HOUSTON Methodist LEADING MEDICINE

Guide to Safe Pain Management

2022 Edition

To be used as a guide only. Healthcare professionals should use the most current evidence and clinical judgment to individualize therapy for each patient.

Contact the Drug Information Center at 713-441-4190 if you require further assistance.

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DEFINITIONS

- **Pain:** An unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage
  - Pain is always a personal experience that is influenced to varying degrees by biological, psychological, and social factors
  - Pain and nociception are different phenomena. Pain cannot be inferred solely from activity in sensory neurons
  - Through their life experiences, individuals learn the concept of pain
  - A person's report of an experience as pain should be respected
  - Although pain usually serves an adaptive role, it may have adverse effects on function and social and psychological well-being
  - Verbal description is only one of several behaviors to express pain; inability to communicate does not negate the possibility that a human or nonhuman animal experiences pain
- **Nociceptive pain:** Pain associated with tissue damage, potential damage, or inflammation; normal response to noxious stimuli
- **Neuropathic pain:** Pain caused by a lesion or damage of the somatosensory nervous system; develops from damage to the nervous system or progression of a disease state (e.g. diabetic peripheral neuropathy, chemotherapy-related neuropathy, etc.)
- **Acute pain:** Sudden, short duration pain typically associated with a specific trigger (e.g. injury, trauma, surgery)
- **Chronic pain:** Pain persisting for ≥ 3-6 months or beyond the expected time of normal tissue healing; may or may not be associated with an identifiable cause
- **Breakthrough pain**: Sudden increase in pain that may occur in patients who are taking a stable regimen of around-the-clock analgesics for baseline pain; also known as a "pain flare"
- **Spasticity:** Caused by upper motor neuron syndromes. Conditions such as multiple sclerosis, spinal cord injury, traumatic brain injury, cerebral palsy, and post-stroke syndrome
- **Spasms**: Caused by peripheral musculoskeletal conditions (involves local muscle groups) resulting in tenderness and muscle pain. Common conditions include fibromyalgia, tension headaches, myofascial pain syndrome, and mechanical low back or neck pain.
- **Morphine milligram equivalents (MME):** Value assigned to opioids representing their relative potencies compared to oral morphine
- **Opioid naïve:** Patients who are not chronically receiving opioid analgesics on a regular basis
- **Opioid tolerant:** Chronic opioid use defined as the use of the following agents or an equianalgesic dose of any other opioid <u>for AT LEAST one week</u>:
  - Oral morphine 60 mg/day
  - Oral oxycodone 30 mg/day
  - Fentanyl patch 25 mcg/hr
  - Oral hydromorphone 8 mg/day
  - Oral oxymorphone 25 mg/day
  - An equivalent dose of any other opioid
- **Opioid tolerance:** Decreased susceptibility to the effects of opioids – both therapeutic and adverse – that may develop in individuals with prolonged use of opioids
- **Opioid dependence:** Physical depends on opioids associated with chronic use; withdrawal symptoms may develop in response to sudden discontinuation of an opioid after continued use

- **Opioid misuse:** Use of an opioid outside of the directed or prescribed indication, regardless of the presence of absence of harm or adverse effects
- **Opioid abuse:** Intentional use of an opioid for a nonmedical purpose, such as euphoria or altering one's state of consciousness
- **Opioid use disorder:** Problematic pattern of opioid use associated with impaired control over drug use, compulsive use, or continued use despite harm
- **Opioid withdrawal**: May occur with abrupt discontinuation of opioids in opioid-dependent patients. Symptoms include nausea, vomiting, diarrhea, anxiety, sweating, rhinorrhea, piloerection and tremors. For patients on long-term/chronic opioid therapy, a gradual taper is recommended to minimize withdrawal.
- **Opioid overdose:** Symptoms may include respiratory depression, constricted pupils, and decreased responsiveness. Naloxone is used to reverse the effects of an opioid.

GENERAL PAIN MANAGEMENT PRINCIPLES

1. Identify relevant co-morbidities that may increase the risk of respiratory depression with opioids

- Co-administration of sedating drugs
- Major organ dysfunction
- Rapid increases opioid dose requirement
- Immediate post-operative period (first 24 hours of opioid therapy)
- Prolonged surgery
- Surgical incisions that impair breathing
- Opioid naïve
- Pre-existing pulmonary disease
- Cardiac disease
- Sleep apnea/sleep disorder
- Obesity
- Smoking
- Snoring
- Younger/older age

2. Identify previous opioid exposure (opioid tolerance)

- **Patients considered opioid-tolerant are those receiving one or more of the following for <u>one week or longer</u>**
  - At least 60 mg oral morphine/day
  - 25 mcg transdermal fentanyl/hour
  - 30 mg oral oxycodone/day
  - 8 mg oral hydromorphone/day
  - 25 mg oral oxymorphone/day
  - An equivalent dose of another opioid

3. Select initial medication therapy and loading doses based on overall pain assessment and prior opioid treatment history

- **Initial Therapy in Opioid Naïve Patients**
  1. First start with scheduled doses of non-opioid analgesics, if not contraindicated
  2. Add an as needed doses of weak or short-acting opioid
  3. Increase as needed doses of opioid by 30-50% if pain persists

- **Initial Therapy in Opioid Tolerant Patients**
  1. Consider scheduled doses of non-opioid analgesics, if not contraindicated
  2. *IMPORTANT* Verify outpatient opioid regimen via patient interview and Prescription Drug Monitoring Program (PDMP) database
  3. Continue baseline outpatient opioid regimen or if pain uncontrolled, increase baseline regimen by 30-50%
  4. For breakthrough pain, add short-acting opioid. Determine dose by calculating 10-15% of 24-hour opioid requirements with frequency of every 3-6 hours depending on the expected duration of action of chosen agent.

