ACUTE PAIN DRUG TABLES

Table 1a. Select Non-Opioid Analgesics for Acute Pain (Oral & Topical)

Name *Trade*, generic	Strength	Adult Dose (Product & CPhA Monographs)	Dose Adjustments (Lexi-Drugs)	Adverse Events	Nova Scotia Pharmacare Status	Cost (McKesson or NS Pharmacare)
ACETAMINOPHEN						
Acetaminophen *Tylenol*, generics	325 mg 500 mg 650 mg (ER)	325-650 mg q4–6h prn 1 g q6h (Extra Strength) 1.3 g q8h prn (ER) **MAX**: 4 g/day	Hepatic: Use with caution (Limited data) Hepatic disease/cirrhosis: ≤2–3 g/ day Hepatic disease/cirrhosis ***and*** active alcohol use: AVOID if possible. Limit to short courses of ≤ 2 g/day Renal: GFR 10–50 mL/min: q6h, GFR <10 mL/ min: q8h	Well tolerated Liver toxicity in higher doses	Not a benefit	$0.03/caplet (325 mg and 500 mg)
Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) ORAL						
Celecoxib *Celebrex*, generics	100 mg 200 mg	400 mg single dose on the first day, then 100–200 mg daily prn **MAX**: 200 mg/day (CV disease, risk factors for CV disease); 400 mg/day	Hepatic: Moderate impairment: ↓ dose by 50% Severe impairment: AVOID Abnormal LFTs (persist/worsen): discontinue Renal: Not recommended in severe impairment and advanced disease	CV: elevated blood pressure, edema CNS: dizziness, hallucinations GI: dyspepsia, ulcer Liver: elevated liver function tests (LFTs) Renal: fluid retention, renal toxicity, increased risk of acute kidney injury in combination with a diuretic and ACEi or ARB	Full Benefit	$0.13-0.25/cap
Diclofenac Potassium *Voltaren Rapide,* generics	50 mg	50 mg q6-8h prn **MAX:** 100 mg/day	Hepatic: No specific dose recommendations. AVOID in patients with severe liver impairment or active liver disease Renal: GFR 30–60 mL/min: reduce the dose GFR <30 mL/min: AVOID		Not a Benefit	$0.39/tab
Diclofenac Sodium *Voltaren,* generics	25 mg, 50 mg 75 mg 100 mg	25 mg TID prn **MAX:** 100 mg/day			Full Benefit	$0.08-0.41/tab
Ibuprofen *Advil, Motrin*, generics	200 mg, 300 mg 400 mg 600 mg	200–400 mg TID–QID prn **MAX:** 1200-2400 mg/day			Full Benefit 300–600 mg tablets	$0.04-0.13/tab
Naproxen *Naprosyn,* generics	250 mg 375 mg 500 mg	250-500 mg BID-TID prn **MAX:** 1500 mg (for limited periods)			Full Benefit	$0.11-0.14/tab
Naproxen Sodium *Aleve, Anaprox,* generics	220 mg 275 mg 550 mg	220 mg q8-12h prn **MAX:** 440 mg/day (OTC) 550 mg loading dose, then 275 mg q6-8h prn **MAX:** 1375 mg/day (by prescription)			Full Benefit	$0.05-0.35/tab
Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) TOPICAL						
Diclofenac sodium solution 1.5% *Pennsaid*, generics		40 drops topically QID	Hepatic: No specific dosage adjustment. Use with caution Renal: AVOID in advanced renal disease NOTE: Use of topical diclofenac with oral NSAIDs is contraindicated in Canada	Local skin reactions; monitor for NSAID related adverse drug reactions	Not a Benefit	$37.36 (60 mL)
Diclofenac diethylamine gel 1.16%, 2.32% *Voltaren Emugel*		1.16%: 2–4 g TID-QID. 2.32%: 2 g BID **MAX:** 4 g/24 h (2.32%) NOTE: 2–4 g= 4–8 cm			Not a Benefit	$6.34 (30 g 2.32%)

Abbreviations: ACEi: angiotensin-converting enzyme inhibitor, ARB: angiotensin II receptor blocker, BID: twice per day, CPhA: Canadian Pharmacists Association, CNS: central nervous system, CV: cardiovascular, ER: extended release GFR: glomerular filtration rate, LFT: liver function test, q: every, OTC: over the counter, prn: as needed, QID: four times per day, TID: three times per day

- See 'Prescribing Considerations' at the end of tables
- For additional prescribing information, see product monographs. For information on other NSAIDs, see product monographs.

