Butorphanol is a Schedule III drug under the US Controlled Substances Act.

**Commonly Prescribed For**
- Management of moderate-to-severe pain, which is defined as pain of intensity >4 on the numerical rating scale 0–10 (where 0 means no pain and 10 the worst pain imaginable). It can be administered parenterally or by using the intranasal spray formulation (management of migraine).
- Preoperative or preanesthetic medication, supplement for balanced general anesthesia, and management of pain during labor. Only parenteral use.

**How the Drug Works**
- Butorphanol exhibits partial agonist activity under some circumstances and in other circumstances antagonist activity at the mu opioid receptor and agonist activity at the kappa opioid receptor. When given alone, the mu-receptor-mediated physiological effects of butorphanol appear to be predominant; however, in combination with naltrexone, some kappa-agonist activity becomes evident. Stimulation of these receptors on CNS neurons causes an intracellular inhibition of adenylate cyclase, closing of influx membrane calcium channels, and opening of membrane potassium channels. This leads to hyperpolarization of the cell membrane potential and suppression of action potential transmission of ascending pain pathways. Because of its kappa-agonist activity, at therapeutic doses butorphanol may increase pulmonary arterial pressure and cardiac work, and cause dysphoria.

**How Long until It Works**
- The analgesic effect of butorphanol is influenced by the route of administration. Onset of analgesia is within a few minutes for IV administration, within 15 minutes for IM injection, and within 15 minutes for the nasal spray doses (butorphanol NS).
- Peak analgesic activity occurs within 30–60 minutes following IV and IM administration and within 1–2 hours following the nasal spray administration.
- The duration of analgesia varies depending on the pain model as well as the route of administration, but is generally 3–4 hours with IM and IV doses as defined by the time 50% of patients required remedication. In postoperative studies, the duration of analgesia with IV or IM butorphanol was similar to morphine, meperidine, and pentazocine when administered in the same fashion at equipotent doses. Compared to the injectable form and other drugs in this class, butorphanol NS has a longer duration of action (4–5 hours).

**If It Works**
- Fewer than 1% of patients using butorphanol had experiences that suggested the development of physical dependence or tolerance. Much of this information is based on experience with patients who did not have prolonged continuous exposure to butorphanol. However, in one controlled clinical trial where patients with chronic pain from nonmalignant disease were treated with butorphanol NS for up to 6 months, overuse (which may suggest the development of tolerance) was reported in 3% of patients.

**If It Doesn’t Work**
- Consider switching to another opioid preparation.
- Consider alternative treatments for moderate to severe pain.

**Best Augmenting Combos for Partial Response or Treatment Resistance**
- Short-acting opioids for breakthrough pain might be used.
- Adding adjuvant analgesics, like 5-HT1 receptor agonists, working predominantly at the B, D, and F subtypes (sumatriptan) also as a NS formulation shows no interaction on butorphanol effect provided always that both administrations are separated by 30 minutes. However, it should be noted that both products are capable of producing transient increases in blood pressure.

**Tests**
- No specific laboratory tests are indicated.
ADVERSE EFFECTS AND PATIENT BEHAVIORS DURING THE COURSE OF OPIOID THERAPY

