

Generic Name	TRADE	Products/Comments	Usual Dosage	Max/d	≅ Dose	\$/30d	Class / Comments
ASA-Plain	ASPIRIN, generic	150 <sup>Ⓢ</sup> & 650 <sup>Ⓢ</sup> mg supp; 80 <sup>Ⓢ</sup> , 325 <sup>Ⓢ</sup> mg tab	325-650mg q4-6h	4g	650mg EC po	\$11	<b>Salicylates</b> ♦ASA: irreversible platelet inhibition ⚠GI-risk if used with other NSAIDs/COXIBs (CLASS)
ASA-Enteric Coated	ENTROPHEN	81 <sup>Ⓢ</sup> , 325, 650, 975 <sup>Ⓢ</sup> mg EC tab	325-975mg QID		QID		
Diflunisal	DOLOBID, generic	250,500mg tab	250-500mg BID	1.5g	250mg po BID	\$37	
Indomethacin	INDOCID, generic	25,50mg cap; 50,100mg supp	25-50mg TID	200mg	25mg po TID	\$17	<b>Indole Acetic Acids</b>
Sulindac	CLINORIL, generic	150 <sup>Ⓢ</sup> , 200 <sup>Ⓢ</sup> mg tab; PD	150-200mg BID	400mg	150mg po BID	\$34	INDOCID SR avail. by Special Access ankylosing spondylitis 613-941-2108
Diclofenac	VOLTAREN, generic	25,50mg EC tab; 50,100mg supp; 75,100mg SR tab	25-50mg BID-TID	150-200mg	50mg po TID 75mg SR po BID	\$40 \$39	<b>Phenylacetic Acids</b> (♦ VOLTAREN RAPIDE 50mg tab Ⓢ Ⓢ \$70; generic diclofenac K 50mg Ⓢ Ⓢ \$48 ) ♦diclofenac 75mg BID ↑LFTs AST >4% in CLASS
Diclofenac + Misoprostol	ARTHROTEC-50 ARTHROTEC-75	(50mg + 200µg) tab (75mg + 200µg) tab	1 tab BID-TID 1 tab OD-BID	200mg/ 800µg	One tab po BID One tab po BID	\$48 \$63	
Ketorolac	TORADOL, generic	#; 10mg tab; 30mg injectable IM formulation available	10mg po q6h x7d max 10-30mg IM q4-6h	40mg 120mg	10mg po QID	\$70#	<b>Pyrolizine Carboxylic Acids</b> ♦inj can be given IM (or IV)
Etodolac	ULTRADOL, gen.	~COX-2 selective; 200,300mg cap	200-600mg BID	1.2g	300mg po BID	\$50	<b>Pyranocarboxylic Acids</b>
Flurbiprofen	ANSAID, generic	50, 100mg tab; 200 <sup>Ⓢ</sup> mg SR cap	50-100mg TID-QID	300mg	100mg po BID	\$32	<b>Propionic Acids</b> ♦ibuprofen & naproxen: similar overall withdrawal rates as celecoxib CLASS & rofecoxib VIGOR respectively ♦naproxen less HTN causing withdrawal (0.1 vs 0.7%) vs rofecoxib VIGOR  Pediatric ibuprofen dose for pain/fever: 5-10mg/kg per dose (≤30mg/kg/day). naproxen 250,375,500mg EC tab Ⓢ Ⓢ: 375mg BID \$41; ♦ANAPROX Ⓢ Ⓢ 275-550 <sup>Ⓢ</sup> mg BID \$50-90(naproxen Na+)
Ibuprofen	MOTRIN, generic	(100mg/5ml, 200mg/5ml susp OTC Ⓢ Ⓢ) 100,200,400mg 300,400,600mg tab	200-800mg TID-QID Peds <sup>RA</sup> , ≤50mg/kg/day	2.4- 3.2g	400mg po TID 600mg po TID	\$12 \$13	
Ketoprofen	ORUDIS, generic	50,100mg EC; 150 <sup>Ⓢ</sup> , 200mg SR tab 50mg cap; 50,100mg supp	25-100mg TID-QID	300mg	50mg po TID	\$25	
Naproxen	NAPROSYN, generic	125,250,375 <sup>Ⓢ</sup> , 500 <sup>Ⓢ</sup> mg; 750mg SR; 125mg/5ml susp; 500mg supp	125-500mg BID >2yr =≤10mg/kg/day	1- 1.5g	375mg po BID 500mg po BID	\$16 \$20	
Oxaprozin	DAYPRO, generic	600 <sup>Ⓢ</sup> mg caplet; long t1/2 (50h)	600-1800mg OD	1.8g	600mg po OD	\$32	
Tiaprofenic Acid	SURGAM, generic	200,300 <sup>Ⓢ</sup> mg tab	200-300mg BID	600mg	200mg po BID	\$36	
Piroxicam	FELDENE, generic	10,20mg cap & 10,20mg supp	10-20mg OD	20mg	20mg po OD	\$33	<b>Oxicams-</b> long t½ (>50h)
