Cancer Pain – Adult

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, pre-procedural, perioperative settings, or currently receiving epidural or intrathecal analgesia.

TABLE OF CONTENTS

Pain Assessment and Treatment - Inpatient ................................................................. Page 2
Pain Assessment and Treatment - Outpatient .............................................................. Page 3
Quick Reference Guide .............................................................................................. Page 4
APPENDIX A: Comprehensive Pain Assessment ....................................................... Page 5
APPENDIX B: Non-opioids .......................................................................................... Page 6
APPENDIX C: Adjuvant “Co-analgesics” for Neuropathic Pain Syndromes and Chronic Pain .......................................................... Pages 7-8
APPENDIX D: Opioid Dose Considerations ............................................................... Pages 9-10
APPENDIX E: Equianalgesic Opioid Dose Conversion ............................................... Pages 11-12
APPENDIX F: Fentanyl ............................................................................................... Pages 13-14
APPENDIX G: Patient Controlled Analgesia (PCA) .................................................. Page 15
APPENDIX H: Opioid Side Effects – Prevention and Management ........................... Pages 16-17
APPENDIX I: Pain Management Education for Patient and Family Prior to Discharge ........................................ Pages 18-19
APPENDIX J: Specialty Services Consultation Guidelines ........................................ Page 20
APPENDIX K: Treatment Services ............................................................................ Page 21
Suggested Readings .................................................................................................... Pages 22-23
Development Credits ............................................................................................... Page 24
Cancer Pain – Adult (Inpatient)

For patients not previously on opioids: choose non-opioids (Appendix B) or if contraindicated, use weak opioids (Appendix D), as needed for pain
- If no side effects, continue current scheduled opioid regimen. For breakthrough pain prescribe short acting opioids (Appendix D) as 10-20% of 24 hour opioid dose every 4 hours as needed. If patient is taking more than 4 breakthrough doses/24 hours, may consider increasing scheduled opioids by 20-30%.
- Manage opioid induced side effects; if indicated, may benefit from decrease/change opioids (Appendix H)

For patients currently taking opioids:
- If pain is greater than or equal to 3 and/or personalized pain goal (PPG) met
  - Pain less than or equal to 3 and/or PPG not met
    - Pain crisis?
    - Reassess as clinically appropriate based on patient’s condition
      - Pain decreased and/or PPG met?
        - Yes
          - Consider starting or adjusting scheduled opioid doses if using more than 3 short-acting doses
        - No
          - Consult specialty services
    - Reassess pain, PPG and opioid side effects at each subsequent visit or interaction
      - Pain decreased and/or PPG met?
        - Yes
          - Consider starting or adjusting scheduled opioid dose if using more than 3 short-acting doses/24 hours
        - No
          - Continue current analgesic regimen
            - If short-acting opioids given, reassess in 1 hour
            - Titrate scheduled and short-acting opioids
            - Consider consult to specialty services
  - Pain greater than or equal to 4 and/or PPG not met
    - For patients not previously on opioids: administer short-acting opioids - choose from weak or strong opioids (Appendix D)
      - Increase opioid dose
        - 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; if indicated, may benefit from decrease/change opioids (Appendix H)
        - Consider specialty consult
      - Consider starting or adjusting scheduled opioids (Appendix D)
        - If no side effects
          - Reassess pain, PPG and opioid side effects at each subsequent visit or interaction

For patients not previously on opioids: choose non-opioids (Appendix B) or if contraindicated, use weak opioids (Appendix D), as needed for pain
- Palliative Specialty consultation services that specialize in pain management
- Consider specialty consult to specialty services

Distress Screening and Psychosocial Management algorithm

1. See Appendix A for Comprehensive Pain Assessment
2. Specialty consultation services that specialize in pain management: Acute Pain, Pain Medicine, Palliative/Supportive Care, and Integrative Medicine; see Appendix J for description of services
3. Pain crisis or emergency is defined as severe pain, new onset or exacerbation of previously stabilized pain, accompanied by significant distress or if present for more than 24 hours
4. For additional information see the Distress Screening and Psychosocial Management algorithm

NOTE: For all patients: Consider using appropriate adjuvants (Appendix C) and/or complementary therapies, bowel regimen (Appendix H), patient education (Appendix I), and psychosocial support (Appendix J) as appropriate
Cancer Pain – Adult (Outpatient)

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, pre-procedural settings, perioperative or currently receiving epidural or intrathecal analgesia.

Assess for pain at each visit or interaction (outpatient)

Yes

Consider referral to Pain Medicine or Supportive Care, evaluation in Emergency Center or hospitalization

No

- Pain in pain crisis?
  - Pain greater than or equal to 4 and/or personalized pain goal (PPG) not met
    - For patients not previously on opioids: choose non-opioids (Appendix B) or if contraindicated, use weak opioids (Appendix D)
    - For patients currently taking opioids: Continue analgesic regimen, opioid regimen/side effects and PPG within 72 hours
  - Pain less than or equal to 3 and/or PPG met
    - Reassess pain, opioid regimen/side effects and PPG within 72 hours
    - Reassess pain, PPG and opioid side effects at subsequent visit or interaction

For patients not previously on opioids: prescribe short-acting opioids - choose from weak or strong opioids (Appendix D)

If pain expected to be continuous, consider scheduling opioids around the clock or long-acting opioids (Appendix D)

For patients currently taking opioids:
- Scheduled opioid: increase dose by 30-50% of prior scheduled dose or equal to calculated prior 24 hour opioid dose, whichever is higher. Administer as around the clock regimen of short-acting opioids or long-acting opioids.
- Calculate short-acting opioids as 10-20% of new opioid regimen and administer every 2 hours as needed
- If opioid induced neurotoxicity (OIN): consider hospitalization and evaluation in the emergency room, opioid rotation (Appendix E), and/or specialty consultation
- Manage other side effects if present (Appendix H)
- Consider specialty consultation

Reassess pain, opioid regimen/side effects and PPG within 72 hours

Side effects resolved and PPG met?