How Drug Causes Adverse Effects

- Via CNS opioid receptors and opioid receptors in the periphery
- Physical dependence
  Physical dependence is defined by the occurrence of an abstinence syndrome (withdrawal) following an abrupt reduction of the opioid dose or the administration of an opioid antagonist. An abstinence syndrome might include myalgias, abdominal cramps, diarrhea, nausea/vomiting, mydriasis, yawning, insomnia, restlessness, diaphoresis, rhinorrhea, piloerection, and chills. Although there is extensive individual variability, it is prudent to assume that physical dependence will develop after an opioid has been administered repeatedly for several days. Physical dependence is not an indicator of addiction. Opioids can be safely discontinued in physically dependent patients. The syndrome is self-limiting, usually lasting 3–10 days, and is not life-threatening (unless occurring in highly debilitated patients or premature infants).
- Tolerance
  Tolerance (“true” analgesic tolerance or pharmacodynamic tolerance) describes the need to progressively increase the opioid dose in order to maintain the same degree of analgesia.
- Opioid-induced hyperalgesia (OIH)
  Hyperalgesia is a form of pain hypersensitivity. Hyperalgesia is a symptom of the opioid withdrawal syndrome seen when opioid administration is abruptly terminated or reversed by the administration of an opioid antagonist. It is still debatable if OIH develops independently from opioid withdrawal or if it becomes more significant during withdrawal because its symptom is no longer opposed by the opioid analgesic effect. OIH has been observed experimentally in animals and humans, but its significance in clinical settings is still unclear. Based on preclinical studies, opioids are thought to have a dual effect: an initial analgesic effect followed by the parallel activation of a hyperalgesic system to counteract the analgesic effect of the opioid. The mechanisms that may contribute to OIH remain uncertain.
- Pseudotolerance
  Pseudotolerance is the patient’s perception that the drug has lost its effect. It requires a differential diagnosis of conditions that mimic “true” analgesic tolerance. These conditions include progression or flare-up of the underlying disease, occurrence of a new pathology, increased physical activity in the setting of mechanical pain, lack of treatment adherence, pharmacokinetic tolerance, manufacturing differences of the same opioid agent, and OIH.
- Addiction
  A primary, chronic, neurobiologic disease, with genetic, psychosocial, and environmental factors influencing its development and manifestations. It is characterized by behaviors that include one or more of the following: impaired control over drug use, craving, compulsive use, and continued use despite harm.

Aberrant behaviors

Opioids are the second most commonly abused drugs in the U.S. Aberrant behaviors include a wide variety of actions, some of criminal purpose:

- selling prescription drugs
- prescription forgery
- stealing another patient’s drugs
- injecting oral formulations
- obtaining prescription drugs from nonmedical sources
- concurrent use of licit or illicit drugs
- multiple unauthorized and uncontrollable dose escalations
- Pseudoaddiction
  Pseudoaddiction refers to the occurrence of problematic behaviors related to extreme anxiety associated with unrelieved pain. This includes unsanctioned dose escalation, aggressive complaining about needing more drugs, and impulsive use of opioids. It can be differentiated from addiction by the disappearance of these behaviors when access to analgesic medications is increased and pain control is improved.
- Opioid-induced constipation (OIC)
  Opioid-induced constipation is a common adverse effect associated with opioid therapy. OIC is commonly described as constipation; however, it refers to a constellation of adverse GI effects, which also includes abdominal cramping, bloating, gastroesophageal reflux disease (GERD), and gastroparesis. The mechanism for these effects is mediated primarily by stimulation of opioid receptors in the GI tract. In patients with pain, uncontrolled symptoms of OIC can add to their discomfort and may serve as a barrier to effective pain management by limiting therapy or prompting discontinuation. Prophylactic treatment should be provided for constipation. Constipation can be managed with peripherally acting opioid antagonist...
compounds (e.g. alvimopan, methylnaltrexone) when available or by a stepwise approach that includes an increase in fluids and osmotic agents (e.g. sorbitol, lactulose), or with a combination stool softener and a mild peristaltic stimulant laxative such as senna or bisacodyl, as needed. Oral naloxone, which has minimal systemic absorption, has also been used empirically to treat constipation without reversing analgesia in most cases.

- **Nausea and vomiting**
  A meta-analysis of opioids in moderate to severe noncancer pain found nausea to affect 21% of patients. Opioids can cause dizziness, nausea, and vomiting by stimulating the medullary chemoreceptor trigger zone, increasing the inner ear vestibular system (i.e., motion sickness), or inducing gastroparesis (or even GERD).
  
  With vomiting, parenteral administration of antiemetics may be required. If nausea is caused by gastric stasis, treatment is similar to that of GERD. Tolerance to nausea usually develops.

- **Biliary tract increased pressures and/or spasm**

- **Drowsiness**
  Common, related to dose, especially observed at initiation of treatment or when dose is increased. Tolerance may develop over time.
  