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Laminate references are available in the Academic Detailing handout:
https://medicine.dal.ca/departments/core-units/cpd/programs/academic-detailing-service/AC-Service-Resources.html

Table 1b. Select Skeletal Muscle Relaxants for Acute Low Back Pain						
Name *Trade,* generic	**Strength**	**Adult Dose** (Product Monographs)	**Dose Adjustments** (Lexi-Drugs)	**Adverse Events**	**Nova Scotia Pharmacare Status**	**Cost (McKesson or NS Pharmacare)**
Cyclobenzaprine generics	10 mg	5-10 mg TID prn **MAX:** 30 mg/24 h	Hepatic: Caution in mild impairment, start lower initial dose. Avoid in moderate to severe cases	Drowsiness, fatigue, dizziness, anticholinergic effects	Full benefit	$0.11/tab
Methocarbamol/ ASA *Robaxisal Extra-Strength,* generics	400/500 mg	2 caplets q6h prn **MAX:** 8 caplets/24 h	Renal: (ASA) Do not use in CrCl <30 mL/min	Lightheadedness, dizziness, drowsiness, mild nausea, constipation (codeine) **NOTE:** high ASA content (>3.6 g/day) more likely to cause GI AE (Ulcer, dyspepsia, heartburn, epigastric distress)	Not a benefit	$0.50/tab
Methocarbamol/ ASA/Codeine *Robaxisal C ½* *Robaxisal C ¼*	400/325/16.2 mg	1 caplet q6-8h prn **MAX:** 8 caplets/24 h				$1.07/tab
	400/325/32.4 mg	1 caplet q6-8h prn **MAX:** 8 caplets/24 h				$1.21/tab
Methocarbamol/ Acetaminophen *Robaxacet* *Tylenol Back Pain* generics	400/500 mg	2 caplets q6h prn **MAX:** 8 caplets/24 h	Hepatic: (Acetaminophen) Use with caution (Limited data) Hepatic disease/cirrhosis: ≤2–3 g/day Hepatic disease/cirrhosis ***and*** active alcohol use: AVOID if possible. Limit to short courses of ≤ 2 g/day Renal: (Acetaminophen) GFR 10–50 mL/min: q6h GFR <10 mL/min: q8h	Lightheadedness, dizziness, drowsiness, mild nausea, liver toxicity, constipation (codeine)	Not a benefit	$0.35- 0.39/tab
Methocarbamol/ Ibuprofen *Robax Platinum* *Motrin Platinum* generics	500/200 mg	1-2 caplets q4-6h prn **MAX:** 6 caplets/24 h	Hepatic: (Ibuprofen) No specific dose recommendations. AVOID in patients with severe liver impairment or active liver disease Renal: (Ibuprofen) GFR 30–60 mL/min: reduce dose GFR <30 mL/min: AVOID	Dyspepsia, ulcer, elevated blood pressure, edema, fluid retention, renal toxicity, elevated liver function tests, dizziness, hallucinations	Not a benefit	$0.36/tab

Abbreviations: AE: adverse events, ASA: acetylsalicylic acid, CrCl: creatinine clearance, GFR: glomerular filtration rate, GI: gastrointestinal, MAX: maximum dose, q: every, QID: four times per day, TID: three times per day

- See 'Prescribing Considerations' at the end of tables
- For additional prescribing information, see product monographs.

