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NSAIDs (Nonselective and COX-2 Selective Agents) Conversion Tools for UW Medicine and WA

Generic NSAIDs Available

NSAID Class	Generic Name	NSAID Class	Generic Name
Salicylates	Salsalate	Acetic acids	Diclofenac potassium
Propionic acids	Fenoprofen		Diclofenac sodium
	Flubriprofen		Etodolac
	Ibuprofen		Sulindac
	Ketoprofen	Oxicams	Piroxicam
	Naproxen	Naphthyl-alkanones	Nabumetone
	Naproxen sodium		
Oxaprozin			

Brand-only NSAIDs:

NSAID Class	Generic Name / Proprietary Name
Semi-selective COX-2 inhibitor	Meloxicam / Mobic®
Selective COX-2 inhibitor	Celecoxib / Celebrex®

Evaluating Patients & Appropriate Use, and Conversion Processes

1. Stratification of Patient Risk

- Cost outcomes studies to date have indicated that the most cost-effective use of COX-2 agents is in patients considered to be at high risk for GI complications.
- Stratification of patients by GI risk is generally recommended in selecting an agent, however it is notable that there are little data to substantiate a lower incidence of GI bleeding or ulceration in high-risk patients. This approach is an extrapolation of the data. In one trial (Francis KL, NEJM 347;26:1104) comparing celecoxib to a diclofenac-omeprazole combination therapy in patients with a recent history of GI bleed, there was no significant difference in the incidence of serious GI outcomes between the treatment groups. However, the relatively high incidence of GI events indicated that none of the treatments protected patients from recurrence of adverse outcomes. Thereby providing a message of caution to treating high-risk patients with any NSAID regimen.

2. Considerations for Use of a COX-2 Selective Agent

- COX-2 agents are not recommended for routine use in patients with acute pain or general musculo-skeletal complaints. COX-2 agents are indicated for patients with confirmed diagnosis of rheumatoid arthritis or osteoarthritis that
 - (per UW and MAA policy) are considered at high-risk for a serious GI event.
 - (per MAA policy) have experienced therapeutic failure with several nonselective NSAIDs.
- Use of non-steroidal anti-inflammatory agents in patients at high risk for serious GI complications should be considered cautiously as both selective and non-selective agents may still increase risks. **Patients considered at the high risk are** those with a previous clinical history of a gastroduodenal ulcer or perforation or GI bleed. Other risk factors include: advanced age (> 65 years), concomitant anticoagulant or glucocorticoid therapy, severe systemic disease).
- Utilization of a proton-pump inhibitor (PPI) in combination with a traditional NSAID agent can improve tolerability and decrease risk of serious GI events. The cost-effectiveness of this combination therapy versus a COX-2 selective agent should be assessed, especially in light of the availability of lower cost, OTC and generic PPI agents.
- All NSAIDs can worsen hypertension and may exacerbate heart failure and have other renovascular effects that may be undesirable in patients with cardiovascular disease. Rofecoxib was voluntarily withdrawn from the market secondary to increased incidence of myocardial infarction in trials comparing the agent to non-selective NSAIDs. While data is inconclusive regarding CV risks selective and nonselective agents, the FDA has

required a black box warning for all NSAIDs in patients with cardiovascular disease and contraindicates the drugs in patients who have recently undergone cardiac bypass surgery.

3. Converting Patients to Preferred NSAIDs

Key Steps in the Assessment and Conversion Process

#1. Determining appropriateness of NSAID therapy and use of non-preferred agents.

- MAA-DSHS has developed a program to decrease morbidity and mortality from NSAID-associated adverse GI event (i.e., bleeding, ulcerations). All patients presenting with a prescription for an NSAID (COX-2 selective or traditional/nonselective) must be evaluated for GI risk. Furthermore, use of non-preferred NSAIDs must meet particular criteria.
- Use the “**NSAID/COX-2 Decision Tree**” (located at end of document) to assist you in working through these criteria. It is advised that the official MAA-DSHS policies be reviewed.

#2. Converting patients to preferred agents via the Therapeutic Interchange Program (TIP) or making recommendations for preferred agents and doses.