  Daytime drowsiness can be minimized by using a low starting dose and titrating progressively. If somnolence does occur, it usually subsides within a few days as tolerance develops. The use of a stimulant (e.g. modafinil, methylphenidate) can be considered if persistent somnolence has a detrimental effect on the patient’s functioning.

- **Delirium**
  Delirium is frequent in elderly patients, particularly those with cognitive impairment. It can be prevented or treated by using low doses of immediate release (IR) opioids and discontinuing other CNS-acting drugs.

- **Hypogonadism**
  Hypogonadism (low testosterone serum levels) can occur in male patients. The testosterone level should be verified in patients who complain of sexual dysfunction or other symptoms of hypogonadism (e.g. fatigue, anxiety, depression). Testosterone supplementation may be effective in treating hypogonadism, but close monitoring of the testosterone serum level as well as screening for benign prostate hypertrophy and prostate cancer should be carried out.

- **Cardiovascular effects**
  Because this compound may increase the work of the heart, especially the pulmonary circuit, its use in patients with acute myocardial infarction (MI), ventricular dysfunction, or coronary insufficiency should be limited to those situations where the benefits clearly outweigh the risk. Severe hypertension has been reported rarely during therapy. In such cases, butorphanol should be discontinued and the hypertension treated with antihypertensive drugs. In patients who are not opioid dependent, naloxone has also been reported to be effective.

### Life-Threatening or Dangerous AEs
- In overdose or when taken with CNS depressants, respiratory depression
- However, though respiratory depression fosters the greatest concern, tolerance to this AE develops rapidly. Respiratory depression is very uncommon if the opioid is titrated according to accepted dosing guidelines

### Weight Gain
- **Unusual**

### Sedation
- **Common**

### What to Do about AEs
- Wait while treat AE symptomatically
- Lower the dose
- Switch to another opioid agent
- The assessment and management of AEs is an essential part of opioid therapy. By adequately treating AEs, it is often possible to titrate the opioid to a higher dose and thereby increase the responsiveness of the pain
- Because different opioids can produce different AEs in a given patient, opioid rotation is an option for the treatment of persistent adverse effects
**DOsing and Use**

**Usual Dosage Range**
- IV: the usual recommended single dose is 1 mg/3–4 hours as necessary
- IM: the usual recommended single dose is 2 mg in patients who will be able to remain recumbent, in the event drowsiness or dizziness occurs
- Nasal spray: the usual recommended dose for initial nasal administration is 1 mg (1 spray in one nostril). Adherence to this dose reduces the incidence of drowsiness and dizziness

**Dosage Forms**
- IV/IM: 1–2 mg/mL
- NS: 10 mg/mL

**How to Dose**
- IV: titrate dose to the needs of the patient. Effective dosage range is 0.5–2 mg/3–4 hours
- IM: titrate dose to the needs of the patient. 2 mg/3–4 hours, as necessary. Effective dosage range depending on the severity of pain is 1–4 mg/3–4 hours. There are insufficient clinical data to recommend single doses above 4 mg
- NS: if adequate pain relief is not achieved after 1 mg, within 60–90 minutes, an additional 1-mg dose may be given. The initial dose sequence outlined above may be repeated in 3–4 hours as required after the second dose of the sequence. Depending on the severity of the pain, an initial dose of 2 mg (1 spray in each nostril) may be used in patients who will be able to remain recumbent in the event drowsiness or dizziness occurs. In such patients single additional 2-mg doses should not be given for 3–4 hours

**Dosing Tips**
- Butorphanol NS is usually used as 1 spray in 1 nostril. If pain relief does not occur within 60–90 minutes, another single spray may be used. This 2-dose sequence usually is repeated every 3–4 hours as needed
- The pump must be primed (made ready to work) if it is not used for 48 hours or longer. One bottle provides approximately 8–10 doses (if priming is needed) or 14 or 15 doses (if no priming is needed between any doses)
- The analgesic effect of butorphanol NS may be diminished when it is administered shortly after sumatriptan nasal spray, but by 30 minutes any such reduction in effect should be minimal. A slower onset can be anticipated if butorphanol NS is administered concomitantly with, or immediately following, a nasal vasoconstrictor
- Because of its opioid antagonist properties, butorphanol is not recommended for use in patients dependent on opioids

