NARCOTICS (OPIOIDS/OPIATES) INFORMATION

Description

Narcotic (*nar-KOT-ik*) analgesics (*an-al-JEE-zicks*) are used to relieve pain. Some of these medicines are also used just before or during an operation to help the anesthetic work better. Codeine and hydrocodone are also used to relieve coughing. Methadone is also used to help some people control their dependence on heroin or other narcotics. Narcotic analgesics may also be used for other conditions as determined by your doctor. Narcotic analgesics act in the central nervous system (CNS) to relieve pain. Some of their side effects are also caused by actions in the CNS. If a narcotic is used for a long time, it may become habit-forming (causing mental or physical dependence). Physical dependence may lead to withdrawal side effects when you stop taking the medicine. These medicines are available only with your medical doctor's or dentist's prescription. For some narcotics, prescriptions cannot be refilled and you must obtain a new prescription from your medical doctor or dentist each time you need the medicine. In addition, other rules and regulations may apply when methadone is used to treat narcotic dependence.

Proper Use of This Medicine

To take *long-acting morphine and oxycodone tablets* :
These tablets must be swallowed whole. Do not break, crush, or chew them before swallowing. *Take this medicine only as directed by your medical doctor or dentist*. Do not take more of it, do not take it more often, and do not take it for a longer time than your medical doctor or dentist ordered. This is especially important for young children and elderly patients, who are especially sensitive to the effects of narcotic analgesics. If too much is taken, the medicine may become habit-forming (causing mental or physical dependence) or lead to medical problems because of an overdose. If you think this medicine is not working properly after you have been taking it for a few weeks, *do not increase the dose*. Instead, check with your doctor.

Dosing - The dose of these medicines will be different for different patients. *Follow your doctor's orders or the directions on the label*. The following information includes only the average doses of these medicines. *If your dose is different, do not change it* unless your doctor tells you to do so. The number of capsules or tablets, depends on the strength of the medicine. Also, *the number of doses you take each day, the time allowed between doses, and the length of time you take the medicine depend on the narcotic you are taking, whether or not you are taking a long-acting form of the medicine, and the reason you are taking the medicine*.

Missed dose - If your medical doctor or dentist has ordered you to take this medicine according to a regular schedule and you miss a dose, take it as soon as you remember. However, if it is almost time for your next dose, skip the missed dose and go back to your regular dosing schedule. *Do not double doses*.

Storage - To store this medicine: Keep out of the reach of children. Overdose is very dangerous in young children. Store away from heat and direct light. Do not store tablets or capsules in the bathroom, near the kitchen sink, or in other damp places. Heat or moisture may cause the medicine to break down. Do not keep outdated medicine or medicine no longer needed. Be sure that any discarded medicine is out of the reach of children.

Additional Information

Once a medicine has been approved for marketing for a certain use, experience may show that it is also useful for other medical problems. Although not specifically included in product labeling, morphine by injection is used in certain pediatric patients with the following medical conditions: Pain, during mechanical ventilation, neonatal Pain, postoperative, neonatal. Other than the above information, there is no additional information relating to proper use, precautions, or side effects for these uses.

Before Using This Medicine

In deciding to use a medicine, the risks of taking the medicine must be weighed against the good it will do. This is a decision you and your doctor will make. For narcotic analgesics, the following should be considered:

Allergies - Tell your doctor if you have ever had any unusual or allergic reaction to any of the narcotic analgesics. Also tell your health care professional if you are allergic to any other substances, such as foods, preservatives, or dyes.

Pregnancy - Although studies on birth defects with narcotic analgesics have not been done in pregnant women, these medicines have not been reported to cause birth defects. However, hydrocodone, hydromorphone, and morphine caused birth defects in animals when given in very large doses. Buprenorphine and codeine did not cause birth defects in animal studies, but they caused other unwanted effects. Butorphanol, nalbuphine, pentazocine, and propoxyphene did not cause birth defects in animals. There is no information about whether other narcotic analgesics cause birth defects in animals. Too much use of a narcotic during pregnancy may cause the baby to become dependent on the medicine. This may lead to withdrawal side effects after birth. Also, some of these medicines may cause breathing problems in the newborn infant if taken just before delivery.

Breast-feeding - Most narcotic analgesics have not been reported to cause problems in nursing babies. However, when the mother is taking large amounts of narcotics, the nursing baby may become dependent on the medicine. Also, butorphanol, codeine, meperidine, morphine, opium, and propoxyphene pass into the breast milk.

Children - Breathing problems may be especially likely to occur in children younger than 2 years of age. These children are usually more sensitive than adults to the effects of narcotic analgesics. Also, unusual excitement or restlessness may be more likely to occur in children receiving these medicines.

Older adults - Elderly people are especially sensitive to the effects of narcotic analgesics. This may increase the chance of side effects, especially breathing problems, during treatment.

Other medicines - Although certain medicines should not be used together at all, in other cases two different medicines may be used together even if an interaction might occur. In these cases, your doctor may want to change the dose, or other precautions may be necessary. When you are taking a narcotic analgesic, it is especially important that your health care professional know if you are taking any of the following:

