

**San Francisco General Hospital / Community Health Network of San Francisco  
Management of Pain Guideline**

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**Pain is defined as:**

- an unpleasant sensory and emotional experience most often associated with actual or potential tissue damage, or described in terms of such damage (International Association for the Study of Pain).
- not just the unpleasant sensation, not just the perception of the sensation, but also the emotional reaction to or experience of the perceived sensation

**Pain is therefore always subjective.**

- This subjectivity creates for the clinician the primary dilemma of pain management: one cannot either prove or disprove the patient's report of pain.
- Self report is the most reliable method to assess pain (AHCPR Cancer Pain Guidelines)
  - Ask the patient if he/she is in pain.
  - Believe the answer you receive unless and until you have overwhelming evidence to distrust the self report and potentially jeopardize your therapeutic relationship.
- Cultural and psychological factors influence the expression of and tolerance for pain.

**Unrelieved pain has consequences for patients:**

- Unnecessary suffering
- Catabolic state
- Respond less well to curative medical or surgical treatments, with higher complication rates.
- More emotional and social disturbance
- In some circumstances, patients with unrelieved pain die sooner

**Factors decreasing pain threshold, i.e., cause the patient to be in more pain:**

- Insomnia
- Anxiety
- Anger
- Fatigue
- Fear
- Shame
- Nausea
- Misunderstanding
- Sadness
- Depression
- Introversion
- Any other discomfort
- The memory of past pain and expectation that pain will recur.

**Factors increasing pain threshold, i.e., cause the patient to have less pain:**

- Relief of other symptoms
- Distraction
- Adequate sleep/rest
- Treatment of psychiatric disorders
- Understanding
- Around the clock pain medication

**Acute pain**

- Follows injury and generally disappears when the injury heals
- Has a well-defined temporal onset
- May be associated with objective physical signs of autonomic nervous activity: tachycardia, diaphoresis, elevated blood pressure, pallor, pupillary dilation - like anxiety.
- May serve as a warning or have a protective purpose
- Is best treated by recognizing and addressing the cause directly and using analgesics administered around the clock to maintain steady blood levels and avoid uncontrolled pain.
- Episodic or procedural pain can be anticipated and is best treated prophylactically.
- Untreated, may lead to development of chronic pain.

**Chronic pain**

- May not have a well-defined cause or temporal onset
- Lasts months to years
- Typically occurs without signs of autonomic nervous system hyperactivity

- Often associated with the signs and symptoms of depression: hopelessness, helplessness, anhedonia, appetite and weight change, sleep disturbance, decreased social interaction.
- Underlying cause may not be identifiable or treatable
- Serves no purpose
- Should be prevented whenever possible
- Is never treated solely on a p.r.n. basis.
- Best managed with an interdisciplinary approach, including
  - psychological and non-pharmacological interventions
  - long-acting medications for 24 hour relief
  - short-acting medications for breakthrough pain

### **Neuropathic pain**

- Is characterized by burning, tingling, numbness, and/or electrical or pins-and-needles dysesthesias, which may radiate along peripheral nerve distribution
- Associated with decreased sensation and/or hypersensitivity.
- Accompanies many medical and surgical conditions (HIV disease, diabetes, alcoholism, shingles, amputations and other trauma, cerebrovascular events, spinal cord injury, etc.)
- Is often undiagnosed.
- Responds to specific anti-neuropathic agents, but may also require non-specific analgesics

### **Muscle spasm**

- Described as tight, pulling, squeezing
- Common with spinal or joint injuries or surgery, and in bed bound patients.
- Responds to heat, massage, stretching, and muscle relaxants such as **baclofen, cyclobenzapine, tizanadine, benzodiazepines** and occasional intraspinal infusion of **local anesthetics**.

### **Pain assessment**

- Facilitates communication about pain intensity among patient, family and clinicians
- Enables the evaluation of pain relief interventions
- Numeric scales such as 0-10 (sometimes 0-5 or 0-3) are used to rate pain intensity or severity, with 0 being no pain and 10 being the worst imaginable pain
- Initial assessment should include
  - Location
  - Intensity
  - Frequency and duration
  - Quality
  - Effect on function
  - Previous pain management strategies and their effectiveness
  - Psychosocial evaluation
  - Substance abuse history
  - Physical examination, especially the neurologic and musculoskeletal exam
  - Appropriate diagnostic work-up to try to determine the cause of the pain
- Reassessment of pain should be done at regular intervals and with changes in clinical condition
- Patients often have multiple pains; each must be assessed separately to ensure appropriate treatment decisions.

