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Comparing NSAIDs

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Aspirin and ibuprofen belong to a class of drugs known as nonsteroidal antiinflammatory drugs (NSAIDs). These medications relieve pain by blocking the production of pain-signaling molecules. One of the steps in this pathway involves certain types of cyclo-oxygenase (COX) enzymes. By blocking the COX-2 type, NSAIDs relieve pain felt in joints, muscles, and other soft tissues.

A related enzyme, COX-1, plays a role in protecting the stomach lining. Because most NSAIDs also block COX-1, they increase the risk of stomach ulcers and gastrointestinal (GI) bleeding. To avoid these adverse effects, NSAIDs selective to blocking COX-2 were developed. However, some selective NSAIDs, along with some of the nonselective NSAIDs, were found to increase the risk of heart attacks.

The "Drug Class Review on Nonsteroidal Antiinflammatory Drugs (NSAIDs)" compares the safety and effectiveness of 28 drugs. A summary of the findings is below.

How do NSAIDs compare in reducing pain?

For short term pain relief (less than 6 months), all NSAIDs have a similar effect on reducing pain in adults with chronic pain from either osteoarthritis, rheumatoid arthritis, soft-tissue pain, back pain, or ankylosing spondylitis. No differences were found among oral NSAIDS, topical NSAIDs, or between oral and topical NSAIDs.

For symptoms of osteoarthritis in a single knee, diclofenac in topical (1.5% solution) and oral forms had a similar short term effect in reducing pain and improving function. Although topical diclofenac has the benefit of being gastroprotective, compared to oral nonselective NSAIDs, dry skin at the application site is more common with the 1.5% solution.

Among topical diclofenac products, limited evidence suggests that the 1.5% solution and 1.0% gel provide similar pain relief, but application site reactions are more common with the solution than with the gel, compared to placebo. [full review]

How do NSAIDs compare in terms of GI adverse events?

All nonselective NSAIDs similarly increase the risk of gastrointestinal adverse events, such as GI bleeding and ulcers, in the short term and in the long term.

Celecoxib is gastroprotective in the short term, but data are lacking for the long term.

For partially selective NSAIDs, only nabumetone is gastroprotective in the short term compared to nonselective NSAIDs. In the long term, no advantage has been found for any partially selective NSAID over nonselective NSAIDs.

To prevent serious ulcer-related events, such as bleeding, either adding the anti-ulcer drug misoprostol to a nonselective NSAID, or taking celecoxib appear to have short term advantages over taking a nonselective NSAID alone. Whereas, to prevent less serious types of ulcers only discovered on endoscopy, there appears to be no difference between different NSAIDS, when taken in combination with an anti-ulcer drug such as a proton pump inhibitor or misoprostol. In patients who recently had a GI bleed from an ulcer, the most recent evidence suggests that the combination of celecoxib plus the proton pump inhibitor esomeprazole is superior to celecoxib alone in preventing a future bleed. [full review]

How do NSAIDs compare in terms of cardiac risks?

Nonselective NSAIDs: With the exception of naproxen, nonselective NSAIDs increase the risk of having a heart attack, with most data on high-dose ibuprofen and diclofenac. Naproxen appears to be risk-neutral with regard to cardiovascular events.

Selective NSAIDs: There is no significant increase in risk of a heart attack or stroke with celecoxib as compared to nonselective NSAIDs. Most evidence comes from short-term studies.

Partially selective NSAIDs: Meloxicam does not appear to increase the risk of heart attack compared to either no drug being taken (after 2 years), or compared to diclofenac being taken (over an unspecified duration). But overall, evidence is limited. [full review]

Does age or other patient factors influence the safety or effectiveness of NSAIDs?

In elderly patients, limited evidence suggests there may be lower risks of serious GI, cardiovascular, and renal adverse events with celecoxib, compared with diclofenac or ibuprofen.

In patients already taking low dose aspirin, the risk of developing an ulcer detected by endoscopy was similar after the addition of either a nonselective NSAID or celecoxib, with or without a proton pump inhibitor.

In the average patient taking aspirin to reduce their risk of cardiac events, taking an additional NSAID did not appear to interfere with the cardioprotective effects of aspirin. However, in patients who already have cardiovascular disease, one observational study found ibuprofen decreased the cardioprotective effects of aspirin. [full review]

Oral drugs included in this review

Generic Name	Trade Names
Celecoxib	Celebrex
Diclofenac Sodium	Voltaren Voltaren SR Voltaren XR
Diclofenac Potassium	Cataflam Voltaren Rapide Zipsor
Diflunisal	
Etodolac	Ultradol
Fenoprofen	Nalfon
Flurbiprofen	Ansaid

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Generic Name	Trade Names
Ibuprofen	Advil Motrin
Indomethacin	Indocin Indocin SR
Ketoprofen	Nexcede
Ketoprofen SR	
Ketorolac tromethamine	Toradol
Meclofenamate	
Mefenamic Acid	Ponstel Ponstan
Meloxicam	Mobic Mobicox
Nabumetone	
Naproxen	Aleve Naprosyn EC-Naprosyn Naprosyn E
Naproxen SR	Naprosyn SR
Naproxen sodium	Anaprox Anaprox DS Naprelan
Oxaprozin	Daypro
Piroxicam	Feldene
Sulindac	Clinoril
Tenoxicam	
Tiaprofenic Acid	
Tolmetin	Tolectin Tolectin 600 Tolectin DS

Topical drugs included in this review

Generic Name	Trade Names
Generic Name	**Trade Names**
Diclofenac epolamine	Flector
Diclofenac sodium	Voltaren Pennsaid Solaraze
Diclofenac diethylamine	Voltaren Emulgen

Further Information

- This PubMed Clinical Q&A was reviewed by Kimberly Peterson, MS.

For the full report and evidence tables, please see:
Peterson K, McDonagh M, Thakurta S, Dana T, Roberts C, Chou R, Helfand M. *Drug Class Review: Nonsteroidal antiinflammatory drugs (NSAIDs). Update 4 final report.* [Internet]. Portland (OR): Oregon Health & Science University; 2010 Nov. Available at http://www.ncbi.nlm.nih.gov/books/NBK53955.