- Carbamazepine (e.g., Tegretol) Propoxyphene may increase the blood levels of carbamazepine, which increases the chance of serious side effects.
- Central nervous system (CNS) depressants or
- Monoamine oxidase (MAO) inhibitor activity (isocarboxazid [e.g., Marplan], phenelzine [e.g., Nardil], procarbazine [e.g., Matulane], tranylcypromine [e.g., Parnate] (taken currently or within the past 2 weeks) or
- Tricyclic antidepressants (amitriptyline [e.g., Elavil], amoxapine [e.g., Asendin], clomipramine [e.g., Anafranil], desipramine [e.g., Pertofrane], doxepin [e.g., Sinequan], imipramine [e.g., Tofranil], nortriptyline [e.g., Aventyl], protriptyline [e.g., Vivactil], trimipramine [e.g., Surmontil])The chance of side effects may be increased; the combination of meperidine (e.g., Demerol) and MAO inhibitors is especially dangerous.
- Naltrexone (e.g., Trexan)Narcotics will not be effective in people taking naltrexone.
- Rifampin (e.g., Rifadin)Rifampin decreases the effects of methadone and may cause withdrawal symptoms in people who are dependent on methadone.
- Zidovudine (e.g., AZT, Retrovir)Morphine may increase the blood levels of zidovudine and increase the chance of serious side effects.
- **Strong CYP3A inhibitors** (Cause ≥ 5-fold increase in AUC of sensitive CYP3A substrate):
    - atazanavir, clarithromycin, indinavir, itraconazole, ketoconazole, nefazodone, nelfinavir, ritonavir, lopinavir/ritonavir, saquinavir/ritonavir, telithromycin
- **Moderate CYP3A inhibitors** (Cause ≥ 2 but < 5-fold increase in AUC of sensitive CYP3A substrate)
    - aprepitant, diltiazem, erythromycin, fluconazole, fosamprenavir, grapefruit juice, verapamil
- **Weak CYP3A inhibitors** (Cause ≥ 1.25 but <2-fold increase in AUC of sensitive CYP3A substrate)
    - Cimetidine
- **CYP2D6 Substrates:**
    - Beta Blockers:, Carvedilol, S-metoprolol, Propafenone, timolol.
    - Antidepressants:, Amitriptyline, clomipramine, desipramine, imipramine, paroxetine.

    - Antipsychotics:, Haloperidol, perphenazine, risperidone_9OH, thioridazine, zuclopenthixol, alprenolol, amphetamine, aripiprazole, atomoxetine, bufuralol, chlorpheniramine, chlorpromazine, codeine (_O-desMe), debrisoquine, dexfenfluramine, dextromethorphan, duloxetine, encainide, flecainide, fluoxetine, fluvoxamine, lidocaine, metoclopramide, methoxyamphetamine, mexilletine, minaprine, nebivolol, nortriptyline, ondansetron, oxycodone, perhexiline, phenacetin, phenformin, promethazine, propranolol, sparteine, tamoxifen, tramadol, venlafaxine.
- **CYP2D6 Inhibitors:** inhibitors may slow metabolism, raising the serum level (SL), extending the duration of its effects, and possibly causing methadone-related toxicity such as oversedation and/or respiratory depression.
    - Bupropion, fluoxetine, paroxetine, quinidine, duloxetine, terbinafine, amiodarone, cimetidine, sertraline, celecoxib, chlorpheniramine, chlorpromazine, citalopram, clemastine, clomipramine, cocaine, diphenhydramine, doxepin, doxorubicin, escitalopram, halofantrine, histamine H1, receptor antagonists, hydroxyzine, levomepromazine, methadone, metoclopramide, mibefradil, midodrine, moclobemide, perphenazine, ranitidine, red-haloperidol, ritonavir, ticlopidine, tripelennamine.
- **CYP2D6 Inducers:** Inducers increase the activity of enzymes involved in metabolism, accelerating the drug's breakdown, and increasing its rate of clearance, abbreviating the duration of effects, lowering serum level (SL), and possibly precipitating opioid-withdrawal syndrome.
    - dexamethasone
    - rifampin

Other medical problems - The presence of other medical problems may affect the use of narcotic analgesics. Make sure you tell your doctor if you have any other medical problems, especially:

- Alcohol abuse, or history of, or
- Drug dependence, especially narcotic abuse, or history of, or
- Emotional problems. The chance of side effects may be increased; also, withdrawal symptoms may occur if a narcotic you are dependent on is replaced by buprenorphine, butorphanol, nalbuphine, or pentazocine.
- Brain disease or head injury or
- Emphysema, asthma, or other chronic lung disease or
- Enlarged prostate or problems with urination or
- Gallbladder disease or gallstones. Some of the side effects of narcotic analgesics can be dangerous if these conditions are present
- Colitis or
- Heart disease or
- Kidney disease or
- Liver disease or
- Underactive thyroid. The chance of side effects may be increased
- Convulsions (seizures), history of Some of the narcotic analgesics can cause convulsions

Precautions While Using This Medicine

If you will be taking this medicine for a long time (for example, for several months at a time), your doctor should check your progress at regular visits.

Narcotic analgesics will add to the effects of alcohol and other CNS depressants (medicines that slow down the nervous system, possibly causing drowsiness). Some examples of CNS depressants are antihistamines or medicine for hay fever, other allergies, or colds; sedatives, tranquilizers, or sleeping medicine; other prescription pain medicines including other narcotics; barbiturates; medicine for seizures; muscle relaxants; or anesthetics, including some dental anesthetics. *Do not drink alcoholic beverages, and check with your medical doctor or dentist before taking any of the medicines listed above, while you are using this medicine*.

This medicine may cause some people to become drowsy, dizzy, or lightheaded, or to feel a false sense of well-being. *Make sure you know how you react to this medicine before you drive, use machines, or do anything else that could be dangerous if you are dizzy or are not alert and clearheaded*.

Dizziness, light-headedness, or fainting may occur, especially when you get up suddenly from a lying or sitting position. Getting up slowly may help lessen this problem.

Nausea or vomiting may occur, especially after the first couple of doses. This effect may go away if you lie down for a while. However, if nausea or vomiting continues, check with your medical doctor or dentist.