4. Additional considerations

- Use the lowest effective dose for the shortest duration possible
- Immediate-release agents recommended over long-acting/extended-release formulations for the treatment of acute pain
- Use the oral route of administration whenever possible and reserve intravenous opioids for certain patient populations (NPO, decreased GI absorption, immediate pain control needed)
- If not contraindicated, make sure appropriate bowel regimen is ordered to prevent opioid-induced constipation
- Consider dose reductions/adjustments and additional monitoring in the following situations:
  - **Adjust for renal/hepatic dysfunction:** Start with lower doses and/or less frequent dosing intervals and titrate slowly as needed
  - **Adjust dose for age:** Start with lower doses and/or less frequent dosing intervals and titrate slowly as needed
  - **Adjust for incomplete cross-tolerance:** When converting from one opioid agent to another reduce the total daily dose of the new opioid by <u>20-50%</u>

PAIN TREATMENT ALGORITHM

Step 1. Identify the INTENSITY of pain

Wong-Baker FACES® Rating Scale

Numerical Rating Scale

Mild Pain	Pain Score 1 – 3
Moderate Pain	Pain Score 4 – 6
Severe Pain	Pain Score 7 – 10

Critical Care Pain Observation Tool (CPOT)

Indicator		Description	Score	
Facial expressions		No muscle tension observed	Relaxed, neutral	0
		Presence of frowning, brow lowering, orbit tightening, and levator contraction or any other change (e.g. opening eyes or tearing during nociceptive procedures)	Tense	1
		All previous facial movements plus eyelid tightly closed (the patient may present with mouth open or biting the endotracheal tube)	Grimacing	2
Body movements		Does not move at all (doesn't necessarily mean absence of pain) or normal position (movements not aimed toward the pain site or not made for the purpose of protection)	Absence of movements or normal position	0
		Slow, cautious movements, touching or rubbing the pain site, seeking attention through movements	Protection	1
		Pulling tube, attempting to sit up, moving limbs/thrashing, not following commands, striking at staff, trying to climb out of bed	Restlessness/Agitation	2
Muscle tension Evaluation by passive flexion and extension of upper limbs when patient is at rest or evaluation when patient is being turned		No resistance to passive movements	Relaxed	0
		Resistance to passive movements	Tense, rigid	1
		Strong resistance to passive movements or incapacity to complete them	Very tense or rigid	2
Compliance with ventilator OR **Vocalization**	**Intubated Patients**	Alarms not activated, easy ventilation	Tolerating ventilator or movement	0
		Coughing, alarms may be activated but stop spontaneously	Coughing but tolerating	1
		Asynchrony: blocking ventilation, alarms frequently activated	Fighting ventilator	2
				OR
	Extubated Patients	Talking in normal tone or no sound		0
		Sighing, moaning		1
		Crying out, sobbing		2
0 = no pain; 8 = maximum pain			**TOTAL**	**0-8**

Step 2. Assess the level of CONSCIOUSNESS using the Pasero Opioid-Induced Sedation Scale (POSS)

Pasero Opioid-Induced Sedation Scale (POSS)	
State	**Dosing Guidance**
0 - Sleepy, easy to arouse	Acceptable; no action necessary; may increase opioid dose if needed.
1 - Awake and alert	Acceptable; no action necessary; may increase opioid dose if needed.
2 - Slightly drowsy, easily aroused	Acceptable; no action necessary; may increase opioid dose if needed.
3 - Frequently drowsy	Unacceptable; decrease opioid dose 25%-50%; monitor respiratory status and sedation level closely until level is < 3 and respiratory status is satisfactory. Consider administering a non-sedating, opioid-sparing non-opioid, such as acetaminophen or an NSAID, if not contraindicated.
4 - Somnolent; minimal or no response to physical stimuli	Unacceptable; stop opioid. Call the Physician and/or a CERT. Consider administering naloxone; monitor respiratory status and sedation level closely until sedation level is < 3 and respiratory status is satisfactory.

Step 3: Assess for response treatment

Response to treatment	Recommended course of action
Positive response: pain relieved and no adverse effects	Consider making dosing adjustments based on frequency of use
Negative response: No pain relief	1. Consider all treatment options available 2. Increase scheduled dose and/or breakthrough pain medication dose 3. Consider inpatient pain consultation
Negative response: Side Effect	Consider discontinuation for severe side effects vs modification for milder side effects

OPIOID DOSING IN ADULT PATIENTS

Drug	Standard Initial Dosing in Adults		Duration (Hr)	Time to Onset (Min)	Sedation/ Respiratory Depression	Hypotension Frequency	Hypotension Severity^
	Age <65 years	Age >65 years					
Codeine	PO: 30 - 60 mg q4 - 6h	PO: 30-60 mg q4-6h	6	30-60	+	PO: moderate	+
Fentanyl	IV: 25 - 50 mcg q1 - 2h Patch: 25 mcg**	IV: 12.5-50 mcg q1-2h Patch: 12-25 mcg*	IV: 2 Patch: 72	IV: 3-5 Patch: 12-24hrs	++	IV: infrequent (1-10%)*	+
Hydrocodone	PO: 5 -7.5 mg q4 - 6h	2.5 – 5 mg PO q4-6h	3-4	PO: 10-20	+	PO: infrequent (1-10%)	N/A
Hydromorphone	IV: 0.2 - 1 mg q2 - 3h PO: 2 - 4 mg q4 - 6h	0.2 – 0.5 mg q2-3h PO: 1 – 2 mg q4-6h	3-4	IV- less than 5 PO- 15-30	++	IV: < 2%	++
Morphine	IV: 2 - 4 mg q3 - 4h PO: 10 - 30 mg q4 - 6h	IV: 1 – 2 mg q3-4h PO: 5 – 10 mg q4-6h	IR: 3-4 ER: 8-12	IV: 3-5 IR: 15-60 SR: 40-60	+++	PO: infrequent (1-10%) IV, IM: moderate (>10%)	+++
Oxycodone	PO: 5 - 10 mg q4 - 6h	PO: 2.5 – 5 mg q4-6h	IR: 3-4 ER: 12	IR/SR: 10-15	++	PO: infrequent (1-10%)	N/A
Oxymorphone	PO: 5 - 10 mg q4 - 6h	PO: 5 mg q 4 – 6h	IR: 4-6 ER: 12	IR: 30 SR: 120	++	PO: moderate (<10%)	N/A
Tapentadol	PO: 25 - 50 mg q 4 - 6h (Max: 600 mg/day)	PO: 25 mg q6h	IR: 4-6 ER: 12	IR: 30 SR:	+	PO: rare (<1%)	N/A
Tramadol	PO: 25 - 50 mg q6h (Max: 400mg/day)	PO: 25 mg q6h (Max: 300mg/day in >75 yrs)	4 - 6	30-60	+	PO: rare (<1%)	N/A