Yes

No

Consider specialty consultation for uncontrolled pain

For patients not previously on opioids: manage opioid induced side effects (Appendix D)

No

For patients currently taking opioids:
- Continue analgesic regimen. Prescribe short-acting opioids, as 10-20% of 24 hour scheduled opioid dose, every 2 to 4 hours as needed. If patient is taking more than 4 breakthrough doses, may consider increasing scheduled opioids by 20-30%.
- Manage opioid induced side effects; if indicated, may benefit from decrease/change opioids (Appendix H)

Reassess pain, opioid regimen/side effects and PPG within 72 hours

Note: For all patients: Consider using appropriate adjuvants (Appendix C) and/or complementary therapies, bowel regimen (Appendix H), patient education (Appendix I), and psychosocial support (Appendix J) as appropriate

1 See Appendix A for Comprehensive Pain Assessment
2 Pain crisis or emergency is defined as severe pain, new onset or exacerbation of previously stabilized pain, accompanied by significant distress or if present for more than 24 hours
3 Specialty consultation services that specialize in pain management: Acute Pain, Pain Medicine, Palliative/Supportive Care, and Integrative Medicine (see Appendix J for description of services)
4 Opioid induced neurotoxicity (OIN) symptoms include drowsiness, cognitive impairment, confusion, hallucinations, myoclonic jerks
5 Opioid induced gastrointestinal side-effects: constipation, nausea, emesis (see Appendix H)

Approved by The Executive Committee of the Medical Staff on 10/31/2017

Copyright 2019 The University of Texas MD Anderson Cancer Center
Quick Reference Guide

- Opioid naïve: Includes patients who are not chronically receiving opioid analgesics on a daily basis and therefore have not developed significant tolerance.
- Opioid tolerant: Patients who are chronically receiving opioid analgesics on a daily basis. The FDA identifies this group as “receiving at least 60 mg of morphine daily, at least 30 mg of oral oxycodone daily, or at least 8 mg of oral hydromorphone daily or an equianalgesic dose of another opioid for a week or longer.”
- Incomplete cross-tolerance: Reduce dose of new opioid by 30 to 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 Pages 2 and 3 of this algorithm for titration recommendations.
- Dosing frequency: For long-acting opioids, dosing frequency is typically every 12 hours to every 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 to 20% of the total daily dose given every 1 to 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 (65 years and older), 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 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, and give 1 mL (0.04 mg) via slow IV push every 2 to 3 minutes until patient 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 (for example, tramadol) or combination opioid preparations (for example, 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 H.
- 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 to 36 hours after transdermal patch removal.
- The Texas Prescription Monitoring Program 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. It can be accessed at https://texas.pmpaware.net/login
## APPENDIX A: Comprehensive Pain Assessment

### The comprehensive pain assessment should include the following:

1. **Pain:**
   - a. For each site of pain, determine intensity level: 0-10 numeric rating scale (NRS) (no pain = 0, mild = 1-3, moderate = 4-6, severe = 7-10).
   - Assess at rest and with activity, location, onset (acute, chronic, acute exacerbation of chronic pain), pathophysiology (somatic, visceral, neuropathic), temporal factors (continuous, intermittent, breakthrough, incidental), etiology (for example, tumor, non-tumor related, fracture).
   - b. Evaluation of medical history includes: oncologic or other significant medical illnesses, medication history, relevant imaging and laboratory studies.
   - c. Physical examination.
   - d. Assess for presence of sedation [inpatient setting, consider Richmond Agitation Sedation Scale (RASS) and common opioid side effects (Appendix H)].

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.

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 which include: 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.

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 (for example, surgery, steroids, radiotherapy, antibiotics) along with an emergent consultation. Oncologic emergencies include:

- Bowel obstruction/perforation
- Leptomeningeal metastasis
- Fracture or impending fracture of weight-bearing bone
- Epidural metastasis/spinal cord compression
- Pain related to infection
APPENDIX B: Non-opioids

CAUTION: All of these agents are antipyretic and may mask fever; use with caution in patients on myelosuppressive chemotherapy. Non-steroidal ant-inflammatory drugs (NSAIDs) may have antplatelet 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 (for example, salsalate, choline magnesium trisalicylate 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.

Non-opioids include acetaminophen and NSAIDs; they may be used alone or in combination with opioids for pain management. NSAIDs are useful adjuvant analgesics for bone pain.

**Recommended Starting Doses:** The choice of non-opioid must depend on the individual risk/benefit balance for each patient. The mechanism of action and side effect profile of each option is different.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Recommended Starting Dose</th>
<th>Maximum Daily Dose</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetaminophen</td>
<td>500-1,000 mg PO every 6 hours as needed</td>
<td>3,000 mg</td>
<td>Available PO and per rectum. At higher doses, can cause fatal hepatotoxicity and renal damage. Avoid use in hepatic dysfunction. Does not have anti-inflammatory effect.</td>
</tr>
<tr>
<td></td>
<td>650 mg IV every 4 hours 1,000 mg IV every 6 hours</td>
<td>Single dose: 1,000 mg/dose; Daily dose: 4,000 mg daily</td>
<td>IV acetaminophen is formulary restricted</td>
</tr>
<tr>
<td>Ibuprofen</td>
<td>200-800 mg PO every 6 hours as needed</td>
<td>3,200 mg</td>
<td>Inhibits platelet aggregation, can cause gastrointestinal side effects or renal failure. Use with caution in patients at high risk.</td>
</tr>
<tr>
<td>Naproxen</td>
<td>500 mg PO initial, then 250 mg every 4 hours as needed</td>
<td>1,500 mg</td>
<td>Inhibits platelet aggregation, can cause gastrointestinal side effects or renal failure. Use with caution in patients at high risk.</td>
</tr>
<tr>
<td>Celecoxib</td>
<td>200-400 mg PO every 12 or 24 hours as needed</td>
<td>400 mg</td>
<td>Does not affect platelet aggregation; can cause renal insufficiency</td>
</tr>
<tr>
<td>Ketorolac</td>
<td>15-30 mg IV or PO every 6 hours as needed</td>
<td>120 mg</td>
<td>Limit treatment to 5 days. Reduce dose by 50% if over 65 years or weight less than 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 and can cause gastrointestinal side effects.</td>
</tr>
</tbody>
</table>