Lying down for a while may also help relieve some other side effects, such as dizziness or light-headedness, that may occur.
Before having any kind of surgery (including dental surgery) or emergency treatment, tell the medical doctor or dentist in charge that you are taking this medicine.
Narcotic analgesics may cause dryness of the mouth. For temporary relief, use sugarless candy or gum, melt bits of ice in your mouth, or use a saliva substitute. However, if dry mouth continues for more than 2 weeks, check with your dentist. Continuing dryness of the mouth may increase the chance of dental disease, including tooth decay, gum disease, and fungus infections.
If you have been taking this medicine regularly for several weeks or more, *do not suddenly stop using it without first checking with your doctor*. Your doctor may want you to reduce gradually the amount you are taking before stopping completely, in order to lessen the chance of withdrawal side effects.
If you think you or someone else may have taken an overdose, get emergency help at once. Taking an overdose of this medicine or taking alcohol or CNS depressants with this medicine may lead to unconsciousness or death. Signs of overdose include convulsions (seizures), confusion, severe nervousness or restlessness, severe dizziness, severe drowsiness, slow or troubled breathing, and severe weakness.
Along with its needed effects, a medicine may cause some unwanted effects. Although not all of these side effects may occur, if they do occur they may need medical attention. *Get emergency help immediately if any of the following symptoms of overdose occur*:
Cold, clammy skin, confusion, convulsions (seizures), dizziness (severe) , drowsiness (severe), low blood pressure, nervousness or restlessness (severe) , pinpoint pupils of eyes, slow heartbeat, slow or troubled breathing, weakness (severe)
Also, check with your doctor as soon as possible if any of the following side effects occur:
Less common or rare
Dark urine (for propoxyphene only), fast, slow, or pounding heartbeat, feelings of unreality , hallucinations (seeing, hearing, or feeling things that are not there), hives, itching, or skin rash , increased sweating (more common with hydrocodone, meperidine, and methadone), irregular breathing, mental depression or other mood or mental changes, pale stools (for propoxyphene only), redness or flushing of face (more common with hydrocodone, meperidine, and methadone), ringing or buzzing in the ears, shortness of breath, wheezing, or troubled breathing, swelling of face, trembling or uncontrolled muscle movements, unusual excitement or restlessness (especially in children), yellow eyes or skin (for propoxyphene only)
Other side effects may occur that usually do not need medical attention. These side effects may go away during treatment as your body adjusts to the medicine. However, check with your doctor if any of the following side effects continue or are bothersome:
More common
Dizziness, light-headedness, or feeling faint, drowsiness, nausea or vomiting
Less common or rare
Blurred or double vision or other changes in vision, constipation (more common with long-term use and with codeine) , decrease in amount of urine, difficult or painful urination, dry mouth, false sense of well-being, frequent urge to urinate, general feeling of discomfort or illness, headache, loss of appetite, nervousness or restlessness, nightmares or unusual dreams, redness, swelling, pain, or burning at place of injection, stomach cramps or pain, trouble in sleeping, unusual tiredness or weakness
After you stop using this medicine, your body may need time to adjust. The length of time this takes depends on the amount of medicine you were using and how long you used it. During this period of time check with your doctor if you notice any of the following side effects:
Body aches, diarrhea, fast heartbeat, fever, runny nose, or sneezing, gooseflesh, increased sweating, increased yawning, loss of appetite , nausea or vomiting, nervousness, restlessness, or irritability, shivering or trembling , stomach cramps, trouble in sleeping, unusually large pupils of eyes, weakness
Other side effects not listed above may also occur in some patients. If you notice any other effects, check with your doctor.

ADVERSEREACTIONS

Major hazards

- Respiratory depression
- Circulatory depression
- Respiratory arrest
- Shock
- Cardiac arrest

Most frequent
- Lightheadedness
- Dizziness
- Sedation
- Nausea
- Vomiting
- Sweating

Central Nervous System
- Euphoria
- Dysphoria
- Weakness
- Headaches
- Insomnia
- Agitation
- Disorientation
- Visual disturbances

Gastrointestinal
- Dry mouth
- Anorexia
- Constipation
- Biliary tract spasms

Cardiovascular
- Facial flushing
- Bradycardia
- Palpitations
- Faintness
- Syncope

Genitourinary
- Urinary retention or hesitancy
- Antidiuretic effect
- Reduced libido and/or potency

Allergic
- Pruritus
- Urticaria
- Skin rashes
- Edema
- Hemorrhagic urticaria (rarely)

Hematologic
- Reversible thrombocytopenia

NOTICE:
The information about drugs contained in this website is general in nature and is intended for use as an educational aid. It does not cover all possible uses, actions, precautions, side effects, or interactions of these medicines, nor is the information intended as medical advice for individual problems or for making an evaluation as to the risks and benefits of taking a particular drug. Side effects contained herein, although possible, maybe extremely rare. Always consult your physician to assess your particular risks.

ADDITIONALINFORMATION
Once a medicine has been approved for marketing for a certain use, experience may show that it is also useful for other medical problems. In certain cases this would mean that the medication may not have FDA approval for a certain use, for which your physician may know it to be appropriate. FDA approval for a specific indication is usually given to those drugs for which the parent pharmaceutical company has

decided to invest money in conduct ingefficacy and safety studies, for the use of the medicine on that particular indication. Occasionally, the condition may be rare and the investment to profit ratio for the pharmaceutical may not warrant their interest in pursuing that indication.

BRAND NAMES:
In the U.S.

Astramorph PF
Buprenex
Cotanal-65
Darvon
Darvon-N
Demerol
Dilaudid
Dilaudid-5
Dilaudid-HP
Dolophine
Duramorph
Hydrostat IR
Kadian
Levo-Dromoran
Methadose
M S Contin
MSIR
MS/L
MS/L Concentrate
MS/S
Nubain
Numorphan
OMS Concentrate
Oramorph SR
OxyContin
PP-Cap
Rescudose
RMS Uniserts
Roxanol
Roxanol 100
Roxanol UD
Roxicodone
Roxicodone Intensol
Stadol
Talwin
Talwin-Nx

BRAND NAMES:
In Canada

Darvon-N
Demerol
Dilaudid
Dilaudid-HP
Epimorph
Hycodan #
Kadian
Leritine
Levo-Dromoran
M-Eslon
Morphine Extra-Forte
Morphine Forte
Morphine H.P.
Morphitec
M.O.S.
M.O.S.-S.R.
M S Contin
MSIR
Nubain
Numorphan
Oramorph SR
OxyContin
Pantopon
Paveral
PMS-Hydromorphone
PMS-Hydromorphone Syrup
Robidone
642
Statex
Statex Drops
Supeudol
Talwin

Other commonly used names are:

dextropropoxyphene
dihydromorphinone
levorphan
papaveretum
pethidine

LIST OF DRUGS CAPABLE OF INTERACTION WITH OPIOIDS/OPIATES

Introduction: Opioids/Opiates can interact with other substances at the pharmacodynamic and/or pharmacokinetic level.

