

**UNIVERSITY OF SOUTH ALABAMA COLLEGE OF MEDICINE  
DEPARTMENT OF FAMILY MEDICINE**

**PAIN MANAGEMENT GUIDELINES**

**I. OVERVIEW**

Detailed narcotic prescribing guidelines are outlined in this chapter, but the basic rules and workflow can be summarized as follows:

- A. Assess the etiology of the patient's pain.
- B. Assess the appropriateness of further diagnostic or therapeutic measures, or specialty referral.
- C. Determine whether or not long-term pain medications are indicated.
- D. If chronic pain medication is to be prescribed, discuss departmental policies with the patient, and have the patient complete a CONTROLLED SUBSTANCES AGREEMENT, including the appropriate RISKS AND SIDE EFFECTS FORM.
- E. Begin prescribing appropriate pain medications, guided by the following principles:
  - 1. Assess the patient's level of pain and the effectiveness of prescribed measures.
  - 2. Use the lowest dose of the mildest medicine necessary for pain management, but make sure pain *is* adequately managed.
  - 3. Unless pain is episodic and relatively infrequent, use both short-acting (breakthrough) and long-acting (maintenance) agents.
  - 4. Anticipate and monitor for side effects, and treat appropriately.
  - 5. Monitor for compliance and appropriate drug usage.
  - 6. Consider adjunctive pharmacologic and nonpharmacologic measures.

**II. ACUTE/SHORT-TERM PAIN MANAGEMENT**

- A. In the event of an apparent acute or short-term need for pain medications, document in the visit note the indication, drug, dosage, and the anticipated timeframe of use.

- B. If the patient's usage starts to exceed the amount or duration of anticipated needs, evaluate further. Consider alternative diagnoses, adjunct pain management modalities, or specialty referral.
- C. If the result of above measures indicates a need for chronic pain management, proceed as discussed below.

### III. CHRONIC PAIN INITIAL PROCEDURES

#### A. Established patient.

1. If the chart contains a clearly documented cause for pain, with no further therapeutic workup indicated, and it is the opinion of the physician that narcotics are the safest, most effective choice for pain management:
  - a. Obtain urine drug screen to look for evidence of appropriate use, diversion, or illicit substance use.
  - b. Continue prescribing, proceeding as discussed below.
2. If there are any questions regarding the diagnosis, medications used, or other treatment options, evaluate these.
  - a. While this evaluation takes place, the physician may continue prescribing the patient's current medications, or make modifications deemed appropriate, before having the patient complete a CONTROLLED SUBSTANCES AGREEMENT.
  - b. Explain to the patient that these steps are being taken as part of a practice-improvement plan with regard to pain management.
  - c. Document on the chart that prescribing is being continued without a CONTROLLED SUBSTANCES AGREEMENT for this interim period. A reasonable timeframe for this evaluation is 30 days, not to exceed 90 days.
  - d. Upon completion of this evaluation, one of the following determinations should be possible:
    - i) The patient has a clearly defined need for chronic pain management.
      - a) Document this.
      - b) Schedule a pain management visit within the next two weeks.

- c) Give the patient copies of the BECK DEPRESSION INVENTORY, the PAIN AND SYMPTOM ASSESSMENT form, and the OPIOID RISK TOOL, with instructions to complete them the morning of the pain management visit.
  - d) The physician may choose to give a short course of pain medication to last until the pain management visit, or to defer treatment until that visit takes place.
- ii) The patient has a problem that can be definitively addressed, obviating the need for chronic pain medications. Treat or refer for such therapeutic management; the physician may continue current pain prescribing while treatment takes place, clearly documenting these measures on the chart.
  - iii) The patient does not have an indication for chronic pain medications. Document on this and inform the patient. Discontinue chronic pain prescribing, considering a brief tapering period if the physician deems appropriate due to concern for withdrawal symptoms. Offer referral for treatment of drug habituation if deemed appropriate or if patient requests.

B. New patient.

For someone coming to our practice with a history of chronic narcotic use from previous healthcare providers, requesting that we take over this prescribing, follow these procedures:

1. Request records, diagnostic study reports, and any other available documentation supportive of the patient's diagnosis and need for chronic pain medications.
2. Based on clinical assessment at this point, the physician may choose to do one of two options:
  - a. Decline to prescribe controlled substances while awaiting further data.
  - b. Prescribe small amounts of pain medications while awaiting further data.
    - i) If this option is chosen, make clear to the patient that the practice is not agreeing to continue long-term pain medications at this point, and that pain meds will not be prescribed longer than one month without receiving prior records or the initiation of further evaluation.
    - ii) Obtain urine drug screen to look for evidence of appropriate use, diversion, or illicit substance use.
3. If the obtained records indicate that patient has a clearly defined need for chronic pain management, and there is no need for further evaluation or therapeutic measures:

- a. Document this.
  - b. Schedule a pain management visit within the next two weeks.
  - c. Give the patient copies of the BECK DEPRESSION INVENTORY, the PAIN AND SYMPTOM ASSESSMENT form, and the OPIOID RISK TOOL, with instructions to complete them the morning of the pain management visit.
  - d. The physician may choose to give a short course of pain medication to last until the pain management visit, or to defer treatment until that visit takes place.
4. If adequate records are not available; there are delays of over a month obtaining records; the patient wishes to have further evaluation without waiting on records; or records indicate the need for further diagnostic or therapeutic measures, recommend further evaluation of the problem and/or referral.
- a. If the patient declines further evaluation, inform the patient that we will be unable to prescribe pain medications.
  - b. If the patient agrees, the physician may prescribe limited pain medications, or decline to do so, until workup is completed, as described in item III.B.2 above.
  - c. If the patient agrees to further evaluation, upon completion of this evaluation, decide upon the appropriate action, as discussed in item III.A.2.d above.

#### IV. CHRONIC PAIN MANAGEMENT POLICIES

##### A. Pain management visits.

1. For any new pain management patient, or for an established patient with a substantial change in pain, an appointment should be made solely to address pain management.
2. When pain is being adequately managed, it is not necessary to have monthly visits just for pain medication refills. These may be handled at visits for other medical problems, or as planned between-visit refills. However, pain management patients will be physically seen in the office at least every three months to continue prescribing.

##### B. CONTROLLED SUBSTANCES AGREEMENT.

1. The USAFM CONTROLLED SUBSTANCES AGREEMENT consists of the following components:
  - a. CONTROLLED SUBSTANCE CONTRACT. This outlines our general controlled substance prescribing rules, and gives the patient the opportunity to acknowledge them.

- b. **RISKS AND SIDE EFFECTS FORM.** This outlines possible adverse effects of the medications to be used, and gives the patient the opportunity to acknowledge them. Note that there are forms for narcotics, sedative/hypnotics, and stimulants, and the physician will need to choose the appropriate page(s).
  - c. **PHARMACY SELECTION FORM.** This specifies the patient's choice of pharmacy, and allows for future changes.
  - d. **TREATMENT PLAN.** This specifies the diagnosis determined to be the etiology of the patient's pain, and medications/therapies used to treat the patient's symptoms. In addition to controlled substances, adjunctive medications and measures used to address side effects should be included.
- 2. The **CONTROLLED SUBSTANCES AGREEMENT** may be given to the patient to review prior to the first pain management visit, or the patient may receive this at the first pain management visit. The patient will be given an opportunity to review the Agreement, and discuss any questions with the physician, social worker, nurse, or other designated practice staff.
  - 3. The patient and physician will sign and date the appropriate locations of the **CONTROLLED SUBSTANCES AGREEMENT**.
  - 4. The patient will receive a copy of the **CONTROLLED SUBSTANCES AGREEMENT**, and the original will remain on the patient's chart.
  - 5. Any future changes to the **PHARMACY SELECTION** or **TREATMENT PLAN** forms will be initialed and dated by the patient and physician, and the patient will receive an updated copy of the effected pages.