1 Manufacturers of over-the-counter acetaminophen recommend no more than 3,000 mg daily
2 Patients at high risk of serious gastrointestinal side effects or renal damage from NSAIDs include: elderly (greater than 60 years old), smokers, previous history of peptic ulcer, currently receiving corticosteroids, anticoagulants, or presence of existing renal disease, cardiac or liver impairment
APPENDIX C: Adjuvant “Co-analgesics” for Neuropathic Pain Syndromes and Chronic Pain

<table>
<thead>
<tr>
<th>Drug Class and Uses</th>
<th>Medication</th>
<th>Recommended Starting Dose</th>
<th>Maximum Daily Dose</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Anticonvulsants</strong> (various NP types)</td>
<td>Gabapentin</td>
<td>100-300 mg PO daily</td>
<td>3,600 mg PO per day in 3 divided doses</td>
<td>Used in PHN and NP. May cause drowsiness, dizziness, peripheral edema. Dose adjust for renal impairment.</td>
</tr>
<tr>
<td></td>
<td>Pregabalin</td>
<td>25-75 mg PO twice daily</td>
<td>600 mg PO per day in 3 divided doses</td>
<td>Used in DN, PHN, FM, and NP. May cause drowsiness, dizziness, peripheral edema. Dose adjust for renal impairment.</td>
</tr>
<tr>
<td></td>
<td>Carbamazepine</td>
<td>100 mg PO twice daily</td>
<td>1,200 mg PO per day in 2 divided doses</td>
<td>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.</td>
</tr>
<tr>
<td></td>
<td>Oxcarbazepine</td>
<td>150-300 mg PO daily</td>
<td>2,400 mg PO per day in 2 divided doses</td>
<td>Used in TGN and NP. Associated with severe dermatologic reactions, hyponatremia. May cause drowsiness, dizziness. Dose adjust for renal impairment.</td>
</tr>
<tr>
<td></td>
<td>Topiramate</td>
<td>25-50 mg PO twice daily</td>
<td>200 mg PO twice per day</td>
<td>Used in NP. May cause acidosis, drowsiness, dizziness, nausea. Dose adjust for renal impairment and hepatic dysfunction.</td>
</tr>
<tr>
<td></td>
<td>Tiagabine</td>
<td>4 mg PO at bedtime</td>
<td>8 mg PO per day</td>
<td>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.</td>
</tr>
<tr>
<td><strong>Tricyclic Antidepressants</strong> (TCA)</td>
<td>Amitriptyline</td>
<td>10-25 mg PO at bedtime</td>
<td>150 mg PO at bedtime</td>
<td>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.</td>
</tr>
<tr>
<td></td>
<td>Nortriptyline</td>
<td>10-25 mg PO at bedtime</td>
<td>75 mg PO at bedtime</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Desipramine</td>
<td>10-25 mg PO at bedtime</td>
<td>150 mg PO at bedtime</td>
<td>Consider duloxetine for NP, DN and musculoskeletal pain. 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.</td>
</tr>
<tr>
<td><strong>Serotonin-Norepinephrine Reuptake Inhibitors</strong> (SNRI)</td>
<td>Duloxetine</td>
<td>20-30 mg PO daily</td>
<td>60 mg PO per day</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Venlafaxine</td>
<td>37.5 mg PO daily</td>
<td>225 mg PO per day</td>
<td></td>
</tr>
</tbody>
</table>

DN = diabetic neuropathy  
NP = neuropathic pain  
PHN = postherpetic neuralgia  
SSRIs = selective serotonin reuptake inhibitors  
SNRIs = serotonin-norepinephrine reuptake inhibitors  
TCAs = tricyclic antidepressants  
TGN = trigeminal neuralgia

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.

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.

This algorithm should not be used to treat pregnant women. 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.

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.

**Antidepressants**

- **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.
  - Nortriptyline: 10-25 mg PO at bedtime, 75 mg PO at bedtime.
  - Desipramine: 10-25 mg PO at bedtime, 150 mg PO at bedtime. Consider duloxetine for NP, DN and musculoskeletal pain. 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.

- **Serotonin-Norepinephrine 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.

**Anticonvulsants** (various NP types)

- Gabapentin: 100-300 mg PO 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. 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.

**Antidepressants**

- **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.
  - Nortriptyline: 10-25 mg PO at bedtime, 75 mg PO at bedtime.
  - Desipramine: 10-25 mg PO at bedtime, 150 mg PO at bedtime. Consider duloxetine for NP, DN and musculoskeletal pain. 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.

**Antidepressants**

- **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.
  - Nortriptyline: 10-25 mg PO at bedtime, 75 mg PO at bedtime.
  - Desipramine: 10-25 mg PO at bedtime, 150 mg PO at bedtime. Consider duloxetine for NP, DN and musculoskeletal pain. 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.

