

General Information for Consumers

**Evidence-based Medicine &
Oregon Evidence-based Practice Center Drug Reviews**

Legal Information & Disclaimers

These materials are not meant to replace the clinical judgment of any health care professional or establish a standard of care. The information contained herein may not be appropriate for use in all circumstances. Decisions to utilize this information must be made by consumers and health care professionals in light of individual circumstances.

These materials were created to assist patients and health care professionals understand the evidence-based drug reviews prepared by the Oregon Evidence-based Practice Center, hereby referred to as "The Oregon EPC." To the best of its ability, *Delfini Group, LLC* has provided an interpretation of the work of the EPC, as of August 7, 2002. At the time of this writing, this work is still in **draft form**.

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General information to help you better understand scientific drug comparisons

This summary of scientific findings compares health benefits and health risks of different drugs. It can help you make a decision about your treatment choices. This information is believed to be the best published scientific research about these drugs at the time of this writing (July 20, 2002).

How This Information Was Gathered and Analyzed

The evidence-based approach used to compare scientific studies about these drugs was done by experts at the **Oregon Evidence-based Practice Center (Oregon EPC)** in Portland, Oregon. This summary of the Oregon EPC's work was prepared by *Delfini Group, LLC*, an evidence-based medicine consulting and medical information company.

Please be sure to **read all legal information and disclaimers** to learn the basis for this information and its status at this time.

How Can I Use This Information

We suggest that the best way to use this information is do the following:

1. Review all this information carefully, including **General Information**.
2. Look closely at the information in the section, **What the Science Has to Say**.
3. Decide what is most important to you.
4. Take this patient information summary to your doctor during your next visit, along with **Information for Your Doctor and You**, which is included here. Or tell your doctor about this Web site.

About Evidence-based Medicine



Evidence-based medicine (EBM) means using science to help doctors understand the best way to practice medicine. Most people believe this is how medicine is already practiced. However, EBM is a *new* and *improved* way to practice medicine. Most doctors do not receive much scientific training during their education. In medical publications, there are good research studies and not-so-good research studies. There are even published studies which are considered “bad” science. This can be very confusing. Our goal is to help make science easier to understand for both doctors and patients.

The best way to do this is through a scientific evaluation of published research studies to find the “best available” evidence and summarize it. This helps doctors and patients predict more accurately the health benefits and health risks that patients might expect from using specific drugs or undergoing specific procedures.

People react differently to the same medication – a medication that works well for someone else might not be the best choice for you. The information provided here is based on what was learned through scientific studies looking at a group of people who may be different from you in important ways. Often there is no way to know ahead of time which drug will work best for a specific person. Frequently, the best that science can tell us are the odds of benefit or risk by examining health results in a group of people. (This is similar to what happens in a lottery. Each person has so many chances to win or lose, based on estimates of the odds of winning or losing.)

Many drugs are so similar that they are considered to be in the same family or “drug class.” Drugs in the same class are often substituted for each other even if research has not been done for each of the specific drugs.

◀ **About Drug Families**
(Also known as “Drug Classes”)

If one type of medication has not worked for you, there may be another drug in the same medication “family” or “drug class” which may work very well. You do not always have to change to a newer, more expensive drug to find a solution. However, sometimes this may be the best solution for you.

About New Drugs



Many of us become hopeful when we learn about a new drug on the market – especially when we feel the old drugs do not work as well as we wish. But when it comes to drugs, **new** does not always mean *improved*. We need good science, through evidence-based medicine, to learn if a new drug really *is* better – or even as good as – the older drug.

Many patients, especially those with chronic conditions such as arthritis, begin treatment with lifestyle changes and older drugs that are frequently “over-the-counter.” Many of these patients do well without ever needing the newer and usually more expensive medications. For example, many people with osteoarthritis achieve satisfactory pain relief and improved joint movement by changing their activities and taking acetaminophen (e.g., Tylenol).

There are some **definite advantages** to taking this more conservative approach:

Safety	<p>Older medications are frequently safer. This is because the newer medications, although advertised and marketed as improvements, are sometimes found after a year or more to have unsuspected side effects or health risks.</p> <p>Most people don't realize that often the long-term risks of newly-approved medications are not known until physicians discover unsuspected side effects in their patients over time. (For example, it took several years before it was discovered that certain drugs used by millions of people to treat irregular heart beats after heart attacks actually <i>increased</i> heart problems.)</p>
Effectiveness	<p>Many newer medications provide little improvement for patients, even though effective advertising and marketing frequently make it appear that the newer medications are “breakthroughs.”</p>
Cost	<p>Cost is a real issue. Older drugs are frequently less expensive than newer medications.</p>

However, many new drugs are significant advances in health care. You need to make a decision on what you feel may be most right for you.

