Consumer Reports

BEST BUY DRUGS™

PROVEN • EFFECTIVE • AFFORDABLE

Treating Osteoarthritis and Pain:

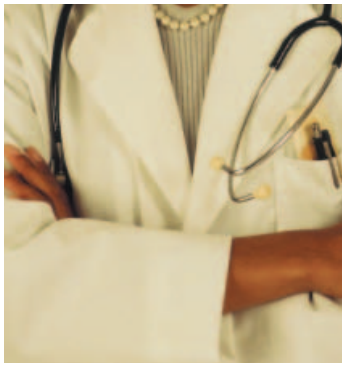
The Non-Steroidal Anti-Inflammatory Drugs

Comparing Effectiveness, Safety, and Price







Our Recommendations

The non-steroidal anti-inflammatory drugs (NSAIDs) are the most frequently used medicines to treat osteoarthritis and mild to moderate pain. Their costs vary from about $25 to about $280 a month.

This class of drugs has been at the center of a two-year controversy. Two NSAIDs – Vioxx and Bextra – have been removed from the market in the last year. The Food and Drug Administration (FDA) in April 2005 issued an important warning about the use and safety of all NSAIDs. This updated *Consumer Reports Best Buy Drugs* report incorporates the FDA's findings and warnings.

It adds our own guidance as well, and the latest cost information – showing how you could save $180 a month ($2,160 a year) or more if you need to take an NSAID. Since individual needs vary, use the information in this report to talk with your doctor about the medicine and dose that is right for you, and the possible risks.

All NSAIDs should be used with caution. All can have dangerous side effects, especially stomach ulcers and gastrointestinal bleeding. The FDA has warned that prolonged use at high doses of any NSAID may raise the risk of heart attack or stroke. NSAIDs (except low-dose aspirin) may not be appropriate for people already at risk of heart disease or stroke. Don't take them for long periods of time without consulting a doctor.

Taking effectiveness, safety and cost into account, we have chosen three generic NSAIDs as *Consumer Reports Best Buy Drugs*:

- **Ibuprofen** – costing an average $26 to $30 per month
- **Naproxen** – costing an average $44 to $50 per month
- **Salsalate** – costing an average $26 to $35 per month

These medicines are less expensive than other NSAIDs and are as effective and safe as any of them when used appropriately. Our advice:

- If you have had a stomach ulcer or bleeding, or are at high risk of either, avoid using NSAIDs. The risk of bleeding from NSAID use increases with age.
- If you have heart disease or are at risk of heart attack or stroke, talk with your doctor about the potential risks of taking any NSAID regularly for long periods.
- Take the lowest dose of an NSAID that brings relief, for the shortest period.
- NSAIDs can interact with other medicines to cause serious side effects. If your doctor prescribes an NSAID, tell him or her about *any other medicine* or dietary supplement you are taking.

Welcome

This report on the pain relievers called NSAIDs (pronounced en-seds) – which stands for "non-steroidal anti-inflammatory drugs" – is part of a Consumers Union and *Consumer Reports* project to help you find safe, effective medicines that give you the most value for your health-care dollar. To learn more about the project and other drugs we've evaluated, go to www.CRBestBuyDrugs.org.

NSAIDs are used by *tens of millions* of Americans everyday to treat osteoarthritis and mild to moderate pain. Most are now available as less expensive generic drugs. And four are available, in lower-dose formulations, as nonprescription over-the-counter drugs. We've put those four at the top of the list on this page.

Other over-the-counter and prescription medicines are available to treat osteoarthritis and mild to moderate pain. Acetaminophen (Panadol, Tylenol) is the one that most people use. *Indeed, many doctors recommend that you try acetaminophen for mild pain before an NSAID and only consider an NSAID if acetaminophen doesn't work for you.* It is only slightly less effective than the NSAIDs, and generally safer. (Acetaminophen in high doses can damage the liver. People with cirrhosis of the liver or hepatitis should use it with caution.) Also, talk to your doctor about topical pain creams and glucosamine and chondroitin supplements; both may help relieve arthritis pain.

This report focuses primarily on the use of NSAIDs to treat osteoarthritis. But you'll also find it helpful if you just use these drugs occasionally to relieve aches and pains, including headaches and muscle soreness. In fact, if you take an over-the counter NSAID several times a week or more, this report will give you some important information about the risks and safe use of these medicines. The report is based on a comprehensive expert analysis of the medical evidence. There's more information on page 14 and at www.CRBestBuyDrugs.org about how we conducted our evaluation.

This report was released in June 2005. It is an update of our original report posted in December 2004.

Generic Name	Brand Name(s)	Available as a Prescription Generic Drug	Available as an OTC Drug[1]
Prescription and Nonprescription			
Acetylated Salicylates	Aspirin, Bayer, Bufferin	Yes	Yes
Ibuprofen	Advil, Motrin, Nuprin	Yes	Yes
Ketoprofen	Orudis, Oruvail	Yes	Yes
Naproxen	Aleve, Anaprox, Naprosyn, Neprelan	Yes	Yes
Prescription Only			
Celecoxib	Celebrex	No	No
Diclofenac	Voltaren, Cataflam	Yes	No
Diflunisal	Dolobid	Yes	No
Etodolac	Lodine	Yes	No
Fenoprofen	Nalfon	Yes	No
Flurbiprofen	Ansaid	Yes	No
Indomethacin	Indocin, Indomethegan	Yes	No
Meloxicam	Mobic	No	No
Nabumetone	Relafen	Yes	No
Nonacetylated Salicylates	Anaflex, Disalcid, Mono-Gesic, Salsalate, Salsitab	Yes	No
Oxaprozin	Daypro	Yes	No
Piroxicam	Feldene	Yes	No
Sulindac	Clinoril	Yes	No
Tolmetin	Tolectin	Yes	No

1. OTC stands for over-the-counter, meaning that the drug is available without a prescription at food, drug and other stores.