Class: Benzodiazepines	
Effect: All can potentiate or increase the side- effects of opioids/opiates, while decreasing their analgesic effects, leading to increased consumption with overdose and death. These medications also stimulate overconsumption of food and fluids. In addition, benzodiazepines are usually prescribed for anxiety, however, even small doses of opioids will block this anxiolytic effect. In other words, taking benzodiazepines and opioids together will increase their side-effects and eliminate their benefits.	
Generic Name	**Brand Name**
Alprazolam	Helex, Ksalol, Xanax, Xanor, Tafil, Alprox, Frontal (Brazil)
Bratazenil	N/A
Bromazepam	Lexaurin, Lexotanil, Lexotan, Lexomil, Somalium, Bromam
Chlordiazepoxide	Librium, Tropium, Risolid, Klopoxid
Cinolazepam	Gerodorm
Clonazepam	Klonopin, Rivotril, Iktorivil
Clorazetape	Tranxene
Cloxazolam	Olcadil (Brazil)
Diazepam	Valium, Pax (South Africa), Apaurin, Apzepam, Stesolid, Vival, Apozepam, Hexalid, Stedon, Valaxona
Estazolam	ProSom
Fludiazepam	Erispan
Flunitrazepam	Rohypnol, Fluscand, Flunipam, Ronal, Rohydorm (Brazil)
Flurazepam	Dalmadorm, Dalmane
Flutoprazepam	Restas
Halazepam	Paxipam
Ketazolam	Anxon
Loprazolam	Dormonoct
Lorazepam	Ativan, Temesta, Tavor, Lorabenz
Lormetazepam	Loramet, Noctamid, Pronoctan
Medazepam	Nobrium
Miadzolam	Dormicum, Versed, Hypnovel, Dormonid (Brazil)
Nimatazepam	Erimin
Nitrazepam	Mogadon, Alodorm, Pacisyn, Dumolid
Nordazepam	Madar, Stilny
Oxazepam	Seresta, Serax, Serenid, Serepax, Sobril, Oxascand, Alopam, Oxabenz, Oxapax
Phenazepam	феназепам
Pinazepam	Domar
Prazepam	Lysanxia, Centrax
Premazepam	N/A
Quazepam	Doral
Temazepam	Restoril, Normison, Euhypnos, Temaze, Tenox
Tetrazepam	Mylostan
Triazolam	Halcion, Rilamir

Class: Opioids/Opiates	
Effect: All can potentiate or increase the effects of other opioids/opiates, leading to overdose and death. Extreme care must be taken with cough medicines, most of which contain codeine, hydrocodone, or dextromethorphan.	
Generic Name	**Brand Name**
Benzylmorphine	Peronine
Buprenorphine	Buprenex, Suboxone, Subutex, Butrans
Codeine	Actifed with Codeine, Airacof, Ala-Hist AC, Allerfrin with Codeine, Allfen CD, Allfen CDX, Alphen, Ambenyl, Ambifed CD, Ambifed CDX, Ambifed-G CD,