### **Goals of pain management**

- Maximal functional status for the patient
- Not necessarily 0 pain
- Are negotiated with the patient
- Anticipation and management of treatment side effects

### **Pain treatment involves a combination of psychosocial/behavioral, rehabilitation, non-pharmacological, and pharmacological techniques, including:**

- Physical therapy
- Exercise
- Acupuncture
- Spiritual exploration
- Hobbies
- Humor
- Distraction
- Visualization
- Meditation

- Biofeedback/autogenic training
- Massage
- Heat and cold
- Enhancement of coping skills
- Self-hypnosis
- Transcutaneous electrical nerve stimulation
- Therapeutic provider-patient relationship

### **Nerve Blocks**

- Regional blocks (brachial plexus, sciatic, popliteal, ankle) may help with acute pain.
- Sympathetic blocks or coeliac plexus blocks for chronic pain are often impermanent, but may provide significant temporary relief for some patients.

### **Principles of Pharmacologic Pain Treatment**

- Medications, including controlled substances, are generally effective provided they are utilized skillfully, with knowledge of pharmacokinetics and without unnecessary fear or restraint.
- Success rates for the management of pain in terminally ill patients have been reported in the range of 90% or higher in hospice programs; whether one should expect equal success in patients who are not terminally ill is not known.
- The dose of the analgesic is adjusted to give the patient adequate pain control; the interval between doses is adjusted so that the analgesic effect is uninterrupted.
- Increase opioid dosage by percentages – 10%, 15%, 20% - not milligrams.
- Prevention of pain is better than treatment - stay ahead of the pain.
- The biologic half-life of an agent must be taken into account when adjusting the dosage and interval. The maximum effect of a given dose may not be seen until the drug has been administered over 4 to 5 half-lives.
- The duration of analgesia may be shorter than the half-life, and the half-life may be prolonged in renal or hepatic failure. In the latter situation one should administer short-acting agents at increased intervals.
- Once pain is controlled satisfactorily, the dose of analgesic usually remains fairly stable; an increase in analgesic requirement most often mean progression of disease or new pathology rather than the development of tolerance.
- Onset of analgesia depends on the route of administration. In general, for IV medications onset is 5-10 minutes, for SQ or IM 20-40 minutes, and for PO 20-60 minutes. Rectal and sublingual onset may be closer to SQ or IM because these routes avoid first pass metabolism in the liver.
- IM, IV, and SQ doses are considered equianalgesic for most agents.

### **Route of administration**

- Oral administration is the preferred route as it usually facilitates a more even blood level, is cheaper, less intimidating, does not require skilled staff, and does not transmit infection as needles do. As a culture we need to move away from the expectation that only a “pain shot” can treat severe pain.
- In special situations other routes of administration may be effective e.g., highly concentrated opioid solutions, IV patient controlled analgesia via pump, transdermal patches, subcutaneous infusions and spinal administration.
- Parenteral opioids may be administered after failure of the oral route, or when the oral route is not available.
- Continuous subcutaneous infusion is usually as effective as intravenous infusion and less invasive. Adding 600 U/L of hyaluronidase allows an increase in the hourly infusible volume to as high as 80 ml (hypodermoclysis).

### **Patient-controlled analgesia (PCA)**

- (PCA), with doses administered by the patient within professionally established limits, has been shown to lessen post-operative pain, decrease surgical complications, lead to earlier hospital discharge, and lessen the total amount of opiate consumed. Though this concept has been applied most frequently to parenteral pumps, it reinforces the desirability of active patient participation in the selection, assessment, and control of analgesic regimens.