What Are NSAIDs and Who Needs Them?

NSAIDs are the most commonly used medicines to treat mild to moderate pain – from arthritis, bursitis, tendinitis, and sprains, as well as premenstrual cramps, headache, dental pain, back ache, and minor injuries. They are also used to reduce fever.

NSAIDs are also the most frequently prescribed treatment for osteoarthritis, a degenerative joint disease that causes pain, stiffness and immobility. The drugs don't cure the disease, but they can relieve its symptoms. Your doctor is most likely to consider an NSAID if you have osteoarthritis symptoms that aren't helped by exercise, other non-drug treatments, or acetaminophen.

About 21 million people in the U.S. have osteoarthritis. But almost everyone older than 60 or so has some arthritic symptoms, which generally worsen as you get older.

The best way to ward off the pain, stiffness and joint "creakiness" of osteoarthritis and aging is regular exercise, stretching, and muscle strengthening. In some case, keeping active and limber can eliminate or sharply reduce the need to take medicines. Be careful, however: if you already have moderate to severe osteoarthritis, strenuous activity can stress weakened joints. Such activity should be undertaken with the advice of a doctor or physical therapist.

Osteoarthritis should not be confused with rheumatoid arthritis. The latter is an autoimmune disease that usually strikes people between the ages of 30 and 50, and causes inflammation (pain, redness, and swelling) of the joints that tends to worsen over time. NSAIDs are often used to relieve the pain and inflammation associated with rheumatoid arthritis. But the underlying disease often needs treatment with other kinds of drugs.

How They Work

NSAIDs work by blocking the body's production of hormones called prostaglandins. Among their other roles, these chemicals help cause pain, inflammation, fever, and muscle cramps and aches. At low doses, the NSAIDs work essentially as pain relievers. At higher doses, though, they can actually reduce the body's inflammatory response to tissue damage, as well as relieve pain.

More specifically, NSAIDs block two different enzymes, called Cox-1 and Cox-2, that the body uses to make prostaglandins. (Cox stands for cyclo-oxygenase). This has turned out to be a serious problem and somewhat of a biological and medical puzzle. You may have heard of this issue as you read or saw media coverage over the last year of the removal from the market of Vioxx and Bextra, two NSAIDs.

One part of the problem is that blocking the Cox-1 enzyme has a big downside. Prostaglandins produced by the Cox-1 enzyme actually *protect* the lining of the stomach from acid. So blocking them leads to an *increase* in the risk of stomach bleeding and ulcers. Some people have an especially high risk of this problem – but it's hard to tell in advance who they are. An estimated 12,000 to 16,000 people die each year as a direct result of gastrointestinal bleeding caused by NSAIDs. And thousands of others may require treatment for the stomach damage.

Heart Risk

Another problem is that blocking the Cox-2 enzyme may, over time, contribute to raising the risk of heart attack and stroke. Exactly how this occurs is not yet clear, but it has raised some troubling questions: (a) if all the NSAIDs (except aspirin, which is discussed below) could have this bad effect, at what dose and over what period of time do NSAIDs become unsafe, to the point that the dangers and ill effects outweigh the benefits; and (b) given that the various NSAIDs have differing effects on the Cox-2 enzyme, what does that mean for their safety?

The short answer to these two questions is that no one knows. Definitive studies have not been done on the potential effects on the heart and blood vessels of most NSAIDs. The evidence strongly suggests, however, that lower doses of NSAIDs used for short periods by most people do not pose any risk of heart disease or stroke. So, if you use NSAIDs only occasionally for, say, headache relief or to ease sore muscle, there is very likely no reason to worry or stop using them.

There's more information below on how to assess and balance your own risk, and use NSAIDs wisely and safely. Most relevant here is that (a) some people may be more prone than others to the heart and stroke risks posed by the NSAIDs, and (b) as the FDA stated in April 2005, "the available data do not permit a rank ordering of these drugs with regard to cardiovascular risk."

Stomach Risk

For stomach bleeding, there's a better sense of the magnitude of the risk, and the population that suffers problems. In any given year, between 5% and 10% of people who take NSAIDs will have stomach bleeding. People with a family or personal history of stomach bleeding and/or ulcers are at higher risk. Talk with your doctor about how to assess your risk of these problems.

As with heart disease risk, the difference between the NSAID drugs in the gastrointestinal (GI) risk they pose is not well understood. Three NSAIDs – Vioxx, Celebrex, and Bextra – were developed in the late 1990s to lower the chances of stomach ulcers and bleeding by blocking the Cox-2 enzyme more than Cox-1. Only one remains on the market – Celebrex. *Importantly, there is no conclusive evidence that Celebrex does in fact carry a lower risk of serious stomach bleeding compared to the older NSAIDs. And it certainly does not lower that risk to zero. Celebrex does, however, reduce the gastrointestinal discomfort that some patients experience.*

The medical puzzle surrounding NSAIDs is further complicated by the fact that the oldest and best known NSAID – aspirin – actually *lowers* the risk of heart attack. Doctors now advise all people at higher risk for heart attack to take a 81 to 162mg of aspirin everyday. Aspirin helps protect the heart by reducing blood clotting.

Even at low doses, however, aspirin carries some risk of stomach bleeding. And at higher doses aspirin

Table 1. Who Needs an NSAID?