IR- immediate release; ER- Extended release

In normal renal and hepatic function patients: + mild, ++ moderate, +++ severe, N/A: not applicable due to limited information

* Opioid induced hypotension is more common in hemodynamically unstable or hypovolemic patients and following rapid intravenous administration. Opioid doses should be reduced and administered slowly in these patients

** Only initiate on patients who are opioid tolerant and on a stable opioid regimen

^ Many opioids release histamine, which may produce flushing, tachycardia, hypotension, pruritus, and bronchospasm. Histamine release is greatest with morphine, codeine and meperidine, and lowest with fentanyl.

a - Multiply the dose for each opioid by the conversion factor to get the equivalent morphine dose (convert between same routes of administration when using the conversion factor)

b - Usual fentanyl dosing is based on mcg, but this table uses mg units for comparison of different agents. Please ensure appropriate unit conversion; **1 mg = 1000 mcg**

OPIOID DOSE ADJUSTMENTS IN RENAL AND HEPATIC DYSFUNCTION

Renal Impairment				Hepatic Impairment
GFR > 50 mL/min		GFR 10 – 50 mL/min	GFR < 10 mL/min, AKI or ESRD	
Codeine	No dose adjustments needed	Do Not Use	Do Not Use	Do Not Use
Morphine	No dose adjustments needed	Reduce original dose by 50%. Increase dosing interval.	Do Not Use. Active metabolite slowly dialyzable.	Increase dosing interval by 2 x the usual time period
Hydrocodone	No dose adjustments needed	Reduce original dose by 50%	Reduce original dose by 75%	Reduce original dose by 50% in severe impairment
Hydromorphone	No dose adjustments needed	Reduce original dose by 50%	Reduce original dose by 75%	Reduce original dose by 25-50% Consider increasing dosing interval in severe impairment
Oxycodone	No dose adjustments needed	Reduce original dose by 50%	Use with caution. Reduce dose and/or increase dosing interval	Reduce original dose by 50-75% and increase dosing interval
Fentanyl	No dose adjustments needed	Reduce original dose by 25%	Reduce original dose by 50%	Dosing adjustment usually not needed
Tramadol¥	No dose adjustments needed	Use q12h dosing interval (Max: IR 200mg/day) Avoid long-acting formulation	Use with caution. 7% of drug and active metabolite dialyzable	Cirrhosis: 50mg q12h Avoid ER formulation in severe impairment

¥ Avoid in patients with seizure disorders or head trauma. Caution in patients receiving multiple serotonergic agents.

OPIOID ANALGESIC EQUIVALENCIES

When switching from one opioid to another, decrease the dose of the new opioid regimen by 20-50% to adjust for incomplete cross-tolerance.

Drug	Parenteral (mg)	Oral (mg)	Conversion Factor (Parenteral Opioid to Oral Opioid)	Conversion Factor (Oral Opioid to Oral Morphine)
Morphine	10	30	3	1
Codeine	100	200	2	0.15
Hydrocodone	N/A	30	N/A	1
Hydromorphone	1.5	7.5	5	4
Oxycodone	N/A	20	N/A	1.5
Oxymorphone	1	10	10	3
Fentanyl	0.1	N/A	N/A	N/A

*Buprenorphine, tramadol, tapentadol, and methadone conversions not included due to additional CNS receptor effects apart from mu-opioid agonism
**Methadone and buprenorphine should only be initiated and managed by clinicians experienced in utilizing these agents

OPIOID ALLERGIES/INTOLERANCES AND CROSS-SENSITIVITY RISKS

Common adverse effects: constipation, dry mouth, sedation, confusion, respiratory depression
Common opioid intolerances (NOT considered a true allergy): nausea, vomiting, itching

Cross-Sensitivity Risk (Based on Opioid Chemical Class)				
PROBABLE	**POSSIBLE**	**LOW RISK**	**LOW RISK**	**LOW RISK**
Buprenorphine* Butorphanol* Codeine Dextromethorphan* Heroin (diacetyl-morphine) Hydrocodone* Hydromorphone* Levorphanol* Methylnaltrexone** Morphine Nalbuphine* Naloxone* Naloxegol* Naltrexone** Oxycodone* Oxymorphone*	Pentazocine	Alfentanyl Fentanyl Meperidine Remifentanil Sufentanil Diphenoxylate Loperamide	Methadone Propoxyphene	Tapentadol Tramadol

*Potential decrease in cross-tolerability due to structural differences to morphine