About NSAIDs and COX-2 Inhibitors

First read, General Information for Consumers: Evidence-based Medicine & Oregon Evidence-based Practice Center Drug Reviews, including all legal information and disclaimers.

About NSAIDs and COX-2 Inhibitors

These drugs are used to relieve pain and improve movement for patients with joint pain. They are used for treatment of other conditions as well, such as muscle pain.

The easiest way to think about these drugs is that there are older ones (1st generation non-steroidal anti-inflammatory drugs – NSAIDs) and newer ones (2nd generation NSAIDs). The newer drugs are called the COX-2s or COX-2 inhibitors. To make this information easy to understand, we will call the older drugs, “older NSAIDs,” and call the newer drugs, “COX-2s,” even though the COX-2s are NSAIDs as well.

Important Information ▼

The information about these drugs treats the **older NSAIDs as one drug family** and the **COX-2s as another drug family**. (If you have not already read the *General Information* section– including *About Drug Families* – we encourage you to read it now.) Research studies have **not** been done comparing each of the drugs. This is common. We have included a special page for you and your doctor which gives the exact details of which comparisons were made. However, drugs in a family are often believed to be similar enough that they are treated alike.

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About NSAIDs and COX-2 Inhibitors

What the Science Has to Say

At the time this summary was prepared, this is what the best available science suggests comparing older NSAIDs with COX-2 inhibitors. The *Notes* following this table will provide you with explanations.

Effectiveness ▶	All of the older and newer NSAID drugs studied (NSAIDs and COX-2s) seem essentially the same in their ability to relieve pain and improve joint movement in patients with joint pain. There is insufficient evidence to know if there are differences in effectiveness among different COX-2s.		
Safety ▶	The COX-2 inhibitors seem nearly equal to the older NSAIDs in safety, but there are some differences that might be important to you. These possible differences are not certain because not all the drugs have been studied thoroughly and not all differences are known.		
Quick Reference Guide	DRUG COMPARISON		
	Topic	Older NSAIDs	COX-2s
	Pain relief	Equal	Equal
	Improved Joint Functioning	Equal	Equal
	Safety	Slight difference – see below ▼	Slight difference – see below ▼
	Older NSAIDs may cause slight increased risk of stomach ulcer problems (e.g., pain, bleeding) compared to COX-2.	1 in 191-199 people who take older NSAIDs for 9 months compared to people who take COX-2s.	--
	COX-2s may cause slight increased risk of heart attack compared to older NSAIDs.	--	1 in 333 people who take COX-2s for 9 months compared to people who take older NSAIDs.
COX-2s may cause slight increased risk of stroke and other blood clot problems compared to older NSAIDs.	--	1 in 162 people who take COX-2s for 9 months compared to people who take older NSAIDs.	

Notes ▼

Age, Gender, Race and Ethnicity:

There is insufficient evidence to know if the drugs reviewed in this report differ in their effectiveness or safety with regard to age, gender or ethnicity.

About NSAIDs and COX-2 Inhibitors

About Potential Stomach Ulcer Problems

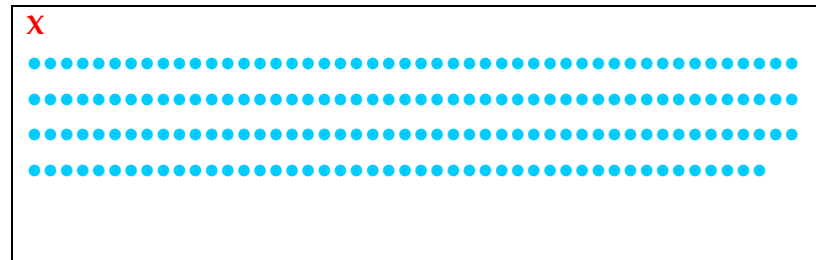
Research suggests that during 9 months of treatment, one person in approximately 191-199 people taking an older NSAID may develop a serious stomach ulcer problem (bleeding, pain, perforation or obstruction of the stomach). If 191-199 people had instead taken Celebrex or Vioxx, it is likely that this one person would not develop a serious stomach ulcer problem.

There is no way to know which one person this might be. Each person making a decision about which medication to take will have different feelings about whether the benefits of the newer medications (COX-2 inhibitors) are important to him or her.

What 1-in-191 Looks Like ►

The “x” represents the one person out of 191 people who might develop a serious stomach ulcer problem taking an older NSAID for 9 months.

We call this calculation the “Number-Needed-to- Harm” (NNH). Here NNH=191.