May Need an NSAID	May Want to Take NSAIDs With Extra Caution	May Want to Avoid NSAIDs[1]
- If you have osteoarthritis with pain, joint inflammation and stiffness unrelieved by an exercise regimen, other non-drug treatments, or acetaminophen. - If you have rheumatoid arthritis and need symptom relief. - If you have moderate pain due to a headache, joint or muscle injury; short-term use only. May want to try acetaminophen first. - If you have low-grade, chronic pain – for example, back pain – unrelated to osteoarthritis, and you either do not need stronger narcotic pain relievers or do not tolerate such pain relievers well.	- If you have frequent stomach upset, irritable bowel syndrome, or a "sensitive" stomach. - If you are 50 or over and have a family history of ulcers or GI problems;[2] and/or a family history of early heart disease – especially if a parent has died of a heart attack at a young age; or you smoke, have high cholesterol or high blood pressure, or kidney problems. - If you have taken NSAIDs regularly for pain relief or osteoarthritis for many years and still need to – especially if you have ever had an ulcer, or GI pain and bleeding associated with NSAID use.	- If you have ever had stomach ulcers or bleeding. - If you have coronary artery disease or any other form of heart disease. - If you have ever had a heart attack. - If you have uncontrolled high blood pressure. - If you have kidney disease. - If you have ever had a stroke or a transient ischemic attack (a mini-stroke).

1. With the exception of aspirin for people with heart disease or who have had a heart attack
2. GI stands for gastrointestinal

poses the same GI risk as other NSAIDs, and possibly even a greater risk than some of them.

Bottom Line

NSAIDs are potent, valuable medicines. But even the nonprescription forms like ibuprofen (Advil, Motrin IB) and naproxen (Aleve) can be dangerous when taken too often and/or in high doses regularly.

Although there are no studies that quantify the extent of the inappropriate or unsafe use of NSAIDs, many doctors and experts believe that Americans overuse them – popping both the nonprescription and prescription versions too often for even mild headaches, and everyday aches and pains, especially those associated with exercise and sports.

Thus, you should:

- Take NSAIDs with more caution than you perhaps have up to now, especially if you use them fairly regularly.
- Consider trying acetaminophen first.
- Don't take NSAIDs on a regular basis to treat osteoarthritis or chronic pain without seeing a doctor to assess your heart and gastrointestinal bleeding risk.

Table 1 on page 5 gives you guidance on who needs an NSAID and who may want to be more cautious in taking them.

Choosing an NSAID – Our *Best Buy* Picks

All the NSAIDs ease the pain and other symptoms of osteoarthritis, and relieve other types of pain, too. At equivalent doses, their effectiveness is essentially the same. As found in our original analysis (December 2004) and as the FDA reconfirmed in April 2005, there is no evidence that any NSAID is superior to others in relieving pain. That includes newer brand-name NSAIDs such as Celebrex and Mobic.

The NSAIDs probably do differ in the risks they pose to your stomach and/or heart. But as discussed above, the evidence is not definitive on this now and does not allow choosing an NSAID based on its risks or safety profile. Rather, your choice of an NSAID and its dose depends on *your risk profile*. Tables 1 and 2 on pages 5 and 7, respectively, will help you gauge your risk and treatment options.

The NSAIDs differ substantially in price – with some nonprescription and generic versions costing about $25 and expensive brands costing $150, $200 or more monthly.

Thus, our choice of the following three *Best Buy* NSAIDs is based primarily on their relatively low cost, but also takes into account their track record and *emerging* evidence on safety and risks:

- **Generic ibuprofen** – costing an average $26 to $30 per month.
- **Generic naproxen** – costing an average $44 to $50 per month
- **Generic salsalate** – costing an average $26 to $35 per month

All three of these medicines have been on the market for more than 20 years. Ibuprofen and naproxen are widely prescribed by doctors and also used heavily (perhaps too heavily) as nonprescription pain relievers. Salsalate is less widely prescribed, and, while an NSAID, is a different type of drug. It is a chemical cousin to aspirin but appears to have some different properties. For example, evidence from studies in the 1980s and early 1990s suggest it may not be as harsh on the stomach as aspirin and some other NSAIDs.

The heart risks of these three drugs relative to other NSAIDs are not known. Some doctors and experts believe that naproxen may carry less risk of a heart attack or stroke than other NSAIDs. But the FDA stated in April 2005 that – while naproxen appears to pose less risk than the Cox-2 drugs (with Celebrex the only one left) – the evidence does "not provide any assurance that naproxen itself confers no increased cardiovascular risk."

Two of our *Best Buys* – ibuprofen and naproxen – are available as nonprescription drugs. If taken at larger (prescription strength) doses, they cost about the same ($28 to $40) per month as prescription pills. However, you will have to take many more pills (12 a day) to get the same dose. A nonprescription ibuprofen pill contains 200mg, and naproxen contains 220mg. Common doses of prescription strength ibuprofen, for example, range from 400mg *three times* per day (six nonprescription pills) to 800 mg *three times* a day (12 pills).

If you have osteoarthritis and need higher doses of an NSAID, and if your insurance covers prescription drugs, your best bet is to take a prescription NSAID under a physician's care. A doctor should be monitoring your response and any side effects to your NSAID, including stomach problems and any developing or worsening heart risks.

Our *Best Buy* NSAIDs, and other generics, will likely cost you only a $5 to $10 co-pay per month under your insurance plan. If you get your medicines through mail order, your out-of-pocket cost could be even lower.

