

These are letters from the FDA issuing warnings and safety alerts for consumers about possible adverse reactions from taking the drug Bextra.

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FDA Issues Public Health Advisory Recommending Limited Use of Cox-2 Inhibitors

Agency Requires Evaluation of Prevention Studies Involving Cox-2 Selective Agents

The Food and Drug Administration (FDA) today issued a Public Health Advisory summarizing the agency's recent recommendations concerning the use of non-steroidal anti-inflammatory drug products (NSAIDs), including those known as COX-2 selective agents. The public health advisory is an interim measure, pending further review of data that continue to be collected.

In addition, FDA today announced that it is requiring evaluation of all prevention studies that involve the Cox-2 selective agents Celebrex (celecoxib) and Bextra (valdecoxib) to ensure that adequate precautions are implemented in the studies and that local Institutional Review Boards reevaluate them in light of the new evidence that these drugs may increase the risk of heart attack and stroke. A prevention trial is one in which healthy people are given medicine to prevent a disease or condition (such as colon polyps or Alzheimer's disease).

FDA is issuing an advisory because of recently released data from controlled clinical trials showing that the COX-2 selective agents (Vioxx, Celebrex, and Bextra) may be associated with an increased risk of serious cardiovascular events (heart attack and stroke) especially when they are used for long periods of time or in very high risk settings (immediately after heart surgery).

Also, as FDA announced earlier this week, preliminary results from a long-term clinical trial (up to three years) suggest that long-term use of a non-selective NSAID, naproxen (sold as Aleve, Naprosyn and other trade name and generic products), may be associated with an increased cardiovascular (CV) risk compared to placebo.

Although the results of these studies are preliminary and conflict with other data from studies of the same drugs, FDA is making the following interim recommendations:

Physicians prescribing Celebrex (celecoxib) or Bextra (valdecoxib), should consider this emerging information when weighing the benefits against risks for individual patients. Patients who are at a high risk of gastrointestinal (GI) bleeding, have a history of intolerance to non-selective NSAIDs, or are not doing well on non-selective NSAIDs may be appropriate candidates for Cox-2 selective agents.

Individual patient risk for cardiovascular events and other risks commonly associated with NSAIDs should be taken into account for each prescribing situation.

Consumers are advised that all over-the-counter (OTC) pain medications, including NSAIDs, should be used in strict accordance with the label directions. If use of an (OTC) NSAID is needed for longer than ten days, a physician should be consulted.

Non-selective NSAIDs are widely used in both over-the-counter (OTC) and prescription settings. As prescription drugs, many are approved for short-term use in the treatment of pain and primary dysmenorrhea (menstrual discomfort), and for longer-term use to treat the signs and symptoms of osteoarthritis and rheumatoid arthritis. FDA has previously posted exTENSive NSAID medication information at <http://www.fda.gov/cder/drug/analgesics/default.htm>.

FDA is collecting and will be analyzing all available information from the most recent studies of Vioxx,

Celebrex, Bextra, and naproxen, and other data for COX-2 selective and nonselective NSAID products to determine whether additional regulatory action is needed. An advisory committee meeting is planned for February 2005, which will provide for a full public discussion of these issues.

FDA urges health care providers and patients to report adverse event information to FDA via the MedWatch program by phone (1-800-FDA-1088), by fax (1-800-FDA-0178), or by the Internet at <http://www.fda.gov/medwatch/index.html>.

The Public Health Advisory is available online at www.fda.gov/cder/drug/advisory/nsaids.htm.