Peri-Operative Pain Management

Disclaimer: *This algorithm has been developed for MD Anderson using a multidisciplinary approach considering circumstances particular to MD Anderson's specific patient population, services and structure, and clinical information. This is not intended to replace the independent medical or professional judgment of physicians or other health care providers in the context of individual clinical circumstances to determine a patient's care. This algorithm should not be used to treat pregnant women.*

Note: This consensus algorithm excludes patients who are in the ICU, intra-operative or pre-procedural settings, or are currently receiving epidural or intrathecal analgesia.

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ASSESSMENT

Pre-Operative Evaluation

- Comprehensive pain assessment (see Appendix A)
- Determine category of procedure (minor, intermediate, major) and consider the following treatment modalities:
  - Minor: local anesthetic infiltration, post-operative oral analgesics
  - Intermediate: minor recommendations in addition to regional analgesic technique if applicable and plan for possible intravenous analgesics post-operatively
  - Major: intermediate recommendations in addition to benefit of starting preoperative medications if appropriate
- Determine previous exposure to opioids
- Anesthesia assessment for PNC or epidural
- Consider Acute Pain consult[1] for assistance in developing peri-operative pain management plan including peripheral nerve blocks (PNB) or peripheral nerve catheters (PNC)
  - For consideration of pre-operative PNC or PNB, consult should be made within 1-2 days of scheduled procedure[2]

Per surgical and anesthesia teams, is there a need for post-operative Acute Pain consult?

- Yes → Consult Acute Pain
- No →

Post-Operative Evaluation

- Complications of surgery and/or anesthesia
- Comprehensive pain assessment (see Appendix A)
- Procedures performed
- Physical constraints (tight straps, bandages, excessive compression, *etc.*)
- Drain output (increased output may indicate coagulopathy)
- Swelling/edema
- Neurovascular assessment
- Activity restrictions/changes (ambulation, performance status, incentive spirometry, bowel function, *etc.*)
- Current pain orders: PCA, epidural, PNC, PNB, or other
- Consider specialty services consultation including Acute Pain, Physical Therapy/Occupational Therapy, and/or Integrative Medicine, as indicated (see Appendix B)

Pain controlled?

- Yes → Continue monitoring; Re-evaluate at appropriate intervals → Pain controlled?
  - Yes →
    - Provide discharge pain plan
    - Consider limited opioid prescription at discharge using a 5x to 7x multiplier based on the 24 hours prior to discharge (*e.g.,* tramadol 50 mg PO taken every 6 hours in the prior 24 hours; 5 x 4 = 20 tablets)
  - No → See Page 3
- No → See Page 3

PCA = patient controlled analgesia

[1] For outpatients, email AcutePainMedicine@mdanderson.org. For inpatients, page (713) 404-2264.

[2] For patients on anticoagulant therapy, see the Peri-Procedure Management of Anticoagulants algorithm

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Note: This consensus algorithm excludes patients who are in the ICU, intra-operative or pre-procedural settings, or are currently receiving epidural or intrathecal analgesia.

Pain not controlled

TREATMENT

Pain score[1] ≤ 3 and/or PPG met

For patients not currently taking opioids:
- Choose non-opioids (see Appendix C) or if contraindicated, use weak opioids (see Appendix D), as needed for pain

For patients currently taking opioids:
- Consider decreasing current analgesic regimen if no side effects. Prescribe short-acting opioid at 10-20% of long-acting dose every 2 to 4 hours as needed (Appendix D for dosing)
- Manage opioid induced side effects and decrease/change opioids if indicated (see Appendix E)

Pain score[1] ≥ 4 and/or PPG not met

For patients not currently taking opioids:
- Maximize non-opioids (see Appendix C)
- Consider administering short acting opioids (see Appendix D)
  Note: Fentanyl should not be used in opioid naïve patients

For patients currently taking opioids:
- Consider increasing scheduled opioid dose by 30-50%; calculate short-acting opioid dose as 10-20% of prior 24 hour opioid dose
- Manage opioid induced side effects and decrease/change opioids if indicated (see Appendix E)
- Consider Acute Pain consult

Severe Pain[3]

Manage both pain and psychosocial distress[4]:
- Rapidly titrate short-acting opioids
- If significant anxiety related to pain, administer opioids prior to sedating anxiolytics
- Ongoing assessment for pain, distress and opioid side effects until patient stable
- Consider Acute Pain consult

Reassess pain, PPG, and opioid side effects at appropriate intervals as clinically indicated[2]

Pain controlled and/or PPG met?

Yes
- Continue current treatment
- Provide discharge pain plan
- Consider limited opioid prescription at discharge using a 5x to 7x multiplier based on the 24 hours prior to discharge (*e.g.,* tramadol 50 mg PO taken every 6 hours in the prior 24 hours; 5 x 4 = 20 tablets)

No

Consult Acute Pain

Note for all patients:
- If patient has a regional anesthetic block, notify appropriate managing service
- Consider Integrative Medicine Services such as acupuncture or mind-body therapies (see Appendix B), Physical Therapy, patient education, and psychosocial support as appropriate
- If frequent prn doses required and pain anticipated for greater than one day, consider patient controlled analgesia (PCA). See Appendix F.

PPG = personalized pain goal

[1] See Appendix A

[2] Refer to Pain Management Policy (#CLN0540)

[3] Severe pain, new onset, or exacerbation of previously stabilized pain, accompanied by significant distress or if present for > 24 hours

[4] For additional information, refer to Distress Screening and Psychosocial Management algorithm