If you do *not* have health insurance or drug coverage, and you take NSAIDs on a regular basis for osteoarthritis, we recommend that you talk to a doctor about using generic ibuprofen, naproxen or salsalate. You, too, should be assessed for risks and monitored periodically.

However, if you are uninsured and/or need to take an NSAID only every once in a while – for example, if your arthritis or pain symptoms are mild on intermittent – you can probably get the pain relief you need by taking nonprescription aspirin, ibuprofen, naproxen, or ketoprofen. You will save money.

Remember, however: regular (and especially every day) use of NSAIDs – prescription or nonprescription – can lead to complications, especially at high doses. That is why the written inserts that accompany all nonprescription NSAIDs say *not* to use them regularly for more than a few days without consulting a physician. Unfortunately, that advice is widely ignored. If you take a nonprescription NSAID several times a week (or more) because of chronic pain, stiffness or to prevent sports injuries or muscle soreness after sports activities, you should consider seeing a doctor to discuss your treatment and use of NSAIDs.

For Osteoarthritis Patients – Your Treatment Options

Table 2 presents another way of looking at treatment options based on your risk. Again, to find the medicine and dose that is right for you, your physician should be asking about and assessing your gastrointestinal and

Table 2. Options in Treating Osteoarthritis

Health Status and Risks	Options
- No or low GI risk[1] - No heart or stroke risk	- Generic ibuprofen, naproxen or salsalate - Other NSAID with lowest out-of-pocket cost for you - Acetaminophen
- GI risk - No or low heart or stroke risk	- Acetaminophen - Lowest possible dose of ibuprofen, naproxen or salsalate (or other generic NSAID) plus a stomach acid reducer
- Heart or stroke risk - No or low GI risk	- Acetaminophen - Aspirin plus a stomach acid reducer. Lowest dose possible.
- Heart or stroke risk - GI risk	- Acetaminophen plus aspirin for heart protection, with a stomach acid reducer. Lowest dose of each drug possible. Stay alert to signs of ulcer.

1. GI stands for gastrointestinal.

heart risk. *You should not agree to take high doses of any NSAID without such an assessment.*

If you have ever had an ulcer or stomach bleeding, you may want to avoid NSAIDs altogether and try acetaminophen. If that does not relieve your pain or other symptoms, you could try taking low doses of an NSAID only when you need one, and always along with a stomach acid reducer.

Acid reducers can lower the incidence of ulcers and GI bleeding in people taking NSAIDs. And this combo has become a commonly prescribed (and advertised) dual treatment. But it is not yet proven whether the combo significantly reduces the risk of the most dangerous kind of ulcers and GI bleeding, and it certainly does not eliminate the risk completely. So be very alert to the signs of an ulcer or GI bleeding, such as burning stomach pain, blood in your stool, or bowel movements that are black and tarry.

Of course, if you do take this drug combination you will have to pay for another medicine. Fortunately, most prescription and nonprescription acid reducers are relatively inexpensive, including over-the-counter omeprazole (Prilosec OTC is one brand). This medicine costs $15 to $25 a month and is a *Consumer Reports Best Buy Drug* in the category of medicines called proton pump inhibitors (PPIs). (Our evaluation of this category is available at www.CRBestBuyDrugs.org.)

If you have ever had a heart attack or stroke, have heart disease, uncontrolled high blood pressure, or are at high risk for those conditions because you smoke or have high cholesterol, you may want to try acetaminophen or aspirin first. Take as low a dose of either as you can. If you take aspirin, talk with your doctor about taking a stomach acid reducer, such as omeprazole (Prilosec OTC), at the same time.

Bear in mind that aspirin plus another NSAID is a potent combination. Taken together, they can increase the risk of ulcers and GI bleeding. Also, at least one non-aspirin NSAID – ibuprofen – reduces the heart protective effects of aspirin. If you are taking aspirin to protect your heart, you may want to avoid ibuprofen and try acetaminophen or naproxen for pain relief.

Table 3 on pages 9-10 presents a full list of NSAIDs and their costs.

Table 3. NSAID Cost Comparison

Generic Name and Dose	Brand Name(s)[1]	Drug is a Generic	Frequency of Dose (per Day)[2]	Average Cost for Month's Supply[3]
Celecoxib 100mg	Celebrex	No	Two	$132
Celecoxib 200mg	Celebrex	No	Two	$214
Diclofenac 50mg	Voltaren, Cataflam	No	Three	$212
Diclofenac 50mg	Generic	Yes	Three	$62
Diclofenac Long-Acting 100mg	Voltaren-XR	No	One	$166
Diclofenac Long Acting 100mg	Generic	Yes	One	$73
Diflunisal 500mg	Dolobid	No	Two	$100
Diflunisal 500mg	Generic	Yes	Two	$72
Diflunisal 250mg	Dolobid	No	Two	$91
Diflunisal 250mg	Generic	Yes	Two	$42
Etodolac 200mg	Lodine	No	Three	$170
Etodolac 200mg	Generic	Yes	Three	$84
Etodolac 400mg	Lodine	No	Three	$184
Etodolac 400mg	Generic	Yes	Three	$74
Etodolac Sustained Release 600mg	Lodine XL	No	One	$105
Etodolac Sustained Release 600mg	Generic	Yes	One	$75
Fenoprofen 300mg	Nalfon	No	Three	$63
Fenoprofen 600mg	Generic	Yes	Three	$50
Flurbiprofen 100mg	Ansaid	No	Three	$282
Flurbiprofen 100mg	Generic	Yes	Three	$63
Ibuprofen 400mg	Motrin	No	Three	$34
CR BEST BUY **Ibuprofen 400mg**	Generic	Yes	Three	$26
Ibuprofen 200mg	Advil[4]	OTC[5]	Six	$14
Ibuprofen 200mg	Advil[4]	OTC	Twelve	$28
Ibuprofen 600mg	Motrin	No	Three	$42
Ibuprofen 600mg	Ibu	No	Three	$31
CR BEST BUY **Ibuprofen 600mg**	Generic	Yes	Three	$29
Ibuprofen 800mg	Motrin	No	Three	$53
Ibuprofen 800mg	Ibu	No	Three	$31
CR BEST BUY **Ibuprofen 800mg**	Generic	Yes	Three	$30
Indomethacin 25mg	Indocin	No	Three	$64
Indomethacin 25mg	Generic	Yes	Three	$31
Indomethacin 50mg	Indocin	No	Three	$107
Indomethacin 50mg	Generic	Yes	Three	$45
Indomethacin 75mg Sustained Release	Indocin SR	No	Two	$151
Indomethacin 75mg Sustained Release	Generic	Yes	Two	$68

