

## Can Patients With Cardiovascular Disease Take Nonsteroidal Antiinflammatory Drugs?

Kathryn A. Taubert, PhD

More than 80 million people in the United States have some form of cardiovascular disease (CVD)—for example, coronary heart disease, stroke, high blood pressure, or heart failure—and millions of others are at increased risk for these diseases. Over half of these people are also affected by arthritis and other disorders of the musculoskeletal system—the muscles, bones, joints, ligaments, tendons, and bursa. The pain associated with these chronic conditions is often treated with a class of medications known as nonsteroidal antiinflammatory drugs (NSAIDs). However, it has been shown that taking some NSAIDs can increase a person's risk of having a heart attack or stroke. This risk is likely greatest in patients who have a prior history of CVD or who are at high risk for CVD. The information here will help you to understand what NSAIDs are and whether it is safe to take them.

### What Are NSAIDs?

NSAIDs can reduce fever, pain, and inflammation (swelling and redness). Some are available over the counter (OTC), whereas others require a prescription. The best known NSAID is

aspirin. Other common NSAIDs are ibuprofen, ketoprofen, and naproxen (all 3 are available both OTC and in prescription strengths). NSAIDs available only by prescription are celecoxib, diclofenac, indomethacin, and sulindac (see Table 1 for a longer list and brand names).

### How Do NSAIDs Work?

NSAIDs work by inhibiting a substance in the body called cyclooxygenase (COX) from doing its work. Two major classes of cyclooxygenase are found in your body, COX-1 and COX-2. COX-1 is produced constantly in most tissues of the body, whereas COX-2 production is stimulated by inflammation (swelling and redness as might occur in association with an infection or arthritis) of a part of the body. Many NSAIDs are called “non-selective” because they inhibit COX-1 and COX-2; others more specifically inhibit COX-2. Nonselective COX inhibitors, such as aspirin or ibuprofen, give pain relief for inflammatory conditions but have a risk of eroding the stomach lining and causing ulcers and/or gastrointestinal bleeding. Newer selective COX-2 inhibitors, which were developed to minimize

irritation to the stomach but still fight pain and inflammation, became available by prescription in the late 1990s.

### What Are the Drawbacks of NSAIDs?

Overall, NSAIDs help to relieve pain and inflammation and reduce fever by inhibiting the production of COX in the body. They can have unwanted side effects, however, some of which can be serious for patients with heart disease or who are at risk for heart disease.

In 2004, the US Food and Drug Administration (FDA) announced that COX-2 selective agents might be associated with an increased risk of heart attack and stroke, especially when they are used for long periods of time or in very high-risk settings (such as immediately after heart surgery). At that time, 3 COX-2 selective agents were on the market, Vioxx, Celebrex, and Bextra.

In 2005, the FDA asked the makers of both prescription and OTC NSAIDs (except aspirin) to make labeling changes to their products by adding more information about the potential cardiovascular and gastrointestinal side effects associated with their use.

The information contained in this *Circulation* Cardiology Patient Page is not a substitute for medical advice, and the American Heart Association recommends consultation with your doctor or healthcare professional.

From the Department of Science and Medicine, American Heart Association, Dallas, Tex.

Correspondence to Kathryn A. Taubert, PhD, American Heart Association National Center, 7272 Greenville Ave, Dallas, TX 75231. E-mail ktaubert@heart.org

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**Table 1. NSAIDs, Generic and Brand Names**

Generic Name	Common Brand Name(s)*
<b>Over the counter NSAIDs</b>	
Aspirin	Bayer, St. Joseph
Ibuprofen	Advil, Motrin, Nuprin
Naproxen	Aleve
Ketoprofen	Actron, Orudis KT
Nonacetylated salicylates	Doan's pills, Arthropan
<b>Prescription NSAIDs</b>	
Celecoxib	Celebrex
Diclofenac	Flector, Cataflam, Voltaren, Arthrotec (combined with misoprostol)
Diflunisal	Dolobid
Etodolac	Lodine, Lodine XL
Fenoprofen	Nalfon, Nalfon 200
Flurbiprofen	Ansaid
Ibuprofen	Motrin, Tab-Profen, Vicoprofen (combined with hydrocodone), Combunox (combined with oxycodone)
Indomethacin	Indocin, Indocin SR, Indo-Lemmon, Indomethagan
Ketoprofen	Oruvail
Ketorolac	Toradol
Mefenamic acid	Ponstel
Meloxicam	Mobic
Nabumetone	Relafen
Naproxen	Naprosyn, Anaprox, Anaprox DS, EC-Naproxyn, Napreelan, Naprapac (copackaged with lansoprazole)
Oxaprozin	Daypro
Piroxicam	Feldene
Sulindac	Clinoral
Tolmetin	Tolectin, Tolectin DS, Tolectin 600

\*Generic versions of many of these medications are available.