NON-OPIOID ANALGESICS FOR PAIN MANAGEMENT

Generic (Brand)	Dose Regimen	Onset of Action (min)	Peak Effect (hrs)	Duration of Action (hrs)	Dose Adjustments	Comments
Acetaminophen (Tylenol®)	325-650 mg PO/PR q4-6h 1000 mg IV q8h (restricted to 24 hr use) Do not exceed APAP 1g/dose or 4g/day	30 - 60	1	3 - 4	Reduce dose in renal or hepatic failure. Consider q8h dosing in patients with CrCl <10 ml/min Max 2 g/day in cirrhosis/severe hepatic impairment	Elderly patients and patients with liver disease or chronic alcohol use may not tolerate max 4 g/day, adjust total daily dose as needed Caution in use with other combination acetaminophen products, G6PD deficiency or chronic malnutrition.
Ibuprofen (Advil®,Motrin®)	200-600 mg PO q4-6h Max: 800 mg/dose or 3200 mg/day	30 - 60	1 - 2	4 - 6		
Ketorolac (Toradol®)	<u>Adults >50 kg and <65 years old</u> IV: 30 mg once OR 30 mg q6h PRN (max: 120 mg/day) IM: 30-60 mg once OR 10-30 mg q4-6h PRN (max: 120 mg/day) PO: 20 mg once then 10 mg q4-6h PRN (max: 40 mg/day) <u>Adults <50 kg or >65 years old</u> IV: 15 mg once OR 15 mg q6h PRN (max: 60 mg/day) IM: 30 mg once OR 10-15 mg q4-6h PRN (max: 60 mg/day) PO: 10 mg q4-6h PRN (max: 40 mg/day) **Oral formulation not recommended for initial therapy** **Use of ketorolac (all formulations) should not exceed 5 days**	IM/IV: 30 PO: 30 - 60	IM/IV: 1-2 PO: 2-3	IM/IV: 4-6 PO: 6-8	Do not use in GFR < 30 mL/min, AKI/ARF, hemodialysis or peritoneal dialysis Use with caution and reduce dose in patients with hepatic impairment. Avoid use in patients with severe hepatic impairment or cirrhosis.	**BBW**-May increase risk of MI/stroke in peri-operative pain in ***CABG*** surgery. **BBW**-Increased risk of GI bleeding, and perforation. Do not use in NSAID-sensitive asthma, urticaria or allergic-type reaction Caution with concomitant use of anticoagulants, hyperkalemia, CHF Use with caution in patients >65 years old; recommend initiating at lowest effective dose
Naproxen (Naprosyn®)	250-500 mg BID Max: 1500 mg/day	30-60	1 - 2	12		
Celecoxib (Celebrex®)	100-200 mg BID Max: 400 mg/day	30-60	3	12		

ADJUVANT AGENTS FOR NEUROPATHIC PAIN SYNDROMES AND CHRONIC PAIN

The following agents should be used with caution in patients >65 years and older. Recommend initiating at lowest effective dose and close monitoring for adverse effects.

Drug Class	Medication	Recommended Starting Dose	Maximum Daily Dose	Renal/Hepatic Considerations	Indication(s)	Comments
Anticonvulsants	Gabapentin (Neurontin®)	100-300 mg PO daily to TID	3,600 mg PO/day in 3 divided doses	Dose adjust for renal impairment (See *Appendix B*)	Postherpetic neuralgia Off-label: fibromyalgia, other neuropathic pain	Caution when combining with other CNS depressants and alcohol May cause drowsiness, dizziness, peripheral edema.
	Pregabalin (Lyrica®)	25-75 mg PO BID	600 mg PO/day in 3 divided doses	Dose adjust for renal impairment (See *Appendix B*)	Fibromyalgia, diabetic peripheral neuropathy, postherpetic neuralgia, neuropathic pain associated with spinal cord injury	Caution when combining with other CNS depressants and alcohol May cause drowsiness, dizziness, peripheral edema.
	Carbamazepine (Tegretol®)	100 mg PO BID	1,200 mg PO/day in 2 divided doses	Avoid in hepatic dysfunction.	Trigeminal neuralgia or glossopharyngeal neuralgia	Associated with aplastic anemia, agranulocytosis, bone marrow suppression, severe dermatologic reactions, hyponatremia. May cause drowsiness, dizziness, nausea. Significant drug interactions.
	Oxcarbazepine (Trileptal®)	150-300 mg PO daily	2400 mg PO/day in 2 divided doses	Dose adjust for renal impairment and hepatic dysfunction.	Off-label: trigeminal neuralgia	Associated with severe dermatologic reactions, hyponatremia. May cause drowsiness, dizziness.
	Topiramate (Topamax®)	25-50 mg PO BID	200 mg PO BID	Recommend 50% dose reduction in CrCl <70 ml/min; supplemental doses may be required after dialysis	Migraine prophylaxis	May cause acidosis, abdominal pain drowsiness, dizziness, nausea.
	Tiagabine (Gabitril®)	4 mg PO at bedtime	8 mg PO/day	Dose adjustment in hepatic impairment; titrate slowly in renal impairment	Off-label: neuropathic pain	May cause drowsiness, dizziness, nervousness, decreased concentration, weakness, tremor, and nausea.

Drug Class	Medication	Recommended Starting Dose	Maximum Daily Dose	Renal/Hepatic Considerations	Indication(s)	Comments
Serotonin-Norepinephrine Reuptake Inhibitors (SNRI)	Duloxetine (Cymbalta®)	20-30 mg PO daily	60-90 mg PO/day	Avoid in severe renal and/or hepatic impairment.	Fibromyalgia, chronic musculoskeletal pain, diabetic peripheral neuropathy Off-label: chemotherapy-induced peripheral neuropathy, other neuropathic pain	Caution in patients with seizures; avoid MAOIs, other SSRIs or SNRIs due to potential for serotonin syndrome. May increase the risk of bleeding events. Concomitant use of aspirin, nonsteroidal anti-inflammatory drugs, warfarin, and other anti-coagulants may add to this risk. Titrate/taper slowly. Avoid abrupt discontinuation.
	Venlafaxine (Effexor®)	37.5 mg XR PO daily	225 mg XR PO/day	Dose adjust for renal and hepatic impairment	Neuropathic pain (various), migraine prevention	
Tricyclic Antidepressants* (TCA)	Amitriptyline (Elavil®)	10 mg PO at bedtime	150 mg PO at bedtime	Dose adjustments recommended in hepatic impairment	Off-label: fibromyalgia, migraine prophylaxis, chronic neuropathic pain, postherpetic neuralgia	Caution in elderly or frail, or patients with history of seizures, cardiac disease. May cause sedation, arrhythmias, dry mouth, orthostasis, and urinary retention. Contraindicated in patients with untreated narrow angle glaucoma. Amitriptyline has high risk for anticholinergic SEs, weight gain, and sexual dysfunction Moderate risk for QTc prolongation; monitor QTc if used in combination with other QTc prolonging agents
	Nortriptyline (Pamelor®)	10 mg PO at bedtime	75 mg PO at bedtime		Off-label: chronic low back pain, neuropathic pain, myofascial pain, postherpetic neuralgia	
	Desipramine (Norpramin®)	25 mg PO at bedtime	150 mg PO at bedtime		Off-label: postherpetic neuralgia	