C. Drug screens.

- 1. Urine drug screens will be performed at the first pain management visit, preferably before narcotics are first prescribed.
- 2. Urine drug screens should be performed at least twice yearly.
- 3. Urine drug screens should be performed at any time the physician has uncertainty as to patient compliance, medication misuse, or illicit drug use.
- 4. The purpose of urine drug screens is two-fold:
  - a. To confirm the patient is using medications as prescribed, rather than diverting them.
  - b. To confirm the absence of unprescribed or illicit drugs.

5. Note the following information regarding the standard University of South Alabama urine drug screen:
  - a. The following drug classes are detected: amphetamines, barbiturates, benzodiazepines, cannabinoids, cocaine, and opiates.
  - b. The following opiates are detected: codeine, heroin, hydrocodone, hydromorphone, meperidine, morphine, oxycodone, and oxymorphone.
  - c. The following agents are *not* detected as opiates: fentanyl, methadone, propoxyphene, and tramadol. If necessary, there are specific assays available to detect these drugs. The most commonly used is the assay for methadone, which is done on a urine specimen.
  - d. While amphetamines are detected, methylphenidate is not.
  - e. Outside reference labs, such as LabCorp, have panels that include methadone and fentanyl.

D. Depression, anxiety, and other mental disorders.

1. Depression is often seen concomitantly with chronic pain, and it complicates pain management. Patients should be evaluated on an ongoing basis for depression.
2. Patients should complete the BECK DEPRESSION INVENTORY either prior to, or the day of, the first pain management visit. This tool may also be used at later visits as dictated by clinical progress.
3. Patients should be offered relatively aggressive medicinal treatment for depression, especially in light of the fact that many antidepressants possess potent analgesic properties. Antidepressant medications that are often used in pain management are discussed below in the section on adjunctive measures.
4. Anxiety is also common in chronic pain patients, but adequate pain management often alleviates much of a patient's anxiety.
5. If anxiety requires medicinal treatment, consider first using antidepressant medications, such as SSRIs/SNRIs, which also possess anxiolytic qualities.
6. Sedatives/hypnotics, such as benzodiazepines, if used at all, are best used on a short-term basis, given the opportunities for habituation and side effects that are additive to those of narcotics. If the physician feels the benefits outweigh the risks, such agents may be prescribed; see the Sedative-Hypnotic Guidelines chapter for further information.

7. In addition to medical treatment, patients should also be offered referral for counseling services, either within the Family Medicine Center Clinic, or, if necessary, with outside consultants. In particularly difficult cases, consider psychiatric consultation.
8. Other major psychiatric diagnoses, such as schizophrenia and bipolar disorder, can make pain management very difficult. Many of these cases will be beyond the scope of a primary care office, and should prompt referral to appropriate psychiatric and pain management consultants.

E. Chronic pain management principles.

1. A good overview of the principles of chronic pain management is available in the PAIN MANAGEMENT READING MODULE, available on the USAFM computer system.
2. A history of previous substance abuse does not preclude pain medication prescribing for appropriate uses. However, there is much greater potential for abuse, requiring very close monitoring, which may well be beyond the scope of most primary care practices.
3. If not completed by the time of the initial pain management visit, the PAIN AND SYMPTOM ASSESSMENT form should be done. It would be advisable to have the patient complete another copy of this form at any time there is a problem with worsening pain or side effects, and at least quarterly.
4. Pain may generally be categorized as follows:
  - a. Mild: Pain score 1-3.
  - b. Moderate: Pain score 4-7.
  - c. Severe: Pain score 8-10.
5. The purpose of chronic pain management is to safely improve function and quality of life through the treatment of pain and other associated symptoms. The complete relief of pain is unlikely to be an achievable goal, and the patient should be made aware this is not a realistic expectation. Negotiate with the patient a target level of relief; often this would be an average pain level of under 4.
6. A general principle to follow, in keeping with the World Health Organization Three-Step Ladder, is to treat mild pain with non-narcotic medications, moderate pain with milder narcotics, and severe pain with more potent narcotics.
7. Short-acting narcotics are immediate-release (IR) preparations; these are also referred to as PRN, rescue, or breakthrough analgesics. Long-acting narcotics are sustained-release (SR) preparations, which may only be required one to two times a day. These are also referred to as extended-release (ER), baseline, or maintenance analgesics.

8. For patients with intermittent pain only, that is, patients who have periods of time with little or no pain, punctuated with occasional episodes of moderate to severe pain, it is proper to prescribe short-acting analgesics for as-needed use. One may wish to consider giving some non-narcotic options for milder pain, and a mild to moderate narcotic for more pronounced pain.
9. If the patient is needing stronger medications more often (perhaps three or more days per week), consider the possibility of a new or overlapping disease process, or progression of the known diagnoses. Investigate and treat accordingly.
10. If it becomes evident that patient is needing stronger medications more frequently, and evaluation fails to reveal a correctable cause, it is time to institute maintenance pain medications.

F. Narcotic usage guidelines.

1. Side effects.

While they will be addressed during the process of completing the CONTROLLED SUBSTANCES AGREEMENT, side effects should be discussed any time medication changes are made, or a new therapy is initiated. The following side effects are particularly common:

a. Sedation and/or lightheadedness.

- i) Tolerance to these side effects generally develops over the first three days in most cases, and by two weeks at worst.
- ii) After the patient has developed tolerance to this side effect, it should be safe for the patient to drive again.

b. Constipation.

- i) Constipation secondary to opioid administration is almost universal. It is the result of opioid effects on the central nervous system, spinal cord, and myenteric plexus of the gut that lead to reduced gut motor activity and increased stool transit time. The colon has more time to desiccate its contents, leaving large, hard stools. Other factors, such as dehydration, poor food intake, and other medications, may further aggravate the problem.
- ii) Tolerance to constipation develops very slowly, and often does not develop at all. It requires anticipatory and ongoing management.
- iii) Dietary interventions, such as increasing fluid and fiber intake are advisable, but are often insufficient.

- iv) Bulk-forming agents, such as psyllium (Metamucil) and methylcellulose (Citrucel), require substantial fluid intake, and are not recommended for those with advanced disease and poor mobility.
  - v) Stimulant laxatives, such as senna (Ex-Lax, Senokot), bisacodyl (Dulcolax), or glycerin, may be useful, though tolerance to their effects may develop.
  - vi) Stool softeners, such as docusate sodium (Colace), are not usually effective by themselves, but may be useful in combination with stimulants.
  - vii) A prokinetic agent, such as metoclopramide (Reglan) may also be useful, though it has a more troublesome side effect profile than the other alternatives for constipation.
  - viii) Osmotic laxatives, in particular polyethylene glycol (MiraLax, GlycoLax), have become a common treatment of choice for narcotic-induced constipation. This may be administered as 17 mg (1 capful/packet) in 8 ounces of fluid twice daily, titrating up or down, aiming for at least one soft bowel movement per day. Other osmotic agents include milk of magnesia, lactulose, and sorbitol.
  - ix) If a patient presents with an already-established pattern of constipation, rule out obstruction, and consider the need for manual disimpaction.
- c. Itching.
- i) Without a rash, itching is *not* indicative of an allergic reaction.
  - ii) It will likely resolve over several days. If it does not, it is possible that another agent will cause less itching.
- d. Respiratory depression. While this is a common concern for prescribers, it is very uncommon at recommended analgesic doses.

## 2. Route of administration.

In general, unless it is unavailable, the preferable route of administration is enteral (oral or feeding tube). After this, use the following routes, listed in order of preference: transcutaneous; subcutaneous; intravenous. The intramuscular route of administration is virtually never required.

