date in patients with or without coronary artery disease, two found evidence of long-term risks from clarithromycin<sup>3,4</sup>, and four did not<sup>5,6,7,8</sup>. Overall, results from the prospective, placebo-controlled CLARICOR trial provide the strongest evidence of the increase in risk compared to the observational study results. Based on these studies, we were unable to determine why the risk of death is greater for patients with heart disease.

Furthermore, there are no prospective, randomized, and controlled trials with prespecified long-term safety outcome measures following clarithromycin treatment in patients who do not have heart disease. Because we currently do not have study information in these patients, and observational studies have shown different results, we cannot determine whether results of the CLARICOR trial can be applied to patients who do not have heart disease.

We previously communicated about this safety issue in [December 2005](#), before the 10-year follow-up results were available for CLARICOR.

We urge health care professionals and patients to report side effects involving clarithromycin and other drugs to the FDA MedWatch program, using the information in the “Contact FDA” box at the bottom of the page.

## References

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4. Mosholder AD, Lee JY, Zhou EH, et al. Long-term risk of acute myocardial infarction, stroke and mortality in adult outpatients treated with clarithromycin: a retrospective cohort study in the Clinical Practice Research Datalink. *Journal of Epidemiology*, kwx319, <https://doi.org/10.1093/aje/kwx319>.
5. Andersen SS, Hansen ML, Norgaard, ML, et al. Clarithromycin use and risk of death in patients with ischemic heart disease. *Cardiology* 2010;116:89-97.
6. Root AA, Wong AY, Ghebremichael-Weldeslassie Y, et al. Evaluation of the risk of cardiovascular events with clarithromycin using both propensity score and self-controlled study designs. *Br J Clin Pharmacol* 2016 Aug;82(2):512-21.

7. Wong AY, Root A, Douglas IJ, et al. Cardiovascular outcomes associated with use of clarithromycin: population based study. *BMJ* 2016 Jan 14;352:h6926. doi: 10.1136/bmj.h6926.
8. Inghammar M, Nibell O, Pastemak B, Melbye M, Svanström H, Hviid A. Long term risk of cardiovascular death with use of clarithromycin and roxithromycin - a nationwide cohort study. *Am J Epidemiol* 2017; Nov 16: doi: 10.1093/aje/kwx359 [Epub ahead of print].

### **Related Information**

- [Clarithromycin \(marketed as Biaxin\) Information](#)
- [Clarithromycin \(by mouth\)](#)
- [The FDA's Drug Review Process: Ensuring Drugs are Safe and Effective](#)
- [Think It Through: Managing the Benefits and Risks of Medicines](#)