Meloxicam	MOBICOX	~COX-2 selective; 7.5,15 <sup>Ⓢ</sup> mg tab	7.5-15mg OD	15mg	7.5mg po OD	\$25	♦meloxicam-well tolerated @7.5mg OD; lacks outcome data for significant reductions in GI ulcers/complications SELECT, MELISSA
Tenoxicam	MOBIFLEX, gen.	20mg tab (only generic in Canada)	20-40mg OD	40mg	20mg po OD	\$37	
Nabumetone	RELAFEN	~COX-2 selective; PD; 500,750mg tab	1-2g OD	2g	1g po OD	\$43	<b>Naphthylalkanones-</b> long t½ (>24h)
Floctafenine	IDARAC, generic	200,400mg tab	200-400mg TID-QID	1.2g	200mg po QID	\$59	<b>Anthranilic Acids</b> ♦mefenamic acid - used for dysmenorrhea; other NSAIDs also effective
Mefenamic Acid	PONSTAN, generic	250mg cap; (initially 500mg x1)	250mg QID x7d max	1.25g	250mg po QID	\$54#	
Celecoxib <sup>32</sup>	CELEBREX	100,200mg cap; Rare SULFA-type rx FAP: 400mg BID (not official indication)	100mg BID (OA) \$54 - 200mg BID (RA)	800mg	200mg OD 200mg BID	\$54 \$99	<b>COXIBs -highly COX-2 selective:</b> equal efficacy & similar renal/CV toxicity to other NSAIDs; less GI ulcer/bleed Non-ASA pts; minimal platelet effects; concern re: ↑cardiac/serious events (VIOXX ≥25mg/d & CELEBREX ≥400mg/d); lumiracoxib TARGET 20;21; warfarin DT's; Valdecoxib BEXTRA: Rare severe skin reactions (exfoliative dermatitis & Stevens-Johnson Sk.)
Rofecoxib DISCONTINUED	VIOXX (withdrawn from world market, Sep04)	-	12.5, 25mg tab; 2.5mg/ml susp {↑heart failure dose related in elderly <sup>22</sup> }	12.5 <sup>OA</sup> , 25mg <sup>OA/RA</sup> OD acute pain: ≤50mg/d x5d	50mg	12.5-25mg OD ≥2yr =≤0.6mg/kg/d	
Valdecoxib SUSPENDED	BEXTRA (suspended from CDN, USA, EU Apr05)	-	10,20mg tab {Rare SULFA-type reactions}	10-20mg OD <sup>OA,RA</sup> 40mg OD <sup>Dysmenorrhea</sup> \$97	40mg	10-20mg OD	
Acetaminophen (= paracetamol)	TYLENOL, generic TYLENOL ARTHRITIS-ER Tab Caution: ingredient of many products!	80,160,325,500mg tab <sup>Ⓢ</sup> Ⓢ 650mg ER tab <sup>Ⓢ</sup> Ⓢ; various susp's <sup>Ⓢ</sup> Ⓢ 120,325,650mg supp <sup>Ⓢ</sup> Ⓢ	325-1000mg TID-QID (Peds: ≤65mg/kg/day)	4g	650mg po QID 1,300mg ER Q8H	\$15 \$25	<b>Non-Anti-inflammatory Analgesic</b> lowest risk GI ulcer/bleed; option in OA; Monitor LFTs: with chronic use & if ↑alcohol use

Ⓢ=EDS=Exception Drug Status Sask. Ⓢ=prior approval for NIHB coverage Ⓢ Non-formulary Sask. Ⓢ=not covered NIHB Ⓢ=covered NIHB DI=drug interaction EC=enteric coated ER=extended release FAP=Familial Adenomatous Polyposis GI=gastrointestinal HTN=hypertension LFT=liver function tests OA=osteoarthritis OTC=over the counter (& non-formulary in SK) PD=Pro-drug RA=rheumatoid arthritis SK=Saskatchewan SR=sustained release supp=suppository susp=suspension Ⓢ=scored tablet COST=generic if avail. with dispensing fee & based on lowest usual anti-inflammatory dose. Lower doses often effective for analgesia. Aspirin induced asthma: common<sup>23</sup>, cross-react with other NSAIDs, rarely with acetaminophen.  