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Quick Reference Guide

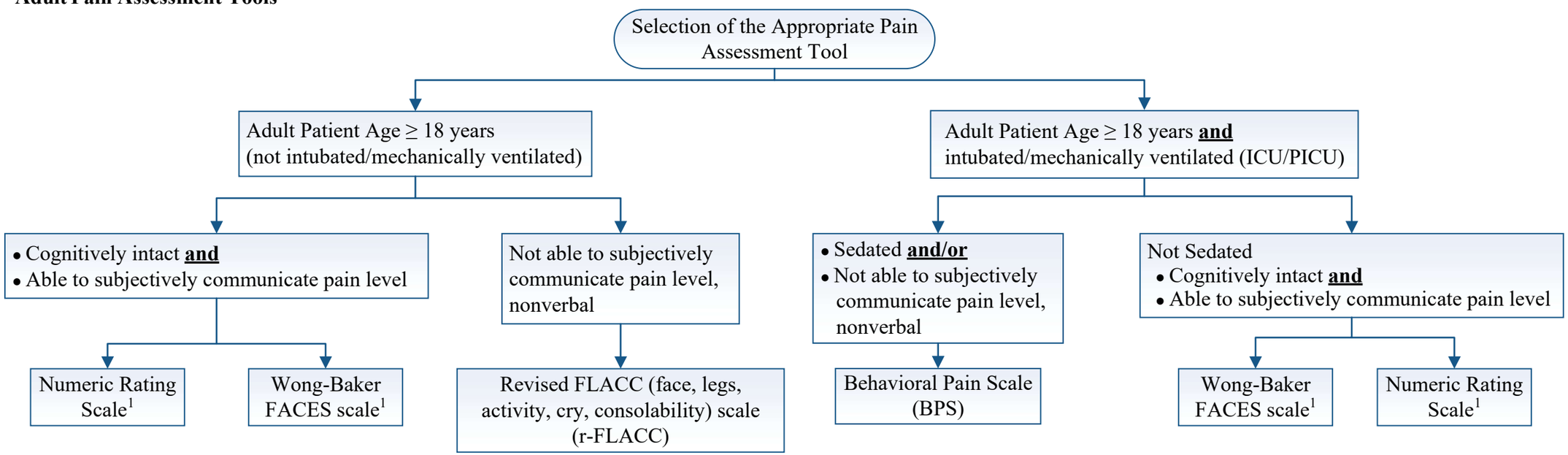
- **Opioid naïve**: Includes patients who are not chronically receiving opioid analgesic on a daily basis and therefore have not developed significant opioid tolerance
- **Opioid tolerant**: Patients who are chronically receiving opioid analgesics on a daily basis. The FDA identifies this group as those receiving at least one of the following for at least 1 week:
  - Morphine 60 mg orally daily
  - Oxycodone 30 mg orally daily
  - An equivalent dose of another opioid
  - Oxymorphone 25 mg orally daily
  - Hydromorphone 8 mg orally daily
  - Transdermal fentanyl 25 mcg per hour
  - Hydrocodone 60 mg orally daily
- **Incomplete cross-tolerance**: Reduce dose of new opioid by 30-50% when switching from one opioid to another to account for tolerance to a currently administered opioid that does not extend completely to other opioids. Consequently, this phenomenon tends to lower the required dose of the new opioid.
- **Dose titration**: Adjusting the dose of an opioid should be individualized for each patient; refer to Page 3 of this algorithm for titration recommendations
- **Dosing frequency**: For long-acting opioids, dosing frequency is typically every 8-24 hours depending on the agent. Refer to Appendix D for Opioid Dose Considerations.
- **Breakthrough pain**: Doses of short-acting opioids for breakthrough pain should be 10-20% of the total daily dose given every 1-4 hours as needed. Breakthrough opioids can be given as frequently as every 1 hour for oral doses or every 15 minutes if IV (assuming normal renal/hepatic function).
- **Elderly/organ dysfunction**: Use additional caution when converting opioids in elderly patients (age ≥ 65 years), and/or patients with hepatic, renal, or pulmonary dysfunction. Codeine, morphine, hydromorphone, and oxycodone should be used with caution in patients with decreased renal function.
- **Opioids NOT recommended for cancer pain**: Meperidine and mixed agonist-antagonists (pentazocine, nalbuphine, butorphanol) should be avoided
- **Withdrawal symptoms**: nausea, vomiting, diarrhea, anxiety, and shivering are common symptoms of opioid withdrawal. A gradual taper is recommended when discontinuing opioids.
- **Overdose**: Symptoms may include respiratory depression, constricted pupils, and decreased responsiveness. Naloxone is used to reverse the effects of an opioid. To administer, dilute naloxone 0.4 mg/mL (1 mL) ampule into 9 mL of sodium chloride 0.9% (NS) for total volume of 10 mL to achieve a 0.04 mg/mL concentration, and give 0.5 mL (0.02 mg) via slow IV push every 2 minutes until patient is more awake and respiratory status improves. DO NOT administer undiluted due to risk of precipitating rapid withdrawal, which may cause severe pain or seizures.
- **Chemotherapy-related, intermittent pain**: This type of pain may be managed with weak opioids (*e.g.,* tramadol) or combination opioid preparations (*e.g.,* hydrocodone with acetaminophen, etc.) See Appendix D for Opioid Dose Considerations, or refer to a drug information reference for additional information.
- **Constipation** is a common side effect with opioid use. Consider starting a bowel regimen in all patients taking opioids. Refer to Appendix E.
- **Duration of drug effect**: Any residual drug in the patient's system must be accounted for and an assessment of any residual effects from discontinued long-acting opioids must be made before any new opioid is started. Example: fentanyl will continue to be released from the skin 12-36 hours after transdermal patch removal.
- **The Texas Prescription Monitoring Program (PMP)** is an electronic database that tracks controlled substance prescriptions. It can help identify patients who may be misusing prescription opioids or other prescription medications and who may be at risk for overdose. Clinicians are encouraged to check the Texas PMP prior to initial opioid prescribing and at regular intervals. The program is now available through OneConnect and can also be accessed at https://texas.pmpaware.net/login. Personal profiles should be reviewed and updated routinely to ensure all states are included.

APPENDIX A: Comprehensive Pain Assessment

The comprehensive pain assessment should include the following:

1. **Pain**:
   a. For each site of pain, determine intensity level using the appropriate pain assessment tool (see below). Tools using 0 to 10 point scales can be categorized as follows: 0 = no pain, 1-3 = mild pain, 4-6 = moderate pain, 7-10 = severe pain
   b. Assess the following at rest and with activity: location and orientation, type (acute, chronic, acute exacerbation of chronic pain), onset, pathophysiology (somatic, visceral, neuropathic), frequency (continuous, intermittent, breakthrough, incidental), temporal factors such as aggravating and alleviating factors, duration, and etiology (*e.g.,* tumor, non-tumor related, fracture)
   c. Evaluation of medical history includes: oncologic or other significant medical illnesses, medication history, relevant imaging and laboratory studies
   d. Physical examination
   e. Assess for presence of sedation and other opioid side effects (Appendix E)