Table 3. NSAID Cost Comparison (continued)

Generic Name and Dose	Brand Name(s)[1]	Drug is a Generic	Frequency of Dose (per Day)[2]	Average Cost for Month's Supply[3]
Ketoprofen 75mg	Orudis	No	Two	$60
Ketoprofen 75mg	Generic	Yes	Two	$48
Ketoprofen 12.5mg	Orudis KT[4]	OTC	Six	NA[6]
Ketoprofen 12.5mg	Orudis KT[4]	OTC	Twelve	NA
Meloxicam 7.5mg	Mobic	No	One	$111
Meloxicam 15mg	Mobic	No	One	$157
Nabumetone 500mg	Relafin	No	Two	$125
Nabumetone 500mg	Generic	Yes	Two	$70
Nabumetone 750mg	Relafin	No	Two	$147
Nabumetone 750mg	Generic	Yes	Two	$82
Naproxen 375mg	Naprosyn	No	Three	$154
CR BEST BUY **Naproxen 375mg**	Generic	Yes	Three	$44
Naproxen 500mg	Naprosyn	No	Three	$187
CR BEST BUY **Naproxen 500mg**	Generic	Yes	Three	$50
Naproxen 220mg	Aleve[4]	OTC	Six	$20
Naproxen 220mg	Aleve[4]	OTC	Twelve	$40
Oxaprozin 600mg	Daypro	No	One	$74
Oxaprozin 600mg	Generic	Yes	One	$32
Oxaprozin 600mg	Daypro	No	Three	$222
Oxaprozin 600mg	Generic	Yes	Three	$96
Piroxicam 20mg	Feldene	No	One	$107
Piroxicam 20mg	Generic	Yes	One	$32
Salsalate 750mg	Disalcid	No	Three	$74
CR BEST BUY **Salsalate 750mg**	Generic	Yes	Three	$26
CR BEST BUY **Salsalate 750mg**	Generic	Yes	Four	$35
Sulindac 150mg	Clinoril	No	Two	$86
Sulindac 150mg	Generic	Yes	Two	$39
Sulindac 200mg	Clinoril	No	Two	$94
Sulindac 200mg	Generic	Yes	Two	$41
Tolmetin 200mg	Generic	Yes	Three	$62
Tolmetin 400mg	Tolectin DS	No	Three	$151
Tolmetin 400mg	Generic	Yes	Three	$101

1. "Generic" means this is a generic drug, as underscored in column three as well.
2. As commonly recommended or prescribed. Many NSAIDs must be taken multiple times per day. Convenience of dosing may be a factor for some patients. If switching from one NSAID to another, talk with your doctor about equivalency of dosing between the different NSAIDs. They come in a wide variety of recommended doses.
3. Monthly cost reflects national average retail prices for March 2005, rounded to the nearest dollar. Data provided by NDCHealth, a healthcare information company.
4. This is a nonprescription medicine. Average monthly prices were obtained from one large national drug store chain for the brand specified. Generic versions or store brand may be less expensive. Varying prices for different size bottles were averaged to yield per-pill prices which were then converted into a monthly price for the given number of pills per day.
5. OTC stands for over-the-counter, meaning it is a nonprescription drug.
6. Not Available. This medicine is not widely sold nationwide but is available in some area and stores.

The Evidence

This section presents more information on the effectiveness and safety of the NSAIDs.

Studies show that NSAIDs are effective pain relievers. But they have serious risks. All NSAIDs increase the risk of bleeding and ulcers in the stomach. NSAIDs also have other risks, such as increasing blood pressure, causing fluid retention, and reducing kidney function. And most recently, the FDA has determined that all NSAIDs when used at high doses for long periods may raise your risk of having a heart attack or stroke.

However, when used only periodically at low doses to relieve pain, aches or soreness, there's no evidence that NSAIDs pose any heart or significant stomach risk, the FDA has said. The agency in April 2005 called for more studies to be done as quickly as possible to assess the magnitude of the heart and stroke risk posed by all NSAIDs used at prescription strength doses. But, practically speaking, it will be years before definitive answers on that risk are available for most of the NSAIDs. The exception may be celecoxib (Celebrex) and naproxen, where studies are already underway or planned.

How Effective Are NSAIDs?

In general, the NSAIDs reduce pain by an average of about 50%. And studies show they enhance mobility in about 60% of people with osteoarthritis. The degree of pain relief you get will depend primarily on the intensity of your pain. But subjective factors also come into play. For example, some people are more tolerant of pain than others. Also, some people may respond to some NSAID drugs better than other drugs because of genetic differences.