	Ambifed-G CDX, Ambophen, Antituss AC, Aprodine with Codeine, Ascomp with Codeine, Biotussin, Bitex, Bromanate DC, Bromanyl, Bromotuss with Codeine, Bromphen DC, Bron-Tuss, Brontex, BroveX CB, BroveX CBX, Brovex PBC, Brovex PBCX, C Tussin, Calcidrine, Capital and Codeine, Chemdal Expectorant, Cheracol with Codeine, Cheratussin, Cheratussin DAC, Co-Histine, Co-Histine DH, Cocet, Codafed, Codafen, Codahistine, Codahistine DH, Codegest, Codehist DH, Codeprex, Codimal PH, Codrix, Colrex, Combiflex ES, Conex, Cophene-X-P, Cotab A, Cotab AX, Cotabflu, Cycofed, Cycofed Expectorant, Cyndal, Decohistine, Decohistine DH, Deconsal C, Demi-Cof, Deproist, Dex-Tuss, Diabetic Tus with Codeine, Diabetic Tussin C, Dicomal-PH, Dihistine, Dihistine DH, Dimetane DC, Duraganidin NR, EZ III, Efasin Expectorant SF, Empirin with Codeine, EndaCof DC, Endacof AC, Endacof C, Endal CD, Endal Expectorant, Enditussin Expectorant, Endotuss, ExeClear-C, Fioricet with Codeine, Fiorinal with Codeine, Fiortal with Codeine, Gani-Tuss NR, Gencofed, Gencofed Expectorant, Giltuss Ped-C, Glydeine, Gua PC, Guai-Co, Guaiatussin AC, Guaiatussin DAC, Guaifen AC, Guaifen C, Guaifen DAC, Guiatuss AC, Guiatuss DAC, Guiatussin DAC, Guiatussin with Codeine, Halotussin AC, Halotussin DAC, Iophen, KG-Fed, KG-Fed Expectorant, Liquihistine CS, M-Clear WC, M-End PE, M-End WC, M-Phen, Mar-cof BP, Mar-cof CG, Margesic #3, Maxifed CD, Maxifed CDX, Maxifed-G CD, Maxifed-G CDX, Maxiflu, Maxiphen CD, Maxiphen CDX, Medent C, Myphetane DC, Mytussin AC, Mytussin DAC, Naldecon CX, Nalex AC, Neo AC, Nortuss-NX, Notuss AC, Notuss DC, Notuss PE, Notuss-NXD, Novadyne DH, Novadyne Expectorant, Novagest, Novahistine Expectorant, Nucochem, Nucodine, Nucodine Expectorant, Nucofed, Nucofed Expectorant, Nucotuss, Pediacof, Pedituss, Pentazine VC, Pentazine with Codeine, Phenaphen with Codeine, Phenco-Care, Phenergan VC with Codeine, Phenergan with Codeine, Phenflu, Phenhist, Phenhist DH, Phenylhistine DH, Phenylhistine Expectorant, Phrenilin with Caffeine and Codeine, Poly CS, Poly-Histine CS, Poly-Tussin AC, Polytine CS, Pro Clear AC, Pro Red AC, Pseudodine C, Pyregesic, Quindal, Robafen AC, Robichem AC, Robitussin AC, Robitussin DAC, Rolatuss, Romilar AC, Ryna C, Ryna CX, Soma Compound with Codeine, Statuss, Sudatuss SF, Suttar, T Koff, TL-Hist CD, TL-Hist CM, Triacin C, Triafed & Codeine, Triaminic Expectorant with Codeine, Trifed C, Trihist CS, Tusnel C, Tussar, Tusshistine CS, Tussi Organidin, Tussiden C, Tussirex, Tusso C, Tylagesic, Tylenol #2, Tylenol #3, Tylenol #4, Tylenol with Codeine, Uni-Multihist CS, Vanacof, Vopac, Z Tuss AC, Zodryl AC, Zodryl DAC, Zodryl DEC, Zotex C
Desomorphine	Dihydrodesoxymorphine, Permonid
Dextromethorphan	Robitussin, NyQuil, Dimetapp, Vicks, Coricidin, Delsym, (Inhibits the antinociceptive effects of nicotine).
Dextropropoxyphene or Propoxyphene	Algaphan, Darvon, Darvocet-N, Di-Gesic, Capadex, Lentogesic, Di-Antalvic, co-proxamol, Doloxene
Diacetylmorphine	Heroin
Dipropanoylmorphine	N/A
Ethylmorphine	codethyline, dionine, Indalgin, Cocillana, Cosylan, Feco Syrup, Solvipect Comp
Fentanyl	Sublimaze, Actiq, Durogesic, Duragesic, Fentora, Onsolis, Instanyl, Matrifen, Innovar
Hydrocodone	Alor, Ambi 5/15/100, Anaplex-HD, Atuss HD, Azdone, BPM-PE-HC, Bromplex-HD, Brovex-HC, Canges-HC, Codal-DH Syrup, CodiCLEAR DH, Cytuss-HC NR, Detussin, Dicomal-DH, Donatussin DC, Donatussin MAX, Drituss HD, Drocon-CS, Dytan-HC, EndaCof-Plus, Endal HD, Entuss-D JR, Excof, Excof-SF, H-C Tussive-NR, Histex-HC, Histinex HC, Histussin D, Histussin-HC, Hycodan, Hycotuss Expectorant, Hydex PD, Hydrocodone CP, Hydrocodone HD, Hydro-DP, Hydromet, Hydrotropine, Hy-KXP, Hyphed, HyTan, Ibudone, Lorcet, Lortab, Lortuss HC, Marcof Expectorant, Max-HC, Mintex-HC, Nalex-DH, Narcof, Nariz HC, Norco, Notuss PD, Notuss, Novasus, Panasal, Phenylephrine HD, Poly-Tussin XP, Procof D, Prolex DH, Protuss, Protuss-D, P-V-Tussin Syrup, Reprexain, Rolatuss with Hydrocodone, Ru-Tuss with Hydrocodone, S-T Forte, Statuss Green, Trimal DH, Tri-Vent-HC, Tusdec-HC, Tusnel-HC, Tussafed-HCG,

	Tussafin, Tussgen, TussiCaps, Tussigon, Tussinate, Tussionex Pennkinetic, Tussplex, Vanacon, VasoTuss-HC, Vetuss HC Syrup, Vicodin, Vicoprofen, Vi-Q-Tuss, Zotex HC, Z-Tuss 2, Zymine HC.
Hydromorphone	Dilaudid, Exalgo, Dilaudid-HP, Hydromorph Contin, Dilaudid Cough Syrup, Hydal, Sophidone, Hydrostat Hydromorfan, Hydromorphan, Laudicon, Hymorphan, Opidol, Palladone, Jurnista
Methadone	Symoron, Dolophine, Amidone, Methadose, Physeptone, Heptadon, Phy, Levo-Polamidone, Polamidone, Heptanone, Heptadone, Heptadon
Morphine	MS Contin, MSIR, Avinza, Kadian, Oramorph, Roxanol, Kapanol, Embeda
Nicomorphine	Vilan
Oxycodone	Combunox, Dazidox, Depalgos, Endocet, Endocodone, Endodan, Endone, ETH-Oxydose, Eucodol, Eukodol, Lynox, Magnacet, Narvox, OxyContin, Oxyfast, Oxy-IR, OxyNorm, Percocet, Percodan, Percodan, Percolone, Perloxx, Primlev, Proladone, Roxicodone, Roxiprin, Roxycet, Targin, Taxadone, Tylox, Xolox
Oxymorphone	Opana, Opana ER, Numorphan, Numorphan HCl
Pethidine or Meperidine	Demerol, isonipecaine, lidol, pethanol, piridosal, Algil, Alodan, Centralgin, Dispadol, Dolantin, Mialgin, Petidin Dolargan, Dolestine, Dolosal, Dolsin, Mefedina
Tapentadol	Nucynta
Thebaine	
Tramadol	Ultram, Ultram ER, Tramal, Ultracet, Trexol, Tramacet, Adolonta, Nobligan, Ryzolt, Sinergix, Tradol, Tradonal, Ultradol, Veldrol, Zaldiar, Zytram, Zytrim