**Anticonvulsants** (various NP types)

- Gabapentin: 100-300 mg PO 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. 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.
APPENDIX C: Adjuvant “Co-analgesics” commonly used for Neuropathic Pain Syndromes and Chronic Pain – continued

<table>
<thead>
<tr>
<th>Drug Class and Uses</th>
<th>Medication</th>
<th>Recommended Starting Dose</th>
<th>Maximum Daily Dose</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Muscle relaxants</td>
<td>Baclofen⁴</td>
<td>5 mg PO twice daily</td>
<td>80 mg PO per day in 3 to 4 divided doses</td>
<td>Caution in patients with seizures, cardiovascular disease, glaucoma, myasthenia gravis, renal or hepatic impairment, patients on TCAs or MAOIs, the elderly. May cause anticholinergic effects and significant drowsiness. Caution additive sedation if used with other central nervous system depressants</td>
</tr>
<tr>
<td>(muscle pain, spasm)</td>
<td>Cyclobenzaprine</td>
<td>5 mg PO three times daily</td>
<td>30 mg PO per day in 3 divided doses</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Diazepam</td>
<td>2 mg to 10 mg PO three to four times daily then 5mg to 10 mg in 3 to 4 hours</td>
<td>Larger doses may be required if associated with tetanus</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Metaxalone</td>
<td>400 mg PO three times daily</td>
<td>3,200 mg PO per day in 3 to 4 divided doses</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Methocarbamol</td>
<td>500 mg PO four times daily 1,000 mg IV every 8 hours</td>
<td>4,000 mg per day in 3 to 6 divided doses; IV for 3 days maximum if PO not possible</td>
<td>Methocarbamol: may repeat course after drug free interval of 48 hours.</td>
</tr>
<tr>
<td></td>
<td>Tizanidine</td>
<td>2-4 mg PO at bedtime</td>
<td>36 mg per day in 2 to 3 divided doses</td>
<td></td>
</tr>
<tr>
<td>Corticosteroids</td>
<td>Dexamethasone</td>
<td>Varies by clinical situation (IV or PO) Standard dose 4 -16 mg/day</td>
<td>Varies by clinical situation</td>
<td>May cause impaired healing, infection, thrush, hyperglycemia, weight gain, myopathy, stomach upset, psychosis, emotional instability.</td>
</tr>
<tr>
<td>(inflammation, nerve compression)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

MAOI = monoamine oxidase inhibitors  
TCAs = tricyclic antidepressants  
⁴Intrathecal formulation not on MD Anderson Cancer Center Formulary

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.
## APPENDIX D: Opioid Dose Considerations

(Weaker medications are listed at the beginning of Appendix D)

<table>
<thead>
<tr>
<th>Opioid</th>
<th>Initial short-acting dose in an opioid naïve patient</th>
<th>Onset (minutes)</th>
<th>Peak effect (hours)</th>
<th>Duration (hours)</th>
<th>Initial scheduled dosing in opioid naïve patients</th>
<th>Available oral dose formulations</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Codeine</td>
<td>PO IV/SC</td>
<td>30 - 60 mg N/A</td>
<td>30 - 60</td>
<td>1-1.5</td>
<td>4 - 8</td>
<td>Short-acting: 15, 30, 60 mg tablets; Long-acting: N/A</td>
<td>Available alone or in combination with 300 mg acetaminophen&lt;sup&gt;1&lt;/sup&gt;. Avoid use in renal and/or hepatic dysfunction.</td>
</tr>
<tr>
<td>Tramadol</td>
<td>PO IV/SC</td>
<td>25-50 mg N/A</td>
<td>30 - 60</td>
<td>1.5</td>
<td>3-7</td>
<td>Short-acting (IR): 50 mg tablets; Long-acting (ER): 100, 200, 300 mg tablets</td>
<td>Increased risk of serotonin syndrome&lt;sup&gt;2&lt;/sup&gt;. May lower seizure threshold. Maximum daily dose 400 mg; consider lower doses if history or increased risk of seizures. Use with caution in renal dysfunction.</td>
</tr>
<tr>
<td>Tapentadol</td>
<td>PO</td>
<td>50 - 100 mg</td>
<td>less than 60</td>
<td>1.25-1.5</td>
<td>4 - 6</td>
<td>Short-acting: 50, 75, 100 mg tablets; Long-acting: 50, 100, 150, 200, 250 mg tablets</td>
<td>Avoid MAOIs, SSRIs, or SNRIs due to potential risk for serotonin syndrome. New medication orders are restricted to Anesthesiology and Perioperative Medicine, Pain Medicine, or Palliative/Supportive Care. Maximum daily doses: tapentadol IR 600 mg and tapentadol ER 500 mg. Avoid use if creatinine clearance is less than 30 mL/min.</td>
</tr>
<tr>
<td>Hydrocodone</td>
<td>PO IV/SC</td>
<td>5-10 mg N/A</td>
<td>10 - 20</td>
<td>1 - 3</td>
<td>4 - 8</td>
<td>Short-acting: 5, 7.5, 10 mg tablets; 2.5 mg/5 mL liquid, in combination with acetaminophen Long-acting: hydrocodone ER (Hysingla&lt;sup&gt;®&lt;/sup&gt; ER) 20 mg PO once daily hydrocodone ER (Zohydro&lt;sup&gt;®&lt;/sup&gt; ER) (non-formulary) PO 10 mg every 12 hours</td>
<td>Doses greater than 160 mg/day of hydrocodone ER (Hysingla&lt;sup&gt;®&lt;/sup&gt; or Zohydro&lt;sup&gt;®&lt;/sup&gt; ER) have been associated with increased risk of QTc prolongation. Use with caution in renal dysfunction.</td>
</tr>
</tbody>
</table>

<sup>1</sup>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.

<sup>2</sup>When used with TCAs, MAOIs, SSRIs, or SNRIs due to potential risk for serotonin syndrome.

<sup>3</sup>Avoid use of tramadol ER when creatinine clearance is less than 30 mL/min.