Hundreds of studies have been done on NSAIDs, with many comparing one NSAID to another. Overall, the differences between them appears to be negligible and study findings do not consistently show any one NSAID to be better than another. That includes Celebrex. Studies have shown, for example, that typical doses of generic ibuprofen, naproxen and diclofenac are just as effective in relieving pain as Celebrex.

How Safe Are NSAIDs?

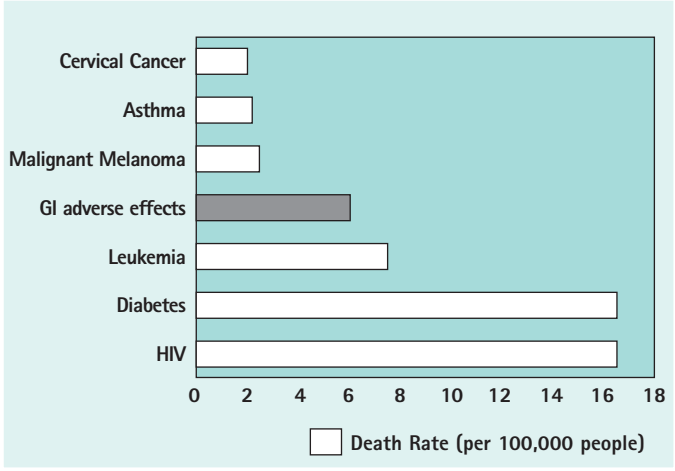
As discussed throughout this report, NSAIDs can cause life-threatening GI bleeding, usually from the stomach. *The risk increases with age,* which is important because the majority of people who take NSAIDs for long periods are 60 or older. As shown in Table 4, a person who is over 75 and takes an NSAID has about a one in 110 chance of having a GI bleed, and a one in 647 chance of dying from that complication.

Table 4. Serious Risks Associated With NSAIDs

Age	Risk of GI bleeding each year	Risk of dying from GI bleeding each year
	Risk in any one year is:	
16-45	1 in 2,100	1 in 12,353
45-64	1 in 646	1 in 3,800
65-74	1 in 570	1 in 3,353
>75	1 in 110	1 in 647

When applied to the population as a whole, NSAID-related deaths are substantial. As shown in Table 5, the rate is higher than that found from cervical cancer, asthma or malignant melanoma, for example.

Table 5. NSAIDs Related Deaths Compared to Other Diseases



The only NSAID ever proven to cause *fewer* serious ulcer or stomach bleeding complications than other NSAIDs is Vioxx, removed from the market in the fall of 2004 after more evidence showed it increased the risk of heart attack and stroke.

A lower risk of ulcers has been assumed for two other drugs – Celebrex and Bextra. Bextra was removed from the market in April 2005, not only because of its heart and stroke risk but also its link to a life-threatening skin reaction and because recent evidence had failed to show that it lowered the risk of serious stomach problems compared to other, older NSAIDs. Similarly, as the FDA stated in April 2005, Celebrex's advantage in lowering the risk of stomach problems compared to other NSAIDS is "uncertain."

More specifically, studies show that the Cox-2 drugs cause fewer "endoscopic ulcers." These are ulcers that usually cause no symptoms or actual bleeding and are found only by performing an endoscopy. This type of ulcer is not as dangerous as ulcers that actually erode the lining of the stomach.

One major study compared Celebrex with two other NSAIDs, ibuprofen and diclofenac. Overall Celebrex was not less likely to cause serious ulcer complications.

Heart Attacks and Strokes

The FDA now requires that a warning be put on the labels of all prescription NSAIDs stating that they have the potential, if used in certain ways, to raise the risk of heart attacks and strokes. This warning joins one for GI risks, required for several years. In addition, the agency will now require nonprescription NSAIDs to carry information about potential heart risks.

These actions were unexpected and represent significant changes in the labeling for these widely used drugs. The labeling is the information available to doctors on the uses of a drug. On nonprescription NSAIDs, the information will be on the package inserts.

Essentially, the FDA decided that although the evidence was uncertain and unsettled, the biological basis for the risk was compelling enough to warn doctors and consumers. Only time and more studies will prove whether this action was judicious. Importantly, however, there is no direct evidence *now* that the older NSAIDs do increase the risk of having a heart attack or stroke. Studies of Celebrex to date are somewhat inconclusive.

Hypertension, Heart Failure, and Kidney Problems

All the NSAIDs can aggravate high blood pressure, which is one way they could raise the risk of heart attack. NSAIDs cause fluid retention, which can lead to slight weight gain or swollen legs even in healthy individuals. In people who have a "weak heart" (left ventricular dysfunction), fluid retention due to NSAIDs can cause congestive heart failure. NSAIDs also reduce kidney function in some individuals, especially those who already have kidney disease from diabetes or other causes. The risk of these problems is similar for different NSAIDs.

Tolerability

All the NSAIDs can cause other *minor* side effects, including stomach upset, abdominal pain and diarrhea. Their frequency is about the same no matter which NSAID you take. About one in five people taking prescription doses of ibuprofen, naproxen, or diclofenac regularly, for example, have one of these side effects. However, most people taking the older NSAIDs do not stop taking the medicines because of side effects.

The NSAIDs can also cause skin rashes, but these are rare.

Age, Race, and Gender Differences

Age is an important factor when considering NSAID treatment, especially long term. The risk of GI bleeding and stomach ulcers increases with age, as seen in Table 4 on page 11. So does heart disease risk. The older you are the more cautious your doctor should be in treating you with NSAIDs for long periods. Some doctors now routinely prescribe a stomach acid reducer to all people aged 65 and over taking an NSAID.

