

Loyola Adult Pain Management Guidelines For patients 18 years and older

Use in conjunction with the Adult Pain Management Orders on the EMR
(Review pain management orders daily; opioid orders expire in 3 days)

Vision: All patients will receive the best level of pain control that can safely be provided.

Principles of Pain Management

1. Pain is whatever the patient says it is. The patient's report of pain must be accepted and addressed.
2. Appropriate assessment, management, and documentation of *pain* are the responsibility of every person on the health care team.
 - Assessment should include quality, severity, and temporal associations.
 - Documentation should include the pain score on the visual analog scale (VAS).
3. Reassessment and documentation of the effect and adequacy of *pain management techniques* is essential to the design of an individualized analgesic regimen.
4. Unresolved pain is an emergent problem.
5. Around-the-clock dosing of analgesics is preferred over PRN dosing.
 - Some patients may not ask for pain medications. They can always refuse a scheduled dose.
 - Pain is more effectively managed when the control is consistent rather than intermittent.
6. Most successful analgesic regimens consist of around-the-clock or long-acting analgesics PLUS short-acting PRN analgesics.
 - VAS scores can be used to determine route and dose of PRN medications.
 - Higher or IV push doses are used for higher VAS scores.
7. Oral or IV routes of administration are preferred over IM injections.
8. Non-pharmacologic options for pain management should be considered in all patients.
9. A plan to avoid and manage adverse effects of analgesics (eg. constipation) must be implemented.
10. Many patients will state they are allergic to morphine; however, very few patients have a true morphine allergy.
 - TRUE ALLERGY: Urticaria & bronchospasm
 - Adverse effects: nausea, vomiting, pruritus, confusion (not dose-related)
 - True morphine allergy will also be a codeine allergy
 - Other opioids are less likely to be cross-reactive.

Recommended Intravenous Opioid Analgesics

1. Patient controlled analgesia (PCA) is the preferred method of intravenous administration. Management of IV PCA is the responsibility of each hospital service. For more information, refer to the IV PCA orders and guidelines on the EMR.

Standard Drug Concentrations for PCA		
Morphine (30 mL vial)	Hydromorphone (pharmacy prep)	Fentanyl (pharmacy prep)
1 mg/mL – peds only	0.2 mg/mL – opioid naïve pts	50 mcg/mL
5 mg/mL – all adults	1 mg/mL or 5 mg/mL – opioid tolerant pts ONLY	

2. IV Push opioids may be used when a patient is experiencing acute, severe pain (VAS 8 or more) or is NPO. If the patient requires more than 3 doses in any 4-hour period, consider changing to PCA. If pain is consistent or predictable, then another method is preferred. Other methods may include IV PCA, transdermal, or oral medications.
3. Peri-spinal analgesia is initiated and managed by the Anesthesia Pain Service. Once peri-spinal analgesia is discontinued, the surgical service assumes responsibility for pain management using the LUHS Adult Pain Management Guidelines. For more information, refer to the Peri-Spinal Analgesia orders and guidelines on the EMR or contact the Anesthesia Pain Service.

4. Intubated/ventilated patients - refer to ICU Adult Analgesia and Sedation Protocol for Patients Receiving Mechanical Ventilation guidelines.
5. Special patient populations (eg. cognitively impaired, dementia, inadequate motor skills to self administer meds) present unique challenges for appropriate pain management. There are two options to consider:
 - o Nurse controlled analgesia: Follow IV PCA orders and the nurse administers demand doses.
 - o IV push medications (eg. morphine, fentanyl, hydromorphone) can be given hourly; however, this is *not the preferred method*. If the patient requires more than 3 doses in a 4-hour period, Nurse controlled analgesia or a continuous basal opioid infusion is recommended.

Recommended Oral Analgesic Medications

Short-acting analgesics

1. Acetaminophen can be used as monotherapy for mild pain (VAS of 3 or less). It may also be used as adjunct PRN therapy for mild pain. Doses up to 1000 mg three to four times daily can be used in most patients. High doses may potentiate the effect of warfarin. Excessive acetaminophen can lead to hepatic compromise in healthy adults.
 - o Total dose of acetaminophen for acute pain is NOT to exceed 4 grams/day from ALL SOURCES.
 - o For chronic pain (over 3 months), total dose of acetaminophen is NOT to exceed 3.2 grams/day.
 - o For chronic pain (over 3 months) in elderly, liver dysfunction, and malnourished patients, total dose is not to exceed 2.4 grams/day.
2. Non-steroidal anti-inflammatory drugs (NSAIDs) can be used as monotherapy for mild pain or for pain due to an inflammatory process. Caution should be used in patients with renal insufficiency or those with increased risk for peptic ulcers, gastritis, or bleeding.
 - o Specific cautions with certain NSAIDs
 - o Ketorolac (Toradol) must be limited to 5-day use
 - o Celecoxib (Celebrex) with caution in patients with congestive heart failure, coronary artery disease or acute coronary syndromes (unstable angina, non Q wave or sub-endocardial MI, and ST segment elevation or transmural MI). Limit use to 5 days for acute pain.
3. Acetaminophen combination products can be used for mild to moderate pain (VAS of 4 to 7) or as an adjunct PRN therapy. Special caution must be used with opioid combination products containing acetaminophen. .