### 3. Narcotic dosing considerations.

- a. Equianalgesic tables are widely available, comparing the relative potency of various narcotic agents, to allow for conversion between them. One is included elsewhere in this chapter.
- b. When starting narcotics on a opiate-naïve patient, begin with the lower end of the dosage range and titrate up.
- c. When converting a patient from PRN narcotics to maintenance therapy, add up the total amount of medication the patient is currently receiving, convert to an equianalgesic dose of a maintenance medication, and give routinely around the clock.
- d. When a patient is given maintenance narcotics, a short-acting agent should also be made available for breakthrough pain. A typical breakthrough dose would be the equivalent of 5-15% of the total daily maintenance dosage. This would be given PRN as often as dictated by the pharmacokinetics of the agent used and the individual response. This might be as frequently as every 1-2 hours orally or 30-60 minutes SC/IV. For continuous infusion, a breakthrough dose can be either the hourly rate given PRN over 15 minutes, or 10% of the total daily dose given over 30-60 minutes. Note that some breakthrough medications are combinations with acetaminophen or NSAIDs, and that these components may actually be the limiting prescribing factor.
- e. Adjust the maintenance dosage upward every 1-3 days in an amount roughly equivalent to the total daily amount of breakthrough usage. This should result in a decrease in the amount of breakthrough medication needed.
- f. When converting from one opioid to another, some experts recommend starting with only 50-75% of the dose calculated using an equianalgesic table. This allows for a margin of safety, given the variability of individual responses to various drugs, but it may also mean the initially chosen conversion dose provides inadequate pain relief, so the patient should be observed for the need for early titration. This dose conversion reduction is particularly important when dealing with high doses of high-potency agents, such as hydromorphone (Dilaudid), methadone, or fentanyl (Duragesic).
- g. Elderly patients, or those with severe renal or liver disease, should be started on half the narcotic dose otherwise calculated, unless recommended otherwise in the prescribing information of the drug in use.
- h. When a patient on chronic maintenance narcotics has surgery, or is temporarily unable to take medications by mouth for other reasons, it may be necessary to change to appropriate doses of immediate-release narcotics for a short period of

time. Resume maintenance doses when the patient's clinical condition has stabilized.

4. Special diagnosis considerations.

a. Back pain.

Data is limited that chronic narcotic usage improves quality of life in patients with back pain over three months' duration. It is advisable to limit prescribing for acute events to a brief period of time, and to maximize non-narcotic drug options and other pain-management modalities. In the event of prolonged back pain, one should completely evaluate the patient for correctable pathology, utilizing appropriate specialty referral, particularly in younger patients. If after such evaluation it is the consensus that there are no other appropriate therapeutic options, chronic narcotics may then be considered.

b. Headache.

In general, narcotics are not advisable choices for headache management, given the side effect profile, and the propensity for inducing rebound worsening of headaches. They may be appropriate for limited, acute treatment of intractable migraines.

c. Sickle cell disease.

Sickle cell disease is often a condition of recurrent, intermittent pain, rather than chronic, daily pain. When possible, it should be managed with immediate-release pain medications on an as-needed basis. However, when pain is becoming more frequent, or when the patient comes to the practice already established on maintenance narcotics, sustained-release prescribing is appropriate. It should also be noted that ketorolac (Toradol) is a potent NSAID that is often especially effective for relieving bone pain in sickle cell patients. It can be given by injection or orally, causes no respiratory depression, and may reduce the amount of opioids required by the patient.

d. Previously-established chronic narcotic usage.

From time to time, patients may come to our practice already established on chronic narcotics through other providers, for conditions for which we would not typically prescribe such medications. Given the rotating nature of the physicians in USAFM, similar patients may also be discovered already within our practice, whose medication prescribing became established prior to the institution of our current pain management policies. Recommendations regarding prescribing for and evaluating these patients appear elsewhere in this document. However, it is recognized that, based upon the clinical judgment of the treating physician, the best course of action may be to continue narcotic prescribing for some patients that we might not have initiated on narcotics if we were the initial treating physicians.

## V. NARCOTIC SELECTION

### A. Immediate-release (breakthrough) narcotics.

#### 1. Tramadol.

##### a. Commonly available forms:

- i) 50 mg tablet (Ultram, generic).
- ii) Acetaminophen/tramadol 325/37.5 mg tablet (Ultracet).

##### b. Dosing: 50-100 mg PO Q 4-6 hours, up to 400 mg/day.

##### c. Notes:

- i) Lowers seizure threshold.
- ii) Not federally classified as a controlled substance; some states classify in Schedule IV, as psychological and physical dependence have occurred.
- iii) If tramadol is sufficient, it is a good initial choice; however, many chronic pain patients are likely to need stronger analgesics.

#### 2. Hydrocodone.

##### a. Commonly available forms:

- i) Acetaminophen/hydrocodone 500/2.5, 500/5, 500/7.5, 500/10 mg tablets; 500/7.5 per 15 ml liquid (Lortab, Vicodin, generics; other combination variants exist).
- ii) Ibuprofen/hydrocodone 200/7.5 mg tablet (Vicoprofen, generic).

##### b. Dosing:

- i) Start at 5 mg PO Q 4 hours, titrating as needed.
- ii) In practicality, dosing is limited by the acetaminophen or ibuprofen component.

##### c. Notes:

- i) A good first choice for breakthrough pain, if the acetaminophen or ibuprofen components are not limiting. Beware of other sources of acetaminophen or NSAIDs patient may be taking.
- ii) Beware of NSAID contraindications for the ibuprofen product.

3. Oxycodone immediate-release.

a. Commonly available forms:

- i) 5, 10, 15, 20, 30 mg IR tablets; 20 mg/ml IR liquid. (Roxicodone, generic). 5, 7.5 mg tamper-resistant tablets (Oxecta)
- ii) Acetaminophen/oxycodone 325/2.5, 325/5, 325/7.5, 325/10, 500/7.5, 650/10 mg tablets (Percocet, Tylox, others, generics; other combination ratios exist).
- iii) Aspirin/oxycodone 325/4.8355 mg tablets (Percodan, generics).
- ii) Ibuprofen/oxycodone 400/5 mg tablets (Combunox).

b. Dosing: 5-30 mg PO Q 4 hr PRN.

c. Notes:

- i) A good choice for breakthrough pain, particularly when there is a need to avoid acetaminophen.
- ii) Acetaminophen component is the limiting factor for the combination product. Beware of other sources of acetaminophen patient may be taking.
- iii) Be careful not to confuse with the extended-release formulation when prescribing; make sure the patient understands the distinction if both IR & ER versions are prescribed.

4. Morphine immediate-release.

a. Commonly available forms:

- i) 10, 30 mg IR tabs; 10, 15, 30 mg soluble IR tabs; 2, 4, 20 mg/ml solution.
- ii) 5, 10, 20, 30 mg suppositories.
- iii) Injectable IV/SC/IM.

b. Dosing:

- i) PO/SL: 10-30 mg Q 3-4 hr PRN; may use soluble tabs or solution buccally.
- ii) Rectal: 10-20 mg Q 4 hr PRN.
- iii) SC/IM/IV: 2.5-10 mg Q 2-6 hr PRN.

c. Notes:

- i) Be careful not to confuse with the extended-release formulation when prescribing; make sure the patient understands the distinction if both IR & ER versions are prescribed.
- ii) Use caution in severe renal failure; accumulation of metabolites can cause agitation, delirium.

5. Hydromorphone (Dilaudid, generic).

a. Commonly available forms:

- i) 2, 4, 8 mg tabs; 1 mg/ml liquid (no generic liquid).
- ii) 3 mg suppository.
- iii) Injectable IV/SC/IM.

b. Dosing:

- i) PO: 2-8 mg PO Q 3-4 hr PRN.
- ii) Rectal: 3 mg Q 6-8 hr PRN.
- iii) SC/IM/IV: 1-4 mg Q 4-6 hr PRN.

c. Notes:

- i) Sometimes effective when analgesia from other narcotics has waned.
- ii) Acceptable with renal disease.
- iii) High equianalgesic potency.

6. Fentanyl immediate-release.

a. Commonly available forms:

- i) 200, 400, 600, 800, 1200, 1600 mcg lozenge (generic); wide variety of branded buccal/sublingual tablets, lozenges, strips, sprays (Abstral, Actiq, Fentora, Onsolis, Subsys); nasal spray (Lazanda)
- ii) Injectable IV/IM.

b. Dosing:

- i) Oral or nasal transmucosal: Start with lowest dose, titrating up as needed, following instructions of the specific agent.
- ii) IV/IM: 50-100 mcg Q 1-2 hr.

c. Notes:

- i) All transmucosal forms are very expensive, including generics.
- ii) The transmucosal forms are not directly interchangeable.
- iii) Do not cut/chew/crush/swallow.
- iv) High equianalgesic potency. Do not depend on equianalgesic conversions to oral fentanyl, as necessary doses correspond poorly with total daily dose of other narcotics.
- v) Do not use in opiate-naïve patients.