---

*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.*

*Copyright 2019 The University of Texas MD Anderson Cancer Center*

*Department of Clinical Effectiveness V11 rev Approved by The Executive Committee of the Medical Staff on 10/31/2017*
APPENDIX D: Opioid Dose Considerations (Weaker medications are listed at the beginning of Appendix D) - continued

<table>
<thead>
<tr>
<th>Opioid</th>
<th>Initial short-acting dose in an opioid naïve patient</th>
<th>Onset (minutes)</th>
<th>Peak Effect (hours)</th>
<th>Duration (hours)</th>
<th>Initial scheduled dosing in opioid naïve patients</th>
<th>Available oral dose formulations</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Morphine</strong></td>
<td>PO: 5-15mg IV/SC: 2-3 mg</td>
<td>30</td>
<td>0.5 - 1</td>
<td>3 - 6</td>
<td>Short-acting: 5-10 mg PO every 4 hours; 2-4 mg IV every 4 hours Long-acting: 15 mg PO every 12 hours, or 20 or 30 mg PO once daily</td>
<td>Short-acting: 15, 30 mg tablets; 10 mg/5 mL, 20 mg/5 mL, 20 mg/mL liquid Long-acting: 15, 30, 60, 100 mg tablets</td>
<td>Available as tablet or liquid preparation. Short-acting preparations can be given via PEG tube. Avoid use in renal dysfunction.</td>
</tr>
<tr>
<td><strong>Oxycodone</strong></td>
<td>PO: 5-10mg IV/SC: N/A</td>
<td>10-15</td>
<td>0.5 - 1</td>
<td>3 - 6</td>
<td>Short-acting: 5 mg PO every 4 hours. Long-acting: 10 mg PO every 12 hours</td>
<td>Short-acting: 5, 15, 30 mg tablets; 5 mg/5 mL, 20 mg/ml liquid Long-acting: 10, 20, 40, 80 mg tablets</td>
<td>Available alone or in combination with acetaminophen (e.g., oxycodone 5 mg with acetaminophen 325 mg in Percocet®). Use with caution in renal dysfunction.</td>
</tr>
<tr>
<td><strong>Oxymorphone</strong></td>
<td>PO: 5-10 mg IV/SC: 0.5 mg</td>
<td>no data</td>
<td>0.5 - 1</td>
<td>3 - 6</td>
<td>Short-acting: 5 mg PO every 4 hours. Long-acting: 5 mg PO every 12 hours</td>
<td>Short-acting: 5,10 mg tablets Long-acting: 5, 10, 20, 40 mg tablets</td>
<td>Poor bioavailability - must be taken on empty stomach. Use with caution in renal dysfunction.</td>
</tr>
<tr>
<td><strong>Hydromorphone</strong></td>
<td>PO: 1-3 mg IV/SC: 0.5-1.5 mg</td>
<td>15 - 30</td>
<td>0.5 - 1</td>
<td>3 - 5</td>
<td>Short-acting: 2 mg PO every 4 hours IV/SC: 0.5-1 mg every 4 hours Long-acting: 8 mg PO every 24 hours</td>
<td>Short-acting: 2, 4, 8 mg tablets; 1 mg/mL liquid Long-acting: 8, 12, 16, 32 mg tablets</td>
<td>Use with caution in renal dysfunction.</td>
</tr>
</tbody>
</table>

1. 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: Equianalgesic Opioid Dose Conversion**

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: The equianalgesic doses (oral and parenteral) can be affected by interpatient variability, type of pain (for example, 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 to 50% to account for incomplete cross tolerance, and to periodically monitor for efficacy and adverse reactions and the dose adjusted accordingly.

<table>
<thead>
<tr>
<th>Opioid</th>
<th>Oral Dose (PO)</th>
<th>Parenteral Dose (IV/SC)</th>
<th>Conversion Factor: Parenteral to Oral Opioid</th>
<th>Conversion Factor: Oral Opioid to Oral Morphine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morphine</td>
<td>30 mg</td>
<td>12 mg</td>
<td>2.5</td>
<td>1</td>
</tr>
<tr>
<td>Oxycodone</td>
<td>20 mg</td>
<td>N/A</td>
<td>N/A</td>
<td>1.5</td>
</tr>
<tr>
<td>Hydrocodone</td>
<td>30 mg</td>
<td>N/A</td>
<td>N/A</td>
<td>1</td>
</tr>
<tr>
<td>Oxytomorphine</td>
<td>10 mg</td>
<td>1 mg</td>
<td>10</td>
<td>3</td>
</tr>
<tr>
<td>Hydromorphone</td>
<td>7.5 mg</td>
<td>3 mg</td>
<td>2.5</td>
<td>4</td>
</tr>
<tr>
<td>Fentanyl 2</td>
<td>N/A</td>
<td>120 mcg</td>
<td>N/A</td>
<td>Should be managed by clinicians experienced in pain management</td>
</tr>
</tbody>
</table>

Methadone and buprenorphine should only be initiated and managed by clinicians experienced in pain management. Consider consult to pain specialists if needed.

1 This Equianalgesic Opioid Dose Conversion chart is based on the CDC’s recommendations (https://www.cdc.gov/drugoverdose/resources/data.html)
2 See Appendix F for transdermal conversion
APPENDIX E: 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).

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

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:

\[
\frac{6 \text{ mg IV morphine}}{120 \text{ mg IV morphine over 24 hours}} = \frac{15 \text{ mg PO morphine}}{X \text{ mg PO morphine over 24 hours}}
\]

\[X = 300 \text{ mg PO morphine}\]

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

\[
\frac{300 \text{ mg PO morphine}}{X \text{ mg PO oxycodone}} = \frac{15 \text{ mg PO morphine}}{10 \text{ mg PO oxycodone}}
\]

\[X = 200 \text{ mg PO oxycodone}\]

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 recommended 120 mg oxycodone dose and administer PRN every 1 hour.
7. Titrate new opioid regimen until adequate analgesia is achieved.

This Equianalgesic Opioid Dose Conversion Chart is also available in Lexicomp.