# Comparative cost: ketorolac & mefenamic; but max. 7 days recommended. **Recently Discontinued Products:** Choline Mg Trisalicylate TRILISATE, Fenoprofen NALFON, Piroxicam BEXIDOL, Salsalate DISALCID, Tolmentin TOLECTIN.  
♦ Fast-acting forms, but non-formulary in Sask. (ANAPROX, VOLTAREN RAPIDE, NOVO-DIFENAC-K); slightly faster onset, but more costly. **PREGNANCY:** weigh risk vs benefit (1<sup>st</sup>/2<sup>nd</sup> trimester likely OK, but D/C ~6-8wks prior to delivery).<sup>24</sup>  
**Topical NSAID:** May be effective in localized pain esp. 5-2weeks<sup>25</sup>; eg. diclofenac Na<sup>+</sup> PENNSAID 1.5% topical soln<sup>Ⓢ</sup> Ⓢ - Apply 40 drops (16mg diclofenac)<sup>26,27</sup> QID to affected knee, allow to dry (\$100/30d). Allow at least 1 wk for effect.  
**GI ULCER Risk Factors<sup>16</sup>:** (x= ↑ in odds ratio risk) Hx of ulcer complications x13.5, Multiple NSAIDs x9, High dose NSAIDs x7, Concomitant anticoagulant use x6.4, Age≥70 x5.6, Age ≥60 x3.1, Concomitant steroids x2.2, Hx of heart disease x1.8  
**Suppository** form NOT safer to GI tract. Ⓢ Possible gastric bleeding; antiplatelet effects of NSAIDs may ↑ risk during anticoagulant therapy. Ⓢ Misoprostol Cytotec Ⓢ 200mcg po bid<sup>S27</sup>, tid<sup>S38</sup>, qid<sup>S48</sup> is cytoprotective.  
**RENAL RISK:** Risk Factors = underlying volume depletion (patients on diuretics, especially high-dose loop), pre-existing renal insufficiency, heart failure, cirrhosis, age ≥70years, previous long-term daily use of NSAIDs/ASA.  
**MONITOR:** CBC, LFTs, SCr, lytes yearly (within 1-2 weeks if cardio/renal risk), signs of HF (e.g. edema, wt gain) Ⓢ ↓ efficacy of antihypertensives (diuretics, β-blockers, ACEI, ARBs); ↑ toxicity (lithium, methotrexate, warfarin).

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- <sup>1</sup> Micromedex 2005
- <sup>2</sup> Silverstein F, Faich G, Goldstein J, et al. Gastrointestinal toxicity with celecoxib versus non-steroidal anti-inflammatory drugs for osteoarthritis and rheumatoid arthritis: the CLASS study: A randomized controlled trial. Celecoxib Long-term Arthritis Safety Study. *JAMA* 2000;284:1247-55.
- <sup>3</sup> Bombardier C, Laine L, Reicin A, et al. Comparison of upper gastrointestinal toxicity of rofecoxib and naproxen in patients with rheumatoid arthritis. VIGOR study group. *N Engl J Med* 2000;343:1520-8.
- <sup>4</sup> Detailed study results for CLASS; FDA Feb 2001 - [http://www.fda.gov/ohrms/dockets/ac/01/briefing/3677b1\\_01\\_searle.pdf](http://www.fda.gov/ohrms/dockets/ac/01/briefing/3677b1_01_searle.pdf) & [http://www.fda.gov/ohrms/dockets/ac/01/briefing/3677b1\\_03\\_med.pdf](http://www.fda.gov/ohrms/dockets/ac/01/briefing/3677b1_03_med.pdf) Access verified, May 6, 2002.
- <sup>5</sup> Detailed study results for VIGOR; FDA Feb, 2001 - [http://www.fda.gov/ohrms/dockets/ac/01/briefing/3677b2\\_01\\_merck.pdf](http://www.fda.gov/ohrms/dockets/ac/01/briefing/3677b2_01_merck.pdf) Access verified, May 6, 2002.
- <sup>6</sup> Singh G, Ramey D, Triadafilopoulos G. Early experience with selective COX-2 inhibitors: safety profile in over 340,000 patient years of use [Abstract]. *Arthritis Rheum* 1999;42(Suppl 9):S296.