7. Oxymorphone immediate-release (Opana, generic).

a. Commonly available forms:

- i) 5, 10 mg IR tablets.
- ii) Injectable IV/SC/IM.

b. Dosing:

- i) PO: 10-20 mg PO Q 4-6 hr PRN, 1 hr before or 2 hours after meals.
- ii) SC/IM: 1-1.5 mg SC/IM Q 4-6 hours PRN.
- iii) IV: 0.5 mg IV Q 4-6 hours PRN.

c. Notes:

- i) Also known as 14-hydroxydihydromorphinone.
- ii) Expensive, even as a generic (though Alabama Medicaid covers as of this writing).
- iii) High equianalgesic potency.

## 8. Methadone.

### a. Commonly available forms:

- i) 5, 10, 40 mg tablets; 1, 2, 10 mg/ml liquid. (40 mg tablet is only available for drug treatment program usage.)
- ii) SC; IM; IV.

### b. Dosing:

- i) PO: 2.5-10 mg Q 8-12 hours PRN in opiate-naïve patients; for conversion, use a very conservative interpretation of equianalgesic tables. Titrate very slowly; see notes below.
- ii) SC/IM/IV: 2.5-5 mg Q 8-12 hours PRN in opiate-naïve patients; for conversion, use a very conservative interpretation of equianalgesic tables. Titrate very slowly; see notes below.

### c. Notes:

- i) Methadone has a very long, variable half-life; it is best used as a maintenance medication. While it may have utility as a breakthrough medication, it should probably only be used when no other alternative is effective. Many would reserve its use to experienced pain management specialists, especially as a breakthrough medication.
- ii) Titrate very slowly to effect; it may take 3-5 days to achieve full analgesic effect. Small dose changes may make big differences in blood levels. It is wise to make dosage changes no more often than every 4-7 days.
- iii) Begin with Q 12 hr dosing. If, after several days of observation, the patient appears to be getting initially adequate pain relief, yet it does not last 12 hours, increase frequency to Q 8 hours. There is considerable individual variability, and some patients have required dosing as often as Q 6 hours, or even Q 4 hours.
- iv) Peak sedation and respiratory depressant effects may occur later than peak pain effect; always write "hold for sedation."
- v) Methadone displays incomplete and variable cross-tolerance with other opiates; deaths have occurred from iatrogenic overdose. When converting from other opiates, it is prudent to start with 10-25% of the published equianalgesic dose and titrate to achieve pain control.
- vi) Do not use methadone as a breakthrough medicine if it is being used as the maintenance medicine.

vii) QT prolongation and torsades de pointes have occurred. Do EKG pre-treatment, after 30 days, and yearly thereafter.

viii) Relatively safe with renal disease.

9. Levorphanol (Levo-Dromoran, generic).

a. Commonly available forms:

i) 2 mg tablet.

ii) SC; IM; IV in some countries.

b. Dosing:

i) PO: 2 mg Q 6-8 hours PRN. Titrate slowly; see notes below.

ii) SC/IM/IV: 2 mg Q 6-8 hours PRN. Titrate slowly; see notes below.

c. Notes:

i) Very long half-life of 16-18 hrs, despite the need for dosing Q 6-8 hrs. Risk of accumulation with repeat dosing. Titrate no more often than Q 72 hrs.

ii) Incomplete cross-tolerance with other opiates; use a very conservative interpretation of equianalgesic tables.

iii) Q 6-8 hr dosing makes it most commonly used as a breakthrough med, though may be useful as maintenance drug in some patients.

10. Tapentadol (Nucynta).

a. Commonly available forms:

i) 50, 75, 100 mg tabs.

b. Dosing: 50-100 mg PO Q 4-6 hours PRN.

c. Notes:

i) Weak mu agonist/norepinephrine reuptake inhibitor.

ii) Perhaps fewer GI effects, same CNS effects, compared to other opioids.

iii) Avoid within 14 days of MAO inhibitor.

## 11. Codeine.

### a. Commonly available forms:

- i) Plain codeine tablet and liquid formulations exist, but are not commonly stocked in pharmacies.
- ii) Acetaminophen/codeine combination is most commonly found form; 300/15, 300/30, 300/60 mg tablets; 120/12 mg per 5 ml liquid with 7% alcohol are usually stocked in pharmacies, and are available generically.
- iii) Codeine/guaifenesin cough syrups are generically available; 10/300; 10/100 mg/5 ml liquids.

### b. Dosing: 15-60 mg PO Q 4-6 hours PRN; acetaminophen is often the limiting factor.

### c. Notes:

- i) Relatively low potency.
- ii) Relatively high incidence of itching and nausea.
- iii) Must be metabolized to morphine to become active; up to 10% of Caucasians lack the cytochrome P450 necessary to do this.
- iv) In contrast, a small number of patients are ultra-metabolizers, and deaths have occurred in children, even at usual doses; it is now contraindicated following tonsillectomy for this reason.
- v) Probably only useful for mild-moderate pain early in the course of pain management.

## B. Extended-release (maintenance) narcotics.

### 1. Oxycodone extended-release.

- a. Commonly available forms: 10, 15, 20, 30, 40, 60, 80 ER tablets (OxyContin; other brand names and generics have existed in ER form in past, but are no longer available as of this writing.)
- b. Dosing: Begin 10 mg PO Q 12 hours, or individualize dose from equianalgesic conversion Q 12 hours.
- c. Notes: A commonly used, first-choice maintenance medicine.

2. Morphine extended-release.

a. Commonly available forms:

- i) 15, 20, 30, 50, 60, 80, 100, 200 mg ER tablets (MS Contin—not all tablet sizes; generic).
- ii) 30, 45, 60, 75, 90, 120 mg modified-release, once-daily capsules/sprinkle (Avinza).
- iii) 10, 20, 30, 40, 50, 60, 70, 80, 100, 130, 150, 200 mg modified-release, once-daily capsules/sprinkle (Kadian).

b. Dosing:

- i) BID PO: Begin 15-30 mg PO Q 12 hours, or individualize dose from equianalgesic conversion Q 12 hours.
- ii) QD PO (Avinza): 30 mg PO Q 24 hours, or individualize dose from equianalgesic conversion. Increase in 30 mg increments no more often than Q 4 days; maximum: 1600 mg/day. Capsules may be swallowed whole or contents sprinkled on applesauce.
- iii) QD to BID PO (Kadian): Begin 15-30 mg PO Q 12 hours, or individualize dose from equianalgesic conversion Q 12 hours. Consider trying to extend to Q 24 hr dosing.

c. Notes:

- i) Be careful not to confuse with the immediate-release formulation when prescribing; make sure the patient understands the distinction if both IR & ER versions are prescribed.
- ii) Sprinkle capsules may be useful in patients with swallowing troubles, but they are branded, and thus are more expensive.
- iii) The QD version is branded, more expensive.
- iv) Caution in severe renal impairment; accumulation of metabolites can cause agitation, delirium.

3. Fentanyl transdermal.

- a. Commonly available forms: 12.5, 25, 50, 75, 100 mcg/hour patches (Duragesic, generic); note that the 12.5 mcg patch is usually dispensed as “12 mcg.”

b. Dosing: Individualize dosage from equianalgesic conversion table; given the high potency, it is advisable to begin around 30-50% of the listed equianalgesic dosage. Patch is replaced Q 72 hours. Some patients may need Q 48 hour dosing or >100 mcg/hour (requiring more than one patch at a time). Titrate dosage every 3-6 days.

c. Notes:

- i) Do not use in opiate-naïve patients.
- ii) Analgesia reaches peak 12 hours after application, and may persist 12-24 hours after removal.
- iii) High equianalgesic potency.