<u>24 Hour Maximum Doses for Some Acetaminophen-containing Products</u>		
Brand	Generic & strength (mg)	No. of tabs
Tylenol	Acetaminophen 325*	12 tabs
Tylenol Extra Strength	Acetaminophen 500	8 tabs
Tylenol Arthritis	Acetaminophen 650	6 tabs
Norco	Hydrocodone/acetaminophen 5/325*, 7.5/325, 10/325	12 tabs
Vicodin	Hydrocodone/acetaminophen 5/500	8 tabs
	Hydrocodone/acetaminophen 7.5/750	5 tabs
Lortab	Hydrocodone/acetaminophen 7.5/500	8 tabs
Percocet	Oxycodone/acetaminophen 5/325*, 10/325	12 tabs
	Oxycodone/acetaminophen 7.5/500	8 tabs
	Oxycodone/acetaminophen 10/650	6 tabs
Ultracet	Tramadol/acetaminophen 37.5/325	12 tabs
Tylenol #3	Codeine/acetaminophen 30/300*	13 tabs
Darvocet N-100	Propoxyphene/acetaminophen 100/650*	6 tabs

*On hospital formulary

4. Tramadol is indicated for moderate pain (VAS 4 to 7). Its use contraindicated in patients with opioid dependence. Use with caution in patients at risk for seizures or in combination with serotonergic drugs (eg. SSRIs, TCAs, MAOIs).
 - o Dosage must be adjusted for renal impairment
 - o Maximum dose in patients over 75 years old: 300 mg/day
5. Immediate release opioids

- Around-the-clock (scheduled) dosing is preferred if patient has moderate to severe pain
- If patient has moderate, unrelieved pain, increase opioid dose by 25-50% q 24 hrs
- If patient has severe, unrelieved pain, increase opioid dose by 50-100% q 24 hrs
- Once pain relief is achieved, convert to long-acting opioids
- See Equianalgesic dosing table for calculating equivalent doses and duration of action of various opioids.
- Immediate release opioids should be ordered as PRN doses in addition to long-acting opioids for breakthrough pain. (See Management of Breakthrough Pain below)

Sustained release (long-acting) opioids

1. Consider the use of sustained released opioids after 5 days of short acting opioids and consistently reported VAS over 4.
2. Dosage is based on the previous 24-hour opioid requirement from all sources (see Equianalgesia table).
3. Ordered doses must be based on available medication strengths. A combination of different strengths may be used to achieve the desired dose.

Standard Long-Acting Opioids			
Brand	Generic	Strengths	Frequency of administration
MSContin (others include Avinza ⁺ , Kadian ⁺)	Morphine controlled-release	15 mg, 30 mg, 60 mg	Every 12 hours (Avinza & Kadian may be every 24 hours)
OxyContin	Oxycodone controlled-release	10 mg, 20 mg, 40 mg, 80 mg	Every 12 hours
Duragesic	Fentanyl transdermal patch	12.5 mcg/hr, 25 mcg/hr, 50 mcg/hr, 75 mcg/hr, 100 mcg/hr	Every 72 hours

4. If VAS is greater than 8 and unrelieved with 3 adjustments in the analgesic regimen, consult the Anesthesia Pain Service.
5. ALWAYS order short-acting (preferred) or IV push analgesics for breakthrough pain when using sustained-release or long-acting opioids. Use the same opioid in short-acting form and the same route that is used for around-the-clock pain management.

Management of Breakthrough Pain

- Breakthrough pain can be predictable (with movement or activity) or unpredictable
- Management of breakthrough pain should always be considered when using sustained release opioids
- Use an immediate release opioid PRN that is the same opioid as the sustained release if possible
- The frequency of breakthrough doses is based on the duration of action of the immediate release opioid; usually q 2-4 hours
- A breakthrough pain dose should be 5-15% of the total daily sustained release opioid dose
 - 15% for severe breakthrough pain (VAS over 7)
 - 5-10% for mild to moderate breakthrough pain (VAS 7 or less)
- If more than 5 breakthrough pain doses are necessary in a 24-hour period, consider increasing sustained

6. Methadone can be used for both acute and persistent pain. It is not a first-line agent. Please consult Anesthesia Pain Service or a pain specialist for assistance with dosing. Repeated dosing results in accumulation that may require a dose reduction after a few days. Methadone is dosed every 8 to 12 hours. It may cause QT prolongation. Use for narcotic addiction must be appropriately documented per hospital policy.

Equianalgesia Conversion

An Equianalgesia table lists opioids at doses that produce approximately the same amount of analgesia. Doses are listed for both oral and parenteral routes, since the absorption and metabolism of the same drug may be different with different routes. For example, 1.5mg of parenteral hydromorphone produces the similar analgesia as 7.5mg of hydromorphone by mouth. Likewise, 20mg of oral oxycodone produces the similar analgesia as 30mg of oral morphine. Calculated equianalgesic doses may need to be decreased by 25 to 30% initially because of increased sensitivity to the new opioid (incomplete cross-tolerance). **These are not suggested starting doses.**

DRUG	ORAL DRUG DOSE	PARENTERAL DRUG DOSE	DURATION of PAIN RELIEF
Morphine (IR)	30 mg	10 mg	3-4 hours
Hydromorphone	7.5 mg	1.5 mg	3-4 hours
Codeine	200mg	130 mg	3-4 hours
Oxycodone	20 mg	-	3-4 hours
Hydrocodone	30 mg	-	3-4 hours
Methadone*	20 mg (acute pain)	10 mg	4-6 hours
Fentanyl	No oral preparation Transdermal (TTS) 15 mcg/h	0.1 mg	48-72 hours TTS; 1-2 hours parenteral

*Methadone is not a first line agent; consult the Anesthesia Pain Service for assistance.