Drug Class	Medication	Recommended Starting Dose	Maximum Daily Dose	Renal/Hepatic Considerations	Indication(s)	Comments
Muscle relaxants (Antispasticity agents) NOTE: Use with caution in elderly patients. Per the 2019 Beers Criteria, "most muscle relaxants are poorly tolerated by older adults due to their anticholinergic effects, sedations, and increased risk of falls."	Baclofen (Lioresal ®)	5 mg PO BID	80 mg PO/day in 3 to 4 divided doses	Dose adjust in renal impairment	Spasticity associated with multiple sclerosis or spinal cord origin (injury or lesions) Off-label: muscle spasms, musculoskeletal pain	Caution when combining with other CNS depressants and alcohol Poor tolerability in patients with previous history of stroke Withdrawal symptoms (hallucinations, seizures) may occur with abrupt discontinuation
	Dantrolene (Dantrium ®)	25 mg PO daily	100 mg PO TID	Contraindicated in acute hepatitis and active cirrhosis	Chronic spasticity associated with upper motor neuron disorders (spinal cord injury, cerebral palsy, multiple sclerosis)	Does not appear to have direct CNS effects Discontinue if no benefit observed after 45 days **BBW:** Symptomatic fatal or nonfatal hepatitis
	Tizanidine (Zanaflex ®)	2-4 mg PO at bedtime	36 mg per day in 2 to 3 divided doses	May cause elevation in LFTs	Spasticity Off-label: muscle spasms and/or musculoskeletal pain	Caution when combining with other CNS depressants and EtOH Contraindicated with CYP1A2 inhibitors (ciprofloxacin, fluvoxamine)
Muscle relaxants (Antispasmodic agents) NOTE: Use with caution in elderly patients. Per the 2019 Beers Criteria, "most muscle relaxants are poorly tolerated by older adults due to their anticholinergic effects, sedations, and increased risk of falls."	Cyclobenzaprine (Flexeril®)	5 mg PO TID	30 mg PO/day in 3 divided doses	Decreased doses and frequency may be required in hepatic impairment; XR formulation not recommended in hepatic impairment	Short-term (2-3 weeks) treatment of muscle spasms associated with acute, painful musculoskeletal conditions Off-label: fibromyalgia, acute temporomandibular disorder	Do NOT use within 14 days of MAOI Caution in patients with seizures, cardiovascular disease, glaucoma, patients taking TCAs or MAOIs May cause anticholinergic effects and drowsiness
	Metaxalone (Skelaxin®)	400 mg PO TID	3,200 mg PO/day in 3 to 4 divided doses	Avoid in renal and hepatic failure	Short-term (2-3 weeks) treatment of muscle spasms associated with acute, painful musculoskeletal conditions	Caution when combining with other CNS depressants Contraindicated in patients with history of anemia

Drug Class	Medication	Recommended Starting Dose	Maximum Daily Dose	Renal/Hepatic Considerations	Indication(s)	Comments
	Methocarbamol (Robaxin®)	500 mg PO four times daily 1,000 mg IV every 8 hours	4,000 mg PO/day in 3 to 4 divided doses 3,000 mg IV/day for 3 days (may repeat after 48-hour drug-free interval)	IV formulation is contraindicated in patients with renal failure due to the presence of polyethylene glycol	Short-term (2-3 weeks) treatment of muscle spasms associated with acute, painful musculoskeletal conditions	Caution when combining with other CNS depressants May cause discoloration of urine (black or green) May exacerbate symptoms of myasthenia gravis
	Orphenadrine (Norflex®)	100 mg PO BID 60 mg IV/IM every 12 hours	200 mg PO/day	Use with caution in hepatic impairment	Short-term (2-3 weeks) treatment of muscle spasms associated with acute, painful musculoskeletal conditions	Caution when combining with other CNS depressants Contraindicated in patients with glaucoma, pyloric or duodenal obstruction, stenosing peptic ulcers, prostatic hypertrophy or obstruction of the bladder neck, cardiospasm, and myasthenia gravis
	Carisoprol (Soma®)	250-350 PO mg TID	1,400 mg PO/day in 3 to 4 divided doses Max duration: 2 to 3 weeks	Use with caution in renal and hepatic impairment.	Short-term (2-3 weeks) treatment of muscle spasms associated with acute, painful musculoskeletal conditions Taper slowly (over 14 days) in patients on long-term therapy	Use not recommended due to high abuse potential and increased risk for addiction. Consider alternative agent CYP2C19 poor metabolizers at risk for increased carisoprodol exposure
Corticosteroids	Dexamethasone	Varies by condition Standard dose: 4-16 mg/day	Varies by condition	No dose adjustments needed	Inflammatory conditions, nerve compression	May increase risk of gastric ulcers in combination with NSAIDs May cause impaired healing, infection, thrush, hyperglycemia, weight gain, myopathy, stomach upset, psychosis, emotional instability.

PATIENT-CONTROLLED ANALGESIA (PCA) DOSING GUIDELINES

RECOMMENDED PCA DOSING FOR OPIOID-NAÏVE PATIENTS

Criteria for Use	Contraindications for Use
▪ Pain anticipated to last more than 10-12 hours ▪ Patient willing and able to take control of their analgesia ▪ Oral route is not appropriate ▪ Severe post-operative pain expected or uncontrolled acute pain ▪ Chronic pain (cancer, sickle cell, burn) **may require higher doses**	▪ **Cognitive impairment (unable to understand concept of PCA)** ▪ **Increased intracranial pressure** ▪ **Patient obtunded, overly sedated** **Respiratory compromise (e.g. severe asthma, COPD)**

THE USE OF CONTINUOUS INFUSIONS (BASAL RATE) IS NOT RECOMMENDED IN OPIOID-NAÏVE PATIENTS.