#### 4. Methadone.

a. Commonly available forms:

- i) 5, 10, 40 mg tablets; 1, 2, 10 mg/ml liquid. (40 mg tablet is only available for drug treatment program usage)
- ii) SC; IM; IV.

b. Dosing:

- i) PO: 2.5-10 mg Q 8-12 hours PRN in opiate-naïve patients; for conversion, use a very conservative interpretation of equianalgesic tables. Titrate very slowly; see notes below.
- ii) SC/IM/IV: 2.5-5 mg Q 8-12 hours PRN in opiate-naïve patients; for conversion, use a very conservative interpretation of equianalgesic tables. Titrate very slowly; see notes below.

c. Notes:

- i) Methadone has a very long, variable half-life; many would reserve its use to experienced pain management specialists.
- ii) Titrate very slowly to effect; it may take 3-5 days to achieve full analgesic effect. Small dose changes may make big differences in blood levels. It is wise to make dosage changes no more often than every 4-7 days.
- iii) Begin with Q 12 hr dosing. If, after several days of observation, the patient appears to be getting initially adequate pain relief, yet it does not last 12 hours, increase frequency to Q 8 hours. There may be some individuals who will still not have pain relief for 8 hours; this situation begins to overlap with

breakthrough usage of methadone, discussed above; if this is occurring, it is advisable to try other maintenance alternatives.

- iv) Peak sedation and respiratory depressant effects may occur later than peak pain effect; always write “hold for sedation.”
- v) Methadone displays incomplete and variable cross-tolerance with other opiates; deaths have occurred from iatrogenic overdose. When converting from other opiates, it is prudent to start with 10-25% of the published equianalgesic dose and titrate to achieve pain control.
- vi) Do not use methadone for both maintenance and breakthrough purposes.
- vii) QT prolongation and torsades de pointes have occurred. Do EKG pre-treatment, after 30 days, and yearly thereafter.
- viii) Relatively safe with renal disease.

5. Oxycodone extended-release (Opana ER, generic).

- a. Commonly available forms: 5, 7.5, 10, 15, 20, 30, 40 mg ER tablets.
- b. Dosing: Start 5 mg PO Q 12 hours in opioid-naïve patients, or individualize dose from equianalgesic conversion. Give 1 hour before or 2 hours after meals.
- c. Notes:
  - i) Also known as 14-hydroxydihydromorphinone.
  - ii) Moderately expensive, even as generic.
  - iii) High equianalgesic potency.

6. Levorphanol.

- a. Commonly available forms:
  - i) 2 mg tablet.
  - ii) SC; IM; IV in some countries.
- b. Dosing:
  - i) PO: 2 mg Q 6-8 hours PRN. Titrate slowly; see notes below.
  - ii) SC/IM/IV: 2 mg Q 6-8 hours PRN. Titrate slowly; see notes below.

c. Notes:

- i) Very long half-life of 16-18 hrs, despite the need for dosing Q 6-8 hrs. Risk of accumulation with repeat dosing. Titrate no more often than Q 72 hrs.
- ii) Incomplete cross-tolerance with other opiates; use a very conservative interpretation of equianalgesic tables.
- iii) Q 6-8 hr dosing makes it most commonly used as a breakthrough med, though may be useful as maintenance drug in some patients.

7. Hydromorphone extended-release (Exalgo).

a. Commonly available forms: 8, 12, 16, 32 mg ER tabs.

b. Dosing: 8-64 mg PO Q 24 hrs, based on daily equianalgesic conversion.

c. Notes:

- i) Not for use in narcotic-naïve patients.
- ii) Decrease dose 50% in moderate renal impairment; 75% in severe renal impairment.
- iii) Very expensive.

8. Morphine extended-release/naltrexone combination (Embeda).

a. Commonly available forms: 20/0.8, 30/1.2, 50/2, 60/2.4, 80/3.2, 100/4 mg caps.

b. Dosing: Based on daily equianalgesic conversion. Try Q 24 hrs; may have to give Q 12 hrs.

c. Notes:

- i) When swallowed, naltrexone is not released; if chewed/crushed/dissolved, naltrexone is released, blocking or blunting euphoria from morphine.
- ii) May be sprinkled on applesauce.
- iii) Very expensive.

9. Tapentadol extended-release (Nucynta ER).

a. Commonly available forms:

- i) 50, 100, 150, 200, 250 mg ER tabs.
- b. Dosing: Start at 50 mg PO Q 12 hrs; may increase by 50 mg every 3 days, up to 500 mg/day.
- c. Notes:
  - i) Weak mu agonist/norepinephrine reuptake inhibitor.
  - ii) Perhaps fewer GI effects, same CNS effects, compared to other opioids.
  - iii) Avoid within 14 days of MAO inhibitor.
  - iv) Do not crush/chew/dissolve.
  - v) Expensive.

10. Tramadol extended-release.

- a. Commonly available forms: 100, 200, 300 ER tablets (Ultram ER, generic).
- b. Dosing: Start at 100 mg PO QD, or equivalent amount of immediate-release tramadol already in use. Titrate 100 mg/day every 5 days; maximum: 300 mg/day.
- c. Notes:
  - i) Low potency, so probably not a practical maintenance choice in most chronic pain settings.
  - ii) Expensive, even as generic.
  - iii) Not federally classified as a controlled substance; some states classify in Schedule IV, as psychological and physical dependence have occurred.

C. Narcotic/analgesic summary table.

<b>Drug</b>	<b>Common Doses</b>	<b>Notes</b>
<i>Immediate-Release</i>	Start low in opiate-naïve patients.	
Codeine	15-60 mg PO Q 4-6 hrs PRN.	Acetaminophen is often the limiting dosing factor. Low potency. Relatively high incidence of itching and nausea. Up to 10% of Caucasians lack the enzyme to activate.
Fentanyl IR (ABSTRAL, ACTIQ, FENTORA, LAZANDA, ONSOLIS, SUBSYS, GENERIC)	Oral or nasal transmucosal: Start with lowest dose, titrating up as needed. 50-100 mcg IV/IM Q 1-2 hrs PRN.	Multiple transmucosal forms (SL/buccal strip, tab, lozenge, oral spray, nasal spray). Even generics are expensive. Various formulations are not directly interchangeable. Do not cut/chew/crush/swallow. High equianalgesic