Copyright 2019 The University of Texas MD Anderson Cancer Center
**APPENDIX F: Fentanyl**

<table>
<thead>
<tr>
<th>Dosage Forms</th>
<th>Onset</th>
<th>Peak</th>
<th>Duration</th>
<th>Doses Available per Formulary</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parenteral (IV/Subcutaneous)</td>
<td>Almost immediate</td>
<td>Several minutes</td>
<td>0.5-1 hour</td>
<td>0.05 mg/mL (5 mL vial for injection) PCA syringe supplied as 2,500 mcg/50 mL</td>
<td></td>
</tr>
<tr>
<td>Transdermal patch¹</td>
<td>12-24 hours</td>
<td>24-72 hours</td>
<td>48-72 hours</td>
<td>12 (delivers 12.5), 25, 50, 75, 100 mcg/hour</td>
<td>Bioavailability 90%; Do not cut patch, apply heat, or use in patients who develop fever - results in faster onset, shorter duration, and possible overdose.</td>
</tr>
<tr>
<td>Transmucosal lozenge (Actiq²)</td>
<td>5-15 minutes</td>
<td>20-40 minutes</td>
<td>Related to blood level</td>
<td>200, 400, 600 mcg</td>
<td>Bioavailability: 50%</td>
</tr>
<tr>
<td>Sublingual Tablet (Abstral³)</td>
<td>5-15 minutes</td>
<td>30-60 minutes</td>
<td>2 hours</td>
<td>100, 200, 300, 400, 600, 800 mcg</td>
<td>Bioavailability: 54%</td>
</tr>
</tbody>
</table>

**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.
- Prior to processing initial prescriptions for rapid onset fentanyl, the prescriber must register with the TIRF REMS Access Program and complete a Prescriber and Patient agreement.

**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 micrograms to micrograms basis.

*Continued on next page*
APPENDIX F: Fentanyl - continued

Transdermal Fentanyl (TDF) Dosing:

Option 1: 2 mg oral morphine is approximately 1 microgram per hour transdermal fentanyl
Example: Total daily dose of morphine 100 mg translates to: approximately 50 micrograms 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

<table>
<thead>
<tr>
<th>Oral Morphine (mg/day)</th>
<th>Transdermal Fentanyl (mcg/hour)</th>
</tr>
</thead>
<tbody>
<tr>
<td>30 to 90</td>
<td>25</td>
</tr>
<tr>
<td>91 to 150</td>
<td>50</td>
</tr>
<tr>
<td>151 to 210</td>
<td>75</td>
</tr>
<tr>
<td>211 to 270</td>
<td>100</td>
</tr>
<tr>
<td>Each additional 60 mg/day</td>
<td>An additional 25 mcg/hour</td>
</tr>
</tbody>
</table>

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.
APPENDIX G: 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)

1. **Opioid naïve patients**

<table>
<thead>
<tr>
<th>Opioid</th>
<th>Demand (PCA) dose (dose range)</th>
<th>Lock out interval (minutes)</th>
<th>1-hour dose limit (optional)</th>
<th>Continuous dose (basal)</th>
<th>Nurse bolus as needed for pain</th>
<th>Nurse bolus interval (hours)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Morphine</strong></td>
<td>1 mg (0.5-2.5)</td>
<td>10-30 min</td>
<td>4 mg</td>
<td>See below</td>
<td>2-4 mg</td>
<td>2</td>
</tr>
<tr>
<td><strong>Hydromorphone</strong></td>
<td>0.2 mg (0.1-0.5)</td>
<td>10-30 min</td>
<td>0.8 mg</td>
<td>See below</td>
<td>0.5-1 mg</td>
<td>2</td>
</tr>
<tr>
<td><strong>Fentanyl</strong></td>
<td>10 mcg (5-25)</td>
<td>10-30 min</td>
<td>40 mcg</td>
<td>See below</td>
<td>25 mcg</td>
<td>2</td>
</tr>
</tbody>
</table>

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, Pain Medicine, Palliative/Supportive Care (see Appendix J 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, Pain Medicine, Palliative/Supportive Care (see Appendix J 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 E) 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 as needed for pain every hour.
## APPENDIX H: Opioid Side Effects – Prevention and Management

<table>
<thead>
<tr>
<th>Side Effect</th>
<th>Prevention</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sedation</td>
<td>● Discontinue other sedating medications if appropriate</td>
<td>● Consider rotation or dose reduction of opioid if sedation persists</td>
</tr>
<tr>
<td></td>
<td>● Educate all patients receiving opioids</td>
<td>● Consider psychostimulant:</td>
</tr>
<tr>
<td></td>
<td>drowsiness may result for a few days following initiation or increase in opioid regimen</td>
<td>1. Methylphenidate (Ritalin®) 2.5-5 mg PO once or twice daily (last dose no later than 4 pm to avoid insomnia). Suggested time 8 am and 12 noon daily. Needs controlled substance Class II (CII) prescription or 2. Consider modafinil 100 mg once or twice daily</td>
</tr>
<tr>
<td>Opioid induced neurotoxicity</td>
<td>Eliminate non-essential CNS activating or depressing drugs (for example: benzodiazepines)</td>
<td>● Consider reversible causes such as metabolic disorders, liver or renal dysfunction, dehydration, hypercalcemia, organic brain disease; treat as appropriate.</td>
</tr>
<tr>
<td>Risk factors:</td>
<td></td>
<td>● Consider one or more of the following:</td>
</tr>
<tr>
<td>High opioid dose</td>
<td></td>
<td>1. Opioid rotation (see Appendix E)</td>
</tr>
<tr>
<td>Dehydration</td>
<td></td>
<td>2. Opioid dose reduction or discontinuation</td>
</tr>
<tr>
<td>Renal failure</td>
<td></td>
<td>3. Discontinue other offending drugs (benzodiazepines)</td>
</tr>
<tr>
<td>Preexisting borderline</td>
<td></td>
<td>4. Hydration</td>
</tr>
<tr>
<td>cognition and/or delirium</td>
<td></td>
<td>5. Symptomatic treatment with haloperidol 1-5 mg PO, IV, or SC every 4 hours as needed</td>
</tr>
<tr>
<td>Use of other psychoactive</td>
<td></td>
<td>● Avoid using naloxone even if delirium is thought to be due to opioid use</td>
</tr>
<tr>
<td>drugs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Respiratory depression</td>
<td>● Monitor sedation and respiratory status (respiratory rate and oxygen saturation) during the first 24 hours in opioid naïve patients</td>
<td>● Call MD, HOLD opioids, provide supplemental oxygen</td>
</tr>
<tr>
<td></td>
<td>● Titrate opioids cautiously</td>
<td>● If patient minimally responsive or unresponsive and respiratory rate less than or equal to 6 breaths per minute, administer naloxone. Recommended dose: naloxone 0.4 mg diluted in 9 mL saline for total volume of 10 mL, give 1 mL (0.04 mg) via slow IV push every 2-3 minutes until patient 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.)</td>
</tr>
<tr>
<td></td>
<td>● Consider dose reduction or opioid rotation if patient has excessive sedation</td>
<td>● If patient is actively dying, DNR (do not resuscitate) and receiving comfort care, naloxone administration may not be appropriate</td>
</tr>
</tbody>
</table>

