FDA Alert for Healthcare Providers
Naproxen

FDA Alert [12/23/04]: Based on emerging information from a long-term prevention trial, the risk of cardiovascular and cerebrovascular events may increase among patients taking naproxen. FDA will be analyzing all available information from these studies to determine whether additional regulatory action is needed.

Prescribing Considerations:

- Healthcare providers who have patients that are currently on naproxen therapy or are considering naproxen therapy for their patients, should carefully weigh the risks and benefits and use the product according to the label.

- For over-the-counter products containing naproxen, healthcare providers should advise their patients to adhere to the recommended daily dose as follows:

  - 1 tablet (220 mg) every 8 to 12 hours while symptoms last
  - 2 tablets (440 mg) may be taken initially within the first hour of symptoms
  - Patients should not exceed 2 tablets (440 mg) in any 8 to 12 hour period and should not exceed 3 tablets (660 mg) in a 24-hour period.

- For prescription use, naproxen should always be prescribed within the recommended dosing range of 250 mg to 500 mg twice a day.

Data Summary:

The National Institutes of Health (NIH) announced on December 20, 2004, that they were halting a clinical trial in patients at risk of developing Alzheimer's Disease treated with non-steroidal anti-inflammatory drugs due to potential increased cardiovascular events associated with drug therapy. The trial, *Alzheimer's Disease Anti-Inflammatory Prevention* Trial (ADAPT) was designed to assess whether the non-steroidal anti-inflammatory drugs (NSAIDs) — naproxen and celecoxib (COX-2 inhibitor) had potential benefit in preventing the onset of Alzheimer's disease. The study enrolled subjects 70 years of age or older who were considered to be at increased risk because of family history, but did not yet have symptoms of the disease.

Approximately 2400 volunteer participants were randomly assigned to receive naproxen (220 mg twice a day), celecoxib, or placebo for periods of time up to three years. Although no significant increase in risk for celecoxib was found in this trial, the study was suspended in part because of findings reported last week from a National Cancer Institute (NCI) colon cancer prevention trial that demonstrated increased cardiovascular events related to celecoxib use. In addition, preliminary data from the *ADAPT* trial indicated an apparent increase in reports of cardiovascular and cerebrovascular adverse events among the participants taking naproxen when

compared with those on placebo. We are continuing to analyze these data to determine the validity of these observations.

To report any unexpected adverse or serious events associated with the use of Naproxen, please contact the FDA MedWatch program at 1-800-FDA-1088 or http://www.fda.gov/medwatch/report/hcp.htm

We encourage you to provide a copy of FDA's Patient Information Sheet to your patient.

Approved Prescription Drug Label
http://www.fda.gov/cder/foi/label/2004/17581s99,100,18164s50,51,18965s9,10,20067s4,6lbl.pdf