**Overdose**
- Confusion, extreme sedation, respiratory depression, and death
- Fatalities have been reported due to overdose both in monotherapy and in conjunction with sedatives, in particular benzodiazepines, or alcohol use

**Long-Term Use**
- The patients will develop physical dependence and may develop tolerance on long-term use
- In patients with addiction vulnerability, risk of aberrant behaviors and addiction

**How to Stop**
- Assuming that the pain has improved, butorphanol administered dose can be decreased by 25% every 3–6 days to prevent or minimize withdrawal symptoms
- Alternatively, butorphanol can be converted to an oral long-acting agent; then similarly, the dose of this agent can be tapered down by 25% every 3–5 days

**Pharmacokinetics**
- Butorphanol is extensively metabolized in the liver. Oral bioavailability is only 5–17% because of extensive first-pass metabolism of butorphanol. It is not known if the effects of butorphanol are altered by other concomitant medications that affect hepatic metabolism of drugs (erythromycin, theophylline, etc.), but physicians should be alert to the possibility that a smaller initial dose and longer intervals between doses may be needed

**Drug Interactions**
- Concurrent use of butorphanol with CNS depressants (e.g. alcohol, barbiturates, tranquilizers, and antihistamines) may result in increased CNS depressant effects. When used concurrently with such drugs, the dose of butorphanol should be the smallest effective dose and the frequency of dosing reduced as much as possible when administered concomitantly with drugs that potentiate the action of opioids
As previously mentioned, the analgesic effect of butorphanol NS may be diminished when it is administered shortly after sumatriptan nasal spray, but by 30 minutes any such reduction in effect should be minimal. A slower onset can be anticipated if butorphanol NS is administered concomitantly with, or immediately following, a nasal vasoconstrictor.

Other Warnings/Precautions
- The safety of butorphanol has not been established in patients below 18 years of age.
- In patients taking opioid analgesics chronically, butorphanol can precipitate withdrawal symptoms.

SPECIAL POPULATIONS

Hepatic or Renal Disease
- In patients with hepatic or renal impairment, the initial dose of butorphanol injection should generally be half the recommended adult dose (0.5 mg IV and 1.0 mg IM). Repeat doses in these patients should be determined by the patient’s response rather than at fixed intervals but will generally be no less than 6 hours apart.
- The initial dose sequence of butorphanol NS should be limited to 1 mg followed, if needed, by 1 mg in 90–120 minutes. The repeat dose sequence in these patients should be determined by the patient’s response rather than at fixed times but will generally be at intervals of no less than 6 hours.

Elderly
- Due to changes in clearance, the mean half-life of butorphanol is increased by 25% (to over 6 hours) in patients over the age of 65 years.
- Elderly patients may be more sensitive to the side effects of butorphanol. In clinical studies of butorphanol NS, elderly patients had an increased frequency of headache, dizziness, drowsiness, vertigo, constipation, nausea and/or vomiting, and nasal congestion compared with younger patients. There are insufficient efficacy data for patients ≥65 years to determine whether they respond differently from younger patients.
- The initial dose of butorphanol injection recommended for elderly patients should generally be half the recommended adult dose (0.5 mg IV and 1.0 mg IM). Repeat doses should be determined by the patient’s response.
- Initially a 1-mg dose of butorphanol NS should generally be used in geriatric patients and 90–120 minutes should elapse before administering a second 1-mg dose, if needed. Butorphanol and its metabolites are known to be substantially excreted by the kidney, and the risk of toxic reactions to this drug may be greater in patients with impaired renal function. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection.
- Due to frequent comorbidities and polypharmacy, as well as increased frailty, older patients are more prone to AEs from opioids. Concerns regarding AEs are held by healthcare professionals, patients, and patients’ families, and can prevent older patients from receiving adequate pain control. Unfortunately, untreated pain also has a detrimental effect on older people, including reduced physical functioning, depression, sleep impairment, and decreased quality of life. The inadequate management of postoperative pain has also been shown to be a risk factor for delirium. Most opioid analgesics can be used safely and effectively in older patients, providing the regimen is adapted to each patient’s specificities and comorbidities (e.g. the presence of renal or hepatic failure, dementia). As in all patients, regardless of age, the opioid should be started at the lowest available dose and titrated slowly, depending on analgesic response and AEs. Slow release (SR), long-acting formulations can be used safely, but they should only be given to patients for whom an effective and safe daily dose of a short-acting opioid has been established. The efficacy of the opioid should be re-evaluated on a regular basis and it should be discontinued if not effective. The presence of AEs should be assessed systematically, and they should be treated where possible. For frequent AEs, it might be appropriate to institute a preventive regimen (e.g. a prophylactic bowel regimen in patients at risk of constipation). Nonopioid analgesics (e.g. acetaminophen), adjuvant analgesics, and nonpharmacologic treatments (e.g. physical therapy, exercise) should be used concurrently with opioid therapy. These will reduce the opioid dose that is required to achieve analgesia, and hence reduce the associated AEs.

