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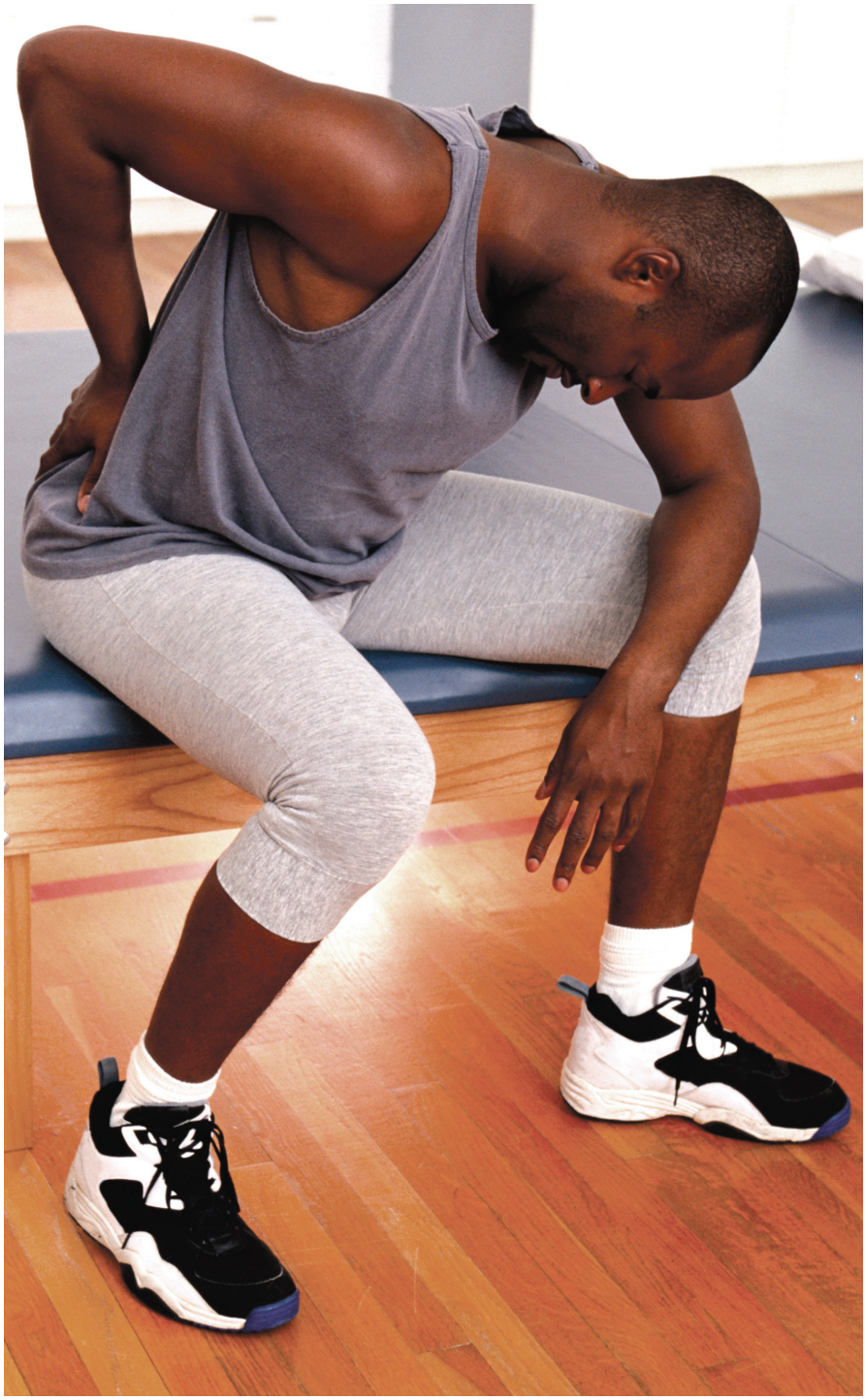
The Benefits and Risks of **PAIN RELIEVERS:**



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Q&A on NSAIDs with Sharon Hertz, M.D.

Sharon Hertz is Deputy Director of FDA's Division of Anesthesia, Analgesia, and Rheumatology Products and has been with FDA for 8 years. Dr. Hertz graduated from SUNY Upstate Medical Center in Syracuse, N.Y., and completed her residency in neurology at SUNY Health Sciences Center at Brooklyn.

Q. What are non-steroidal anti-inflammatory drugs (NSAIDs)?

A. NSAIDs are a group of drugs used to temporarily relieve pain and inflammation. They work by blocking the production of prostaglandins, or chemicals believed to be associated with pain and inflammation.