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Table 1c. Select Oral Opioids for Acute Pain								
Name *Trade,* generic	**Dosage Form/Strength**	**Starting Dose for Opioid-Naïve Adults**	**Dose Titration/Taper**	**Dose Adjustments** (Lexi-Drugs)	**Adverse Events**	**Nova Scotia Pharmacare Status**	**Morphine Equivalents** (50 mg/day)	**Cost** (McKesson or NS Pharmacare)
Codeine +/- **Acetaminophen** +/- **Caffeine** *Tylenol # 1, 2, 3, 4,* generics	• IR tab: 15 mg, 30 mg • Syrup: 5 mg/mL • Tab with 300 mg or 325 mg acetaminophen: 8, 15, 30, 60 mg	15-30 mg q4h prn* (codeine) T1, T2, T3 do not exceed 12 tabs/24 hours T4 do not exceed 6 tabs/24 hours	Adjust according to clinical response to lowest effective dose. Taper to avoid withdrawal symptoms if prolonged use required, see links: https://cep.health/media/uploaded/20180305-Opioid-Tapering-Tool-Fillable.pdf https://www.deprescribingnetwork.ca/tapering	Hepatic: use lowest possible dose Renal: use lowest possible dose Combination products with acetaminophen are contraindicated in severe hepatic and renal impairment. *Individual dosing requirements vary considerably based on each patient's age, weight, severity of pain, and medical and analgesic history. Formulations with acetaminophen: **MAX:** 4 g/day	Constipation Nausea Opioid-use disorder Respiratory depression Sedation	Full benefit (T1 not a benefit)	334 mg/day	$0.02-0.37/tab
Morphine *Doloral, MS-IR, Statex,* generics	• IR tab: 5, 10, 20, 25, 30, 50 mg • IR cap: 5, 10, 20, 30 mg • Syrup: 1 mg/mL, 5 mg/mL	5-10 mg q4h prn *				Full benefit	50 mg/day	*Tablets:* $0.16-0.52/tab *Liquid:* $0.05/ml
Oxycodone +/- **Acetaminophen** *Oxy-IR, Percocet, Supeudol,* generics	• IR tab: 5, 10, 20 mg • Tab: 5 mg with 325 mg acetaminophen	5-10 mg q6h* (oxycodone)				Full benefit	33 mg/day	$0.12-0.79/tab
Hydromorphone *Dilaudid*, generics	• IR tab: 1, 2, 4, 8 mg • Syrup: 1 mg/mL	2-4 mg q4-6h prn*				Full benefit	10 mg/day	*Tablets:* $0.10-0.35/tab *Liquid:* $0.09/ml
Tramadol +/- **Acetaminophen** *Ultram, Tramacet*	• IR tab: 50 mg • Tab: 37.5 mg with 325 mg acetaminophen	25 mg once daily* (tramadol) **MAX:** 400 mg/day		Do not use in severe hepatic or renal impairment Formulations with acetaminophen: **MAX:** 4 g/day	As above + increased seizure risk when used with SSRIs, SNRIs, TCAs, or other tricyclic compounds	Not a benefit	300 mg/day	$0.63-0.64/tab

Abbreviations: IR: immediate release, MAX: maximum dose, prn: as needed, q: every, SNRI: serotonin-norepinephrine reuptake inhibitor, SSRI: selective serotonin reuptake-inhibitor, tab: tablet, TCA: tricyclic antidepressant
*Individual dosing requirements vary considerably based on each patient's age, weight, severity of pain, and medical and analgesic history.
• Dosing obtained from product monographs
• See 'Prescribing Considerations' at the end of tables
• For additional prescribing information, see product monographs.

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PRESCRIBING CONSIDERATIONS: *NOTE: not all-inclusive, see product monographs for more information

Many combination products exist over-the-counter that could contain the same ingredient (or class of ingredients) as prescribed medications (e.g. acetaminophen). Additive adverse effects can occur as a result of combining these.

Nonsteroidal Anti-Inflammatory Drugs (NSAIDs) [1]