Children and Adolescents
- Butorphanol should not be used in patients under 18 years of age.
Pregnancy
- Category C
- There are no adequate and well-controlled studies. However, pregnant rats treated subcutaneously with butorphanol at 1 mg/kg (5.9 mg/m²) had a higher frequency of stillbirths than controls. Butorphanol at 30 mg/kg oral (360 mg/m²) and 60 mg/kg oral (720 mg/m²) also showed higher incidences of postimplantation loss in rabbits.

Breast-Feeding
- Butorphanol is excreted in human milk
- The amount an infant would receive is probably clinically insignificant

THE ART OF PAIN PHARMACOLOGY

Potential Advantages
- Butorphanol has high lipid solubility, low molecular weight, and high potency, making it suitable for intranasal preparation

Potential Disadvantages
- Relatively weak analgesic effects

Primary Target Symptoms
- Acute pain
- Management of acute migraine
- Preoperative or preanesthetic medication, supplement for balanced general anesthesia, and management of pain during labor

Pearls
- In general, “agonist/antagonist” type opioids should never be used to treat long-term chronic pain
- Comfortable intranasal absorption in patients with migraine headache. Should be utilized cautiously and infrequently
- Butorphanol, like other mixed agonist/antagonists with a high affinity for the kappa receptor, may produce unpleasant psychotomimetic effects in some individuals
- Because of its opioid antagonist properties, butorphanol is not recommended for use in patients dependent on opioids
- In patients taking opioid analgesics chronically, butorphanol has precipitated withdrawal

symptoms such as anxiety, agitation, mood changes, hallucinations, dysphoria, weakness, and diarrhea

Universal Precautions and Risk Management Plan
- Opioids are highly effective drugs for treating moderate to severe pain. However, both patients’ and physicians’ fears of drug abuse and addiction (and potential associated legal sanctions) are an important barrier to the effective use of opioids for this indication. Unfortunately, this can result in the undertreatment of pain
- The physician is responsible for assessing whether the patient is at a relatively low or high risk of addiction and/or abuse. Risk factors for addiction can be divided into three categories:
  - Genetic factors (e.g. family history of addiction). One of the most consistent predictors of addiction is a personal or family history of substance abuse
  - Psychosocial factors (e.g. depression, anxiety, personality disorder, childhood abuse, unemployment, poverty)
  - Drug-related factors (e.g. neuroadaptation associated with craving)
- The application of a standardized approach to managing chronic pain patients with opioids has been referred to as UNIVERSAL PRECAUTIONS. An integral component of such precautions is the implementation of a risk management plan, including strategies to monitor, detect, manage, and report addiction or abuse. The following points are of relevance:
  1. Interview and examine the patient
  2. Try to establish the pain diagnosis, outline the differential diagnosis
  3. Recommend the appropriate diagnostic work-up
  4. Discuss opioid therapy, benefits and risks, and potential exit strategies. The criteria for stopping opioid therapy should be discussed with the patient prior to starting therapy, and a written exit strategy should be in place, in case the patient:
    ✓ fails to show decreased pain or increased function with opioid therapy
    ✓ experiences unacceptable adverse effects or toxicity
    ✓ violates the opioid treatment agreement (see below)
    ✓ displays aberrant drug-related behaviors