Adult Pain Assessment Tools



[1] The Numeric Rating Scale is the first choice for adult patients who are able to subjectively communicate pain level unless deemed appropriate based on patient preference

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APPENDIX A: Comprehensive Pain Assessment - continued

2. **Function**:
   a. Evaluate patient's ability to ambulate, perform activities of daily living (ADL), range of motion (ROM), deep breathing, and coughing
   b. Assess restrictions related to pain
   c. Document patient's functional ability
3. **Psychosocial issues**:
   a. Evaluate patient distress, family support, psychiatric history, patient/family knowledge and beliefs surrounding pain and its management, and risk factors for under treatment of pain including underreporting, prior treatment of pain and response to other pain medications, concerns about addiction to pain medications or side effects, extremes of age, gender, cultural barriers, communication barriers, and prior history of drug abuse
   b. Document patient's assessment of psychological distress
4. **Personalized Pain Goal (PPG):**
   Determine the verbal or written goal stated by the patient describing the desired level/intensity of pain that will allow the patient to achieve comfort in physical, functional, and psychosocial domains

In addition to Comprehensive Pain Assessment, rule out or treat pain related to oncologic emergencies[1]

[1] Pain related to an oncologic emergency requires assessment and treatment (*e.g.,* surgery, steroids, radiotherapy, antibiotics) along with an emergent consultation.
Examples of oncologic emergencies include:

- Bowel obstruction/perforation
- Brain metastasis
- Leptomeningeal metastasis
- Fracture or impending fracture of weight-bearing bone
- Epidural metastasis/spinal cord compression
- Pain related to infection

APPENDIX B: Post-Op Specialty Services and Consultation Guidelines

Integrative Medicine Clinic services relative to pain management include:

- Acupuncture
- Meditation/mind-body techniques
- Massage
- Music therapy
- A variety of individual and group services are also available for long-term issues

Note: For Integrative Medicine Center services, submit a referral order for a specific service or an evaluation of the use of integrative therapies for symptom management.

Rehabilitation Services

Physical Medicine and Rehabilitation (PM&R)

- Consider PM&R referral for evaluation of patient's pain and related impairments, coordination with physical and occupational therapy on treatment, and management of functional expectations

Physical and Occupational therapy services and programs relative to pain management:

- Education and activity modification
- DME and adaptive equipment recommendation and issue
- Modalities: thermal, ultrasound, electrical stimulation, IFC (interferential current), paraffin wax, TENS
- Positioning and joint protection
- Exercise and activity prescription

Physical Therapy specialized inpatient and outpatient services:

- Lymphedema management, assessment and treatment, compression garment assessment and recommendation
- TENS (IFC, biofeedback or equivalent) trial and issue
- Ergonomics assessment and training
- Low back pain programs
- Manual therapy, soft tissue mobilization and joint mobilization techniques
- Amputee programs: desensitization, mirror therapy
- Orthotics and prosthetics evaluation and recommendation
- Assistive device (walker, cane, crutches) evaluation and prescription
- Hydrotherapy and wound care

Occupational Therapy specialized inpatient and outpatient services:

- ADL, work and leisure activity modification
- Fatigue management/energy conservation
- Upper extremity amputee programs
- Custom splinting and bracing
- Psychosocial support
- Adaptive equipment assessment and prescription
- Wheelchair evaluation and recommendation (custom or rental)
- Seat and back cushion evaluation and recommendation

MD Anderson offers three coordinated pain specialty core services, consisting of Acute Pain Medicine, Chronic Pain Medicine, and Supportive Care. Guidelines for consultation to these services are indicated below.

Specialty Service Consultation Guidelines for Post-Operative Pain Management:

- Pre-operative evaluation: Consult Pain Acute Pain Medicine for any of the following:
  - Patient will require either a peripheral nerve catheter (PNC), peripheral nerve block (PNB), or epidural
  - Patient has been followed by either Chronic Pain Medicine or Supportive Care, consult Acute Pain Medicine
- Post-operative evaluation:
  - Patient with uncontrolled pain after discontinuation of PNC, PNB, or epidural, consider consulting Chronic Pain Management
  - Patient with uncontrolled pain accompanied by symptom burden **or** in the context of cancer in the palliative stage of end of life, consider consulting Supportive Care
- For patients with suspected opioid addiction, request a consult to one of the specialty core services for a referral to a treatment program. See Appendix G for Substance Use Disorder Treatment Services.

ADL = activities of daily living DME = durable medical equipment TENS = transcutaneous electrical nerve stimulation

Peri-Operative Pain Management

APPENDIX C: Non-opioids

- Non-opioids may be used alone or in combination with other non-opioids or with opioids for a multi-modal approach to pain management
- Non-steroidal anti-inflammatory drugs (NSAIDs) are useful adjuvant analgesics for bone pain

Drug Class	Drug	Recommended Starting Dose	Maximum Daily Dose	Comments
Analgesic	**Acetaminophen PO**	500-1,000 mg PO every 6 hours as needed	Single dose: 1,000 mg/dose; Daily dose: Weight < 50 kg: 3,750 mg Weight ≥ 50 kg: 4,000 mg[1]	At higher doses, can cause fatal hepatotoxicity and renal damage. Avoid use in hepatic dysfunction. Does not have anti-inflammatory effect.
	Acetaminophen IV	1,000 mg IV every 6 hours		IV acetaminophen is formulary restricted
	Acetaminophen PR	650 mg PR every 6 hours as needed		Use rectal route with caution in patients with thrombocytopenia and/or neutropenia
NSAID analgesic	**Ibuprofen[2]**	200-800 mg PO every 6 hours as needed	3,200 mg[3]	Inhibits platelet aggregation, can cause gastrointestinal side effects or renal failure. Use with caution in patients at high risk[4].
	Naproxen[2]	500 mg PO initial, then 250 mg every 4 hours as needed	1,500 mg	Inhibits platelet aggregation, can cause gastrointestinal side effects or renal failure. Use with caution in patients at high risk[4].
	Celecoxib[2]	100-200 mg PO every 12 or 24 hours as needed	400 mg	Can cause renal insufficiency
	Ketorolac[2]	15-30 mg IV or PO every 6 hours as needed	120 mg	Evaluate after 8 doses and limit treatment to 5 days. Reduce dose by 50% if age > 65 years or weight < 50 kg. Use is contraindicated in patients with advanced renal impairment or patients at risk for renal failure due to volume depletion. Inhibits platelet aggregation, can cause gastrointestinal side effects.
	Meloxicam[2]	Tablet 7.5-15 mg PO daily Capsule 5-10 mg PO daily[5]	Tablet: 15 mg Capsule: 10 mg[5]	Inhibits platelet aggregation, can cause gastrointestinal side effects or renal failure. Use with caution in patients at high risk[4]. Tablets and capsules do not have equivalent systemic exposure and are not interchangeable, even if the total milligram strength is the same; do not substitute similar dose strengths of other meloxicam products.