Class: MAO inhibitors	
Effect: Certain combinations can be lethal. The can trigger a **Noradrenergic Syndrome** (Hypertensive Crisis) and/or **Serotonin Syndrome** (Hyperpyrexic crisis). They can interact with the pharmacokinetics of the opioids, potentially causing side-effects and toxicity.	
Generic Name	**Brand Name**
Asagiline	Azilect
Furazolidone	Furoxone, Dependal-M (used as an antibacterial – treatment of cholera and giardiasis)
Isocarboxazid	Marplan
Isoniazid	Laniazid, Nydrazid
Isoniazid rifampin	Rifamate, Rimactane
Linezolid	Zyvox, Zyvoxid, Zyvoxam, (an oxazolidinone antibiotic)
Moclobemide	Aurorix, Manerix
Pargyline	Eutonyl
Phenelzine	Nardil
Procarbazine	Matulane (US), Natulan (Canada), Indicarb (India) (used as a cancer drug)
Selegiline	Eldepryl, Emsam
Tranylcypromine	Parnate
St. John's Wart	St. John's Wart

Class: Antibiotics	
Effect: All can potentiate or increase the effects of opioids/opiates, leading to overdose and death. They can interact with the pharmacokinetics of the opioids, potentially causing side-effects and toxicity.	
Generic Name	**Brand Name**
Azithromycin	Zithromax
Ciprofloxacin	Cipro
Clarithromycin	Biaxin
Erythromycin	Erythrocin, E-Mycin, Ery-Tab (Increases side-effects)
Itraconazole	Sporanox
Ketoconazole	Nizoral
Metronidazole	Flagyl
Rifampicin	Rifampin (Decreases analgesic-effects)
Telithromycin	Ketek
Voriconazole	Vfend

Class: Antiviral Agents	
Effect: They can interact with the pharmacokinetics of the opioids, potentially causing side-effects and toxicity.	
Generic Name	**Brand Name**
Abacavir	Ziagen
Amprenavir	Agenerase
Atazanavir	Reyataz
Didanosine	Videx
Efavirenz	Sustiva
Fosamprenavir	Lexiva, Telzir
Indinavir	Crixivan
Lopinavir	Kaletra
Nelfinavir	Viracept
Nevirapine	Viramune
Ritonavir	Norvir
Saquinavir	Invirase, Fortovase
Stavudine	Zerit
Zidovudine	Retrovir

Class: Antifungals	
Effect: They can interact with the pharmacokinetics of the opioids, potentially causing side-effects and toxicity. They slow down the hepatic metabolism of opioids (i.e.: fentanyl, alfentanil, etc.)	
Generic Name	**Brand Name**
Abafungin	Abasol
Bifonazole	Canespor
Butoconazole	N/A
Clotrimazole	Canesten, Lotrimin
Econazole	Spectazole, Ecostatin, Pevaryl, Ecostatin Vaginal Ovules, Endix-G, Ecosone, Vivicome Cream
Fenticonazole	Falvin, Fenizolan, Fentiderm, Fentigyn, Fentizol, Gynoxin, Laurimic, Lomexin, Micofulvin, Mycodermil, Mycofentin, Terlomexin.
Fluconazole	Diflucan, Trican, Alfumet
Isavuconazole	N/A
Isoconazole	N/A
Itraconazole	Sporanox
Ketoconazole	Nizoral, Sebizole
Miconazole	Oravig, Desenex, Micatin, Monistat-Derm, Daktarin, Decocort, Daktacort, Miconazex, Monistat, Femizol or Gyno-Daktarin
Nefazodone	Serzone, Nefadar
Omoconazole	N/A
Oxiconazole	Oxistat, Oxizole
Posaconazole	Noxafil, Posanol
Ravuconazole	N/A
Sertaconazole	Ertaczo, Dermofix
Sulconazole	Exelderm
Terconazole	N/A
Tioconazole	N/A
Voriconazole	VFEND

Class: Antacids	
Effect: They can interact with the pharmacokinetics of the opioids, potentially causing side-effects and toxicity.	
Generic Name	**Brand Name**
Cimetidine	Tagamet
Ranitidine	Zantac

Metoclopramide	Maxolon, Reglan, Degan, Maxeran, Primperan, Pylomid, Cerucal, Pramin

Class: Anticonvulsants	
Effect: They can interact with the pharmacokinetics of the opioids, potentially causing side-effects and toxicity. They can all precipitate withdrawals.	
Generic Name	**Brand Name**
Carbamazepine	Biston, Calepsin, Carbatrol, Epitol, Equetro, Finlepsin, Sirtal, Stazepine, Telesmin, Tegretol, Teril, Timonil, Trimonil, Epimaz, Carbama, Carbamaze, Amizepin, Hermolepsin, and Degranol
Fosphenytoin	Cerebyx, Prodilantin
Mephenytoin	Mesantoin
Phenobarbital	Luminal,
Phenytoin	Phenytek, Dilantin, Dilantin Kapseals, Dilantin Infatabs, Eptoin, Epanutin, Дифенин, Diphenin, Dipheninum
Primidone	Mysoline, Prysoline, Apo-Primidone, Liskantin, Desitin, Resimatil, Mylepsinum, and Sertan

Class: Barbiturates	
Effect: They can interact with the pharmacokinetics of the opioids, potentially causing side-effects and toxicity.	
Generic Name	**Brand Name**
Butalbital	Axocet, Bucet, Bupap, Cephadyn, Dolgic, Phrenilin, Phrenilin Forte, Sedapap, Fioricet, Esgic, Esgic-Plus, Axotal, Fiorinal, Fiormor, Fiortal, Fortabs, Laniroif,
Mephobarbital	Mebaral
Methohexital	Brevital
Pentobarbital	Nembutal
Phenobarbital	Luminal
Thiamylal	Surital
Thiopental	Sodium Pentothal, thiopental, thiopentone sodium, or Trapanal