There is scant data on any differences by gender or race in response to any NSAID. However, an important recent study found that aspirin's heart and stroke protective effect was different in men and women. The study found that while women taking low dose aspirin regularly had a lower incidence of strokes (a benefit not seen in men), they did not get the same benefit as men in prevention of a first heart attack. The reason for this difference in unknown. It raises the possibility that women and men may also respond differently to other NSAID drugs.

Talking With Your Doctor

It's important for you to know that the information we present in this report is not meant to substitute for a doctor's judgment. But we hope it will help your doctor and you arrive at a decision about which NSAID or dose is best for you, and which gives you the most value for your health-care dollar.

Bear in mind that many people are reluctant to discuss the cost of medicines with their doctors and that studies show doctors do not routinely take price into account when prescribing medicines. Unless you bring it up, your doctors may assume that cost is not a factor for you.

Many people (including physicians) also believe that newer drugs are always or almost always better. While that's a natural assumption to make, the fact is that it's not true. Studies consistently show that many older medicines are as good as, and in some cases better than, newer medicines. Think of them as "tried and true," particularly when it comes to their safety record. Newer drugs have not yet met the test of time, and unexpected problems can and do crop up once they hit the market.

Of course, some newer prescription drugs are indeed more effective and safer. Talk with your doctor about the pluses and minuses of newer versus older medicines, including generic drugs.

Prescription medicines go "generic" when a company's patents on a drug lapse, usually after about 12 to 15 years. At that point, other companies can make and sell the drug.

Generics are almost always much less expensive than newer brand name medicines, but they are not lesser quality drugs. Indeed, most generics remain useful medicines even many years after first being marketed. That is why today about 47% of all prescriptions in the U.S. are for generics.

Another important issue to talk with your doctor about is keeping a record of the drugs you are taking. There are several reasons for this:

- First, if you see several doctors, each may not be aware of medicines the others have prescribed.
- Second, since people differ in their response to medications, it is very common for doctors to prescribe several medicines before finding one that works well or best.
- Third, many people take several prescription medications, nonprescription drugs and dietary supplements at the same time. These can interact in ways that can either reduce the benefit you get from the drug, or be dangerous.
- And fourth, the names of prescription drugs – both generic and brand – are often hard to pronounce and remember.

For all these reasons, it's important to keep a written list of all the drugs and supplements you are taking, and to periodically review this list with your doctors.

Always be sure, too, that you understand the dose of the medicine being prescribed for you and how many pills you are expected to take each day. Your doctor should tell you this information. When you fill a prescription at the pharmacy, or if you get it by mail, you may want to check to see that the dose and the number of pills per day on the pill bottle match the amounts that your doctor told you.

How We Picked the *Best Buy* NSAIDs

Our evaluation is primarily based on an independent scientific review of the evidence on the effectiveness, safety and adverse effects of the NSAIDs. A team of physicians and researchers at the Oregon Health & Science University Evidence-based Practice Center conducted the analysis as part of the Drug Effectiveness Review Project, or DERP. DERP is a first-of-its-kind 12-state initiative to evaluate the comparative effectiveness and safety of hundreds of prescription drugs.

A synopsis of DERP's analysis of the NSAIDs forms the basis for this report. A consultant to *Consumer Reports Best Buy Drugs* is also a member of the Oregon-based research team, which has no financial interest in any pharmaceutical company or product.

The full DERP review of NSAIDs is available at http://www.ohsu.edu/drugeffectivness/reports/final.cfm. (This is a long and technical document written for physicians.)

This update is also based in part on the FDA's April 2005 findings and regulatory actions on the NSAIDs.

The drug costs we cite were obtained from a health-care information company which tracks the sales of prescription drugs in the U.S. Prices for a drug can vary quite widely, even within a single city or town. All the prices in this report are national averages based on sales of prescription drugs in retail outlets. They reflect the cash price paid for a month's supply of each drug in March 2005.

Consumers Union and *Consumer Reports* selected the *Best Buy Drugs* using the following criteria. The drug (and dose) had to:

- Be approved by the FDA for treating at least one form of arthritis.
- Have a safety record equal to or better than other NSAIDs.
- Have an average price for a 30-day supply that is substantially lower than the most costly NSAID meeting the first two criteria.

The *Consumers Reports Best Buy Drugs* methodology is described in more detail in the Methods section at www.CRBestBuyDrugs.org.

About Us

Consumers Union, publisher of Consumer Reports magazine, is an independent and non-profit organization whose mission since 1936 has been to provide consumers with unbiased information on goods and services and to create a fair marketplace. It is solely responsible for the content of this report. Its main Web sites are www.consumersunion.org and www.consumerreports.org. You may also want to visit www.ConsumerReportsMedicalGuide.org. This subscription Web site can help you evaluate your medical treatment options, and contains in-depth information on prescription drugs.

Consumer Reports Best Buy Drugs is a public education project administered by Consumers Union. Two outside sources of generous funding made the project possible. They are a major grant from the Engelberg Foundation, a private philanthropy, and a supporting grant from the National Library of Medicine, part of the National Institutes of Health. A more detailed explanation of the project is available at www.CRBestBuyDrugs.org.

We followed a rigorous editorial process to ensure that the information in this report and on the *Consumer Reports Best Buy Drugs* Web site is accurate and describes generally accepted clinical practices. If we find, or are alerted to, an error we will correct this as soon as possible. However, *Consumer Reports* and its authors, editors, publishers, licensors and any suppliers cannot be responsible for medical errors or omissions, or any consequences from the use of the information on this site. Please refer to our user agreement at www.CRBestBuyDrugs.org for further information.