[1] Manufacturers of over-the-counter acetaminophen recommend no more than 3,000 mg daily

[2] Non-steroidal anti-inflammatory drugs (NSAIDs) may have antiplatelet effects that can increase the risk of bleeding in patients who are thrombocytopenic or on myelosuppressive chemotherapy and likely to become thrombocytopenic. Non-acetylated salicylates (*e.g., salsalate, choline magnesium salicylate)* and the COX-2 selected NSAID (celecoxib) may have less effects on platelets, but should still be used with caution in a patient on myelosuppressive chemotherapy.

[3] Due to increased adverse effects with higher doses, recommended maximum daily dose for chronic use is 2,400 mg

[4] Patients at high risk of serious gastrointestinal side effects or renal damage from NSAIDs include: elderly (age > 60 years), smokers, previous history of peptic ulcer, currently receiving corticosteroids, anticoagulants, or presence of existing renal, cardiac or liver impairment

[5] Not on MD Anderson Cancer Center Formulary

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APPENDIX C: Non-Opioids - continued

Drug Class and Uses	Medication	Recommended Starting Dose	Maximum Daily Dose	Comments
Anticonvulsants (various NP types)	Gabapentin	100-300 mg PO one to three times daily	3,600 mg PO per day in 3 divided doses	Used in PHN and NP. May cause drowsiness, dizziness, peripheral edema. Dose adjust for renal impairment.
	Pregabalin	25-75 mg PO twice daily	600 mg PO per day in 3 divided doses	Used in DN, PHN, FM, and NP. May cause drowsiness, dizziness, peripheral edema. Dose adjust for renal impairment.
	Carbamazepine	100 mg PO twice daily	1,200 mg PO per day in 2 divided doses	Used in TGN and NP. Associated with aplastic anemia, agranulocytosis, bone marrow suppression, severe dermatologic reactions, hyponatremia. May cause drowsiness, dizziness, nausea. Significant drug interactions. Avoid in hepatic dysfunction.
	Oxcarbazepine	150-300 mg PO daily	2,400 mg PO per day in 2 divided doses	Used in TGN and NP. Associated with severe dermatologic reactions, hyponatremia. May cause drowsiness, dizziness. Dose adjust for renal impairment.
	Topiramate	25-50 mg PO twice daily	200 mg PO twice per day	Used in NP, cluster headaches, and migraine prevention. May cause acidosis, drowsiness, dizziness, nausea. Dose adjust for renal impairment and hepatic dysfunction.
	Tiagabine	4 mg PO at bedtime	8 mg PO per day	Used in NP. May produce seizures in patients with prior seizure history. May cause drowsiness, dizziness, diarrhea. Use with caution if hepatic dysfunction. Higher doses resulted in increased side effects.
Tricyclic Antidepressants (TCA)	Amitriptyline	10-25 mg PO at bedtime	150 mg PO at bedtime	Consider for continuous and shooting neuropathic pain. Caution in elderly or frail, or patients with glaucoma or arrhythmias. May cause sedation, arrhythmias, dry mouth, orthostasis, urinary retention. Consider duloxetine for NP, DN. Caution in patients with seizures; avoid MAOIs, other SSRIs or SNRIs due to potential for serotonin syndrome. Duloxetine 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. Taper slowly.
	Nortriptyline	10-25 mg PO at bedtime	75 mg PO at bedtime	
	Desipramine	10-25 mg PO at bedtime	150 mg PO at bedtime	
Serotonin-Norepinprine Reuptake Inhibitors (SNRI)	Duloxetine	20-30 mg PO daily	60 mg PO per day	
	Venlafaxine	37.5 mg PO daily	225 mg PO per day	

DN = diabetic neuropathy
PHN = post herpetic neuralgia
FM = fibromyalgia
SSRIs = selective serotonin reuptake inhibitors
MAOI = monoamine oxidase inhibitors
TGN = trigeminal neuralgia
NP = neuropathic pain

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APPENDIX C: Non-Opioids - continued

Drug Class and Uses	Medication	Recommended Starting Dose	Maximum Daily Dose	Comments
Muscle relaxants (muscle pain, spasm)	Baclofen[1]	5 mg PO twice daily	80 mg PO per day in 3 to 4 divided doses	Caution in patients with seizures, cardiovascular disease, glaucoma, myasthenia gravis, renal or hepatic impairment, patients on tricyclic antidepressants or MAOIs, or the elderly. May cause anticholinergic effects and significant drowsiness. Caution with additive sedation if used with other central nervous system depressants. Methocarbamol IV: may repeat course after drug free interval of 48 hours. **Note:** IV route is contraindicated in patients with renal dysfunction due to presence of polyethylene glycol.
	Cyclobenzaprine	5 mg PO three times daily	30 mg PO per day in 3 divided doses	
	Metaxalone	400 mg PO three times daily	3,200 mg PO per day in 3 to 4 divided doses	
	Methocarbamol	500-750 mg PO every 8 hours 1,000 mg IV every 8 hours	4,000 mg per day in 3 to 6 divided doses; IV maximum dose is 3,000 mg per day for 3 days maximum if PO not possible	
	Tizanidine	2-4 mg PO at bedtime	36 mg PO per day in 2 to 3 divided doses	
Corticosteroids (inflammation, nerve compression)	Dexamethasone	Varies by clinical situation (IV or PO) Standard dose 4 -16 mg/day	Varies by clinical situation	May cause impaired healing, infection, thrush, hyperglycemia, weight gain, myopathy, stomach upset, psychosis, emotional instability. Perineal burning/itching may occur with IV.