- <sup>7</sup> Mukherjee D, Nissen SE, Topol EJ. Risk of cardiovascular events associated with selective COX-2 inhibitors. *JAMA*. 2001;286:954-9.
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- <sup>10</sup> Guidelines for the management of rheumatoid arthritis: 2002 Update. *Arthritis Rheum*. 2002 Feb;46(2):328-46.
- <sup>11</sup> Treatment Guidelines: Drugs for Rheumatoid Arthritis. *The Medical Letter*: January, 2003; (5) pp. 25-32.
- <sup>12</sup> Hawkey C, Kahan A, Steinbruck K, et al. Gastrointestinal tolerability of meloxicam compared to diclofenac in osteoarthritis patients. International MELISSA Study Group. *Br J Rheumatol* 1998;37:937-45.
- <sup>13</sup> Dequeker J, Hawkey C, Kahan A, et al. Improvement in gastrointestinal tolerability of the selective cyclooxygenase (COX)-2 inhibitor meloxicam, compared with piroxicam: Results of the Safety and Efficacy Large-scale Evaluation of COX-inhibiting Therapies (SELECT) trial in osteoarthritis. *Br J Rheumatol* 1998;37:946-51.
- <sup>14</sup> <http://www.oregonrx.org/OrgrxPDF/NSAIDS%20review/NSAID%20Uupdate%20Report/5-12-03%20NSAID%20update.pdf>
- <sup>15</sup> <http://www.oregonrx.org/OrgrxPDF/NSAID%20Review.htm>
- <sup>16</sup> Hunt RH, Barkun AN, Baron D, et al. Recommendations for the appropriate use of anti-inflammatory drugs in the era of the coxibs: defining the role of gastroprotective agents. *Can J Gastroenterol*. 2002 Apr;16(4):231-40.
- <sup>17</sup> Nussmeier NA, Whelton AA, Brown MT, et al. Complications of the COX-2 Inhibitors Parecoxib and Valdecoxib after Cardiac Surgery. *N Engl J Med*. 2005 Feb 15; [Epub ahead of print]
- <sup>18</sup> Bresalier RS, Sandler RS, Quan H, Bolognese JA, Oxenius B, Horgan K, Lines C, Riddell R, Morton D, Lanas A, Konstam MA, Baron JA. Cardiovascular Events Associated with Rofecoxib in a Colorectal Adenoma Chemoprevention Trial. *N Engl J Med* 2005; 352:1092-102. (InfoPOEMs: For every 62 patients who take rofecoxib instead of placebo for 3 years, 1 additional patient will experience a serious cardiovascular event. Remember, there is no greater symptomatic relief with COX-2 inhibitors than with older drugs; acetaminophen is a very safe alternative. The decrease in risk of serious gastrointestinal complications is marginal with COX-2 inhibitors and the cost is high. (LOE = 1b))
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- <sup>20</sup> Farkouh ME, Kirshner H., Harrington RA. Comparison of lumiracoxib with naproxen and ibuprofen in the Therapeutic Arthritis Research and Gastrointestinal Event Trial (TARGET), cardiovascular outcomes: randomised controlled trial. *Lancet* 2004;364:675-84.
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- <sup>28</sup> Bjordal JM, Ljunggren AE, Klovning A, Slordal L. Non-steroidal anti-inflammatory drugs, including cyclo-oxygenase-2 inhibitors, in osteoarthritic knee pain: meta-analysis of randomised placebo controlled trials. *BMJ*. 2004 Dec 4;329(7478):1317. Epub 2004 Nov 23.
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- <sup>30</sup> Savage R. Cyclo-oxygenase-2 inhibitors : when should they be used in the elderly? *Drugs Aging*. 2005;22(3):185-200.
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- <sup>33</sup> Arrich J, Piribauer F, Mad P, et al. Intra-articular hyaluronic acid for the treatment of osteoarthritis of the knee: systematic review and meta-analysis. *CMAJ*. 2005 Apr 12;172(8):1039-43. (InfoPOEMs: The evidence that intra-articular hyaluronic acid helps patients with knee osteoarthritis is of poor quality. Improvements in pain at rest and pain during exercise is seen in a minority of studies, and those studies were of lower quality than those showing no benefit. There is no evidence of functional improvement. Injections like this have a potentially powerful placebo effect, so any benefit seen in unblinded studies without concealed allocation is likely represent the placebo effect rather than any effect of the drug. (LOE = 1a-))
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