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5. Perform a psychosocial assessment of the patient including screening for low or high risk of addictive disorders; proactive screening strategies should be employed, based on the perceived level of risk. Validated screening tools and questionnaires for patients with pain include: (1) Opioid Risk Tool (ORT) www.painknowledge.org/physician tools/ORT/ORT%20Patient%20Form.pdf, (2) Screener and Opioid Assessment for Patients with Pain (SOAPP) www.painedu.org/soapp-development.asp. If appropriate, obtain urine drug testing (UDT) at baseline.

6. Document informed consent and treatment agreement

7. Initiate trial of opioid therapy ± adjuvant medications

8. Assess ANALGESIA, ACTIVITY, ADVERSE EFFECTS, and ABERRANT BEHAVIORS (4As) at follow-ups. For assessments of pain and function may use the Brief Pain Inventory (BPI). Pill count and urine drug testing are the most common strategies to assess compliance. UDT can be performed to check for the presence of prescribed medications as evidence of their use, and for the presence of illicit drugs. A negative test for prescribed medications does not necessarily indicate diversion, but could be due to laboratory test inaccuracy or to inadequate dosing or problematic use. This result would, however, merit further discussion with the patient. The aim of UDT is not simply to ensure adherence, but to enhance the doctor–patient relationship by providing documentation of adherence to the treatment plan. If problematic or aberrant behavior is identified, the physician should reassess the patient to provide a potential diagnosis (e.g. pseudoaddiction, pseudotolerance, cognitive impairment, encephalopathy, anxiety or personality disorder, depression, addiction, criminal activity).

9. Continue or discontinue opioid therapy, or discharge patient from practice. On the basis of the severity of the problematic behavior, patient history, and the findings of the reassessment, the physician must make a decision regarding treatment continuation and referral (e.g. to an addiction specialist). Treatment should only be continued if pain relief and maintained function are evident, control over the therapy can be reacquired, and there is improved monitoring. Any changes in the treatment plan must be comprehensively documented. All physicians should follow federal and state laws regarding the prescribing of controlled substances. Regarding the prescription of opioids to a reliable and clinically stable patient who is affected by a chronic disabling painful disorder, federal regulations are articulated under the Controlled Substances Act (CSA) and monitored by the Drug Enforcement Administration (DEA).

10. Avoid withdrawal symptoms if you discontinue opioid therapy by using a slow tapering schedule (reducing the opioid dose by 10–20% each day). Anxiety, tachycardia, sweating, and other autonomic symptoms that persist may be lessened by slowing the taper. Clonidine at a dose of 0.1–0.3 mg/day over 2–3 weeks can be recommended for individuals who are known to have a history of a problematic withdrawal.

Opioid Treatment Agreement

- Before the start of therapy, the expectations and obligations of both the patient and physician should be clearly established in a written or verbal agreement. The opioid agreement facilitates informed consent, patient education, and adherence to the treatment plan.
- As a tool, the opioid agreement may also describe the treatment plan for managing pain, provide information about the side effects and risks of opioids, and establish boundaries and consequences for opioid misuse or diversion.
- The agreement can help to reinforce the point that opioid medications must be used responsibly, and assure patients that these will be prescribed as long as they adhere to the agreed plan of care. An example of an agreement is available for perusal at www.ampainsoc.org/societies/mps/downloads/opioid_medication_agreement.pdf.

Patient Education

- Patient education is an essential part of opioid therapy; it should begin before therapy is instituted, and continue throughout the course of treatment. The physician has to address the following components of education while talking to the patient:
- Opioids are powerful pain-relieving drugs, and are effective in a number of painful disorders.
However, they are strictly regulated and must be used as directed, and only by the patient to whom they are prescribed.