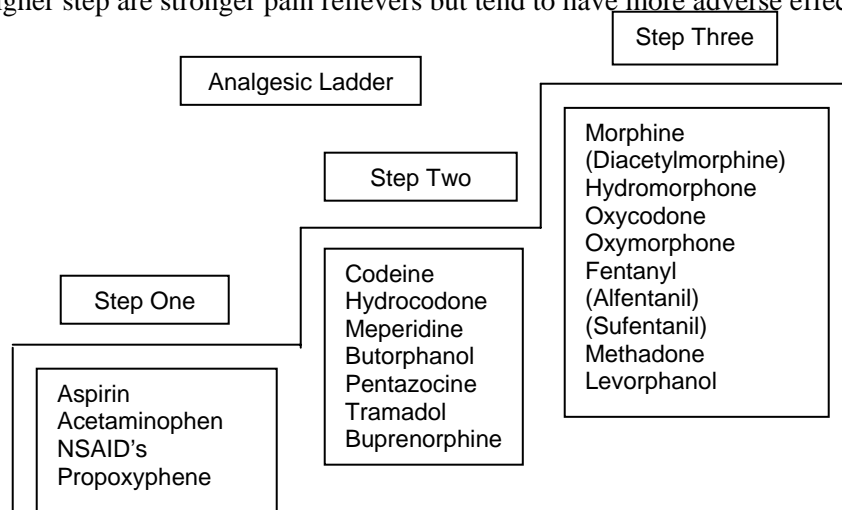
- Basal rates of infusion of opioids via PCA pumps are potentially problematic in patients with any hepatic or renal functional abnormalities, elderly patients, or patients with changing pain, such as post-op patients. Basal rates may be indicated in patients with chronic stable pain.
- The initial hourly dosage of a constantly infused drug should be one fourth the every-4-hour bolus dose. Boluses of the 1 - to 2 - hour equivalent amount may be given as a loading dose, before painful procedures, and/or every 15 minutes for breakthrough pain.
- Intraspinal (epidural or intrathecal) regimens can provide analgesia at lower dosages and may reduce systemic side effects. This route may be especially useful in acute post-operative pain, particularly after thoracic, abdominal, or pelvic surgery. The equianalgesic epidural dosage of morphine is about one tenth the parenteral dosage, whereas the intrathecal dosage is about one tenth the epidural dosage. The intraspinal route is invasive, expensive, requires close monitoring, and necessitates involvement of an anesthesiologist or pain specialist.

### Treatment of neuropathic pain

- tricyclic agents - specific anti-neuropathic effect, separate from antidepressant effect occurs at lower doses (10-75mg vs 150-300mg) and sooner (1-3days vs weeks); all tricyclics seem to work; choose one with fewest side effects, avoiding **amitriptyline**, choosing **desipramine**, **nortriptyline**, **imipramine** instead; selective serotonin re-uptake inhibitors lack analgesic properties, **venlafaxine** or **duloxetine** may be useful
- anticonvulsants - **carbamazepine**, **topiramate**, **lamotrigene**, **phenytoin**, **valproic acid**, even **clonazepam** tried, **gabapentin** now best studied, with minimum effective dose 900mg in an adult and upper limit not defined (6gms per day and more sometimes used).
- **mexilitene** - antiarrhythmic, an oral form of lidocaine (150-200mg TID to 1200mg qd); avoid in patients prone to arrhythmias. **Lidocaine** infusion or topical application effective; do not keep lidocaine patches on for more than 18 hours per day. Other anti-arrhythmics not well studied.
- **baclofen** up to 20mg QID may be useful in neuropathy as well as spasm
- **capsaicin**, topical agent derived from chili peppers, burns when applied; **analgesic balm** sometimes used
- these agents are often combined, and opiates may be added if these more specific approaches are ineffective

### Analgesic ladder

- Progressively stronger medications often used, especially for somatic or visceral pain.
- Agents on the higher step are stronger pain relievers but tend to have more adverse effects.



### Step 1 Agents

- non-steroidal agents have analgesic and anti-inflammatory properties; for non-inflammatory conditions (most degenerative joint disease), 800mg **ibuprofen** not much stronger than 400mg or 1gm acetaminophen; for inflammatory conditions (rheumatoid arthritis), 800mg provides much more pain relief. No published data show one NSAID provides more pain relief than another, including **indomethacin** and **ketorolac**. The latter has a high incidence of side effects, is expensive, and should be restricted to situations where one needs an anti-inflammatory and the oral route cannot be used.

**Salsalate, choline magnesium trisalicylate and nabumetone** do not affect platelet function. Cox-2 inhibitors, such as **celecoxib** and **rofecoxib** have been associated with cardiovascular toxicity; a proton pump inhibitor may be added to a non-specific NSAID to decrease GI bleeding. NSAIDs and acetaminophen are synergistic and have non-overlapping toxicities.