Patient Age Group:		12 years – 18 years	19 years – 65 years	Over 65 years	Comments
MorPHINE:					
PCA MODE ONLY	PCA DOSE Lockout Interval MAX Limit (4 hour) Loading Dose	0.5 mg–2 mg 10-20 minutes Up to 30 mg 2 mg–5 mg	0.5 mg–2 mg 10-20 minutes Up to 30 mg 1 mg–4 mg	0.5 mg–1.5 mg 10-20 minutes Up to 24 mg 1 mg–3 mg	**Avoid use in patients with poor renal function (CrCl <30 ml/min) and dialysis patients**
HYDROmorPHONE:					
PCA MODE ONLY	PCA DOSE Lockout Interval MAX Limit (4 hour) Loading Dose	0.05 mg–0.4 mg 5–15 minutes Up to 6 mg 0.2 mg–0.4 mg	0.1 mg–0.4 mg 10-15 minutes Up to 6 mg 0.2 mg–0.4 mg	0.05 mg–0.2 mg 10-15 minutes Up to 4 mg 0.2 mg–0.4 mg	Initiate at a lower dose in patients with moderate renal impairment (CrCl <50 ml/min). Monitor closely
FENTANYL					
PCA MODE ONLY	PCA DOSE Lockout Interval MAX Limit (4 hour) Loading Dose	10 mcg–20 mcg 5–10 minutes Up to 200 mcg 25 mcg–50 mcg	10 mcg–20 mcg 5–10 minutes Up to 200 mcg 25 mcg–50 mcg	10 mcg–15 mcg 5–10 min Up to 150 mcg 15 mcg–30 mcg	

PCA CONSIDERATIONS

- Educate patient and family members/caregivers on proper PCA use. Reiterate that no one other than the patient, or designated person, is allowed to press the button (PCA by proxy).
- Monitor for adequate pain relief and adverse effects (oversedation, respiratory depression, etc)
- Monitor for sedation and respiratory depression. Pulse oximetry or capnography is recommended in high-risk patients and if a continuous (basal) infusion is added.

PCA INTERVENTIONS – IMPROVEMENT OF PAIN CONTROL AND REDUCTION OF ADVERSE EFFECTS

Clinical Situation	Recommended Intervention
Pain relief: None/insufficient **Adverse effects: None**	1. Verify PCA system is functioning properly, correctly assembled, loaded and programmed correctly. 2. Confirm lockout interval is appropriate. 3. Administer a clinician/nursing loading dose (if needed). 4. Increase PCA bolus dose by 25-100% or shorten lockout interval
Pain relief: None/insufficient **Adverse effects: Yes**	1. Treat adverse effects 2. Add or increase non-opioid or adjuvant analgesics, if appropriate. 3. Decrease opioid dose by 25% 4. Rotate to a different opioid (reduce for cross-tolerance)
Pain relief: Yes **Adverse effects: Yes**	1. Treat adverse effects 2. Decrease opioid dose by 25-50% (potentially more if excessive sedation and/or respiratory depression) 3. Rotate to a different opioid (reduce for cross-tolerance)
Pain relief: Yes **Adverse effects: Yes (only after PCA bolus dose administration)**	1. Treat adverse effects 2. Decrease PCA bolus dose by 25-50% AND shorten the lockout interval (give smaller doses more often) 3. Rotate to a different opioid (reduce for cross-tolerance)
Pain relief: Yes (except during activity) **Adverse effects: None**	Remind patient to use PCA prior to activity (at least 10-15 minutes prior) and continue to self-administer during activity
Maximum programmed amount used (4-hour lockout reached)	1. If patient still in pain, administer clinician/nursing loading dose 2. Verify that 4-hour lockout limit was calculated appropriately 3. Determine amount of pain relief obtained and adjust accordingly (if none or tolerable adverse effects): a. If <50%, increase 4-hour limit by 100% b. If >50% but less than optimal, increase 4-hour limit by 50%
Somnolence, difficult to arouse, and/or respiratory depression	1. If opioid-naïve, discontinue the PCA. If opioid-tolerant, consider decreasing the dose by 75%, in order to avoid precipitating opioid withdrawal 2. Consider administering low-dose naloxone (see Opioid Reversal, page 19) 3. Add a non-sedating non-opioid analgesic 4. If resuming PCA, reduce dose to 50% of previous once adverse effects are resolved 5. Close monitoring for adverse effects every 1 to 2 hours
Disproportionate number of demands vs. delivered doses	1. Ensure that no one other than the patient is pressing the demand button (PCA by proxy) 2. Determine if patient understands the use of the demand button and re-educate if needed 3. Determine the ratio of doses delivered to demands: a. If ratio is 1 dose delivered per <2 to 3 demands and pain is controlled, continue current settings b. If ratio is 1 dose delivered per <2 to 3 demands and pain is **uncontrolled** with tolerable adverse effects, administer clinician/nursing loading dose and increase PCA bolus dose by 25-100% c. If ratio is 1 dose delivered per >2 to 3 demands and pain is controlled with tolerable adverse effects, consider administering clinician/nursing loading dose and remind patient to self-administer dose *before* pain gets uncontrolled. Ask patient to wait until length of lockout interval prior to re-dosing to evaluate for dose effect.

CONVERSION TRANSDERMAL FENTANYL (DURAGESIC ®)

Total 24-Hour Oral Morphine Equivalent (mg/day)	Fentanyl Patch Dose (mcg/hr)
45-134	25
135-224	50
225-314	75
315-404	100
405-494	125
495-584	150
585-674	175
675-764	200
765-854	225
855-944	250
945-1034	275
1035-1124	300

Transdermal fentanyl should be **reserved** for patients with chronic pain and have stable opioid requirements. Current HM policy states that the inpatient initiation of fentanyl patches are "restricted to home continuation or conversion from oral therapy in opioid tolerant patients" (See definition of opioid tolerant, page 2). ***The manufacturer's conversion table should ONLY be used for converting FROM an oral opioid to a fentanyl patch***

- It may be necessary to provide patients with breakthrough pain doses of an immediate release or parenteral opioid during the initiation of transdermal fentanyl
- Increase patch dose based on breakthrough medication used during the initial 3-day period
- Avoid titrating patch until 3 days after initiation and every 6 days thereafter
- If rotating off transdermal patch, remove patch and start new opioid 12 hours later. Breakthrough medication may be needed during this time period.

