Alert for Healthcare Professionals

Celecoxib (marketed as Celebrex)

FDA Alert [04/07/05]:

Celebrex has been associated with an increased risk of serious adverse cardiovascular (CV) events in a long-term placebo controlled trial. Based on the currently available data, FDA has concluded that an increased risk of serious adverse CV events appears to be a class effect of non-steroidal anti-inflammatory drugs (NSAIDs) (excluding aspirin). FDA has requested that the package insert for all NSAIDs, including Celebrex, be revised to include a boxed warning to highlight the potential increased risk of CV events and the well described risk of serious, and potentially life-threatening, gastrointestinal bleeding. FDA has also requested that the package insert for all NSAIDs be revised to include a contraindication for use in patients immediately post-operative from coronary artery bypass (CABG) surgery.

This information reflects FDA's current analysis of all available data concerning this drug. FDA intends to update this sheet when additional information or analyses become available.

Recommendations

- Physicians are encouraged to carefully weigh the potential benefits and risks of Celebrex and other treatment options for the condition to be treated before a decision is made to use Celebrex. If Celebrex is selected for an individual patient, FDA encourages use of the lowest effective dose for the shortest duration consistent with individual patient treatment goals.
- Celebrex should not be used in patients who are immediately post-operative from CABG surgery.

Data Summary

- In the National Cancer Institute's Adenoma Prevention with Celecoxib (APC) trial in patients at risk for recurrent colon polyps, a 2-3 fold increased risk of serious adverse CV events was seen for Celebrex compared to placebo after a mean duration of treatment of 33 months. There appeared to be a dose response relationship, with a hazard ratio of 2.5 for Celebrex 200 mg twice daily and 3.4 Celebrex 400 mg twice daily for the composite endpoint of death from CV causes, myocardial infarction (MI), or stroke.
- In the nearly identical Prevention of Spontaneous Adenomatous Polyps (PreSAP) trial, the APC results were not replicated. Based on preliminary, unpublished data presented by the investigators at the February 16-18, 2005, FDA meeting of the Arthritis Advisory Committee and the Drug Safety and Risk Management Advisory Committee, the hazard ratio was 1.1 for celecoxib 400 mg once daily compared to placebo for the composite endpoint of death from CV causes, MI, or stroke. (Extensive data related to the cardiovascular safety of Celebrex and other COX-2 selective and non-selective NSAIDs were presented at this Advisory Committee meeting. This information is available on the following website: http://www.fda.gov/ohrms/dockets/ac/cder05.html#ArthritisDrugs).

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- Another long-term controlled trial, the National Institute of Aging's Alzheimer's Disease Anti-Inflammatory Prevent Trial (ADAPT), compared Celebrex 200 mg twice daily to placebo in patients at risk for Alzheimer's disease. Data are not yet available from this trial; however, a preliminary report released by NIH on December 20, 2004, (http://www.nih.gov/news/pr/dec2004/od-20.htm) suggested that no increased risk of serious adverse CV events was found for Celebrex compared to placebo.
- The only available data from a long-term comparison of Celebrex to other NSAIDs come from the Celebrex Long-Term Arthritis Safety Study (CLASS) in which Celebrex 400 mg twice daily was compared to diclofenac and ibuprofen in approximately 8,000 patients with osteoarthritis. No differences were observed for serious adverse CV events between Celebrex and the two NSAID comparators in this trial.
- In two short-term placebo-controlled clinical trials in patients immediately post-operative from CABG surgery, valdecoxib, another COX-2 selective NSAID, was associated with an approximately two-fold increased risk of serious adverse CV events compared to placebo. No data are available for Celebrex in the post-CABG surgery population; however, pending receipt of further data, FDA has concluded that all NSAIDs, including Celebrex, should be contraindicated in patients immediate post-operative from CABG surgery.