Steps in Equianalgesia Conversion

- Add up the total amount of the **current** drug given in 24 hours (X). Remember to add in both scheduled and PRN doses. Keep the total of IV and oral doses separate.
- Plug numbers into the following equation:

$$\frac{\text{Equivalent dose of Opioid A (from Table)}}{\text{Equivalent dose of Opioid B (from Table)}} = \frac{\text{X mg of Opioid A (from step 1)}}{\text{Solve for Y mg of Opioid B}}$$

- Solve for **Y** by cross multiplying:

- $(X \text{ mg of Opioid A}) \times (\text{Equivalent dose of Opioid B}) = (\mathbf{Y \text{ mg}} \text{ of Opioid B}) \times (\text{Equivalent dose of Opioid A})$
- $\frac{(X \text{ mg of Opioid A}) \times (\text{Equivalent dose of Opioid B})}{\text{Equivalent dose of Opioid A}} = \mathbf{Y \text{ mg}} \text{ of Opioid B}$
- **Y mg** of Opioid B is the 24 hour total dose

- Find the duration of action (the dosing interval) of the **new** drug in the Equianalgesia table. Divide **Y mg** by the number of doses the patient will take each day. This gives the amount for each scheduled dose of the new opioid. Take into account the dose strengths available (i.e. do not order fractions of a capsule or sustained-release tablets). Round to the nearest strength, erring on the side of caution, as appropriate.

Note: This process is the same for converting from oral to parenteral doses (or vice versa). The doses to be placed in the equation will be the *oral* equivalent dose and the *parenteral* equivalent dose. See Table.

Medications NOT Recommended for Pain Management

Meperidine (Demerol)

Normeperidine is a non-opioid metabolite of meperidine and is renally excreted. The half-life is 12 to 18 hours and is longer in neonates and elderly. Accumulation may cause CNS excitation and seizures. Naloxone will NOT reverse this CNS excitotoxicity. Concomitant use of MAOI inhibitors is contraindicated as it may result in a hypermetabolic lethal reaction.

Limit use to:

1. Prevention and treatment of drug-induced or blood product-induced rigors and treatment of post-anesthesia shivering. Recommended dose 12.5 to 25 mg via slow IV push.
2. True allergy to all other opioids (eg. fentanyl, hydromorphone, morphine, codeine).
3. **All IV Meperidine PCA's must be approved by the Anesthesia Pain Service (APS) Call 6-8777 #10580.**
4. Conscious sedation used prior to adult procedures requiring pre-procedure analgesia, where rapid onset and short duration may improve patient care. Meperidine 12.5 to 50mg IV may be given, preferably in increments, 5 to 10 minutes prior to procedures.
5. **Less than 600mg parenterally (IV/IM) per 24-hour period.**
6. **Maximum duration of 48 hours.**

Propoxyphene (Darvon, Darvocet)

Provides minimal analgesia. Analgesic efficacy is no greater than aspirin alone. It is 1/2 to 1/3 as potent as codeine. Norpropoxyphene metabolite has a half-life of 30 to 36 hours and is renally excreted. With repeated doses, it can result in pulmonary edema and cardiac toxicity.

Adjuvant Pain Medications

Adjuvant medications can be used in addition to opioids or may be used for neuropathic pain. If used in addition to opioids, the patient may require lower doses of opioid. They should *not* be used as a sole medication for pain management if vas is over 3.

Neuropathic Pain Medications

1. Many antiepileptic drugs have been shown to be effective in treating neuropathic pain.
 - Gabapentin (Neurontin) and pregabalin (Lyrica; non-formulary) are renally excreted and patients should be monitored for adverse effects of accumulation. Agents cause drowsiness and should be initiated at night.
2. Antidepressants that belong to the *tricyclic* (TCAs) or *serotonin-norepinephrine reuptake inhibitor* (SNRIs) antidepressant classes can be used for neuropathic pain. Agents cause drowsiness and should be initiated at night.
 - Amitriptyline and nortriptyline (TCAs) should not be avoided in patients with cardiac conduction or structural abnormalities, seizure disorder, or history of tardive dyskinesia. Use with caution in the elderly due to anticholinergic properties. The preferred TCA for elderly patients is nortriptyline.
 - Duloxetine (Cymbalta; non-formulary) is an SNRI that may be used in outpatients.
3. Clonazepam (a benzodiazepine) has a long half-life. Start at bedtime due to sedation effects.

Others

1. Calcitonin (Miacalcin) or bisphosphonates can be used for pain due to fractures or osteoporosis.
2. Topical agents can be used for localized neuropathic pain. They should be applied to intact skin.
 - Lidocaine 5% (Lidoderm) patches should be worn no more than 12 hours in a 24 hour period.
3. Muscle relaxants or antispasmodics can be used if pain is of musculoskeletal origin.