Class: Antidepressants (SSRIs)	
Effect: All can **inhibit CYP2D6**, thereby decreasing opioid/opiate metabolism, leading to accumulation and overdosage. They can interact with the pharmacokinetics of the opioids, potentially causing side-effects and toxicity. Specifically Tramadol can precipitate seizures and serotonin syndrome/Toxidrome.	
Generic Name	**Brand Name**
Citalopram	Celexa, Cipramil, Cipram, Dalsan, Recital, Emocal, Sepram, Seropram, Citox, Cital
Dapoxetine	Priligy
Escitalopram	Lexapro, Cipralex, Seroplex, Esertia
Fluoxetine	Prozac, Fontex, Seromex, Seronil, Sarafem, Ladose, Motivest, Fluctin, Fluox, Depress, Lovan
Fluvoxamine	Luvox, Fevarin, Faverin, Dumyrox, Favoxil, Movox
Indalpine	Upstene (discontinued)
Paroxetine	Paxil, Seroxat, Sereupin, Aropax, Deroxat, Divarius, Rexetin, Xetanor, Paroxat, Loxamine
Sertraline	Zoloft, Lustral, Serlain, Asentra
Zimelidine	Zelmid, Normud (discontinued)

Class: Tricyclic Antidepressants	
Effect: All can **inhibit CYP2D6**, thereby decreasing opioid/opiate metabolism, leading to accumulation and overdosage. They can interact with the pharmacokinetics of the opioids, potentially causing side-effects and toxicity. They increase blood levels of opioids.	
Generic Name	**Brand Name**
Amineptine	Survector, Maneon, Directim – (Norepinephrine-dopamine reuptake inhibitor)
Amitriptyline	Elavil, Tryptizol, Laroxyl, Sarotex, Lentizol
Amitriptylinoxide	Amioxid, Ambivalon, Equilibrin
Butriptyline	Evadyne

Clomipramine	Anafranil
Demexiptiline	Deparon, Tinoran
Desipramine	Norpramin, Pertofrane
Dibenzepin	Noveril, Victoril
Dimetacrine	Istonil, Istonyl, Miroistonil
Dosulepin/Dothiepin	Prothiaden
Doxepin	Adapin, Sinequan
Imipramine	Tofranil, Janimine, Praminil
Imipraminoxide	Imiprex, Elepsin
Iprindole	Prondol, Galatur, Tetran – (5-HT_2 receptor antagonist)
Lofepramine	Lomont, Gamanil
Melitracen	Deanxit, Dixeran, Melixeran, Trausabun
Metapramine	Timaxel
Nitroxazepine	Sintamil
Nortriptyline	Pamelor, Aventyl
Noxiptiline	Agedal, Elronon, Nogedal
Opipramol	Insidon, Pramolan, Ensidon, Oprimol – (σ receptor agonist)
Pipofezine	Azafen/Azaphen
Propizepine	Depressin, Vagran
Protriptyline	Vivactil
Quinupramine	Kevopril, Kinupril, Adeprim, Quinuprine
Tianeptine	Stablon, Coaxil, Tatinol – (Selective serotonin reuptake enhancer)
Trimipramine	Surmontil – (5-HT_2 receptor antagonist)

Class: Phenothiazines	
Effect: They can interact with the pharmacokinetics of the opioids, potentially causing side-effects and toxicity. Known to cause **extrapyramidal side effects** (EPSE).	
Generic Name	**Brand Name**
Chlorpromazine	Thorazine, Chlor-PZ, Klorazine, Promachlor, Promapar, Sonazine, Chlorprom, Chlor-Promanyl, Largactil
Fluphenazine	Prolixin, Permitil, Modecate, Moditen
Levomepromazine in Germany and Methotrimeprazine in America	Nozinan, Levoprome
Mesoridazine	Serentil
Methylene blue	
Perphenazine	Trilafon, Etrafon, Triavil, Phenazine
Prochlorperazine	Compazine, Stemetil
Promazine	Sparine
Thioridazine	Mellaril, Novoridazine, Thioril
Trifluoperazine	Stelazine
Triflupromazine	Stelazine, Clinazine, Novaflurazine, Pentazine, Terfluzine, Triflurin, Vesprin

Class: Antiemetics	
Effect: All can **inhibit CYP2D6**, thereby decreasing opioid/opiate metabolism, leading to accumulation and overdosage. They can interact with the pharmacokinetics of the opioids, potentially causing side-effects and toxicity. Known to cause **extrapyramidal side effects** (EPSE).	
Generic Name	**Brand Name**
Alizapride	Litican, Plitican, Superan, Vergentan (Dopamine antagonist)
Chlorpromazine	Thorazine, Largactil (Dopamine antagonist)
Dolasetron	Anzemet (5-HT_3 Serotonin receptor antagonist)
Domperidone	Motilium, Motillium, Motinorm, Costi (Dopamine antagonist)
Droperidol	Droleptan, Dridol, Inapsine (Dopamine antagonist)
Granisetron	Kytril, Sancuso (5-HT_3 Serotonin receptor antagonist)
Haloperidol	Aloperidin, Bioperidolo, Brotopon, Dozic, Duraperidol, Einalon S, Eukystol, Haldol, Halosten, Keselan, Linton, Peluces, Serenace, Serenase, Sigaperidol. (Dopamine

	antagonist)
Metoclopramide	Reglan (Dopamine antagonist)
Mirtazapine	Remeron (5-HT_3 Serotonin receptor antagonist)
Ondansetron	Zofran (5-HT_3 Serotonin receptor antagonist)
Palonosetron	Aloxi (5-HT_3 Serotonin receptor antagonist)
Prochlorperazine	Compazine, Stemzine, Buccastem, Stemetil, Phenotil (Dopamine antagonist)
Promethazine	Phenergan, Promethegan, Romergan, Fargan, Farganesse, Prothiazine, Avomine, Atosil, Receptozine, Lergigan (H_1 histamine receptor antagonists) (Dopamine antagonist)
Tropisetron	Navoban (5-HT_3 Serotonin receptor antagonist)