*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.*
## APPENDIX H: Opioid Side Effects – Prevention and Management - continued

<table>
<thead>
<tr>
<th>Side Effect</th>
<th>Prevention</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea, Vomiting</td>
<td><strong>Prevention</strong></td>
<td><strong>Management</strong></td>
</tr>
<tr>
<td></td>
<td>• Titrate opioid dose slowly and steadily.</td>
<td>1. Investigate for other causes of nausea (for example, constipation, bowel obstruction, chemotherapy or other medications) and treat per guidelines. Initiate scheduled antiemetics. Example: metoclopramide 5 to 10 mg PO, IV, or SC every 6 hours.</td>
</tr>
<tr>
<td></td>
<td>• Provide antiemetics available with opioid prescription.</td>
<td>2. Add or increase non-opioid or adjuvant medications for additional pain relief so opioid dose can be reduced.</td>
</tr>
<tr>
<td></td>
<td>• Metoclopramide 10 mg PO</td>
<td>3. If analgesia is satisfactory, reduce opioid dose by 25%.</td>
</tr>
<tr>
<td></td>
<td>• Patients at high risk of nausea consider scheduled antiemetics for 5 days and then change to as needed.</td>
<td>4. Consider opioid rotation if nausea remains refractory.</td>
</tr>
<tr>
<td>Constipation</td>
<td><strong>Prevention</strong></td>
<td><strong>Management</strong></td>
</tr>
<tr>
<td></td>
<td>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.</td>
<td>1. Assess potential causes of constipation (such as recent opioid dose increase, use of other constipating medications, new bowel obstruction)</td>
</tr>
<tr>
<td></td>
<td>1. Stimulant laxative plus stool softener:</td>
<td>2. Increase Senokot-S® (or senna and docusate tablets if using separate) and add 1 or both of the following:</td>
</tr>
<tr>
<td></td>
<td>For example: Senokot-S® (senna 8.6 plus docusate 50 mg), 2 tablets/day and titrate up maximum 9 tablets/day.</td>
<td>a. Milk of magnesia oral concentrate (1,200/5 mL) 10 mL PO every 2-4 times daily.</td>
</tr>
<tr>
<td></td>
<td>2. Ensure adequate fluids, dietary fiber and exercise if feasible.</td>
<td>b. Polyethylene glycol (Miralax®) 17 grams in 8 ounce beverage daily.</td>
</tr>
<tr>
<td></td>
<td>3. Prune juice followed by warm beverage may be considered.</td>
<td>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</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• If impacted: disimpact manually if stool is soft. If not, soften with mineral oil fleet enema before disimpaction. Follow up with milk of molasses enemas until clear with no formed stools.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Consider use of short-acting analgesics before disimpaction.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• If not impacted on rectal examination, patient may still have higher level impaction. Consider abdominal imaging and/or administer milk of molasses enema along with 8 ounces of PO magnesium citrate.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• See Bowel Management SmartSet</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4. Methylnaltrexone (Relistor®) may be given to patients who meet the following criteria:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Patient experiencing opioid-induced constipation</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Patient has not demonstrated an adequate response to other laxative therapy</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Patient does not have a known or suspected mechanical gastrointestinal obstruction</td>
</tr>
</tbody>
</table>
APPENDIX I: Pain Management Education for Patient and Family Prior to Discharge

Management of cancer pain is an integral component of cancer care. Patient education in the following areas should be provided to patients.

1. **General Pain Education**: Specific teaching information is available in Patient Education- On Line (Patient Packet 1). Education should include the following:
   A. Relief of pain is important and there is no benefit to suffering with pain
   B. Expect optimal treatment for pain and side effects
   C. Pain can usually be well controlled with oral medications. There are many options available to control pain.
   D. Communication with healthcare team is critical to pain management and avoiding serious side effects. Communication should include:
      • Patient understanding about how to rate their pain type, severity/intensity, and personalized pain goals (PPG). A numeric pain scale should be provided with explanation.
      • Potential problems or side-effects of pain medications
      • Concerns about difficulty in obtaining medications (such as cost, or inadequate amount of tablets)

2. **Specific information related to Opioid Use** (such as morphine and related medications). Specific teaching information is available in Patient Education- On Line. (Patient Packet 2)
   A. Morphine and morphine-like medications are often used to relieve pain
   B. When opioids are used to treat cancer pain, addiction is rarely a problem
   C. Taking opioids now will not affect later effectiveness
   D. Discuss potential side effects of opioids, and its prevention and management
   E. Prevention of constipation will be needed by most patients
   F. Opioids are controlled substances that need to be properly safeguarded in the home
   G. Opioids must be used with caution, and should not be mixed with alcohol or illicit substances