MAOI = monoamine oxidase inhibitors

[1] Intrathecal formulation not on MD Anderson Cancer Center Formulary

APPENDIX D: Opioid Dose Considerations (Medications are listed from weakest to strongest at the beginning of Appendix D)

Opioid	Initial short-acting dose in an opioid naïve patient		Onset (minutes)	Peak effect (hours)	Duration (hours)	Available oral dose formulations and frequency	Comments
	Route	Dose					
Codeine	PO IV/SC	30-60 mg N/A	30-60 -	1-1.5 -	4-8 -	Short-acting[1]: 15, 30, 60 mg tablets Frequency: every 6 hours	Available alone or in combination with 300 mg acetaminophen[2]. Avoid use in renal and/or hepatic dysfunction[3].
Tramadol	PO IV/SC	25-50 mg N/A	30-60 -	1.5 -	3-7 -	Short-acting (immediate release [IR][1]: 50 mg tablets Frequency: every 6 hours Long-acting (extended release [ER])[4]: 100, 200, 300 mg tablets Frequency: daily	Available alone or 37.5 mg dose in combination with 325 mg acetaminophen[2,5]. Increased risk of serotonin syndrome[6]. May lower seizure threshold. Maximum daily dose 400 mg; consider lower doses if history or increased risk of seizures. Use with caution in renal and/or hepatic dysfunction[3].
Tapentadol	PO	50-100 mg	< 60	1.25-1.5	4-6	Short-acting (IR)[1]: 50, 75, 100 mg tablets Frequency: every 4-6 hours Long-acting (ER)[4]: 50, 100 mg tablets Frequency: every 12 hours	Avoid MAOIs, SSRIs, or SNRIs due to potential risk for serotonin syndrome. Maximum daily doses: tapentadol IR 600 mg and tapentadol ER 500 mg. Use with caution in renal and/or hepatic dysfunction[3]. Avoid use if creatinine clearance < 30 mL/minute[3].
Hydrocodone	PO IV/SC	5-10 mg N/A	10-20 -	1-3 -	4-8 -	Short-acting[1]: 5, 7.5, 10 mg tablets; 2.5 mg/5 mL liquid (in combination with acetaminophen[2]) Frequency: every 6 hours Long-acting[4]: hydrocodone ER (Hysingla®ER) 20, 30, 40, 60, 80, 100, 120 mg tablets Frequency: daily hydrocodone ER[5] (Zohydro® ER) 10, 15, 20, 30, 40, 50 mg tablets Frequency: every 12 hours	Doses greater than 160 mg/day of hydrocodone ER (Hysingla® or Zohydro® ER) have been associated with increased risk of QTc prolongation. Use with caution in renal and/or hepatic dysfunction[3].

MAOI = monoamine oxidase inhibitors SNRIs = serotonin-norepinephrine reuptake inhibitors SSRIs = selective serotonin reuptake inhibitors TCAs = tricyclic antidepressants

[1] Short acting formulations may be given via enteral tubes (*e.g.*, nasogastric tube, percutaneous endoscopic gastrostomy (PEG) tube, gastric tube)

[2] Must consider all forms of acetaminophen (combination and individual) when determining total daily dosing. Manufacturers of over-the-counter acetaminophen recommend no more than 3,000 mg daily.

[3] Refer to Appendix H for Renal Dosing for Opioids

[4] Do not crush, chew, or dissolve long-acting formulations

[5] Not on MD Anderson Cancer Center Formulary

[6] When used with TCAs, MAOIs, SSRIs, SNRIs, and/or CYP262 or CYP3A4 inhibitors

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APPENDIX D: Opioid Dose Considerations - continued (Medications are listed from weakest to strongest at the beginning of Appendix D)

Opioid	Initial short-acting dose in an opioid naïve patient		Onset (minutes)	Peak Effect (hours)	Duration (hours)	Available oral dose formulations and frequency	Comments
	Route	Dose					
Morphine	PO IV/SC	5-15 mg 2-3 mg	30 5-10	0.5-1 -	3-6 -	Short-acting[1]: 15, 30 mg tablets; 10 mg/5 mL, 20 mg/5 mL, 20 mg/mL liquid Frequency: every 4 hours Long-acting[2]: 15, 30, 60, 100, 200 mg tablets Frequency: every 12 hours for 15 mg dose, or daily for higher doses	Oral formulations available as tablet or liquid preparation. Avoid use in renal dysfunction[3]. Use with caution in liver dysfunction.
Oxycodone	PO IV/SC	5-10 mg N/A	10-15 N/A	0.5-1 N/A	3-6 N/A	Short-acting[1]: 5, 10, 15, 30 mg tablets; 5 mg/5 mL, 20 mg/mL liquid Frequency: every 4 hours Long-acting[2]: 10, 15, 20, 30, 40, 60, 80 mg tablets Frequency: every 12 hours	Oral formulations available as tablet or liquid preparation. Available alone or in combination with acetaminophen[4] (*e.g.*, oxycodone 5 mg with acetaminophen 325 mg in Percocet®). Use with caution in renal and/or liver dysfunction[3].
Oxymorphone	PO IV/SC	5-10 mg 0.5 mg	no data 5 - 10	0.5-1 N/A	3-6	Short-acting[1]: 5,10 mg tablets Frequency: every 4 hours Long-acting[2]: 5, 10, 15, 20, 30, 40 mg tablets Frequency: every 12 hours	Poor bioavailability - must be taken on empty stomach. Use with caution in renal and/or liver dysfunction[3].
Hydromorphone	PO IV/SC	1-3 mg 0.5-1.5 mg	15-30 15-30	0.5-1 N/A	3-5 4-5	Short-acting[1]: 2, 4, 8 mg tablets; 1 mg/mL liquid Frequency: every 4 hours Long-acting[2]: 8, 12, 16, 32 mg tablets Frequency: daily	Oral formulations available as tablet or liquid preparation. Use with caution in renal and/or liver dysfunction[3]

[1] Short acting formulations may be given via enteral tubes (*e.g.*, nasogastric tube, percutaneous endoscopic gastrostomy (PEG) tube, gastric tube)

[2] Do not crush, chew, or dissolve long-acting formulations

[3] Refer to Appendix H for Renal Dosing for Opioids

[4] Must consider all forms of acetaminophen (combination and individual) when determining total daily dosing. Manufacturers of over-the-counter acetaminophen recommend no more than 3,000 mg daily.