Per the Institute of Safe Medication Practices (ISMP) update for 2020-2021, fentanyl patches should NOT be used for opioid-naïve patients and/or for the treatment of acute pain

OPIOID REVERSAL

The opioid antagonist naloxone (Narcan®) is the reversal agent used in the setting of an opioid overdose.

Inpatient Naloxone Administration in Adults (Intravenous Naloxone)

1. Criteria for intravenous naloxone administration:
    a. Known or suspected recent administration of an opioid agent
    b. Minimal or no response to physical and/or verbal stimulation, difficult to arouse, POSS >3
    c. Shallow respirations or respiratory rate less than 8 breaths per minute
    d. Pinpoint pupils
2. Stop administration of any opioids and other CNS depressants.
3. Summon help. Call the CERT team and notify the ordering physician.
4. To prepare naloxone, dilute 0.4 mg/mL (1 mL) ampule into 9 mL of normal saline for total volume of 10 mL to achieve a 0.04 mg/mL concentration. **DO NOT administer** undiluted due to risk of precipitating rapid withdrawal, which may cause severe pain or seizures.
5. Administer via slow IV push (0.5 mL over 2 minutes) and monitor for patient response. A second dose (total of 0.8 mg or 20 mL) may administered if no response within 1 to 2 minutes.
6. Continue to closely monitor sedation and respiratory status.

Outpatient Naloxone Prescribing (Intranasal Naloxone Spray)

An intranasal naloxone prescription should be considered for patients who are prescribed opioid medications and who:

- Are prescribed medicines to treat opioid use disorder
- Are prescribed opioid pain medications who are at increased risk for overdose:
    - Concomitant use of benzodiazepines or other CNS depressants
    - Chronic opioid treatment with total daily opioid >50 MME
    - History of opioid use disorder
    - History of opioid overdose
- Have household members or other close contacts who may be at risk for accidental ingestion or opioid overdose (children, pets, family members/friends with substance use history)

Patient Education: How to Respond to an Overdose
If someone is not breathing or you think they may have overdosed: 1. Check for response to yelling and shaking. 2. Call 911. 3. Administer 1 spray of naloxone into 1 nostril. If no reaction in 2 to 3 minutes, administer a second dose in the other nostril. 4. Give rescue breaths or administer CPR. Follow 911 dispatcher instructions. 5. Stay with the person until help arrives.

DISCHARGE AND OUTPATIENT OPIOID PRESCRIBING
TEXAS CONTROLLED SUBSTANCES LAW UPDATES

- As of January 1, 2021, the electronic prescribing of ALL controlled substances (Schedule II through V) is now mandatory, with the exception in limited circumstances or unless a waiver has been granted to the prescribing provider by the appropriate agency. See the e-prescribing tip sheet here.
- As of March 1, 2020, it is required to check the patient's prescription monitoring program (PMP) history *prior to* prescribing or dispensing of opioids, benzodiazepines, barbiturates, or carisoprodol. The Texas PMP website is available here.
- As of September 1, 2019, prescriptions for opioids for acute pain may not exceed a maximum of 10 days. Exceptions include prescriptions for cancer pain, hospice or end-of-life care, palliative care, or opioids approved by the FDA for the treatment of substance use disorder.

RECOMMENDED OPIOID QUANTITIES[5,17]

The quantities listed below are expert panel recommendations of opioid tablet quantities to prescribe for opioid-naïve patients based on *select* procedures. **Initiation of acetaminophen PO 1 g every 8 hours ± ibuprofen 400 mg PO every 8 hours (unless contraindicated) is also recommended.**

Procedure	Oxycodone (Hydrocodone) 5 mg Tablets
Dentistry	
Dental extraction	0
Otolaryngology	
Thyroidectomy, partial or total	0-15
Cochlear implant	0
Cardiac Surgery	
Coronary artery bypass grafting	0-20
Cardiac catheterization	0
Carotid endarterectomy	0-10
Surgical Oncology	
Breast biopsy or lumpectomy	0-5
Lumpectomy + sentinel lymph node biopsy	0-5
Sentinel lymph node biopsy only	0-5
Wide local excision ± sentinel lymph node biopsy	0-20
Simple mastectomy ± sentinel lymph node biopsy	0-20
Partial mastectomy ± sentinel lymph node biopsy	0-15
Modified radical mastectomy or axillary lymph node dissection	0-30
Thoracic Surgery	
Video-assisted thoracoscopic wedge resection	0-20
Cardiac surgery via median sternotomy	0-25
Gynecologic Surgery and Obstetric Delivery	
Hysterectomy (laparoscopic or vaginal)	0-15
Hysterectomy (abdominal)	0-20
Uncomplicated caesarean delivery	0-20
Uncomplicated vaginal delivery	0

Procedure	Oxycodone (Hydrocodone) 5 mg Tablets
Otolaryngology	
Thyroidectomy	0-5
Urologic Surgery	
Prostatectomy	0-10
General Surgery	
Anti-reflux (Nissen), laparoscopic	0-10
Appendectomy, laparoscopic or open	0-10
Cholecystectomy, laparoscopic	0-10
Cholecystectomy, open	0-15
Donor nephrectomy, laparoscopic	0-10
Inguinal hernia repair, open	0-10
Umbilical hernia repair, open	0-15
Sleeve gastrectomy	0-10
Colon and Rectal Surgery	
Colectomy, laparoscopic	0-10
Colectomy, open	0-15
Ileostomy/colostomy creation, revision, closure	0-15
Small bowel resection or enterolysis – open	0-15
Orthopedic Surgery	
Arthroscopic partial meniscectomy	0-10
Arthroscopic ACL/PCL repair	0-20
Arthroscopic rotator cuff repair	0-20
ORIF of the ankle	0-20
Total hip arthroplasty	0-30
Total knee arthroplasty	0-50

NON-PHARMACOLOGIC TREATMENT OPTIONS

There is strong literature supporting non-pharmacologic interventions in both acute and chronic pain. This multimodal treatment approach has advantages over traditional pharmacologic/interventional pain management because of their opioid-sparing effects and decreased incidence of adverse events. Non-pharmacologic treatments often are used to augment and complement pharmacologic treatments.