- The goals of pain management are to help the patient feel better and live a more active life. It takes more than pain medications: wellness program, comprehensive assessment, exercises, appropriate diet, physical therapy, and relaxation are also very important.
- These medicines cannot be stopped abruptly, and they need to be tapered off gradually and only under and according to the physician’s directions.
- Common adverse effects include nausea, dry mouth, and drowsiness with cognitive impairment, impaired voiding, and itchy skin. These usually last 1–2 weeks until tolerance develops. They can be managed. Nausea and itch may be prevented by antiemetics.

Opioid Rotation

- Opioid rotation refers to the switch from one opioid to another, and it can be recommended when AEs or onset of analgesic tolerance limit the degree of analgesia obtained with the current opioid; opioid rotation is commonly recommended and performed between pure opioid agonists. In pain management, opioid rotation of mixed opioid agonist–antagonists to/from pure opioid agonists can be difficult and clinically unfeasible to be carried out. If necessary, it is recommended that the initial opioid (e.g. a pure agonist) be tapered down and almost discontinued before starting with the upward titration of the new opioid.
- According to clinical experience and observations, opioid rotation may result in clinical improvement in >50% of patients with chronic pain who have had a poor response to one opioid.
- Opioid rotation should always be based on an equianalgesic opioid conversion table, which provides values for the relative potencies among different opioid drugs. The first step is to determine the patient’s current total daily opioid utilization. This can be accomplished by adding up the doses of all long-acting and short-acting opioids taken by the patient per day. If the patient is on multiple opioids, convert all of them to morphine equivalents using standard equianalgesic tables.
- Usually, when switching from opioid A to opioid B, it is initially prudent to reduce the calculated equianalgesic dose of opioid B by 50%. If opioid B is methadone, and you are switching from

Goals of Opioid Therapy

- The goal of opioid therapy is to provide analgesia and to maintain or improve function, with minimal AEs. The careful use of opioid analgesics may be considered in the treatment of pain when nonopioid analgesics (e.g. acetaminophen, NSAIDs, calcium channel alpha-2-delta ligands, duloxetine) and nonpharmacologic options have proven inadequate for pain control. When medically appropriate, opioid analgesics can be recommended for chronic, moderate to severe pain, which, for practical purposes, is defined as pain of intensity >4 on the numerical rating scale 0–10 (where 0 means no pain and 10 the worst pain imaginable).
- Opioids are still considered among the most potent and effective “broad-spectrum” analgesics in the treatment of acute and chronic pain. As such, they have been prescribed to patients suffering from moderate to severe disabling pain of both cancer and noncancer origin. The indications for the use of opioids in moderate to severe chronic pain of noncancer origin are osteoarthritis, musculoskeletal pain, and neuropathic pain, with the common denominator that various pharmacologic and nonpharmacologic procedures have proved unsuccessful.
- It is crucial to recognize that patients will respond differently to various opioids in terms of both potency and effectiveness. Variability among patients can be quite profound. This can extend towards both the analgesic effects and the AEs. Reports of lack of analgesic effects should be regimen and adherence. Predicting a patient’s response to medication has long been a goal of clinicians; it is possible that pharmacogenomics may, in due course, become in common use for screening for variations in the expression of drug-metabolizing enzymes (e.g. cytochrome CYP3A4), and thus provide a potent tool for improving pain management.

BUTORPHANOL
>200 mg/day dose of morphine or morphine equivalent, the initially calculated dose of methadone should be reduced by 90%, and given in divided doses not more often than every 8 hours. If you are rotating to opioid B and opioid B is transdermal fentanyl, then maintain the equianalgesic dose.

- The initial dose of opioid B should also be further reduced based on clinical circumstances, for example, in the elderly or in the patients who have significant cardiopulmonary, hepatic, or renal disease.

- The patient must remain under close clinical supervision to prevent overdose. Under supervision, a safe, effective, and rapid opioid rotation and titration (RORT) can also be performed via IV patient-controlled analgesia. This option should be considered for patients with severe disabling pain who are on large daily doses of opioids, including oral methadone or multiple opioids, and for frail or elderly patients.

Suggested Reading