		potency; do not use in opiate-naïve patients.
Hydrocodone (LORTAB, VICODIN)	5-10 mg PO Q 4 hrs PRN.	A good first choice for breakthrough pain, if the acetaminophen or ibuprofen components are not limiting.
Hydromorphone (DILAUDID, GENERIC)	2-8 mg PO Q 3-4 hrs PRN. 3 mg rectally Q 6-8 hrs PRN. 1-4 mg SC/IV/IM Q 4-6 hrs PRN.	Sometimes effective when analgesia from other narcotics has waned. Acceptable with renal disease, but reduce dose 50-75% in moderate-severe CRF. High equianalgesic potency.
Levorphanol (LEVO-DROMORAN, GENERIC)	2-4 mg PO Q 6-8 hrs PRN. Parenteral form available in some countries.	Very long half-life of 16-18 hrs, despite the need for dosing Q 6-8 hrs. Incomplete cross-tolerance with other opiates; use a very conservative interpretation of equianalgesic tables. Risk of accumulation; wait 72 hrs between dosage increases.
Methadone	2.5-10 mg PO Q 8-12 hrs PRN. 2.5-5 mg SC/IV Q 8-12 hrs PRN.	Very long, variable half-life; better used as maintenance drug rather than a breakthrough med. See discussion under ER meds below.
Morphine IR (GENERIC)	10-30 mg PO/SL Q 3-4 hrs PRN. 10-20 mg Q 4 hr rectally PRN. 2.5-10 mg SC/IV Q 2-6 hrs PRN.	Be careful not to confuse with the extended-release formulation when prescribing. Caution in severe renal failure; accumulation of metabolites can cause agitation, delirium.
Oxycodone IR (ROXICODONE, GENERIC) Oxycodone IR tamper-resistant (Oxecta)	5-30 mg PO Q 4 hrs PRN.	A good choice for breakthrough pain, particularly when there is a need to avoid acetaminophen. Be careful not to confuse with the extended-release formulation when prescribing.
Oxycodone IR/acetaminophen or NSAID or ASA combinations (TYLOX, PERCOCET, others, GENERIC)	5-30 mg hydrocodone PO Q 4 hrs PRN.	Acetaminophen/NSAID often becomes the dose-limiting factor. Be careful not to confuse with extended-release formulations when prescribing.
Oxymorphone IR (OPANA, GENERIC)	10-20 mg PO Q 4-6 hrs PRN. 1-1.5 mg SC/IM Q 4-6 hrs PRN. 0.5 mg IV Q 4-6 hrs PRN.	Expensive, even as generic—though may be Alabama Medicaid-covered. Give PO doses 1 hr before or 2 hours after meals. High equianalgesic potency.
Tapentadol (NUCYNTA)	50-100 mg PO Q 4-6 hrs PRN.	Weak mu agonist/norepinephrine reuptake inhibitor. Weaker than morphine, perhaps fewer GI effects, same CNS effects.
Tramadol (ULTRAM)	50-100 mg PO QID PRN.	Central opioid agonist/SNRI. A good initial choice for mild pain. Lowers seizure threshold.
<i>Extended-Release</i>	Base initial dosing on equianalgesic conversion table.	
Fentanyl Transdermal (DURAGESIC, GENERIC)	Individualize dosage, based on equianalgesic conversion table. Replace patch Q 72 hrs.	Titrate slowly. Analgesia reaches peak 12 hrs after application; may persist 12-24 hrs after removal. High equianalgesic potency; do not use in opiate-naïve patients.
Hydromorphone ER (EXALGO)	8-64 mg PO Q 24 hrs, based on equianalgesic conversion table.	Very expensive. Sometimes effective when analgesia from other narcotics has waned. Acceptable with renal disease, but reduce dose 50-75% in moderate-severe CRF. High equianalgesic potency; do not use in opiate-naïve patients.
Levorphanol (LEVO-DROMORAN, GENERIC ER)	2-4 mg PO Q 6-8 hrs PRN. Parenteral form available in some countries.	Very long half-life of 16-18 hrs, despite the need for dosing Q 6-8 hrs. Incomplete cross-tolerance with other opiates; use a very

		conservative interpretation of equianalgesic tables. Risk of accumulation; wait 72 hrs between dosage increases. Q 6-8 hr dosing makes it most commonly used as a breakthrough med, though may be useful as maintenance drug in some patients.
Methadone	2.5-10 mg PO Q 8-12 hrs. 2.5-5 mg SC/IV Q 8-12 hrs.	Very long, variable half-life. Titrate very slowly to effect; it may take 3-5 days to achieve full analgesic effect. Peak sedation and respiratory depressant effects may occur later than peak pain effect; always write "hold for sedation." Incomplete cross-tolerance with other opiates; use a very conservative interpretation of equianalgesic tables. Relatively safe with renal disease.
Morphine ER Twice-Daily (MS CONTIN, GENERIC ER)	15-30 mg PO Q 12 hrs.	There are once-daily and sprinkle versions, but they are branded, more expensive. Caution in severe renal failure; accumulation of metabolites can cause agitation, delirium.
Morphine ER Once-Daily (KADIAN, AVINZA)	See brands for cap sizes/dosing. Can try once-daily dosing, though still may need twice daily. Unlike regular morphine, there are brand-specific maximal doses. May open cap & sprinkle, but do not crush/chew/dissolve.	Combination of immediate & delayed-release. Very expensive. Caution in severe renal failure; accumulation of metabolites can cause agitation, delirium.
Morphine ER/Naltrexone tamper-resistant (EMBEDA)	Individualize based on equianalgesic conversion table. Q 24 hrs, to Q 12 hrs if necessary. May open cap & sprinkle, but do not crush/chew/dissolve.	Naltrexone passes through gut unabsorbed if taken correctly; if abuse attempted by crushing/dissolving, it at least partially blocks euphoria from morphine. Expensive.
Oxycodone ER (OXYCONTIN)	10-80 mg PO Q 12 hrs.	A commonly used, first-choice maintenance medicine.
Oxymorphone ER (OPANA ER, GENERIC ER)	5-40 mg PO Q 12 hrs.	Expensive, even as generic. Give PO doses 1 hr before or 2 hours after meals. High equianalgesic potency.
Tapentadol ER (NUCYNTA ER)	Start at 50 mg PO Q 12 hrs; may increase by 50 mg every 3 days, up to 500 mg/day. Do not crush/chew/dissolve.	Weak mu agonist/norepinephrine reuptake inhibitor. Weaker than morphine, perhaps fewer GI effects, same CNS effects.
Tramadol ER (ULTRAM ER, GENERIC ER)	100-300 mg/day.	Expensive, even as generic. Low potency, so probably not a practical maintenance choice in most chronic pain settings.

#### D. Unrecommended agents.

1. Meperidine (Demerol).
  - a. Poorly absorbed orally.
  - b. Short half-life.

- c. Principal metabolite has no analgesic properties, has a longer half-life, is renally excreted, and produces significant adverse effects—tremulousness, dysphoria, myoclonus, and seizures.
  - d. As a result of the above, routine dosing at therapeutic levels exposes the patient to unnecessary risk of adverse effects, particularly if renal clearance is impaired.
2. Propoxyphene (Darvon, Darvocet). [Removed from U.S. market 2010.]
- a. Typically administered at doses that produce relatively little analgesia.
  - b. Dose escalation can lead to accumulation of a toxic metabolite.
  - c. Dose escalation of the acetaminophen combination product can lead to excessive acetaminophen dosage.
3. Mixed opioid agonist-antagonists.
- a. Examples: Pentazocine (Talwin), butorphanol (Stadol), buprenorphine (Buprenex, Subutex, Butrans), nalbuphine (Nubain).
    - i) Note that a buprenorphine patch (Butrans) is marketed for chronic pain, though it remains a dubious choice for the reasons stated below.
    - ii) Usually expensive, branded.
  - b. Should not be used in a patient already taking a pure opioid agonist, as they may cause a withdrawal reaction.
  - c. Not advisable as routine analgesics, since their dosing is limited by a ceiling effect.
  - d. Pentazocine and butorphanol are associated with a relatively high risk of psychotomimetic adverse effects.
4. Barbiturates and barbiturate combinations.
- a. Examples: Acetaminophen/butalbital/caffeine (Esgic, Fioricet), aspirin/butalbital/caffeine (Fiorinal).
  - b. Barbiturates are CNS depressants, with no inherent analgesic properties. In fact, there is evidence that, in low doses, they actually *hyperalgesic*, partially negating the analgesic effect of the other components.
  - c. Barbiturates are habituating, and thus have a high abuse potential. Psychological and physical dependence may occur; the severity of withdrawal symptoms are determined by the amount, duration, and continuity of their use.

E. Equianalgesic narcotic conversions.

1. Equianalgesic conversions generally compare to a standard dose of morphine 10 mg parenterally, which is equivalent to morphine 30 mg orally.
2. Theoretically, tramadol 400 mg would be equivalent to 30 mg morphine orally, but this is not a recommended dose.
3. Dosing conversions are approximate, given the variability of individual response and incomplete cross tolerance.
4. Given this variability, it is wise to begin with 50-70% of the calculated equianalgesic dose, and titrate to effect; for the more potent narcotics, many would advise starting at 30-50% of the calculated equianalgesic dose. Also note the specific dosing considerations for methadone discussed above.