Non-Pharmacologic Options

1. Non-pharmacologic options for pain management should be considered for all patients. They include
 - Repositioning
 - Diversional activity
 - Physical Therapy evaluation for TENS units (call ext 65300)
2. To request a Behavioral Medicine Evaluation/Consult for non-pharmacologic approaches, the MD must request by calling 327-2133. These include
 - **Relaxation Techniques:** progressive muscle relaxation, imagery, meditation, breathing techniques, clinical hypnosis to reduce muscle tension levels & stress reactivity
 - **Cognitive Behavioral Techniques:** to modify non-productive thought and behavior patterns that affect a patient's pain behavior and coping processes.

Side Effect Management

Side effect management must be considered proactively when prescribing opioids. Side effects include constipation, anxiety, confusion, respiratory suppression, nausea, vomiting, and pruritus. A tolerance will develop to most side effects, except constipation.

Constipation

Initiate a bowel regimen in all patients except in cases of bowel surgery. Rectal exams and suppositories are contraindicated in patients with neutropenia.

1. Begin all patients on stool softener (docusate, Colace®) and/or a stimulant laxative (senna, Senokot® S).
2. If no bowel movement (BM) in any 48-hour period, do one of the following:
 - Increase dose or add stimulant laxative
 - Add milk of magnesia or bisacodyl.
3. If no BM by 72 hours, perform rectal examination to rule out impaction.
4. If none of the above measures produce a BM, consider other treatments for constipation, such as lactulose or polyethylene glycol (Miralax).
5. If pain well controlled, consider decreasing opioid dose by 10-15%.

Anxiety

Sedation is not a replacement for analgesia. Titrate opioids before prescribing anything for anxiety. Avoid use of anxiolytics in patients with altered mental status.

Nausea & vomiting

Prochlorperazine (Compazine) is the preferred drug and can be given orally or by rectal suppository. Oral prochlorperazine can be used for nausea if the patient is not vomiting. Alternative therapies include promethazine (Phenergan), ondansetron (Zofran), naloxone, metoclopramide (Reglan), and corticosteroids. Suppositories are contraindicated in patients with neutropenia. Use metoclopramide with extreme caution in elderly patients due to the potential for extrapyramidal symptoms. If patient is responsive to intermittent naloxone, consider a naloxone infusion, titrated to treat the side effect without reversing analgesia.

Pruritus

Consider pruritus to be severe when the patient cannot eat, fall asleep, or concentrate on any activity because of itching. If severe, consider switching to another opioid. If unresolved after 3 doses of naloxone, call Anesthesia Pain Service.

Excessive sedation & opioid overdose

Naloxone may be given in bolus doses or a continuous infusion to reverse the effects opioids. Use caution when giving naloxone to patients with chronic pain or who are opioid dependent. Opioid withdrawal may be more common and severe in these patients. Naloxone may be given in bolus doses or as a continuous infusion. For reversal of long-acting opioids, repeat boluses or an infusion may be required.

Discharge Instructions

1. Continue use of effective analgesic for two weeks following surgery.
2. Instruct the patient to decrease dose by 10% per day if pain VAS decreases and analgesia is satisfactory.
3. Acetaminophen for long term use includes the following maximum doses:
 - 3.2 g/day
 - 2.4 g/day for elderly, liver dysfunction, and malnourished patients

Consultation with the Anesthesia Pain Service

Pager 68777 #10580

1. Pain management is the responsibility of each hospital service, including PCA management.
2. Suggested guidelines for referral to the Anesthesia Pain Service include:
 - Perioperative Epidural Analgesia
 - If the patient's VAS is greater than 8 and unrelieved after 3 titrations of the analgesic regimen
 - Management of opioid tolerant patients when standard pain medications are inadequate

This guideline should be used in conjunction with information from the medical literature to make decisions about the best approach to pain relief for individual patients.

References:

American Pain Society: Principles of Analgesic Use in the Treatment of Acute Pain and Cancer Pain, 5th Ed. Glenview, IL, American Pain Society, 2003.

McCaffery M, Pasero C: Pain: Clinical Manual, ed 2. St. Louis, Mosby, Inc., 1999.

Meperidine References:

Latta, KS, Ginsberg, B., Barkin, RL: Meperidine: A critical review. American Journal of Therapeutics 9 (1): 53-68, Jan-Feb 2002.

Austrup ML, Korean G: Analgesic agents for the postoperative period; Opioids. Surgical Clinics of North America 79(2): 253-273, 1999.

Kaiko, RF, Foley Km, Grabinski PY, et al: Central nervous system excitatory effects of Meperidine in cancer patients. Annals of Neurology 13(2): 180-185, 1983.

Propoxyphene References:

Reisine T, Pasternak G: Opioid Analgesics and Antagonists. In Hardman, JG, Limbird, LM, editors: Goodman & Gillman's the Pharmacologic Basis of Therapeutics, ed 9, pgs 521-555. NY 1996, McGraw-Hill.

Barkin, RL, Lubenow, TR, Bruehl S et al: Management of Chronic Pain, Disease-A-Month 42 (7): 389-454. 1996.

Acetaminophen References:

Ostapowicz G, Lee WM. Acute hepatic failure: a Western perspective. Journal of Gastroenterology Hepatology 15(5): 480-8, May 2000.

Moore A, Collins, S, Carroll D, McQuay H. Paracetamol with and without codeine in acute pain: a systematic review. Pain 70 (2-3): 193-201, April 1997.

Csete M, Sullivan JB. Vicodin induced fulminant hepatic failure. Anesthesiology 79(4): 857-60, 1993.

