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Quick Pulse

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PPIs Do Not Cause Heart Problems but Association with Hip Fractures Still Under Study

The FDA announced on December 10, 2007, that it has determined that proton pump inhibitors (PPIs) – e.g., AstraZeneca's Prilosec (omeprazole) and Nexium (esomeprazole) – do not cause heart attacks or cardiac problems. After issuing a written statement, FDA officials spoke by teleconference with reporters about the decision.

On May 29, 2007, AstraZeneca sent the FDA data from two long-term studies in patients with severe gastroesophageal reflux disease (GERD) that were being treated with either Prilosec or Nexium…During the studies, cardiovascular events raised a question about whether long-term use of these drugs increases the risk of heart attacks, heart failure, and heart-related sudden death in patients taking either of those drugs vs. patients who received surgical treatment. Then, on August 9, 2007, the FDA issued an "Early Communication of an Ongoing Safety Review" of those drugs. In that initial review, the FDA determined that there was no increased risk of cardiac problems associated with long-term use of either drug, but the FDA asked AstraZeneca to submit additional data, and it undertook a comprehensive review of the cardiac safety of these PPIs.

Dr. Paul Seligman, associate director for Safety Policy and Communication in the FDA's Center for Drug Evaluation and Research (CDER), said the FDA review found no cardiac safety problem, "We have completed our safety review, and our current assessment is the difference seen in the earlier analysis of two small studies, which has been supplemented by additional information from those studies as well as a review and analysis of 14 other comparative studies, including 4 that were placebo-controlled – (are not substantiated). It is our assessment that those studies do not show a risk for heart attacks or heart-related problems."

The FDA has not asked AstraZeneca or the manufacturers of any other PPIs for additional data on PPIs and cardiac safety, so this cardiac safety issue should be settled unless and until there is new evidence of a cardiac risk. However, **PPI safety is *still under review*** for a different reason.

There was a report in the ***Journal of the American Medical Association*** (JAMA) in December 2006 about hip fractures in older people taking PPIs long term, and Dr. Seligman said that article prompted an FDA review. Thus, the FDA has an ongoing review related to PPIs and hip fractures. Dr. Joyce Korvick, deputy director of the FDA's Division of Gastroenterology Products, Office of Drug Evaluation III, CDER, explained, "Internally, we've looked at the issue and asked all the sponsors to send us additional information and analyses on this area, and that is under review. That is all I can say right now."

At this point, the FDA does not appear to be planning to issue an early communication on hip fractures any time soon. Dr. Seligman said, "We have not issued an early communication on that (hip fracture) review, but we generally like to do early communications when we have information in house that is not otherwise generally accessible to the public. When something is published in a major medical journal and is well-known to the public, it in some ways obviates our need to do an early communication."

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