Adapted from US Food and Drug Administration's Medication Guide for Non-Steroidal Antiinflammatory Drugs. Available at: <http://www.fda.gov/cder/drug/infopage/COX2/NSAIDmedguide.htm>.

Serious possible side effects from NSAIDs use are:

- heart attack
- stroke
- high blood pressure
- heart failure from body swelling (fluid retention)
- kidney problems including kidney failure
- bleeding and ulcers in the stomach and intestine
- low red blood cells (anemia)
- life-threatening skin reactions
- life-threatening allergic reactions
- liver problems including liver failure
- asthma attacks in people who have asthma

Other possible side effects can include stomach pain, constipation, diarrhea, gas, heartburn, nausea, vomiting, and dizziness.

If you need to take an NSAID on a long-term basis, the lowest effective dose for the shortest duration that is consistent with treatment goals should be used (Table 2).

**Does Aspirin Have All of These Side Effects?**

Aspirin does not increase the chance of a heart attack. In fact, aspirin can lower your risk of having a heart attack or stroke. Both of these conditions are triggered by the formation of a blood clot that blocks blood flow to a part of

**Table 2. Who Should Not Take NSAIDs?\***

Do not take NSAIDs

If you have ever had an asthma attack, hives, or other allergic reaction with aspirin or any other NSAID medicine

If you experience pain right before or after heart bypass surgery

If you have just experienced a heart attack or an episode of severe angina

\*Patients routinely taking NSAIDs (except for aspirin) before having a heart attack should stop those medications at the time of diagnosis of a heart attack because of the increased cardiovascular risks. At the time of discharge from the hospital, your doctor will discuss pain management options with you.

the heart or brain; regular aspirin use can lessen the chances of that blood clot forming. Regular aspirin use is often recommended to people at high risk for a heart attack or stroke because aspirin can reduce the ability of the blood to clot.

Aspirin can cause possible side effects in a small number of patients, however. It can cause bleeding in the brain, stomach, and intestines, as well as ulcers in the stomach and intestines.

**Are There Non-NSAIDs Pain Relievers Available OTC?**

OTC pain relievers are divided into 2 main categories, NSAIDs and acetaminophen. Acetaminophen is available as the brand Tylenol and in generic form. Acetaminophen reduces pain and fever but does not have an antiinflammatory effect. It also does not upset the gastrointestinal tract.

**Can People With CVD Take an NSAID?**

If you have cardiovascular disease, you should discuss taking OTC NSAIDs with your doctor. Taking medications such as acetaminophen or other pain medications may be more appropriate for you. If your physician determines that you do need an NSAID, it is important to take it exactly as prescribed, at the lowest dose possible for your treatment, and for the shortest time needed. The American Heart Associ-

ation recommends a “stepped care” approach to medication therapy for people with CVD who have musculoskeletal aches and pains. A person would be started on medications that have the lowest reported risk for cardiovascular events, and then, if needed, move step by step to other medications, with consideration of the risks versus the benefits at each step. For example,

- Start with OTC medications acetaminophen or aspirin, the prescription medication tramadol, or short-term painkillers containing a narcotic. If necessary, go to
- Aspirin-like drugs (nonacetylated salicylates). If necessary, go to
- Non-COX-2 selective NSAIDs. If necessary, go to
- NSAIDs with some COX-2 activity. If necessary, go to
- COX-2 selective NSAIDs.

Some traditional NSAIDs may interfere with the regular aspirin that CVD patients are asked to take to help decrease their risk of a heart attack or stroke. In 2007, the FDA issued an advisory that alerted individuals who take low-dose aspirin and who also take ibuprofen that they should take the ibuprofen at least 30 minutes after aspirin ingestion or at least 8 hours before aspirin ingestion to avoid any potential interaction. This is another important topic to discuss with your healthcare provider (Table 3).

### Disclosures

None.

### Additional Resources

The American Heart Association Web site has information on prevention and treatment cardiovascular diseases and their risk factors at <http://www.americanheart.org>.

The FDA has a medication guide for NSAIDs at <http://www.fda.gov/cder/drug/infopage/COX2/NSAIDmedguide.htm>.

### Table 3. Special Precautions

NSAIDs may increase the chance of a heart attack or stroke that can lead to death. This chance increases:

With longer use of NSAIDs

For people who have heart disease

NSAIDs should never be used right before or after a heart surgery called a coronary artery bypass graft (CABG)

NSAIDs can cause ulcers and bleeding in the stomach and intestines at any time during treatment. Ulcers and bleeding:

Can happen without warning symptoms

May cause death

NSAIDs should only be used:

Exactly as prescribed

At the lowest doses possible for your treatment

For the shortest time needed

The American College of Rheumatology has information about NSAIDs for patients at <http://www.rheumatology.org/public/factsheets/nsaids.asp?aud=pat>.

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