APPENDIX E: Opioid Side Effects – Prevention and Management

Side Effect	Prevention	Management
Sedation Inpatient setting: Assess sedation using the Richmond Agitation Sedation Scale (RASS) as indicated	• Discontinue other sedating medications if appropriate • Educate all patients receiving opioids that drowsiness may result for a few days following initiation or increase in opioid regimen	• Consider rotation or dose reduction of opioid if sedation persists • Consider psychostimulant: 1. Methylphenidate (Ritalin®) 2.5-5 mg PO once or twice daily (last dose no later than 4 pm to avoid insomnia). Suggested times: 8 am and 12 noon daily. Needs controlled substance Class II (CII) prescription **or** 2. Consider modafinil 100 mg once or twice daily
Opioid induced neurotoxicity Risk factors: • High opioid dose • Dehydration • Renal failure • Preexisting borderline cognition and/or delirium • Use of other psychoactive drugs	Eliminate non-essential CNS activating or depressing drugs (*e.g.,* benzodiazepines)	• Evaluate for reversible causes such as metabolic disorders, liver or renal dysfunction, dehydration, hypercalcemia, organic brain disease; treat as appropriate. • Consider one or more of the following: 1. Opioid rotation (see Appendix I) 2. Opioid dose reduction or discontinuation 3. Discontinue other offending drugs (benzodiazepines) 4. Hydration 5. Symptomatic treatment with haloperidol 1-5 mg PO, IV, **or** SC every 4 hours as needed • Avoid using naloxone even if delirium is thought to be due to opioid use • Refer to Delirium – Adult Inpatient algorithm as indicated
Respiratory depression	• Monitor sedation and respiratory status (respiratory rate and oxygen saturation) during the first 24 hours in opioid naïve patients • Titrate opioids cautiously • Consider dose reduction or opioid rotation if patient has excessive sedation	• Call MD, HOLD opioids, provide supplemental oxygen • If patient minimally responsive or unresponsive and respiratory rate is ≤ 8 bpm, administer naloxone. Recommended dose: naloxone 0.4 mg diluted in 9 mL sodium chloride (0.9%) for total volume of 10 mL, give 0.5 mL (0.02 mg) via slow IV push every 2 minutes until patient is more awake and respiratory status improves. *(Half life of naloxone is short and patient may need naloxone infusion for long-acting opioids. If no change with naloxone, rule out other causes for the respiratory depression.)* • If patient is actively dying, DNR (do not resuscitate) and receiving comfort care, naloxone administration may not be appropriate

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APPENDIX E: Opioid Side Effects – Prevention and Management - continued

Side Effect	Prevention	Management
Nausea, Vomiting	• Nausea and vomiting may be associated with opioid initiation or high doses of opioids • Titrate opioid dose slowly and steadily • Patients at high risk of nausea consider scheduled antiemetic for 5 days and then change to PRN	1. Evaluate for other causes of nausea [for example, constipation, bowel obstruction, chemotherapy (refer to Adult Antiemetic Management of Chemotherapy-Induced Nausea and Vomiting (CINV) algorithm) or other medications] and treat per guidelines. Initiate scheduled antiemetics, if indicated. Example: metoclopramide 5 to 10 mg PO, IV, or SC every 6 hours. 2. Add or increase non-opioid or adjuvant medications for additional pain relief so opioid dose can be reduced 3. If pain control/regimen is satisfactory, reduce opioid dose by 25% 4. If nausea remains refractory, consider opioid rotation (see Appendix H) 5. Refer to Post-Op Nausea and Vomiting Management algorithm as indicated
Constipation	Unless alterations in bowel patterns such as bowel obstruction or diarrhea exist, all patients receiving opioids should be started on laxative bowel regimen and receive education for bowel management. 1. Stimulant laxative plus stool softener: For example: Senokot-S (senna 8.6 plus docusate 50 mg), 2 tablets/day and titrate up maximum 9 tablets/day 2. Ensure adequate fluids, dietary fiber and exercise if feasible 3. Prune juice followed by warm beverage may be considered	1. Evaluate for causes of constipation (such as recent opioid dose increase, use of other constipating medications, new bowel obstruction) 2. Increase Senokot-S®(or senna and docusate tablets if using separate) and add 1 or both of the following: a. Milk of magnesia oral concentrate (1,200/5 mL) 10 mL PO every 2-4 times daily b. Polyethylene glycol (MiraLAX™) 17 grams in 8 ounce beverage PO daily 3. If no response to above, perform digital rectal exam (DRE) to rule out low impaction (do not perform if neutropenic, thrombocytopenic, or post-operative bowel surgery) Continue above steps **and** • If impacted: disimpact manually if stool is soft. If not, soften with mineral oil fleet enema before disimpaction. Follow up with milk and molasses enemas per rectum until clear with no formed stools. • Consider use of short-acting analgesics before disimpaction • If not impacted on rectal examination, patient may still have higher level impaction. Consider abdominal imaging and/or administer milk and molasses enema per rectum along with 8 ounces of PO magnesium citrate. 4. Methylnaltrexone (Relistor®) may be given to patients who meet the following criteria: • Patient experiencing opioid-induced constipation • Patient has not demonstrated an adequate response to other laxative therapy • Patient does not have a known or suspected mechanical gastrointestinal obstruction

APPENDIX F: Patient Controlled Analgesia (PCA)

Suggested initial PCA settings: All opioid doses must be individualized. Use the institutional order set for all new PCA orders and dose changes. Refer to Patient Controlled Analgesia (PCA) Administration Procedure (#ATT1857) for assessment and monitoring guidelines.

1. Opioid naïve patients

Opioid	Demand (PCA) dose (maximum dose)	Lock out interval (minutes)	1-hour dose limit (optional)	Continuous dose (Basal)	Nurse bolus prn dose (maximum dose)	Nurse bolus interval (hours)
Morphine (milligrams)	0.5 mg (2.5 mg)	10-30 minutes	4 mg	See below	1 mg (4 mg)	2
Hydromorphone (milligrams)	0.1 mg (0.5 mg)	10-30 minutes	0.8 mg	See below	0.25 mg (1 mg)	2
Fentanyl (micrograms)	5 mcg (25 mcg)	10-30 minutes	40 mcg	See below	12.5 mcg (25 mcg)	2

a. Patient should be alert and demonstrate ability to administer demand dose for pain. If concerns about cognitive failure or significant anxiety, consider Specialty Consultation: Acute Pain, Chronic Pain, Supportive Care (see Appendix B for description of services).

b. Carefully consider adding continuous (basal) dose after 12-24 hours if using frequent demand doses or if pain not controlled. Suggested basal dose is 30-50% of average hourly dose. Example: The 12 hour total morphine demand dose is 20 mg, calculate continuous dose as 20/12 = 1.7 mg/hour then 1.7 X 0.3 (30%) = 0.5 mg/hour basal rate.