- **acetaminophen** can cause significant hepatotoxicity, especially in those with underlying active liver disease. In general, limit to 4 gms per day for acute use, monitor LFT's in chronic use.
- **propoxyphene**, a synthetic opioid, is no stronger than acetaminophen and has a metabolite that accumulates in the body

### Step 2 Agents

- Like Step 1 drugs, and unlike Step 3 drugs, these have a maximum dosage. They are frequently combined with Step 1 agents.
- **codeine** has a maximum dose of about 120mg q4h in an adult
- **hydrocodone** also cannot be continuously titrated; beware combinations with high dose acetaminophen because of acetaminophen toxicity
- **meperidine** is a short acting agent with a metabolite that accumulates with repeated dosing and which lowers the seizure threshold; if used at all for pain, limit to comfortable patients who will be uncomfortable for a short time only, i.e., during a colonoscopic or other procedure. Repeated doses should not be given. Agent of choice for treatment of rigors.
- **pentazocine, butorphanol**, and other mixed agonist-antagonists have a high incidence of psychotomimetic adverse effects, cannot be titrated as other opiates can be, and must be left to wear off before one can administer an effective agent because of antagonist properties.
- **tramadol**, although chemically not an opiate, fits into the  $\mu$  opiate receptor and is thus prone to abuse like other Step 2 drugs; centrally active and lowers seizure threshold
- **buprenorphine** is a partial opiate agonist with a long half life which binds tightly to receptors; expensive; must be administered several times per day when given for pain.
- **oxycodone** can be titrated like other Step 3 agents, i.e. without upper limit, but dosage must be limited when it is combined with aspirin or acetaminophen as in percocet or percodan.

### Step 3 Agents

- **morphine** is the standard against which other analgesics are measured. Titrate the dose against the pain with short acting morphine, then divide the twenty four hour total in half and administer it as the sustained release preparation q12 hrs. Oral dosing is preferred and effective - use two to three times the parenteral dose. As the long-acting preparations are made by suspending the drug in a matrix, do not crush these tablets. Long-acting pills are well absorbed rectally; concentrated oral solutions usually well absorbed buccally.
- **hydromorphone** is slightly shorter acting, with similar properties to morphine
- **oxycodone** comes as a short-acting and long acting preparation.
- **oxymorphone** is recently available as short- and long-acting preparations.
- **methadone** can be used for pain relief but requires q6-8 hour dosing for this indication. Its lipophilicity causes it to accumulate, sometimes requiring a reduction in dose after two or three days. Equianalgesic tables inaccurate at higher doses of this agent.
- **levorphanol** has properties similar to methadone
- **fentanyl**, a short-acting agent when given intravenously or buccally, has been converted into a q72 hr (in some patients a q48 hr) agent when administered by transdermal patch.
  - Use patches only for chronic stable pain, never in post-op or unpredictable pain
  - Onset of analgesia can take more than 12 hours, and the agent's effects can last more than 18 hours after patch is removed.
  - Allergic skin reactions to the patch are common; use of a topical spray from a respiratory steroid inhaler prevents the rash and allows the patch to stick.
  - Absorption from the patch may increase if the patient is febrile or even with elevated ambient temperature.

### Adverse Effects of Opiates

- **Constipation** almost universal in patients taking opiates and should be anticipated
  - the one effect to which patients do not become tolerant
  - prophylactic treatment better than p.r.n.
  - stool softeners and senna propulsants are useful, as is sorbitol
  - avoid bulk agents
- **Nausea** common with opiates, and often caused by constipation. Useful agents:
  - antihistamines
  - butyrophenones (**haloperidol, droperidol**)
  - phenothiazines (**prochlorperazine, promethazine**)
  - scopolamine
  - rarely, benzodiazepines
- **Itching** may respond to antihistamines, and is often self-limited
- **Sedation** may be temporary with initiation of therapy. If persistent:
  - try reducing the dose of medication
  - increase the interval between doses
  - switch agents
  - add **caffeine**, or rarely **dextroamphetamine** or **methylphenidate**
- **Respiratory depression** rare in chronic opioid therapy
  - observe patient closely; physical stimulation may be sufficient
  - if **naloxone** required, dilute 0.4mg ampule in 10cc NS and administer 0.5ml IV push q 2 minutes. Titrate dose to avoid withdrawal, seizures, severe pain.
- **Decreased libido, fertility** with long term use.

