Nonsteroidal Anti-Inflammatory Drugs — Safety Update

• Based on a comprehensive review of new safety information, the FDA announced that they are strengthening existing label warnings for both prescription and over-the-counter (OTC) non-aspirin, nonsteroidal anti-inflammatory drugs (NSAIDs) regarding the increased risk of a heart attack or stroke, either of which may lead to death.

— Current prescription NSAID labels and the Drug Facts labels of over-the-counter (OTC) non-aspirin NSAIDs already contain information on heart attack and stroke risk.

• Patients taking NSAIDs should seek medical attention immediately if they experience symptoms such as chest pain, shortness of breath or trouble breathing, weakness in one part or side of their body, or slurred speech.

• Patients who take low-dose aspirin for protection against heart attack and stroke should know that some NSAIDs, including those in OTC products such as ibuprofen and naproxen, can interfere with aspirin’s protective effect.

• Prescription and OTC NSAIDs are widely used to treat pain and fever from many different long- and short-term medical conditions such as arthritis, menstrual cramps, headaches, colds, and the flu.

— Examples of NSAIDs include ibuprofen, naproxen, diclofenac, and celecoxib. A list of non-aspirin NSAIDs is located here.

• The risk of heart attack and stroke with NSAIDs was first described in 2005 in the Boxed Warning and Warnings and Precautions sections of the prescription drug labels. Since 2005, the FDA has discussed and reviewed new safety information during an Advisory Committee Meeting held in 2014.

• Based on the FDA’s review and the Advisory Committee’s recommendations, the prescription NSAID labels will be revised to reflect the following:

— The risk of heart attack or stroke can occur as early as the first weeks of using an NSAID. The risk may increase with longer use of the NSAID.

— The risk appears greater at higher doses.

— It was previously thought that all NSAIDs may have a similar risk. Newer information makes it less clear that the risk for heart attack or stroke is similar for all NSAIDs; however, this newer information is not sufficient for the FDA to determine that the risk of any particular NSAID is definitely higher or lower than that of any other particular NSAID.

— NSAIDs can increase the risk of heart attack or stroke in patients with or without heart disease or risk factors for heart disease. A large number of studies support this finding, with estimates varying from 10% to > 50%, of how much the risk is increased, depending on the drugs and the doses studied.

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— In general, patients with heart disease or risk factors for it have a greater likelihood of heart attack or stroke following NSAID use than patients without these risk factors because they have a higher risk at baseline.

— Patients treated with NSAIDs following a first heart attack were more likely to die in the first year after the heart attack compared to patients who were not treated with NSAIDs after their first heart attack.

— There is an increased risk of heart failure with NSAID use.

- Similar updates will be made to the existing heart attack and stroke risk information in the Drug Facts labels of OTC non-aspirin NSAIDs.

- Additional information for healthcare providers:
  - Remain alert for the development of cardiovascular (CV) adverse events throughout the patient’s entire treatment course, even in the absence of previous CV symptoms.
  - To minimize the risk for an adverse CV event in patients treated with an NSAID, the lowest effective dose for the shortest duration possible should be prescribed.
  - Some NSAIDs, including those in OTC products such as ibuprofen and naproxen, can interfere with the antiplatelet action of low dose aspirin used for cardioprotection by blocking aspirin’s irreversible COX-1 inhibition.

- A large, ongoing randomized clinical trial (PRECISION) comparing CV event rates among patients with high CV risk randomized to celecoxib, naproxen, or ibuprofen was evaluated at the 2014 Advisory Committee meeting and is expected to provide additional safety information.