Analgesic dosing:

American Geriatrics Society Clinical Practice Guidelines: The Management of Chronic Pain in Older Persons. J Amer Geriatr Soc, 1998, 46:635-651.

American Hospital Formulary Service. McVoy, Gerald, ed. *Drug Information*. Bethesda, MD, American Society of Health-System Pharmacists, Inc, 2002.

Burnham, Teri Hines, ed. *Drug facts and comparisons*. St. Louis, Wolters Kluwer Co, 2002.

Davies, G, Kingswood C, Street M. Pharmacokinetics of opioids in renal dysfunction. Clin Pharmacokinet. 1996; 31:410-22.

Jacox AK, Carr DB, Payne R, et al. *Management of Cancer Pain. Clinical Practice Guideline, No. 9*. Rockville, Md: Agency for Health Care Policy and Research; 1994. AHCPR publication 94-0592.

Teketomo, Carol K, Hodding, Jane H., Krause, Donna M. *Pediatric Dosage Handbook, 8th Ed*. Cleveland, Lexi-Comp, Inc, 2001.

Equianalgesia Conversion Factors:

American Pain Society: Principles of Analgesic Use in the Treatment of Acute Pain and Cancer Pain, 4th ed. Skokie, Illinois, American Pain Society, 1999.

Anderson, R, Saiers, J, Abram, S, et al. Accuracy in Equianalgesia dosing: conversion dilemmas. J Pain Symptom Manage 2001; 21:397-406

Stevenson, K., Gordon, D., & Ford Roberts, K. Wisconsin Cancer Pain Initiative, 1996.

General Principles/ SE Management:

Friedman, JD, Buono, FA. Opioid antagonists in the treatment of opioid-induced constipation and pruritis. AnnPharmacother 2001; 35:85-91

Foley, K. The treatment of cancer pain. N Engl J Med 1995. 313, 84-95.

Grossman, SR, Benedetti C, Brock C, et al. NCCN practice guidelines for cancer pain. Oncology. 2000; 14: 135-150.

Liu, M, Wittbrodt E. Low-dose oral naloxone reverses opioid-induced constipation and analgesia. J Pain Symptom Manage 2002; 23:48-53.

Meissner W, Schmidt U, Hartman M, et al. Oral naloxone reverses opioid-associated constipation. Pain. 2000; 84: 105-109.

National Cancer Institute pain management website: http://www.cancer.gov/cancer_information/doc_pdq.aspx?version=provider&viewid=66d23623-3e9c-4bcf-8c09-902c2afe0f06

Portenoy, RK. Cancer pain management. Semin Oncol. 1993;2 (suppl 1) ;19-35.

Sykes, NP. An investigation of the ability of oral naloxone to correct opioid-related constipation in patients with advanced cancer. Palliat Med 1996; 10:135-144.

(Authoring Department: _____ Last revision date: _____)

LUHS Formulary Pain Medications

NON-OPIOID ANALGESICS AVAILABLE AT LUMC-MILD PAIN (VAS 1-3)			
	DOSAGE FORMS	USUAL DOSE	COMMENTS
ACETAMINOPHEN	SOLN: 160mg/5ml TAB: 325,650mg SUPP: 80,120, 650mg	ADULTS: 650mg q 4-6 h GERIATRICS: 325-650mg q 4 h PEDS: 10-15mg/kg PO q 4-6 h 10-20mg/kg PR q 4-6 h	MAX daily adult doses: <10 days: 4000mg chronic use: 3200mg alcoholic, malnourished: 2400mg MAX peds dose: 75mg/kg/day PO (100mg/kg/day PR)
ASPIRIN	CHEW TAB: 81mg TAB: 325 SUPP: 300,600mg TAB: 100, 200 mg	ADULTS: 650mg q 4 h GERIATRICS: 325-650mg q 4 h PEDS: 10-15mg/kg q 4-6 h	MAX adult dose: 4000mg/day
CELECOXIB	TAB: 100, 200 mg	ADULTS: 400mg x1; 100-200mg q 12 h GERIATRICS: same as adult PEDS: 50-100 mg q 12 h	MAX adult dose: chronic use 400mg/day ↓dose in hepatic impairment Not usually used in peds
DICLOFENAC <i>(Voltaren®)</i>	TAB: 25, 50 mg	ADULTS: 25-75mg q 12 h GERIATRICS: 25mg q 8 h PEDS: (0.5-0.75mg/kg q 6-8 h)	MAX adult dose=225mg/day (extended release=once daily tabs not on formulary) Not usually used in peds
IBUPROFEN	SOLN: 100 mg/5ml TAB: 200, 400, 600, 800mg	ADULTS: 400-800mg q 6-8 h GERIATRICS: 200-600mg q 6-8 h PEDS: 4-10mg/kg q 6-8 h	MAX adult dose: 3200mg/day [2400mg/day geriatrics] MAX peds dose: 50mg/kg/day
INDOMETHACIN	SUSP: 25 mg/5ml CAP: 25, 50 mg	ADULTS: 25-50 mg q 8-12 h GERIATRICS: 25mg q 8-12 h PEDS: (0.5mg/kg q6-12 h)	MAX adult dose = 200mg/day ↓ dose for renal dysfunction Not usually used in peds
KETOROLAC (IM/IV) (Toradol®)	INJ: 30 mg	ADULTS: 60mg x1; 30mg q 6 h GERIATRICS: 30mg x1; 15mg q 6 h PEDS: 0.5 mg/kg q 6 h	MAX adult dose 150mg day 1, then 120mg/day MAXIMUM 5 DAYS Avoid if renal failure/bleeding MAX peds dose: 30mg (IM), 15mg (IV)
KETOROLAC (PO) <i>(Toradol®)</i>	TAB : 10 mg	ADULTS: 20mg x1; 10mg q 6 h GERIATRICS: 20mg x1; 10mg q 6 h PEDS: Not established	MAX adult dose= 40mg/day MAXIMUM 5 DAYS
NAPROXEN	TAB: 250 mg	ADULTS: 500mg x1; 250mg q 6-8 h or 500mg q 12 h GERIATRICS: 250mg q 8-12 h PEDS: 5-7mg/kg q 8-12 h	MAX adult dose 1250-1500mg/day [MAX 1000mg/day geriatrics] MAX peds : 20mg/kg/day