2. Opioid tolerant patients (currently receiving opioid therapy).

PCA orders should take into account the patient's current opioid regimen, clinical situation (severity and etiology of the pain, side-effects from opioids, baseline drowsiness, need for opioid rotation). If there are significant side effects, drowsiness, confusion, respiratory or central nervous system concerns, it is recommended to call for Specialty Consultation: Acute Pain, Chronic Pain, Supportive Care (see Appendix B for description of services) for PCA ordering.

a. Calculate total dose of opioid (scheduled and PRN doses) used in the previous 24 hour period

b. Use equianalgesic opioid dose conversion table (Appendix I) to calculate dose of IV opioid being considered for PCA. Decrease dose by 30-50% to adjust for lack of complete cross tolerance to obtain new IV dose.

c. Divide new IV dose (from above step) by 24 hours, to obtain hourly (basal) dose

d. Calculate demand (PCA) dose as 10-20% of new IV opioid dose to use PRN every hour

APPENDIX G: Substance Use Disorder Treatment Services

Note: Most treatment facilities require insurance coverage or sufficient money to cover treatment. If patient has insurance, call the customer service number to find a facility in-network to avoid a large out-of-pocket debt. Refer to Case Management for assistance.

- Treatment Facilities for Alcohol and Drug Abuse
  Houston, Texas
  1-800-304-2219
- Bay Area Recovery Center
  1807 FM 517
  East Dickinson, Texas 77539
  (713) 705-3457
- The Council on Recovery
  Houston, Texas
  www.councilonrecovery.org
- Clearinghouse for treatment, education, and recovery groups, *etc.*
  303 Jackson Hill St.
  Houston, Texas 77007
  (713) 914-0556, (281) 866-7557
- UT Health Houston Behavioral and Biomedical Science Building
  941 East Rd. First floor
  Houston, Texas 77054
  (713) 500-3784
- Hazelden Betty Ford
  Multiple locations around the country
  1-866-831-5700
- The Treehouse
  Scurry, Texas (South of Dallas)
  1-888-683-1406
- St. Joseph Hospital
  1401 St. Joseph Parkway
  Houston, Texas 77002
  (713) 575-1000; 1-800-466-0792
- West Oaks Hospital (Dr. George Santos)
  https://westoakshospital.com
  6500 Hornwood
  Houston, Texas 77074
- UT Health Harris County Psychiatric Center (HCPC)
  2800 South MacGregor Way
  Houston, TX 77021
  (713) 741-5000
- SAMHSA, Substance Abuse and Mental Health Services Administration
  Behavioral Health Treatment Services Locator:
  https://www.samhsa.gov/find-treatment
  Enter patient's address and zip code on website
  1-800-622 4357
- The Menninger Clinic
  12301 S. Main St.
  Houston, Texas 77035-6207
  (713) 275-5000
- Narcotics Anonymous
  www.na.org
  Houston area Narcotics Anonymous
  www.hascona.org
  (713) 661-4200

APPENDIX H: Renal Dosing for Opioids

Opioid	Renal Dosing
Pure mu-opioids (morphine, codeine and codeine products, hydrocodone, hydromorphone, oxycodone, oxymorphone, fentanyl, methadone)	CrCl < 15 mL/minute: • Consider dose reduction of 25-50% of usual dose and greater dosing interval (every 6-8 hours) • Preferred opioids in renal failure: fentanyl, methadone, hydromorphone • Avoid morphine and codeine if possible • Avoid initiating long-acting opioid and consult pain specialty team Dialysis: Dialysis depends on mode of dialysis and filter, please refer to UpToDate® Lexidrug™ for further dosing guidance
Tramadol	CrCl < 30 mL/minute: • Increase dosing interval to every 12 hours • Maximum dose is 200 mg/day • Extended release (ER) formulation should be avoided Dialysis: • Initiate immediate release 25 mg PO every 12 hours • Maximum dose is 100 mg/day (uremic state may lower seizure threshold) • ER formulation should be avoided
Tapentadol	CrCl < 30 mL/minute: Use not recommended

APPENDIX I: Equianalgesic Opioid Dose Conversion

Note: This chart is based on the Centers for Disease Control and Prevention (CDC) recommendations (https://www.cdc.gov/opioids/providers/prescribing/guideline.html). The equianalgesic doses (oral and parenteral) can be affected by interpatient variability, type of pain (*e.g.,* acute versus chronic), chronic administration, and tolerance. The following table should serve as a guide when switching from one opioid to another. It is recommended to reduce the dose of the new opioid by 30-50% to account for incomplete cross tolerance, and to periodically monitor for efficacy and adverse reactions and the dose adjusted accordingly.

Opioid	Oral Dose (PO)	Parenteral Dose (IV/SC)	Conversion Factor: Parenteral to Oral Opioid	Conversion Factor: Oral Opioid to Oral Morphine
Morphine	15 mg	6 mg	2.5	1
Oxycodone	10 mg	N/A	N/A	1.5
Hydrocodone	15 mg	N/A	N/A	1
Oxymorphone	5 mg	0.5 mg	10	3
Hydromorphone	4 mg	1.5 mg	2.5	4
Fentanyl [1]	N/A	60 mcg	N/A	Should be managed by clinicians experienced in pain management
Methadone and buprenorphine should only be initiated and managed by clinicians experienced in pain management. Consider consult to pain specialists if needed.				