3. **Pain Education Discharge/Resource Checklist**:
   A. A written plan for pain medications, listing all medications to be used with dosage and frequency. Provide patient with printed copy of updated medication reconciliation.
   B. Written information on who to call (provider, service, phone number) for pain issues and plan for follow up care. Instruct patient/caregiver to call if:
      • Problems in obtaining prescriptions or taking the medication
      • New pain, change in pain, or pain not relieved with medication
      • Nausea and vomiting that prevents eating for 1 day
      • No bowel movements for 3 days
      • Difficulty arousing the patient from sleep easily during daytime
      • Confusion

Continued on next page
APPENDIX I: Pain Management Education for Patient and Family Prior to Discharge - continued

3. Pain Education Discharge/Resource Checklist - continued:

C. MDACC has multiple resources for pain management
   - Online resources – MD Anderson has multiple on-line resources for patients and families. Patient education online is available at http://www.mdanderson.org/departments/patedu/ or via https://my.mdanderson.org. Please ask for a guide to the website.
   - Specialty services for pain management at MD Anderson include: Acute Pain Medicine, Pain Medicine and Palliative/Supportive Care, and Integrative Medicine. Referral from primary service is required. Pain Medicine, Palliative/Supportive Care, and Integrative Medicine have clinics 5 days a week. Integrative Medicine services such as acupuncture, massage, and mind-body therapies are available through Online Consults or by calling 713-794-4700.
   - Website: http://www.mdanderson.org/departments/integrative-medicine-program. Located in the Main Building, Floor 1, outside and east of Clark Clinic main entrance - Main, free-standing building located outside and east of the Clark Clinic main entrance, near the Aquarium (R1.2000); Mays Clinic, Floor 2, near The Tree Sculpture
   - The Learning Center(s) provide the latest information about health, cancer, and cancer prevention. Available resources include:
     - Journals, consumer health magazines and newsletters
     - Online journals, electronic books and databases
     - Free booklets
     - Topic-specific binders
     - Books, audios and videos
     - DVDs and videotapes

   Law Learning Center, Main Building, Floor 4, Elevator A R4.1100 713-745-8063
   Levit Learning Center, Mays Clinic, Floor 2, Near Tree Sculpture ACB2.1120 (Mon-Fri 9 am-4 pm 713-563-8010)
APPENDIX J: Specialty Services Consultation Guidelines

MD Anderson offers three coordinated pain specialty core services, consisting of Acute Pain Medicine, Pain Medicine and Palliative/Supportive Care, and Integrative Medicine. Guidelines for consultation to these services include the following:

A. Consult to one of the specialty core services should be considered for any patient whose pain remains uncontrolled for over 24 hours. Special patient population in which pain assessment and management may be especially challenging include the following:

- Substance use disorders - except tobacco (current or past history)
- Emotional, behavioral, and mental disorders
- Cognitive disorders
- Communicative disorders
- Developmental disabilities
- Vision and hearing impairments and disabilities
- Refractory symptoms and dying patient

B. For postoperative and perioperative pain: Acute Pain Medicine and Integrative Medicine

C. For acute pain in inpatients: Pain Medicine in cases of pre-existing chronic pain

D. For patients with chronic pain and no evidence of active cancer: Pain Medicine (Chronic Pain) and Integrative Medicine

E. For patients with evidence of active cancer with pain as the sole or predominant symptom: Pain Medicine or Palliative/Supportive Care Service, or Integrative Medicine

F. For patients with evidence of active cancer and pain accompanied by multiple symptoms: Palliative/Supportive Care or Integrative Medicine

G. For patients with pain in the context of cancer in the palliative stage or end of life: Palliative/Supportive Care and Integrative Medicine

H. 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 K for Treatment Services.

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.
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: 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.

- 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 Alcohol and Drugs
  Houston, Texas
  [website]
- 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)
  (888) 683-1406

- St. Joseph Hospital
  1401 St. Joseph Parkway
  Houston, Texas 77002
  (713) 575-1000 (800) 466-0792
- West Oaks Hospital (Dr. George Santos)
  [website]
  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: [website]
  Enter patient’s address and zip code on website
  (800) 622 4357
- The Menninger Clinic
  12301 S. Main St.
  Houston, Texas 77035-6207
  (713) 275-5000
- Narcotics Anonymous
  [website]
  Houston area Narcotics Anonymous
  [website]
  (713) 661-4200
SUGGESTED READINGS

Agency for Healthcare Research and Quality (AHRQ): Management of Cancer Pain Volumes I and II
SUGGESTED READINGS - continued


DEVELOPMENT CREDITS:

This practice consensus statement is based on majority opinion of the cancer pain experts at the University of Texas MD Anderson Cancer Center for the patient population. These experts included:

- Eduardo Bruera, MD (Palliative Care Medicine)
- M. Kay Garcia, DrPH, LAc (Integrative Medicine Research)
- Diana Cauley, PharmD (Pharmacy Clinical Programs)
- Keyuri U Popat, MD (PeriOperative Medicine)
- Shalini Dalal, MD (Palliative Care Medicine)
- Dhanalakshmi Koyyalagunta, MD (Pain Medicine)
- Larry Driver, MD (Pain Medicine)
- Suresh K. Reddy, MD (Palliative Care Medicine)
- Olga Fleckenstein
- Eden Mae C. Rodriguez, PharmD (Pharmacy Clinical Programs)
- Carmen Gonzalez, MD (Emergency Medicine)
- Alan D. Valentine, MD (Psychiatry)
- Larry Driver, MD (Pain Medicine)
- Olga Fleckenstein

The document is based upon the consensus of pain experts. Evidence regarding specific clinical outcomes associated with the use of this or similar pain algorithms applied in comprehensive cancer centers is sparse. Other algorithms or approaches may produce similar or better outcomes.

[T Core Development Team Lead
[C Clinical Effectiveness Development Team

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.