5. Equianalgesic narcotic conversion table:

Medication	Equianalgesic Doses	
	Parenteral	Oral
Morphine	10 mg	30 mg
Codeine	120 mg	200 mg
Fentanyl (DURAGESIC)	0.1 mg	individualize
Hydrocodone (LORTAB)	N/A	30 mg
Hydromorphone (DILAUDID)	1.5 mg	7.5 mg
Levorphanol (LEVO-DROMORAN)	2 mg (single dose; reduce to 1 mg for chronic dosing)	4 mg (single dose; reduce to 1 mg for chronic dosing)
Methadone	5 mg	10 mg
Oxycodone (TYLOX, OXYCONTIN)	N/A	20 mg
Oxymorphone (OPANA)	N/A	10 mg
Tapentadol (NUCYNTA)	N/A	Not formally established; clinical trials suggest 100 mg
Fentanyl (DURAGESIC) Patch	24 Hour Oral MS Dose = Initial Patch Dose	
	45 mg	12 mcg/hr
	90 mg	25 mcg/hr
	180 mg	50 mcg/hr
	360 mg	100 mcg/hr

VI. ADJUNCTIVE PHARMACOLOGIC MEASURES

A. Acetaminophen and nonsteroidal anti-inflammatory drugs (NSAIDs).

1. Acetaminophen is generally safe, with mild analgesic effects additive to other agents. One must note that acetaminophen is a component of many narcotic combination agents, and the total dosage of acetaminophen may actually be the limiting dosing factor.
2. Nonsteroidal anti-inflammatory drugs can provide analgesic effects additive to other agents; they are sometimes included in narcotic combination products. One must take note of their known gastrointestinal, hepatic, and renal toxicities, which may preclude use in many patients.

B. Antidepressants.

Depression is often concomitant with chronic pain, and antidepressants can treat this problem; in addition, they may be directly effective for pain in the absence of depression. The possibility of at least initially increased suicidal ideation at the start of antidepressant therapy should be considered.

1. Tricyclics.
  - a. There is good evidence of efficacy in chronic pain, especially neuropathic pain.
  - b. Most are generic and inexpensive.
  - c. Anticholinergic side effects are common, especially in the tertiary amines, such as amitriptyline and imipramine, so they would be best avoided in the elderly. The sedative effect could be useful in some patients, however.
  - d. The secondary amines, such as desipramine and nortriptyline, have fewer anticholinergic effects.
  - e. Other considerations include cardiac conduction abnormalities, and narrow-angle glaucoma exacerbation.
2. Selective serotonin reuptake inhibitors (SSRIs).
  - a. Evidence of efficacy in chronic pain is relatively sparse.
  - b. Several branded and generic options are available.
  - c. Side effects include nausea, constipation, sedation or agitation, serotonin syndrome, weight gain, sexual dysfunction, decreased libido, and insomnia. However, often they are better-tolerated and safer than tricyclics.
3. Serotonin and norepinephrine Reuptake inhibitors (SNRIs).
  - a. There is good evidence of efficacy in chronic pain.
  - b. Venlafaxine (Effexor) is available generically; it exhibits only serotonergic effects below doses of 150 mg. Duloxetine (Cymbalta) and milnacipran (Savella) are not available generically, but are marketed specifically for treatment of pain. Desvenlafaxine (Pristiq) may have efficacy similar to venlafaxine; it is only marketed for depression.
  - c. Side effects are similar to those of the SSRIs: nausea, constipation, sedation or agitation, serotonin syndrome, weight gain, sexual dysfunction, decreased libido, and insomnia.
4. Bupropion (Wellbutrin).
  - a. Evidence of efficacy in chronic pain is very limited.
  - b. While both are available generically, the SR generic is cheaper than the XL generic.

- c. The SR version has to be dosed BID; the XL version is dosed once daily.
- d. Side effects include agitation or sedation, insomnia, weight loss, and lowering of seizure threshold.

### C. Anticonvulsants.

#### 1. First generation agents.

- a. There is good evidence of efficacy in chronic pain.
- b. Several branded and generic options are available.
- c. Examples include carbamazepine (Tegretol, Carbatrol), oxcarbazepine (Trileptal), valproate (Depakene), divalproex (Depakote), and phenytoin (Dilantin).
- d. Side effects include dizziness, sedation, ataxia, confusion, nausea, gingival hypertrophy; rarely blood dyscrasias, hepatotoxicity, and other severe hypersensitivity reactions are seen.

#### 2. Second generation agents.

- a. There is good evidence of efficacy in chronic pain, especially neuropathic pain.
- b. Examples include gabapentin (Neurontin, generic), pregabalin (Lyrica), and lamotrigine (Lamictal, generic).
- c. Side effects include dizziness, sedation, ataxia, fatigue, nausea, weight gain, and serious toxic rashes (with lamotrigine).
- d. It may take several weeks to see maximum efficacy with gabapentin.
- e. Pregabalin and lamotrigine are scheduled, but there is low risk of abuse.

### D. Corticosteroids.

- 1. May be useful in the presence of acute nerve compression, increased intracranial pressure, bone pain, visceral pain (obstruction and/or capsular distention), anorexia, nausea, and depressed mood.
- 2. Dexamethasone is often the drug of choice, due to its long half-life and minimal mineralocorticoid effect.
- 3. Given the well-known side effects of chronic steroids, they are often best reserved for episodic use, or in the face of terminal illness.

4. Steroid psychosis should be considered if an agitated delirium appears.

E. Miscellaneous.

1. Caffeine 65-200 mg/dose may increase the analgesic effect of acetaminophen, aspirin, and non-steroidal anti-inflammatory drugs.
2. Hydroxyzine 25-50 mg parenterally or 50-100 mg PO may add to the analgesic effect of opiates while also relieving nausea.
3. For bone pain, bisphosphonates (alendronate, pamidronate), calcitonin, radiopharmaceuticals, and external beam radiation may be useful adjuncts to opioids, NSAIDs, and corticosteroids.
4. For bowel obstruction not amenable to mechanical or surgical intervention, anticholinergics, such as dicyclomine (Bentyl) and scopolamine, may be useful.
5. Topical anesthetics, such as capsaicin and the lidocaine 5% patch, may be effective for episodic, localized pain flare-ups; they may be particularly useful for neuropathic pain. They have not been extensively studied for long-term use, and their practical usefulness may be limited by body geography or poor tolerance of localized burning.

F. Adjunctive pain medication summary table. (Partially adapted from Maizels, Morris, and Bill McCarberg; Antidepressants and Antiepileptic Drugs for Chronic Non-Cancer Pain; Am Fam Physician 2005;71:483-90.)

DRUG	DOSAGE	SIDE EFFECTS, CAUTIONS, & NOTES
<b>Antidepressants</b>		
<i>Tricyclics</i>		SE: Dry mouth, constipation, urinary retention, sedation, weight gain, possibility of at least initially increased suicidal ideation. CI: Cardiac conduction abnormalities, recent cardiac events, narrow-angle glaucoma. Notes: Good evidence of efficacy in chronic pain; most all generic.
Amitriptyline (ELAVIL) Imipramine (TOFRANIL)	10-25 mg QHS; increase by 10-25 mg every 3 wks to effect or 150 mg.	Notes: Tertiary amines have greater anticholinergic effects—avoid use in elderly.
Desipramine (NORPRAMIN) Nortriptyline (PAMELOR)	25 mg QHS; increase by 25 mg every 3 wks to effect or 150 mg.	Notes: Secondary amines have fewer anticholinergic effects.
<i>Selective Serotonin Reuptake Inhibitors</i>		SE: Nausea, constipation, sedation or agitation, serotonin syndrome, weight gain, sexual dysfunction, decreased libido, insomnia, possibility of at least initially increased suicidal ideation. Notes: Efficacy in chronic pain is relatively poor; several branded & generic.