*All Adult doses are for patients <65y/o, > 50kg

- Risk factors for acute kidney injury with NSAIDs in patients with pre-existing renal disease: age ≥65, hypertension or chronic heart failure, and concomitant use of diuretics and angiotensin-converting enzyme inhibitors.
- NSAIDs may interact with other highly protein-bound drugs like warfarin, methotrexate, digoxin, cyclosporine, oral antidiabetic agents, and sulfa drugs. Such interactions may enhance therapeutic or toxic effects of either drug.
- The American Geriatric Society (AGS) Clinical Practice guidelines [JAG 46:635-65,1998] recommends APAP for chronic use in geriatric patients. When NSAIDs are used chronically in the elderly, they should be used PRN, rather than ATC.
- NSAIDs & non-enteric coated ASA products should be taken with food to reduce GI irritation.

**OPIOID, COMBINATION OPIOID & NSAID PRODUCTS AVAILABLE AT LUMC-MILD/MODERATE PAIN
(VAS 4-7)**

	DOSAGE FORMS	USUAL DOSE	COMMENTS
CODEINE	INJ: 30, 60 mg TAB: 15, 30, 60mg	ADULTS: 15-60 mg PO q 4-6 h GERIATRICS: 15-60 mg PO q 4-6 h PEDS: 0.5-1 mg/kg PO q 4-6 h (IM/SQ approx ½ doses)	MAX adult dose: 1.5 mg/kg 7% of Caucasians have CYP 2D6 deficiency resulting in diminished analgesia ↓ dose renal dysfunction
CODEINE + ACETAMINOPHEN (<i>Tylenol® # 3</i>)	ELIX: 12 mg +120 mg APAP / 5 ml TAB: 30 mg +300 mg APAP	ADULTS: 15-60mg q 4-6 h GERIATRICS: 15-60mg q 4-6 h PEDS: 0.5-1 mg/kg q 6-8 h (doses based on codeine content)	MAX adult dose: 165ml or 13 tabs/day 7% of Caucasians have CYP2D6 deficiency resulting in diminished analgesia ↓ dose renal & hepatic dysfunction
HYDROCODONE + ACETAMINOPHEN (<i>Norco®, Lortab®, Vicodin®</i>)	ELIX: 7.5 mg + 500mg APAP/15 ml TAB: 5/325, 7.5/325, 10/325 TAB: 5/500, 7.5/500, 10/500 TAB: 7.5/750	ADULTS: 5-10 mg q 4 h GERIATRICS: 2.5-10 mg q 4 h PEDS: 0.15mg/kg q 4 h (doses based on hydrocodone content)	MAX adult dose: 120ml or 8 tabs/day Pts with CYP2D6 deficiency have possible diminished analgesia ↓ dose renal & hepatic dysfunction
OXYCODONE + ACETAMINOPHEN (<i>Percocet®</i>)	TAB: 5 mg + 325 mg APAP	ADULTS: 5-10 mg q 4 h GERIATRICS: 5-10 mg q 4-6 h PEDS: 0.05-0.15mg/kg/d q 4-6 h (doses based on oxycodone content)	MAX adult dose: #12 tabs / day ↓ dose renal/hepatic dysfunction Pts with CYP2D6 deficiency have possible diminished analgesia
OXYCODONE + ASPIRIN (<i>Percodan®</i>)	TAB: 5 mg + 325 ASA	ADULTS: 5-10 mg q 4 h GERIATRICS: 5 mg q 4-6 h PEDS: 0.05-0.15mg/kg/d q 4-6 h (doses based on oxycodone content)	MAX adult dose: #12 tabs / day ↓ dose renal dysfunction Pts with CYP2D6 deficiency have possible diminished analgesia
PROPOXYPHENE HCl (<i>Darvon®</i>)	CAP: 65 mg	ADULTS: 65mg q 4 h prn GERIATRICS: Not recommended PEDS: Not recommended	MAX adult dose: 8 caps / day Analgesic potency is similar to that of APAP ↓ dose renal & hepatic dysfunction
PROPOXYPHENE NAPSYLATE W/APAP (<i>Darvocet® N 50 & 100</i>)	TAB: (N 50): 50 mg +325 mg APAP TAB: (N 100): 100 mg +650mg APAP	ADULTS: 100mg q 4 h prn GERIATRICS: Not recommended PEDS: Not recommended	MAX adult dose: 6 tabs N-100 / 12 tabs N-50 /day 100mg propoxyphene napsylate = 65mg propoxyphene ↓ dose renal & hepatic dysfunction
TRAMADOL (<i>Ultram®</i>)	TAB : 50mg ORAL SOLN (PEDS): 5mg/ml	ADULTS: 50-100mg q 4-6 h GERIATRICS: 50-100mg q 6-8 h PEDS: Not established	Do not use or use cautiously with TCAs, SSRIs, or MAOI inhibitors MAX adult dose: 400mg/day (300mg geriatrics)
<ul style="list-style-type: none"> • ALL DOSES OF COMBINATION PRODUCTS LIMITED BY APAP OR ASA CONTENT TO 4GM/DAY (ADULTS) OR 75MG/KG (PEDS) • Take pain medications with food to decrease the incidence of nausea • Propoxyphene may increase serum levels of warfarin, some anticonvulsants, & TCAs • Plain codeine tablets not readily available in community pharmacies 			