Non-pharmacologic/integrative medicine modalities include:

- Acupressure
- Acupuncture – Available at HM (outpatient only)
- Aromatherapy
- Interdisciplinary Rehabilitation
- Massage Therapy – Available at HM per request
- Music Therapy – Available at HMH via consult
- Osteopathic and Spinal Manipulation
- Pain Psychology
- Pet Therapy – Available at HM per request
- Physical/Occupational Therapy – Available at HM via consult
- Psychological Therapies

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APPENDIX A: SAMPLE CALCULATIONS

CONVERT FROM ORAL AND PARENTERAL OPIOID TO ORAL OPIOID REGIMEN

Convert the following regimen to hydrocodone: **oxycodone 10 mg q4h prn moderate pain and hydromorphone IV 0.5 mg q3h severe pain**.
Past 24 hours use: oxycodone 10 mg x 2 doses and hydromorphone IV 0.5 mg x 4 doses

STEP 1	*Convert total 24-hour IV opioid to PO equivalent dose*	Hydromorphone IV 0.5 mg x 4 doses = Hydromorphone IV 2 mg Per dose conversion chart: *Using conversion factor of 5* **IV Hydromorphone 2 mg x 5 = PO Hydromorphone 10 mg**
STEP 2	*Convert each PO opioid to oral morphine equivalent (total oral opioid plus IV opioid conversion from Step 1)*	Oxycodone 10 mg x 2 doses = 20 mg Per dose conversion chart: *Using a conversion factor of 1.5 for oxycodone* **PO Oxycodone 20 mg x 1.5 = PO Morphine 30 mg** Per dose conversion chart: *Using a conversion factor of 4 for hydromorphone* **PO Hydromorphone 10 mg x 4 = PO Morphine 40 mg**
STEP 3	*Combine oral morphine equivalents for the two opioids in order to obtain total daily dose*	Morphine PO 30 mg + Morphine PO 40 mg = Morphine PO 70 mg
STEP 4	*Reduce total daily dose by 20-50% to account for cross-tolerance*	Reducing by 20-50% yields: **35–56 mg morphine PO**
STEP 5	*Convert oral morphine to oral hydrocodone (1:1 conversion)*	**Morphine PO 45 mg = Hydrocodone PO 45 mg total daily dose** Divide by 6 for q4h dosing: **Hydrocodone/APAP 7.5-325 mg q4h prn**

CONVERT FROM A PCA TO AN ORAL OPIOID REGIMEN

Patient is on Hydromorphone PCA 15 mg/30 mL with a basal rate of 0.5 mg/hr and PCA bolus dose of 1 mg Q 15 minutes
***Patient used the PCA Patient button 2 times in the previous 24 hours. No bolus doses needed.*

STEP 1	*Calculate 24-hour IV opioid dose* *(Basal infusion rate x 24 hrs) + (PCA dose x # times used in past 24 hrs) + (bolus doses x # doses administered in past 24 hours)*	0.5 (24) + 1 (2) + 0 = **14 mg IV Hydromorphone in 24 hours**
STEP 2	*Convert 24-hour IV opioid dose to 24-hour PO opioid dose*	Per dose conversion chart: *Using a conversion factor of 5* **IV Hydromorphone 14 mg x 5 = PO Hydromorphone 70 mg**
STEP 3	*Calculate the 24-hour PO opioid dose (from step 2) to the equivalent dose of the oral opioid of choice*	Per dose conversion chart*: Using a conversion factor of 4* **PO Hydromorphone 70 mg x 4 = PO Morphine 280 mg**
STEP 4	*Reduce the total dose by 20-50% to account for cross-tolerance*	Reducing by 20-50% yields: **PO Morphine 140 mg–210 mg**
STEP 5	*Divide 24-hour PO opioid by dosing frequency* *Round dose to nearest tablet or multiple of tablets size*	For BID (extended release formulation) divide by 2: **MS Contin 70-100 mg Q12H** For Q4H (immediate release) divide by 6

APPENDIX B: RENAL DOSE ADJUSTMENT RECOMMENDATIONS FOR GABAPENTINOIDS

Gabapentin (Neurontin ®)		
CrCl (mL/min)	**Total Daily Dose Range (mg/day)**	**Dose Regimen**
Normal (≥60)	900-3600	TID
>30 to 59	400-1400	BID
>15 to 29	200-700	Daily
15*	100-300	Daily
Post-Hemodialysis Supplemental Dosage (mg)		
Patients on 100 mg daily regimen: One supplemental dose of 125 mg Patients on 125 mg daily regimen: One supplemental dose of 150 mg Patients on 200 mg daily regimen: One supplemental dose of 200 mg Patients on 250 mg daily regimen: One supplemental dose of 250 mg Patients on 300 mg daily regimen: One supplemental dose of 300 mg		

Pregabalin (Lyrica ®)					
CrCl (mL/min)	**Total Daily Dose (mg/day)**				**Dose Regimen**
Normal (≥60)	150	300	450	600	BID or TID
>30 to 59	75	150	225	300	BID or TID
>15 to 29	25-50	75	100-150	150	Daily
15*	25	25-50	50-75	75	Daily
Post-Hemodialysis Supplemental Dosage (mg)					
Patients on 25 mg daily regimen: One supplemental dose of 25 mg or 50 mg Patients on 25-50 mg daily regimen: One supplemental dose of 50 mg or 75 mg Patients on 50-75 mg daily regimen: One supplemental dose of 75 mg or 100 mg Patients on 75 mg daily regimen: One supplemental dose of 100 mg or 150 mg					