### Regulatory Barriers

- Fear of regulators has been shown to play a role in the repeatedly studied and documented under-treatment of pain
- CA Health and Safety Code section 11159.2 allows providers with their own DEA numbers to use regular prescriptions for controlled substances for those terminally ill patients expected to live one year or less
- California is only the second state to discipline one physician for under-prescribing pain medication. On average, the California Medical Board discipline 17 physicians per year for over-prescribing.
- One California physician has been successfully sued for elder abuse for under-treatment of pain.
- Thorough documentation is the best defense against over-zealous regulators.

### Physical dependence, drug abuse, drug addiction, pseudoaddiction

- **physical dependence** occurs when, after a period of continuous use, abrupt discontinuation of an agent causes physical symptoms (withdrawal or abstinence syndrome)
  - physical dependence is a common feature of opioids, corticosteroids, barbiturates, benzodiazepines, antihypertensives and other agents.
  - physical dependence is easily managed by gradually tapering the drug if it is no longer needed
- **drug abuse** is the inappropriate use of a medication for a non-medical problem, i.e., to escape family, work, social or financial problems.
- **addiction** is a chronic neurobiologic disease with genetic, psychosocial and environmental factors influencing its development and manifestations, characterized by behaviors that include impaired control over drug use, compulsive use, continued use despite harm, and craving.
  - The medical use of opiates is not associated with the development of addiction, with the exception of the individual in recovery from opiate addiction, who may be at risk of relapse.
- Screening for drug abuse or addiction:
  - “Have you ever tried to stop using or cut down?”
  - “Has your family or anyone else ever complained about or discouraged your use?”
  - “Have you ever had trouble with driving while under the influence?”
  - “Did you ever get into trouble or have difficulty at work or school due to your use?”
  - “Have you ever been injured while under the influence?”

- **pseudoaddict**
  - patient with a chronic painful condition who requires opiates to function normally
  - may exhibit behaviors which providers label as manipulative, obsessive or drug seeking in order to find sufficient relief from pain to fully participate in life. These behaviors stop promptly after adequate analgesia is provided.
- **Behaviors that may or may not predict addiction:**
  - having more than one prescription provider, obtaining analgesics from emergency departments or drop-in settings
  - increasing prescribed analgesic dose or frequency
  - seeking early refills
  - losing prescriptions / medications
  - forging a prescription
  - obtaining opioids from street sources
  - requesting drugs of higher street value or rapid-onset formulations or routes of administration
  - hoarding unused medications
  - non-adherence to recommended non-opioid treatments or evaluations
  - supplementing analgesics with alcohol or other psychoactive drugs
  - using analgesics to relieve symptoms other than pain.

### **Urine toxicology** – know your laboratory

Approximate duration of detectability of drugs in urine by commonly used screening tests:

Amphetamines	2-4 days
Barbiturates	3 days
Phenobarbital	2 weeks or longer
Cannabinoids	
Infrequent user	up to 10 days
Chronic user	30 days or longer
Cocaine metabolite	2-3 days
Methadone	2-4 days
Other opiates	2-3 days
Propoxyphene	3-7 days
Phencyclidine (PCP)	3-8 days

Confirmatory tests: gas liquid chromatography with or without mass spectrometry, high performance liquid chromatography.

Beating the test: substitution, adulteration with chemicals, dilution – Substance Abuse and Mental Health Services Administration uses a cut off of specific gravity of 1.003 and urine creatinine concentration of 40 mg/dl

Know the **street value** of drugs which may be diverted.

It is in the patient's best interest to insist on certain conditions for prescribing controlled substances, e.g. concurrent treatment for substance abuse and/or mental health problems.

The provider-patient relationship, like most human relationships, is two sided. The provider and the patient both have rights and both have responsibilities. Sometimes these should be made explicit.

**Prescribing rules.** Establish the rules early. Be prepared to enforce them.

When the prescribing rules are violated there is no necessity to stop seeing the patient - we should not abandon the patient unnecessarily. We should refuse to prescribe controlled substances for that patient, at least temporarily, while providing other kinds of care.

When treating an individual with a history of addiction:

- Do not overuse intramuscular and intravenous analgesics - avoid needles
- Patients using / taking chronic opioids will require higher doses than those patients not using / taking chronic opioids.
- Use long acting, not short acting, opiates.

- Use scheduled, not prn, dosing of those opiates.
- Consider having one prescriber of all psychoactive medications
- Obtain information from sources other than the patient
- Include non-controlled substances and non-pharmacologic approaches as indicated
- Consult early and often
- Document what you do
- Be aware of the environment, but keep your eye on the patient.