Nine months is important because that is the length of the study, so that is the time period for which we have scientific information.

This does **not** mean that if you take a drug for nine months with **no** stomach ulcer problem that you will *never* have a stomach ulcer problem using this drug. Also, this does **not** mean that the research data can be recalculated to create **reliable** predictions longer than 9 months.

We only know what the science tells us about this particular group of patients that were studied for 9 months.

◀ **Why Do We Emphasize 9 Months?**

About NSAIDs and COX-2 Inhibitors

Are There Other Choices I Could Make if I am Concerned About Heartburn and Stomach Ulcer Problems?

- ◆ Cytotec (misoprostol) appears to be a useful medication to take **in addition to older NSAIDs** to prevent stomach ulcer problems caused by older NSAIDs. Doctors would have to treat 263 patients for 6 months with Cytotec in addition to the patient's usual older NSAID medication to prevent one stomach ulcer problem. This is called the "Number-Needed-to-Treat" or NNT. Here NNT=263 over 6 months of treatment.

However, Cytotec increases patients' risks of other intestinal discomforts such as nausea, gas or diarrhea.

- ◆ Proton pump inhibitors (PPIs), such as omeprazole or pantoprazole, and Histamine 2-receptor antagonists ("H2-blockers"), such as cimetidine and ranitidine, are effective medications for decreasing some abdominal symptoms such as heartburn in patients taking older NSAIDs.

However, there is no proof that PPIs or H2-blockers reduce the risk of stomach ulcer problems. The PPI and H2-blocker studies did not show differences in how much the ulcers bothered patients. They did show that there was a reduction in stomach ulcers when patients were examined using endoscopes (scopes inserted through the mouth and then moved into the stomach to look for ulcers). One of the problems with the use of endoscopy in these studies is that it found small ulcers which might have healed without any treatment and without bothering the patients – in other words, ulcers which may not have ever been noticed by patients or ever have caused a problem for them.

About "Patient-oriented Evidence that Matters" ►

Sometimes research studies find things which are unlikely to affect patients, or the effects of which are unknown. An example of this might be if a research study found that a certain medication causes a very slight reddening of the sinus cavity. If a sinus cavity being a little more red does not have a harmful effect to a patient, or if we do not know if it is important, then the finding of that research study isn't very meaningful in caring for a patient.

Evidence-based medicine focuses on looking at research findings which seem most meaningful in caring for a patient.

About NSAIDs and COX-2 Inhibitors

Information for Your Doctor and You

Scientific Evidence Summary for Patients Comparing Different Non-steroidal Anti-inflammatory Drugs (NSAIDs and COX-2s)

This information was made available to your patient through an initiative to summarize for patients the results of evidence-based reviews performed to compare these drugs by experts at the Oregon Evidence-based Practice Center (Oregon EPC) in Portland, Oregon. This summary of the Oregon EPC's work was prepared by *Delfini Group, LLC*, an evidence-based medicine consulting and medical information company.

This information was produced to assist patients and their doctors in understanding the "best available evidence," at the time of this writing on the benefits and risks of the various NSAIDs, paying particular attention to the older as compared to the newer NSAIDs (COX-2 inhibitors).

How This Information Was Gathered and Analyzed

The Oregon EPC used methods that are widely accepted as the best way to evaluate health care practices. The evidence-based process reduces bias by using explicit, systematic methods to locate scientific studies, collecting the same information in the same manner from each study, and assessing the *validity* (or quality) of each study. They looked for evidence of bias in each study by determining factors such as whether patients and researchers were kept unaware of which patient group got which drug, whether the patients studied were similar to people who would take these drugs, and if the studies reported results using appropriate statistical methods. You can obtain more information in the following ways:

For access to the site of the Oregon Evidence-based Practice Center (EPC) ►	http://medir.ohsu.edu/~brodnerr/
For information on <i>Delfini Group, LLC</i> ►	www.delfini.org
To read the full report from the Oregon EPC ►	www.oregonrx.org

About NSAIDs and COX-2 Inhibitors

What the Science Has to Say

At the time this summary was prepared, this is what the best available science suggests comparing older NSAIDs with COX-2 inhibitors. The *Notes* following this table will provide you with explanations.