Consumer Reports Best Buy Drugs should not be viewed as a substitute for a consultation with a medical or health professional. This report and the information on www.CRBestBuyDrugs.org are provided to enhance communication with your doctor rather than to replace it.

Sharing this Report

References

1. Topol EJ, Falk GW. A coxib a day won't keep the doctor away. *Lancet* 2004; 364: 639-640.
2. Topol, EJ. Failing the public health – refecoxib, Merck, and the FDA. *New England Journal of Medicine* 2004; 351 (17): 1707-1709.
3. Dubois RW, Melmed GY, Henning JM, Laine L. Guidelines for the appropriate use of non-steroidal anti-inflammatory drugs, cox-2 inhibitors and proton pump inhibitors in patients requiring chronic anti-inflammatory therapy. *Alimentary Pharmacologic Therapy* 2004; 19 (2)197-208.
4. Bombardier C. Comparison of upper gastrointestinal toxicity of rofecoxib and naproxen in patients with rheumatoid arthritis. VIGOR Study Group. *New England Journal of Medicine* 2000;343:1520.
5. Chan FK, Hung LC, Suen BY, et al. Celecoxib versus diclofenac and omeprazole in reducing the risk of recurrent ulcer bleeding in patients with arthritis. *New England Journal of Medicine* 2002; 347(26):2104-10.
6. Farkouh ME, Kirshner H, Harrington RA, et al. Comparison of lumiracoxib with naproxen and ibuprofen in the Therapeutic Arthritis Research and Gastrointestinal Event Trial (TARGET), cardiovascular outcomes: randomised controlled trial. *Lancet* 2004;364(9435):675-84.
7. FitzGerald GA, COX-2 and beyond: approaches to prostaglandin inhibition in human disease. *Nat. Rev. Drug Discov.* 2003;2:879-90.
8. Fitzgerald GA. Coxibs and cardiovascular disease. *New England Journal of Medicine* 2004;351(17):1709-11.
9. Food and Drug Administration. Medical Officer review, 1999: Vioxx. NDA 21-042. http://www.fda.gov/cder/foi/nda/99/021042_52_vioxx.htm (accessed Nov.12, 2004).
10. Garcia Rodriguez LA, Varas-Lorenzo C, Maguire A, et al. Non-steroidal anti-inflammatory drugs and the risk of myocardial infarction in the general population. *Circulation* 2004;109(24):3000-6.
11. Gøtzsche PC. Reporting of outcomes in arthritis trials measured on ordinal and interval scales is inadequate in relation to meta-analysis. *Ann. Rheum. Disease* 2001;60:349-352.
12. Krum H, Liew D, Aw J, Haas S. Cardiovascular effects of selective cyclooxygenase-2 inhibitors. *Expert Review of Cardiovascular Therapy* 2004;2(2):265-70.
13. Moore R. Quantitative systematic review of topically applied non-steroidal anti-inflammatory drugs. British Medical Journal1998;316:333-338.
14. Mukherjee D. Selective cyclooxygenase-2 (COX-2) inhibitors and potential risk of cardiovascular events. *Biochemical Pharmacolog.* 2002;63(5):817-21.
15. Ray WA, Stein CM, Daugherty JR, Hall K, Arbogast PG, Griffin MR. Cox-2 selective non-steroidal anti-inflammatory drugs and risk of serious coronary heart disease. *Lancet* 2002;360(9339):1071-3.
16. Ray WA, Stein CM, Hall K, Daugherty JR, Griffin MR. Non-steroidal anti-inflammatory drugs and risk of serious coronary heart disease: an observational cohort study. *Lancet* 2002;359(9301):118-23.
17. Schnitzer T, Update of ACR guidelines for osteoarthritis: role of the coxibs. *J. Pain Symptom Management* 2002;23(4 Suppl):S24-30; discussion S31-4.
18. Silverstein FE, Faich G, Goldstein JL, et al. Gastrointestinal toxicity with celecoxib vs non-steroidal anti-inflammatory drugs for osteoarthritis and rheumatoid arthritis: the CLASS study. *Journal of the American Medical Association* 2000;284(10):1247-1255.
19. Solomon DH, Schneeweiss S, Glynn RJ, et al. Relationship between selective cyclooxygenase-2 inhibitors and acute myocardial infarction in older adults. *Circulation* 2004;109(17):2068-73.
20. Strand V, Hochberg MC. The risk of cardiovascular thrombotic events with selective cyclooxygenase-2 inhibtors. *Arthritis Rheum* 2002;47:349–355.
21. Zhang W, Jones A, Doherty M. Does paracetamol (acetaminophen) reduce the pain of osteoarthritis? A meta-analysis of randomized controlled trials. *Ann Rheum Disease* 2004;63(8):901-7.
22. Hopper L, Brown TJ, Elliot RA et al. The effectiveness of five strategies for the prevention of gastrointestinal toxicity induced by non-steroidal anti-inflammatory drugs: a review. *British Medical Journal Online* 2004 (October 8); 10.1136.
23. Bjordal JM, Ljunggren AE, Klovning A, Slordal L. Non-steroidal anti-inflammatory drugs, including cox-2 inhibitors, in osteoarthritic knee pain; meta-analysis of randomized placebo controlled trials. *British Medical Journal Online* 2004 (November 23); 10.1136
24. Jenkins, JK and Seligman, PJ, FDA Memorandum – Analysis and recommendations for agency action regarding non-steroidal anti-inflammatory drugs and cardiovascular risk. April 6, 2005. Available at www.fda.gov/cder/drug/infopage/cox2/NSAIDdecisionmemo.pdf