[1] See Appendix J for transdermal fentanyl conversion

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APPENDIX I: Equianalgesic Opioid Dose Conversion - continued

Steps for Opioid Rotation:

1. Stop current opioid regimen
2. Calculate total dose of current opioid (scheduled and PRN doses) used in the previous 24 hour period
3. Calculate the dose of the new opioid using the equianalgesic dose conversion table (from previous page) and conversion equation (below)

$$\frac{\text{Equianalgesic dose per route of CURRENT opioid}}{\text{24 hour dose per route of CURRENT opioid}} = \frac{\text{Equianalgesic dose per route of NEW opioid}}{\text{24 hour dose per route of NEW opioid}}$$

4. Calculate for incomplete cross-tolerance between opioids. Decrease the target dose from step 3 by 30-50% to obtain the new opioid dose.
5. Calculate scheduled pain dose. Divide the new opioid dose (from step 4) by number of doses to be given over 24 hours and administer as scheduled doses.
6. Calculate breakthrough pain dose as 10-20% of calculated new opioid dose to administer PRN every 1 hour
7. Titrate new opioid regimen until adequate analgesia is achieved

Opioid Rotation Example: Rotation from morphine PCA (total daily dose of 120 mg IV) to oral oxycodone

1. Stop current opioid regimen
2. Calculate dose of current opioid (scheduled and PRN doses) used in the previous 24 hours which equals 120 mg IV morphine.
3. Calculate the dose of the new opioid using the equianalgesic dose conversion table and conversion equation (below):

   a. Calculate IV morphine to PO morphine based on conversion table and conversion equation:

$$\frac{\text{6 mg IV morphine}}{\text{120 mg IV morphine over 24 hours}} = \frac{\text{15 mg PO morphine}}{\text{X mg PO morphine over 24 hours}} \quad X = 300 \text{ mg PO morphine}$$

   b. Calculate PO morphine to PO oxycodone based on conversion table:

$$\frac{\text{300 mg PO morphine}}{\text{X mg PO oxycodone}} = \frac{\text{15 mg PO morphine}}{\text{10 mg PO oxycodone}} \quad X = 200 \text{ mg PO oxycodone}$$

4. Calculate for incomplete cross-tolerance. After a 30-50% dose reduction, the oxycodone dose calculated above should be between 100 and 140 mg per day.
5. Calculate scheduled pain dose. Extended release (ER) oxycodone is dosed every 12 hours; recommend ER oxycodone 60 mg every 12 hours (based on tablet availability).
6. Calculate breakthrough pain dose as 10-20% of 120 mg oxycodone dose and administer PRN every 1 hour
   a. Immediate release (IR) oxycodone is between 12 and 24 mg per dose and may be administered every 1 to 4 hours
   b. Based on tablet availability recommend IR oxycodone 10 to 20 mg every 1 to 4 hours as needed for breakthrough pain
7. Titrate new opioid regimen until adequate analgesia is achieved

APPENDIX J: Fentanyl

Dosage Forms	Onset	Peak	Duration	Doses Available per Formulary	Comments
Parenteral (IV/Subcutaneous)	Almost immediate	Several minutes	0.5-1 hour	0.05 mg/mL (5 mL vial for injection) PCA syringe supplied as 2,500 mcg/50 mL	
Transdermal patch[1]	12-24 hours	24-72 hours	48-72 hours	12 (delivers 12.5), 25, 50, 75, 100 mcg/hour	Bioavailability 90%; Do *not* cut patch, apply heat, or use in patients who develop fever - results in faster onset, shorter duration, and possible overdose. After transdermal patch removal, continued absorption of fentanyl occurs from the skin. Delayed administration of another long-acting opioid should be considered due to persistent serum levels of fentanyl. Due to differences in bioavailability, fentanyl products are not interchangeable on a microgram-to-microgram basis.

Drug specific characteristics:

- Fentanyl is 80 to 100 times more potent than morphine. Fentanyl is not recommended for initial use in opioid naïve patients. Use in non-opioid tolerant patients may lead to fatal respiratory depression.
- Transdermal fentanyl should only be used in patients with stable opioid requirements. Due to its long half-life of 17 hours, the dose may be difficult to titrate if pain is not well-controlled.
- When initiating transdermal fentanyl, patients should use short-acting opioids as needed until efficacy is obtained (peak effect 24-72 hours).
- Titrate patients on transdermal fentanyl no more frequently than every 3 days after initial dose, and then every 6 days thereafter. Initial evaluation of maximum analgesic effect should not be made before 24 hours.
- Caution with CYP450 3A4 inhibitors, which can increase fentanyl plasma concentrations
- May be used in patients with renal dysfunction

Morphine to Fentanyl conversion: 1 mg of IV morphine or 2.5 mg of oral morphine = 10 micrograms of IV fentanyl

Example: Conversion from oral morphine ER 90 mg every 12 hours to IV Fentanyl

1. 24 hour morphine dose is 90 + 90 = 180 mg
2. Decrease 180 mg by 30% for incomplete tolerance = 126 mg
3. 1 mg IV morphine = 2.5 mg oral morphine = 10 micrograms IV fentanyl, then new 24 hour morphine dose of 126 mg = 24 hour IV fentanyl dose of 504 micrograms
4. Divide 24 hour fentanyl dose calculated by 24 hours = 21 micrograms/hour

Thus an appropriate starting dose for IV fentanyl/hour (as basal rate in PCA) is 20 micrograms/hour

[1] After Transdermal patch removal, continued absorption of fentanyl occurs from the skin. Delayed administration of another long-acting opioid should be considered due to persistent serum levels of fentanyl. Due to differences in bioavailability, fentanyl products are not interchangeable on a mcg to mcg basis.

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APPENDIX J: Fentanyl - continued

Transdermal Fentanyl (TDF) Dosing:

Option 1: 2 mg oral morphine approximately 1 mcg ***per hour*** transdermal fentanyl
Example: Total daily dose of morphine 100 mg translates to approximately 50 mcg transdermal patch, to be applied every 72 hours

Option 2: Calculate the total daily dose of morphine and then use the following table to select the appropriate patch strength

Oral Morphine (mg/day)	Transdermal Fentanyl (mcg/hour)
30 to 90	25
91 to 150	50
151 to 210	75
211 to 270	100
Each additional 60 mg/day	An additional 25 mcg/hour

- **Note:** This table should **NOT** be used to convert from TDF to other therapies because this conversion to **TDF** is conservative. Use of this table for conversion to other analgesic therapies can overestimate the dose of the new agent.
- To convert patients to another opioid, remove the transdermal fentanyl patch and titrate the dose of the new analgesic based upon the patient's report of pain until adequate analgesia has been attained. Upon system removal, 17 hours or more are required for a 50% decrease in serum fentanyl concentrations.
- Must prescribe short-acting opioid for breakthrough pain

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MD Anderson Institutional Policy#CLN0540 - Pain Management Policy

MD Anderson Institutional Policy Attachment #ATT1857 - Patient Controlled Analgesia (PCA) Administration Procedure

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