“The aim of medicine is surely not to make men virtuous; it is to safeguard and rescue them from the consequences of their vices.” H.L. Mencken

### Know how to get appropriate help in your medical setting.

10/06

#### Equianalgesic Dosing Table for Opioids

Use this table for determining approximate dose conversions when changing from one route of administration to another or from one drug to another.

Doses in each column should give about the same amount of pain relief. Use a lower than equianalgesic dose when changing drugs, then re-titrate to the desired clinical response in each patient.

(Pediatric dosing [persons weighing < 50kg])

Drug	Approximate equianalgesic oral dose	Approximate equianalgesic parenteral dose	How supplied (non-parenteral)
<b>Codeine</b>	130mg q3-4hr (0.5-1mg/kg q3-4hr)	75mg q3-4hr (not recommended)	15, 30, 60mg tablets, tyco #2, #3, #4; soln. 5ml =12.5mg codeine + 120mg acetaminophen or 30mg codeine + 160mg acetaminophen
<b>Hydrocodone</b> in Vicodin, Lortab, etc.	30mg q3-4hr (0.2mg/kg q3-4hr)	not available	2.5, 5, 7.5 and 10mg tablets with 500mg ASA or 500-750mg acetaminophen
<b>Buprenorphine</b> Buprenex, Subutex also in Suboxone	1mg q6hr	0.3mg q6-8hr 2-6µg/kg q6-8hr	2, 8mg tablets  same strengths with naloxone
<b>Oxycodone</b> Roxicodone, Intensol; also in Percocet, Percodan, Tylox, Roxicet, Roxiprin, Endodan, Endocet. Oxycontin sustained release (q8-12hr)	20mg IR q3-4hr (0.2mg/kg q3-4hr)	not available in US	5mg per combination tablet; 5, 15, 30mg tablet; 1mg/ml, 20mg/ml soln., 10, 20, 40, 80mg sustained release tablet
<b>Meperidine (Pethidine)</b> Demerol	300mg q2-3hr (not recommended)	100mg q2-3hr (0.75mg/kg q2-3hr) not recommended for around the clock dosing	50, 100mg tabs, 10mg/ml syrup
<b>Morphine</b> MSIR, OMS, Roxanol; MS Contin, Oramorph SR sustained release (q8-12hr) Kadian (q12-24hr), Avinza (q24hr)	30mg IR q3-4hr, (0.15mg/kg q3-4hr) round the clock; 60mg single dose or intermittent dosing	10mg q3-4hr (0.15mg/kg q3-4hr neonates 0.03mg/kg, <6months 0.05mg/kg)	2mg/ml, 20mg/ml and other oral solutions; 15, 30, 60, 100, 200mg sustained release tablet. various
<b>Hydromorphone</b> Dilaudid	7.5mg q3-4hr (0.03-.08mg/kg q3-4hr)	1.5mg q3-4hr (0.015-.03mg/kg q3-4hr)	1mg/ml oral soln; 2,4,8mg tab, 3mg rectal suppositories
<b>Oxymorphone</b> Numorphone, Opana,	10mg IR q3-4hr	1mg q3-4hr (not recommended)	5, 10mg tablet, 5, 10, 20, 40mg sustained release tablet 5mg rectal suppositories
<b>Methadone</b> Dolophine	20mg q8hr (0.2mg/kg q8h)	10mg q8h (0.1-0.2mg/kg q8h)	5, 10mg tablet, 1, 2, and 10mg/ml soln
<b>Levorphanol</b> Levo-Dromoran	4mg q8h (0.04mg/kg q8h)	2mg q8h (0.02mg/kg q8h)	2mg tablet
<b>Fentanyl</b> Sublimaze; Duragesic transdermal patch (q72hr)	not available	2.5mg/hr morphine IV = 30mg q3h morphine PO = 25µg/hr (1-3µg/kg/hr) fentanyl IV infusion or patch	25, 50, 75, 100µg transdermal patch; 200, 300, 400µg transmucosal lozenge

Recommended dosing schedules do not apply to patients with renal and/or hepatic insufficiency or other conditions affecting drug metabolism and kinetics.

These dosing recommendations do not apply to babies less than 6 months to one year except as noted.

Dosing of aspirin or acetaminophen must be considered when titrating combination preparations.

Rectal administration of morphine and hydromorphone is possible, with dosing approximately the same as the oral route.

Codeine doses above 120 mg q4h are not useful due to diminishing incremental analgesia but continually increasing constipation and other adverse effects.

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