Q. What conditions do NSAIDs treat?

A. Prescription NSAIDs are an important treatment for many debilitating conditions such as osteoarthritis and rheumatoid arthritis. Some prescription NSAIDs also are used to treat pain. Over-the-counter versions of some NSAIDs are used to treat fever and pain associated with dental problems, tendonitis, strains, sprains and other injuries. NSAIDs are also commonly used to relieve pain associated with menstrual cramps.

Whether you're taking a prescription NSAID or an OTC NSAID, following directions is important.

Q. What are non-selective NSAIDs and COX-2 selective NSAIDs?

A. Non-selective NSAIDs work by inhibiting two enzymes that are involved with inflammation—cyclooxygenase-1 and cyclooxygenase-2 (COX-1 and COX-2).

There are several non-selective NSAIDs on the market, including diclofenac, ibuprofen, ketoprofen, meloxicam, naproxen, and oxaprozin. Ibuprofen, ketoprofen, and naproxen are available in both prescription and over-the-counter (OTC) versions. The doses in OTC NSAIDs are lower than the doses of prescription versions and should only be used for up to 10 days without seeing a doctor. So, if you take OTC ibuprofen (Advil and Motrin) or naproxen (Aleve), the doses are about half the doses of prescription versions.

COX-2 selective inhibitors are a newer type of medicine that primarily block the COX-2 enzyme. The only COX-2 selective inhibitor currently on the market in the United States is the prescription drug Celebrex (celecoxib), which is marketed by Pfizer. It was believed that COX-2 inhibitors may be less likely to cause the stomach problems associated with the older NSAIDs, but all NSAIDs carry the risk of stomach problems.

Q. What are the risks of taking NSAIDs?

A. Like all drugs, there is the potential for an allergic reaction to NSAIDs. Symptoms may include hives, facial swelling, wheezing, and skin rash.

There is the potential for gastrointestinal bleeding associated with all NSAIDs. The risk of bleeding is low for people who use NSAIDs intermittently. The risk of stomach problems goes up for people who take them every day or regularly, especially for people who are over 65, people with a history of stomach ulcers, and people who take blood thinners or corticosteroids (prednisone). Alcohol use can also increase the risk of stomach problems.

Long-term continuous use of all NSAIDs, except for aspirin, may increase the risk of heart attack or stroke. Aspirin is a non-selective NSAID, but it has been shown in clinical trials to reduce the risks of cardiovascular events. Aspirin is sold in generic forms and under brand names such as Bayer and St. Joseph's.

All NSAIDs also carry the risk of potential skin reactions. Patients should be alert for symptoms such as the skin reddening, rash, or blisters.

Q. Which people are at highest risk for cardiovascular adverse events associated with NSAIDs?

A. People who have coronary artery disease (known angina or who have had a heart attack), people who have high blood pressure, and people who have had a stroke are at the greatest risk. Also, people who have just had cardiovascular bypass surgery are at risk for heart attacks with use of NSAIDs.

Q. Which Cox-2 selective inhibitors have been taken off the market?

A. Merck voluntarily withdrew Vioxx (rofecoxib) in 2004 after finding out the results of a study that showed patients who took Vioxx had a higher risk for heart attacks than patients who took a placebo. FDA asked Pfizer to withdraw Bextra (valdecoxib) from the market in 2005 because the overall risk/benefit profile was unfavorable. The request was based on many factors. Along with the other risks associated with NSAIDs, there were a higher than expected number of reports of serious and potentially life-threatening skin reactions, including death.

An increased risk of cardiovascular adverse events has been shown for all COX-2 inhibitors, including Celebrex, which is still on the market in the United States. Based on available data, FDA determined that the benefits of Celebrex outweigh the potential risks in properly selected and informed patients. FDA asked Pfizer to include a boxed warning on the Celebrex label, and asked manufacturers of all prescription NSAIDs to revise their labeling too. The boxed warning highlights the potential for increased risk of cardiovascular events as well as serious, potentially life-threatening gastrointestinal bleeding. It is important to know that FDA also determined that the risk for cardiovascular events was most likely present for the non-selective NSAIDs as well, and all of the manufacturers of these drugs were asked to add important warnings to their labels.

Q. What can consumers do to lower their risks with NSAIDs?

A. Tell your doctor about your complete medical history, including any history of cardiovascular disease or stomach ulcers. This will help you and your doctor weigh the risks and benefits. You can also ask your doctor what you can do to lesson the chance for stomach irritation such as taking medication with a meal. Also, ask what steps you can take to lower the risk of cardiovascular disease and report medication side effects to your doctor. Whether you're taking a prescription NSAID or an OTC NSAID, following directions is important. Available scientific data don't suggest an increased risk of serious cardiovascular events for short-term, low-dose use of OTC NSAIDs. But be aware that the OTC labeling states that if you take an NSAID for longer than 10 days, you should see your doctor. The lowest effective dose should be used for the shortest time. FDA