

January 2017 ~ Resource #330101

Safety Comparison of NSAIDs

The following chart compares COX-2 selectivity, GI risk, and cardiovascular risk of available NSAIDs. Also keep in mind that NSAIDs carry varying risks of rare **hepatotoxicity** (diclofenac poses the highest risk). Also, NSAIDs can cause **renal injury** by reducing renal blood flow or through other mechanisms.¹¹ In older patients, theoretically, COX-2 inhibitors may be safer from a renal standpoint because in the elderly renal blood flow is mostly COX-1 dependent.¹² Other options that may have relatively low renal risk are nabumetone or nonacetylated salicylates (e.g., diflunisal).^{13,14} COX-2 selectivity is not necessarily associated with better GI safety or worse CV outcomes.

Drug	COX-2 selectivity (<i>in vitro</i>) ^{b,1-3}	GI Risk ^{4-7,15}	Cardiovascular Risk ^{a,4,8-10,16}
Aspirin	Low	Moderate	Low
Celecoxib (<i>Celebrex</i>)	High	Low	Moderate to High
Diclofenac (<i>Voltaren</i> [Canada], generics)	High	Moderate	High
Diflunisal	Moderate	Moderate	Data not available ^a
Etodolac	High	Low	Moderate
Fenoprofen (U.S. only)(<i>Nalfon</i> , generics)	Moderate	Moderate	Data not available ^a
Flurbiprofen	Low	High	Data not available ^a
Ibuprofen	Moderate	Low	Moderate to High
Indomethacin (<i>Indocin</i> [U.S.], generics)	Low	Moderate to High	Moderate
Ketoprofen (<i>Anafen</i> [Canada], generics)	Low	Moderate	Data not available ^a
Ketorolac (<i>Toradol</i> [Canada], generics)	Low	High	Data not available ^a

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Drug	COX-2 selectivity (<i>in vitro</i>)^{b,1-3}	GI Risk^{4-7,15}	Cardiovascular Risk^{a,4,8-10,16}
Meclofenamate (U.S. only)	Moderate	High	Data not available ^a
Mefenamic acid (<i>Ponstel</i> [U.S.], <i>Ponstan</i> [Canada], generics)	High	Low to Moderate	Data not available ^a
Meloxicam (<i>Mobic</i> [U.S.], <i>Mobicox</i> [Canada], generics)	High	Low	Moderate
Nabumetone	Moderate	Low	Data not available ^a
Naproxen (<i>Anaprox DS</i> , etc, generics)	Low	Moderate	Low to Moderate
Oxaprozin (<i>Daypro</i> , generics)	Low	High	Data not available ^a
Piroxicam (<i>Feldene</i> [U.S.], generics)	Moderate	High	Low
Salsalate (U.S. only)	Unavailable	Low	Data not available ^a
Sulindac	Moderate	Moderate	Data not available ^a
Tolmetin (U.S. only)	Low	Moderate	Data not available ^a

- a. For patients with cardiovascular disease or risk factors for ischemic heart disease, the American Heart Association recommends for pain (in the order listed): acetaminophen, aspirin, tramadol, opioids (short-term), nonacetylated salicylates (e.g., diflunisal), NSAIDs with low COX-2 selectivity, NSAIDs with some COX-2 selectivity, and COX-2 selective agents.⁸
- b. Note that the selectivity ratio in the table above is based on *in vitro* assay studies and should be interpreted with caution as different assay methods give different results. Moreover, no assay method can predict what will happen when the drug is given to patients. Clinical studies are the best way to determine the effects of NSAIDs in patients.¹

Users of this resource are cautioned to use their own professional judgment and consult any other necessary or appropriate sources prior to making clinical judgments based on the content of this document. Our editors have researched the information with input from experts, government agencies, and national organizations. Information and internet links in this article were current as of the date of publication.

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Project Leader in preparation of this clinical resource (330101): *Melanie Cupp, Pharm.D., BCPS*

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