- *Diclofenac* most commonly associated with hepatic adverse drug reactions.
- *Celecoxib* may cause an allergic reaction in patients with hypersensitivity to sulfonamides.
- NSAIDs inhibit platelet aggregation and can increase bleeding risk. Use them with caution in patients with platelet disorders or hemophilia or who take anticoagulant drugs.
- Consider lower doses in the elderly due to an increased potential for toxicity.
- Both COX-2 inhibitors and non-selective NSAIDs have the potential for adverse gastrointestinal and cardiovascular events; however not all people are at equal risk and there are differences between agents. Please refer to the NSAID risk section and risk factor assessment tools.
    - As an example, ketorolac is associated with a high risk of GI toxicity (up to 5.5 times greater than other NSAIDs) especially in higher doses, older patients, and for use > 5 days.
- Contraindications:
    - History of asthma or allergic-type reactions after taking NSAIDs or ASA including ASA intolerance and the Aspirin Triad (asthma, nasal polyps, and ASA intolerance), since fatal anaphylactoid reactions are possible. Cross-reactivity among structurally different nonselective NSAIDs occurs.
    - Perioperative setting of coronary artery bypass graft surgery (CABG) because of the risk of thrombotic events.
    - Severe uncontrolled heart failure since exacerbations can occur.

Skeletal Muscle Relaxants [2]

- *Cyclobenzaprine*: Use of monoamine oxidase inhibitors is contraindicated with skeletal muscle relaxants as well as within the preceding 14 days. A starting dose of 5 mg tid prn reduces adverse effects and provides similar pain relief as higher doses.
- Methocarbamol and cyclobenzaprine may impair the ability of the patient to engage in potentially hazardous activities such as operating machinery or driving a motor vehicle; ambulatory patients should, therefore, be cautioned accordingly.
- Patients should be cautioned about combined effects of methocarbamol and cyclobenzaprine with alcohol and with other CNS depressants.

Opioids [3]

- *Codeine* is a prodrug that needs to be converted by CYP2D6 to an active metabolite. Genetically determined variations in metabolism mean codeine has an unpredictable effect. In patients who are CYP2D6 ultra-rapid metabolizers, toxicity from codeine can occur even at therapeutic doses. Poor metabolizers of CYP2D6, or patients taking drugs that inhibit CYP2D6, will experience less analgesic effect.
- *Tramadol* in its unconverted state binds weakly to opioid receptors but inhibits the reuptake of norepinephrine and serotonin. Tramadol is converted by CYP2D6 and its' main active metabolite is an opioid. Tramadol metabolism can be highly variable. In patients who are CYP2D6 ultra-rapid metabolizers, opioid associated toxicity with tramadol is more likely to occur even at therapeutic doses. Alternatively, poor CYP2D6 metabolizers are at increased risk of serotonin syndrome due to enhanced inhibition of serotonin reuptake by tramadol. Variable pharmacokinetics along with drug interactions mean tramadol can have unpredictable therapeutic and safety effects.
- Use of monoamine oxidase inhibitors should be avoided while using opioids and within 14 days of use.
- Serotonin syndrome is possible if any opioid is combined with serotonergic drugs.
- Avoid concomitant use of benzodiazepines, alcohol, and other CNS depressants (e.g. gabapentinoids) while using opioids due to additive sedative properties.
- There is no safe dose of opioids. Harms and complications can happen at any dose, but are less likely at lower morphine mg equivalents/day (< 50 morphine equivalents).
- Patients should be educated on overdose risk and use of *Naloxone kits*. Naloxone only partially reverses the symptoms of tramadol overdose and can increase the risk of tramadol associated seizures.
- *Combination products* that contain both an opioid and non-opioid analgesic (e.g. acetaminophen, NSAID, or ASA) may result in serious adverse effects. Effects of high doses may include liver toxicity, gastric perforation, hemorrhage and peptic ulcer, renal failure, chronic blood loss anemia and low blood potassium (with potential fatal heart and neurological complications). Unintentional overdose can occur due to cumulative exposures from ingestion of multiple and/or combination OTC products containing the non-opioid analgesics. ***Note:** the use of combination opioid/non-opioid products does not allow routine dosing of non-opioid analgesics and PRN dosing of opioids as recommended after surgery.

ASA: acetylsalicylic acid, CNS: central nervous system, NSAID: non-steroidal anti-inflammatory drug, SNRI: serotonin norepinephrine reuptake inhibitor, SSRI: selective serotonin reuptake inhibitor, [1]NSAIDS Canadian Pharmacists Association (CPhA) monograph, [2]Cyclobenzaprine (CPhA) and Robaxin monographs, [3]Opioids CPhA monograph, Ultram monograph.
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