Effectiveness ▶	All of the older and newer NSAID drugs studied (NSAIDs and COX-2s) seem essentially the same in their ability to relieve pain and improve joint movement. There is insufficient evidence to know if there are differences in effectiveness among different COX-2s.		
Safety ▶	The COX-2 inhibitors seem nearly equal to the older NSAIDs in safety, but there are some differences that might be important to you. These possible differences are not certain because not all the drugs have been studied thoroughly and not all differences are known.		
Quick Reference Guide	DRUG COMPARISON		
	Topic	Older NSAIDs	COX-2s
	Pain relief	Equal	Equal
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	Safety	Slight difference – see below ▼	Slight difference – see below ▼
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Notes ▼

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About NSAIDs and COX-2 Inhibitors

Studies Comparing COX-2 Inhibitors to Each Other ►

Very few studies have compared COX-2 inhibitors to each other. Several studies have compared Celebrex to Vioxx and have shown no meaningful difference between the two in efficacy or safety. No studies have compared Bextra to Celebrex or Vioxx.

Summary



At this writing, the best available evidence suggests that all Cox-2 inhibitors are **equivalent** in terms of their ability to **relieve pain** and **improve functioning**. They appear to be **nearly equal in safety**.

Studies Comparing COX-2 Inhibitors to other NSAIDs ►

- ◆ Celebrex (evaluation of the seven best studies)
- ◆ Vioxx (evaluation of the nine best studies)
- ◆ Mobic (evaluation of the eight best studies)

Summary



Benefits

In evaluating the best studies comparing these three COX-2 inhibitors to older NSAIDs for **pain relief** and **improved joint movement**, **no clinically meaningful differences between the COX-2 inhibitors and the comparison older drugs were found**.

Note: Most of the patients who participated in these studies had been diagnosed as having osteoarthritis or rheumatoid arthritis.

About NSAIDs and COX-2 Inhibitors

Studies Comparing COX-2 Inhibitors to other NSAIDs ►	<ul style="list-style-type: none"> ◆ Celebrex (evaluation of the seven best studies) ◆ Vioxx (evaluation of the nine best studies) ◆ Mobic (evaluation of the eight best studies) <p style="text-align: center;">Summary ▼</p>			
Possible Harms				
Risk	Evidence Notes	Results	Period	Favoring
Stomach Ulcer Problems	In one study, the VIGOR trial , Vioxx was compared to Naprosyn in patients with rheumatoid arthritis. Patients taking Naprosyn were found to have more significant stomach ulcer complications (bleeding, pain, perforation or obstruction of the stomach) than patients taking Vioxx.	The VIGOR Trial ARR = 0.52% NNH = 191 for ulcer problems ►	9 months	+Vioxx - Naprosyn
	In the CLASS Study , comparing Celebrex to ibuprofen and diclofenac in patients diagnosed as having osteoarthritis or rheumatoid arthritis, patients taking the older NSAIDs were found to have more significant stomach ulcer complications (bleeding, pain, perforation or obstruction of the stomach) than patients taking Celebrex.	The CLASS Study ARR = ½ of 1% NNH = 199 for ulcer problems ►	9 months	+ Celebrex - NSAIDs
Heart, Stroke and Blood Clot Risks	One good quality study (VIGOR) reported more heart attacks in the patients taking COX-2s. For every 333 patients taking Vioxx instead of Naprosyn for approximately 9 months there was one additional heart attack.	The VIGOR Study NNH=333 for a heart attack ►	9 months	+NSAID - Vioxx
	The VIGOR study also reported an increased risk of serious blood clot problems, defined as strokes, unstable angina pectoris, cardiac arrest, transient ischemic attack (a warning of stroke), sudden death and heart attack. Of 162 patients taking Vioxx instead of Naprosyn for approximately nine months, one additional patient experienced one of the above-mentioned serious blood clot problems.	The VIGOR Study NNH=162 for serious blood clot problems ►	9 months	+ NSAID - Vioxx

About NSAIDs and COX-2 Inhibitors

Other Ulcer Prevention Medications That Can be Taken with NSAIDs	
Cytotec (misoprostol) NNT=263 (TIME)	Cytotec (misoprostol) when taken with the older NSAIDs probably prevents stomach ulcer pain and ulcer complications. Doctors would have to treat 263 patients with Cytotec along with the patients' NSAID medication in order to prevent one serious ulcer complication (NNT=263 over 6 months). Cytotec was associated in this study with more diarrhea, upset stomach and "gas".
PPIs and H2 Antagonists	Proton pump inhibitors, such as omeprazole or pantoprazole, and H2 antagonists, such as cimetidine and ranitidine, decreased some gastrointestinal symptoms. (The studies did not focus on meaningful differences in patients' ulcer symptoms—instead they focused on visible ulcers when the researchers examined the stomach using endoscopes. There is no data on whether the ulcers found by endoscopy had any impact on the patients.) There is no proof that PPIs or H2-blockers reduced the risk of stomach ulcer problems.