SHORT ACTING OPIOIDS AVAILABLE AT LUMC- MODERATE/SEVERE PAIN (VAS 8-10)

SHORT ACTING OPIOID	DOSAGE FORMS	OPIOID NAÏVE STARTING DOSES (Titrate to effective analgesic dose with least side effects)	CAUTIONS
MORPHINE <i>(Roxanol[®], MSIR[®])</i>	ORAL SOLN: 4, 20 mg/ml TABLET: 15, 30 mg SUPPOSITORY: 10 mg INJ: 1,2,4,8,10,15 mg/ml PCA: 1, 5 mg/ml 30 ml	ADULTS: 10-30mg PO/PR q 3-4 h 2-10mg IV/IM/SQ q 3-4 h GERIATRICS: 10-30mg PO/PR q 4-6 h 2-10mg IV/IM/SQ q 4-6 h PEDS: 0.2-0.5mg/kg PO/PR q 3-4 h 0.05-0.1mg/kg IV/IM/SQ q 3-4 h	↓ dose in renal dysfunction
FENTANYL IV/Subcut <i>(Sublimaze[®])</i>	INJ: 50 mcg/ml (2, 5ml) PCA: 50 mcg/ml 30 ml	ADULTS: 0.25-1mcg/kg IV/SQ q 10min GERIATRICS: 0.25-1mcg/kg IV/SQ q 10min PEDS: 0.25-1mcg/kg IV/SQ q 10min	
HYDROMORPHONE <i>(Dilaudid[®])</i>	TABLETS : 2, 4 mg SUPPOSITORY: 3 mg INJ: 2,4,10 mg PCA: 0.2mg/ml 20ml, 1mg/ml 30ml	ADULTS: 1-4mg PO/PR q 2-3 h 0.5-2mg IV/IM/SQ q 2-3 h GERIATRICS: 1-4mg PO/PR q 4-6 h 0.5-1mg IV/IM/SQ q 4-6 h PEDS: 0.03-0.08mg/kg PO/PR q 4-6 h 0.015-0.03mg/kg IV/IM/SQ q 4-6 h	With prolonged use, the equianalgesic potency of IV hydromorphone to IV morphine may decrease from 7:1 to 3:1.
OXYCODONE <i>(Roxicodone[®])</i>	ORAL SOLN: 1 mg/ml TABLET: 5 mg	ADULTS: 5-20mg PO q 3-4 h GERIATRICS: 2.5-5mg PO q 3-4 h PEDS: 0.05-0.2mg/kg PO q 3-4 h	
MEPERIDINE <i>(Demerol[®])</i>	TABLET: 50 mg INJ: 25,50, 75, 100 mg/ml ORAL SOLN: 50 mg/5ml	Only recommended use is for rigors, post operative shivering and true opioid allergy. IV PCA must be approved by Anesthesia Pain Service (68777, #10580)	Avoid in renal dysfunction or history of seizures. ↓ dose in hepatic dysfunction Max dosing: 48hrs or less → 600mg/24h

LONG ACTING OPIOIDS AVAILABLE AT LUMC-MODERATE/SEVERE PAIN (VAS 8-10)

	LONG ACTING OPIOID	DOSAGE FORMS	DOSING INTERVAL	TIME TO ONSET [PEAK] (HR)	CAUTIONS
Sustained release products	MORPHINE CR (<i>MS Contin®</i> <i>Oramorph® SR</i>)	TABS: 15, 30, 60 mg	8-12 h	1 [2-3]	↓ dose in renal dysfunction SR products not interchangeable
	OXYCODONE CR (<i>Oxycontin®</i>)	TABLETS: 10, 20mg	12 h	1 [2-3]	
Other long acting products	FENTANYL (<i>Duragesic®</i>)	PATCHES: 12, 25,50,75,100 mcg/hr	72 hr	12 [24-48]	To determine dose, divide the total daily morphine (or equivalent) dose by 2-4. Example: total morphine 50 mg/day = ~25 mcg fentanyl patch Continue short acting opioid for 12-24 hrs after application of patch because of slow onset of analgesia. When discontinuing patch, remove patch & begin new opioid 12 hrs later.
	METHADONE (<i>Dolophine®</i>)	TABLET: 5, 10mg ORAL SOLN: 1mg/ml	4-8 h	1 [4]	Unpredictable t 1/2 and duration of action because of accumulation with continued use. When converting to methadone, titrate slowly by adding 1/3 of methadone dose and removing 1/3 of old opioid dose q 3-7 days.