- Determine which NSAID products the patient has used in the past and avoid converting to those associated with therapeutic failures or intolerances.
- For patients requiring routine NSAID therapy (i.e., OA, RA), use the **Conversion Dosing Guide for Chronic NSAID Therapy** (Table 2) to assist you with selecting a preferred agent and dose. You may also refer to the **Comparative Table of Adverse Effects of Nonselective NSAIDs** (Table 3).
- For patients requiring intermittent (PRN) NSAID therapy for mild to moderate pain, select an agent with a shorter duration of action or a non-sustained release formulation and use the low to moderate dose recommendations in Table 2. Ibuprofen and naprosyn are the most widely used agents for these types of indications.
- Inpatient variability in response to NSAIDs is common and can lead to therapeutic failures. Patients often need consecutive trials with several agents. Traditional recommendations have been to switch to agents in different chemical classes and, while there is no harm in this approach, there is no data to support its effectiveness.

#3. Patient education and consultation

- The patient should be counseled on the rationale behind this conversion.
- The patient should be specifically instructed to stop the previous NSAID agent and begin taking the new agent with emphasis on the risk of using both medications (including OTC preparations).
- Counseling should include advising the patient on adverse reactions that may occur with all NSAID medications and what to do should they experience any significant reactions (ie, blood in stool)
- The patient should be advised to contact the pharmacy for any questions related to the medication or to contact their physician/prescriber for any health-related concerns.

#4. Notification of Prescriber Regarding Conversion

- All WA Rx therapeutic interchanges necessitate notification of the prescriber. It is recommended that this notification be completed within 24 hours by the pharmacist making the conversion and, for UW Medicine prescribers, that the documentation is completed in Powerchart.

Table 2: Conversion Dosing Guide for Chronic NSAID Therapy*

NSAID Agent	Low Dose	Medium Dose	High or Max Dose
Salsalate	500-750mg bid	750mg tid	1000mg tid
Fenoprofen	200-300mg qid	600mg tid-qid	800mg qid
Flubriprofen	50mg bid	50mg tid-qid	100mg tid
Ibuprofen	400mg tid	600mg tid-qid	800mg qid**
Ketoprofen	25-50mg tid	75mg tid	IR =300mg/day (divide), SR =200mg/day
Naproxen	250mg tid	500mg bid	1250mg/day (divided)
Naproxen sodium	275mg tid	550mg bid	1375mg/day (divided)
Oxaprozin	600mg qd	1200mg qd	1200mg qd
Diclofenac potassium	50mg bid	50mg tid	50mg qid (in OA/RA only)
Diclofenac sodium	50mg bid	75mg bid	50mg qid or 100mg SR bid (in RA only)
Etodolac	200mg tid	400mg bid	1200mg max (IR or SR divided doses)
Sulindac	150mg bid	200mg bid	200g bid
Piroxicam	10mg qd	20mg qd	40mg per day (not indicated for OA or RA)
Nabumetone	1000mg qd	1000mg bid	2000mg/day (qd or divided bid)
Meloxicam/Mobic®#	7.5mg qd	7.5mg qd	15mg qd
Celecoxib/Celebrex®#	200mg qd	200mg bid	200mg bid
Rofecoxib/Vioxx®#	12.5mg qd	25mg qd	50mg qd for max of 5 days (acute pain)
Valdecoxib/Bextra®#	10mg qd	10mg qd	20mg bid (primary dysmenorrhea only)

*This table does not represent exact or equivalent dosing conversions. It is based on FDA approved dosing ranges and comparative doses from clinical trials. Practitioners should exercise common sense in the practical application of this guide, including consideration for the patient's NSAID history and current clinical status (i.e., renal function).

Preferred Agents per WA Rx PDL [UW PDF Agents](#)

#NON-preferred agents on Washington State Preferred Drug List. Require prior authorization

Table 3: Comparative Table of Adverse Effects of Nonselective NSAIDs (Miyoshi, Boyce)

Class	Analgesic	Gastrointestinal system		Platelets	Renal toxicity	Hepatic toxicity
		Dyspepsia	Bleeding			
Salicylates	Salsalate	+	+	0	+	+
Propionic acids	Fenoprofen	+	+	+	++	+
	Flubriprofen			+	++	
	Ibuprofen	++	+	+	++	+
	Ketoprofen	+	+	+	++	++
	Naproxen	+++	++	+	++	+
Acetic acids	Oxaprozin	++	+	+	++	++
	Diclofenac	++	++	+	++	++
	Etodolac	++	+	0/+	+	+
Oxicams	Sulindac	++	+	+	+	+
	Piroxicam	++	+	+	++	+
Alkanones	Meloxicam	+	+	0	+	+
	Nabumetone	+	+	0	+	+

0=no effect, + minimal effect, ++ moderate effect, +++ strong effect, ++++ maximum effect

WA Rx NSAID/COX-2 Decision Tree