<i>Serotonin &amp; Norepinephrine Reuptake Inhibitors</i>		SE: Nausea, constipation, sedation or agitation, serotonin syndrome, weight gain, sexual dysfunction, decreased libido, insomnia, possibility of at least initially increased suicidal ideation. Notes: Good evidence of efficacy in chronic pain.
Duloxetine (CYMBALTA)	20-60 mg QD; for pain consider 60 mg BID.	
Milnacipran (SAVELLA)	50 mg BID; for pain consider 12.5 mg QD x1 day, then 12.5 mg BID x2 days, then 25 mg BID x4 days, then 50 mg BID; Max: 200 mg/day.	
Venlafaxine (EFFEXOR)	Start at 37.5 mg QD; increase to 75 mg/150 mg/225 mg/max 300 mg every 3 wks.	Notes: Only serotonergic effects below 150 mg; generic.
<i>Novel Antidepressants</i>		
Bupropion (WELLBUTRIN)	Start at 150 mg XL QAM; increase to 300 mg in a wk if necessary.	SE: Agitation or sedation, insomnia, weight loss, lowering of seizure threshold, possibility of at least initially increased suicidal ideation. Notes: Evidence of efficacy in chronic pain is very limited; the SR generic is cheaper than the XL generic, but it has to be dosed BID.
<b>Anticonvulsants</b>		
<i>First-Generation Agents</i>		Notes: Good evidence of efficacy in chronic pain; many generics.
Carbamazepine (TEGRETOL, CARBATROL)	Start at 100 mg BID; titrate to 1200 mg/day divided BID-QID.	SE: Dizziness, sedation, rarely aplastic anemia & other severe hypersensitivity reactions. Notes: There are branded ER formulations.
Oxcarbazepine (TRILEPTAL, GENERIC)	Start at 300 mg BID; titrate 600 mg/day weekly up to 1200 mg BID.	SE: Same as carbamazepine, though usually less severe.
Phenytoin (DILANTIN)	Start at 100 mg QHS; titrate every 1-3 wks, to 500 mg QHS max.	SE: Dizziness, sedation, ataxia, confusion, nausea, gingival hypertrophy, rarely blood dyscrasias, hepatotoxicity, & other severe hypersensitivity reactions. Notes: There are branded ER formulations.
Valproate (DEPAKENE), Divalproex (DEPAKOTE)	Start at 250 mg BID, titrate rapidly to lowest effective dose, typically as high as 500 mg TID.	SE: Dizziness, sedation, ataxia, confusion, nausea, rarely blood dyscrasias, hepatotoxicity, pancreatitis, & other severe hypersensitivity reactions. Notes: There are generic versions of valproate.
<i>Second-Generation Agents</i>		Notes: Good evidence of efficacy in chronic pain.
Gabapentin (NEURONTIN)	Start at 300 mg QD; titrate every few days to max 3600 mg/day divided TID.	SE: Dizziness, sedation, ataxia, fatigue, nausea, weight gain. Notes: Maximum efficacy may be seen several wks after initiation; generic.
Lamotrigine (LAMICTAL)	Start at 50 mg QD; titrate every 2 wks to max 400 mg/day divided QD-BID.	SE: Dizziness, nausea, constipation, rarely serious toxic rashes. Notes: Scheduled, but low risk of abuse; generic.

Pregabalin (LYRICA)	Start at 75 mg BID; titrate every few days to max 300 mg/day divided BID-TID.	SE: Dizziness, sedation, ataxia, fatigue, nausea, weight gain. Notes: Scheduled, but low risk of abuse.
<b>Corticosteroids</b>		
Dexamethasone, several others	2-20 mg or more QD.	SE: Proximal myopathy, candidiasis, bone loss, and other toxicities are possible, but are seldom a problem in the setting of terminal disease. Observe for steroid-induced psychosis. Notes: Dexamethasone is preferred, due to its long half-life and minimal mineralocorticoid effect.
<b>Nonsteroidal Anti-inflammatory Drugs</b>		
Many	Various.	SE: Gastrointestinal, hepatic, and renal toxicities. Notes: NSAIDs can provide analgesic effects additive to other agents, but their toxicities may preclude use in many patients.
<b>Miscellaneous</b>		
Caffeine	65-200 mg per opiate dose.	May increase the analgesic effect of acetaminophen, aspirin, and NSAIDs.
Hydroxyzine	25-50 mg parenterally or 50-100 mg PO per opiate dose.	May add to the analgesic effect of opiates while also relieving nausea.
Topical analgesics (lidocaine, capsaicin, diclofenac, others)	Various.	Helpful for neuropathic and localized orthopedic pain.

Dosing information and cautions are abbreviated; see prescribing information for individual agents. SE = Side Effects. CI = Contraindications.

## VII. ADJUNCTIVE NONPHARMACOLOGIC MEASURES

### A. Physical therapy: exercise and rehabilitation.

1. Rehabilitative strategies are especially appropriate in patients with persistent nonmalignant pain associated with impairment in physical functioning and deconditioning. While they may not provide adequate pain relief when used alone, they often lead to demonstrable improvements in quality of life and functional ability.
2. Therapeutic exercise (physical therapy) can be an extremely helpful adjuvant to pain management. Patients with persistent pain may restrict activity, believing it makes their pain worse or does physical harm. This results in physical deconditioning, which further complicates chronic pain syndromes. Once serious underlying physical pathology has been excluded, patients should be educated that “hurt does not equal harm;” in fact, when physical deconditioning is reversed with gentle and appropriate exercise, pain levels may decrease. Moderate levels of physical activity should be maintained, even if the pain persists, and the program should include exercises that improve flexibility, strength, and endurance.
3. External mechanical supports, such as braces and splints, may provide relief from movement-related pain.
4. Other rehabilitative strategies include work hardening programs, vocational training, and occupational therapy.

### B. Physical therapy: pain management modalities.

1. In addition to exercise and function-oriented interventions, physical therapists can also provide a variety of pain management modalities. Evidence-based data is often limited or conflicting, and there appears to be a good deal of individual variability with regard to response.
2. Heat, cold, or alternating heat and cold may be helpful in chronic pain, especially for episodic exacerbations.
3. Therapeutic massage, perhaps augmented by liniment, vibration, or ultrasound, may also relieve pain. Massage is thought to transiently alter physiological responses to pain, and to induce relaxation.
4. Transcutaneous electrical nerve stimulation (TENS) involves pulsed transcutaneous electrical stimulation, under the gate control theory of pain, which states that non-noxious dorsal horn stimulation may inhibit transmission of pain information from the periphery to the brain. Although it has been difficult to show benefit from TENS in controlled trials, individual successes have occurred, and a trial is justified in selected patients.

### C. Invasive/interventional modalities.

1. Various sensory nerve blocks, sympathetic nerve blocks, and injection therapies may provide pain relief in selected, difficult to manage cases.
2. There is limited to moderate evidence that epidural steroid injections can provide long-term relief from cervical pain or lumbar pain.
3. Specialists may be able to provide implant therapies, such as dorsal column stimulation and neuraxial infusion pumps, in highly selected patients.

### D. Cognitive behavioral therapy (CBT).

1. Cognitive-behavioral therapy encompasses the gamut of psychological interventions that can be taught to patients to lessen pain intensity, improve coping, increase function, and reduce overall disability. Studies have demonstrated that patients are often receptive to such measures.
2. Persistent pain sufferers may demonstrate negative thought patterns, such as overgeneralization, catastrophizing, all-or-none-thinking, jumping to conclusions, selective attention, and negative predictions, all of which can increase the emotional difficulty of living with pain.
3. Examples of psychological approaches to pain management include relaxation, imagery, hypnosis, biofeedback, art therapy, music therapy, distraction methods, coping techniques, time management, sleep hygiene training, and psychotherapy.
4. Multidisciplinary consultation may be necessary to take full advantage of many of these methods.

### E. Alternative therapies.

1. Acupuncture is among the oldest interventions for pain, though it has remained a source of controversy among physicians not trained in this discipline, because there is no clear understanding of its physiological effects that is acceptable to Western concepts of medicine. Nonetheless, existing evidence indicates that it can be effective for pain.
2. Chiropractic and manipulative therapy focuses on the relationship between bodily structure and function, and how that relationship affects the preservation and restoration of health; these are also concepts that can be difficult to reconcile with Western concepts of medicine. Studies, primarily on back pain, have shown short-term positive results with regard to pain and disability, superior to sham therapies, but not superior to effective conventional treatments.

3. Herbs and nutritional supplements are commonly embraced by patients, though there is not an abundance of controlled studies supporting them. Given the variability of the available preparations, and the possibility of interaction with several over-the-counter and prescription medications, their use is not widely recommended.

## VIII. REFERENCES AND FURTHER READING

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