- Methadone not readily available at most retail pharmacies. Prescriptions must read “for pain”.
- THE EQUIANALGESIC DOSE RATIO OF MORPHINE TO METHADONE HAS BEEN A MATTER OF CONFUSION AND CONTROVERSY. The equianalgesic ratio of methadone and morphine correlates with total morphine dose administered before switching to methadone. Among patients receiving low doses of morphine (30 to 300 mg oral morphine), the equianalgesic ratio for oral morphine to methadone is 4:1 to 6:1 and at high doses (more than 300 mg oral morphine), 10:1 TO 12:1. [J Pain Symptom Manage 2001; 21:397-406 + JCO 1999;17:3307-3312; Cancer 1998;82: 1167-1173]

MANAGEMENT OF OPIOID-ASSOCIATED ADVERSE EFFECTS

SIDE EFFECT	MANAGEMENT	DOSING OF RECOMMENDED AGENTS		COMMENTS/ALTERNATIVE TREATMENTS
CONSTIPATION	<p>PROPHYLACTIC STIMULANT LAXATIVE + STOOL SOFTENER SHOULD BE USED IF OPIOID USE IS CHRONIC</p> <p>Stool softener alone may be adequate for limited opioid use</p> <p>If possible increase PO fluids, dietary fiber, & exercise</p>	ADULTS	PEDIATRICS	<p>Avoid bulk laxatives</p> <p>If no BM in 48°, increase dose of Senokot S or add MOM or Bisacodyl</p> <p>IF no BM in 72°, r/o impaction</p> <p>Oral naloxone (2-20mg) to reverse opioid-induced constipation effective in a few small studies</p>
		<p>Docusate 100-200mg daily or BID (range 50-500mg in 1-4 divided doses)</p> <p>Senokot S 2 tabs daily (max 4 tabs BID) Senokot+docusate</p> <p>Bisacodyl 10mg daily (range 10-15mg)</p> <p>Milk of Magnesia 30ml daily (range 30-60ml)</p>	<p>Docusate 10-150mg in 1-4 divided doses</p> <p>Senokot S Senakot (syrup) doses: 1-5 yrs: 2.5-5ml daily 5-15 yrs: 5-10ml daily</p> <p>Bisacodyl 5-10mg PO or 0.3mg/kg/dose qday PR: age <2: 5mg qday</p> <p>Milk of Magnesia 1-2ml/kg/dose BID (up to adult dose)</p>	
NAUSEA/ VOMITING	<p>PRN antiemetics recommended</p> <p>Tolerance usually develops in 1-3 days</p>	ADULTS	PEDIATRICS	<p>Ondansetron is expensive but is less sedating than other antiemetics</p> <p>If ondansetron is ineffective for a Peds patient ADD promethazine</p>
		<p>Prochlorperazine (1st choice) 5mg PO/ 25mg rectal q 6 h prn</p> <p>Promethazine 12.5-25mg IV/PO q 4 h prn</p> <p>Metoclopramide 10-20mg IV/PO q 6 h prn</p> <p>Ondansetron 4mg IV/PO 6h prn</p>	<p>Ondansetron (1st choice) 0.05-0.1mg/kg (up to 4mg) IV/PO q 6h prn</p> <p>Promethazine (alternate) 0.25-0.5mg/kg IV/PO q 4-6 h prn</p>	
PRURITUS	<p>Tolerance usually develops</p>	ADULTS	PEDIATRICS	<p>If persistent, try equianalgesic dose of a “more potent” opioid</p>
		<p>Diphenhydramine (1st choice) 25mg PO/IV q 6h prn</p> <p>Hydroxyzine 25mg PO /IM q 6h prn</p>	<p>Diphenhydramine (1st choice) 2-<6: 6.25mg q 4-6 h prn 6-12: 12.5mg q 4-6 h prn</p> <p>Hydroxyzine 0.5mg/kg PO/IM q 6-8 h prn</p>	

SEDATION	<p>Tolerance usually develops</p> <p>Initiate lower doses for elderly</p> <p>If sedation is dose limiting, consider CNS stimulant</p>	<p>If sedation persists after 1 week consider adding (adults): Caffeine 100-200 mg PO q 6h -OR- Methylphenidate 5-10 mg q am & noon</p> <p>In extreme cases: use low dose IV naloxone</p>	<p>Eliminate other sedating medications if possible</p> <p>If pain is under control, consider lowering the dosage</p> <p>Consider adjuvant medication to allow opioid dose reduction</p>
RESPIRATORY DEPRESSION	<p>Tolerance develops rapidly</p> <p>If life-threatening respiratory depression occurs, use low doses of naloxone</p>	<p>Naloxone: ADULTS: 0.1mg IV (IM if no IV access) q 5min x 3 prn OR 0.2mg IV q 15min x 3 doses prn. PEDS < 20kg: 0.1mg/kg q 2-3 minutes prn ≥ 20kg: 2mg/dose q 2-3 minutes prn</p>	<p>Titrate naloxone to reverse respiratory depression/excessive sedation; however, be aware of rapid reversal of analgesia.</p>
<p>Senokot S[®] tablets = 8.6mg sennosides + 50mg docusate per tablet Senokot Children's Syrup[®] = 8.8mg sennosides per 5ml [=218mg std senna concentrate per 5ml]</p>			