Class: Cardiovascular	
Effect: They can interact with the pharmacokinetics of the opioids, potentially causing side-effects and toxicity.	
Generic Name	**Brand Name**
Diltiazem	Adizem, Altiazem, Angiozem, Angizem, Angizem CD, Cardizem, Cartia XT, Dilatam, Dilatem, Dilcardia, Dilcontin SR in India (Sustained Release), Dilt-CD, Diltelan, Diltime, Dilt-XR, Dilzem, Dyalec, Filazem, Herben, Progor, Tiamate, Tiazac, Tiazac XC, Tildiem, Tildiem in particular in Europe, Vasmulax, Vasocardol & Vasocardol CD, in Australia, Viazem, Zandil, Zemtrial
Verapamil	Isoptin, Verelan, Verelan PM, Calan, Bosoptin, Covera-HS

Class: Antihistamines (H_1 histamine receptor antagonists)	
Effect: All can **inhibit CYP2D6**, thereby decreasing opioid/opiate metabolism, leading to accumulation and overdosage. They can interact with the pharmacokinetics of the opioids, potentially causing side-effects and toxicity.	
Generic Name	**Brand Name**
Cyclizine	Valoid, Marezine, Marzine, Emoquil
Dimenhydrinate	Dramamine, Driminate, Gravol, Gravamin, Vomex, Vertirosan, Viabom, Dramin, Daedalon, Antimo
Diphenhydramine	Benadryl, Dimedrol, Nytol, Unisom, Tylenol PM, Midol PM and Advil PM
Hydroxyzine	Vistaril, Atarax, Equipose, Masmoran, Paxistil, Alamon, Aterax, Durrax, Tran-Q, Orgatrax, Quiess, Tranquizine
Meclizine	Bonine, Bonamine, Antivert, Postafen, Sea Legs, Emesafene
Promethazine	Phenergan, Promethegan, Romergan, Fargan, Farganesse, Prothiazine, Avomine, Atosil, Receptozine, Lergigan, Pentazine, Promacot

Class: Antipsychotics	
Effect: All can **inhibit CYP2D6**, thereby decreasing opioid/opiate metabolism, leading to accumulation and overdosage. They can interact with the pharmacokinetics of the opioids, potentially causing side-effects and toxicity.	
Generic Name	**Brand Name**
Amisulpride	Solian
Aripiprazole	Abilify
Asenapine	Saphris
Chlorpromazine	Thorazine, Largactil
Chlorprothixene	Cloxan, Taractan, Truxal
Clopenthixol	Sordinol
Clozapine	Clozaril
Droperidol	Droleptan
Flupenthixol	Depixol, Fluanxol
Fluphenazine	Prolixin - Available in decanoate (long-acting) form
Haloperidol	Haldol, Serenace
Iloperidone	Fanapt
Levomepromazine	Levomepromazine (Nozinan
Mesoridazine	Serentil
Olanzapine	Zyprexa

Paliperidone	Invega
Pericyazine	Neulactil
Perphenazine	Trilafon
Pimozide	Orap
Prochlorperazine	Compazine
Promazine	Sparine
Promethazine	Phenergan
Quetiapine	Seroquel
Risperidone	Risperdal
Sertindole	Serdolect, and Serlect
Thioridazine	Mellaril, Melleril
Thiothixene	Navane
Trifluoperazine	Stelazine
Triflupromazine	Vesprin
Ziprasidone	Geodon
Zotepine	Nipolept, Losizopilon, Lodopin, Setous
Zuclopenthixol	Cisordinol, Clopixol, Acuphase

Disclaimer: This is not a complete list. There are over-the-counter medications, as well as illegal substances that have not been included. For further information, always consult your pharmacist. In anesthesiology and Pain Management, unlike most medical disciplines, pharmacodynamic drug interactions are frequently produced by design. Not all drugs listed here may cause clinically significant drug interactions, however, caution and vigilance must be exercised when considering using these medications in addition to narcotic opioids/opiates.

PHARMACOKINETIC INTERACTIONS: CYP2D6 LIGANDS

Selected inducers, inhibitors and substrates of CYP2D6

Effects: Cytochrome P_{450} 2D6 (abbreviated **CYP2D6**), is an important enzymes involved in the metabolism of certain opioids/opiates. **Inhibitors** will lead to the accumulation of the opioid/opiate, possibly leading to overdosage, while **inducers** will cause the rapid elimination of the medication, with subsequent decreased effects. A **substrate** is a molecule upon which an enzyme acts, thereby, when present, competing against other substrates. Opioid/opiate "pro-drugs" would act differently.

Substrates

Major:

- beta-blockers
  - metoprolol
  - carvedilol
  - timolol
- debrisoquine (antihypertensive)
- Class I antiarrhythmics
  - flecainide
  - lidocaine
  - propafenone
  - encainide
  - mexiletine
- All tricyclic antidepressants, e.g.
  - imipramine
  - amitriptyline
  - etc.
- Most SSRIs (antidepressant), e.g.
  - fluoxetine
  - paroxetine
- venlafaxine (SNRI antidepressant)
- **opioids**
  - **codeine**
  - **tramadol**
  - **oxycodone**
- antipsychotics, e.g.
  - haloperidol
  - risperidone
  - perphenazine
  - thioridazine
  - zuclopenthixol
  - remoxipride
  - aripiprazole
- dextromethorphan (antitussive)
- ondansetron (antiemetic)

Minor:

- alprenolol (beta-blocker)
- atenolol (beta-blocker)
- mianserin (tetracyclic

Inhibitors

Strong:

- SSRIs
  - citalopram
  - fluoxetine
  - paroxetine
- Some other antidepressants
  - bupropion
  - duloxetine
- terbinafine (antifungal)
- quinidine (class I antiarrhythmic agent)
- MDMA (recreational empathogen)
- hyperforin (St. Johns Wort)

Weak:

- buprenorphine (in opioid addiction)

Unspecified:

- amiodarone (antiarrhythmic)
- dronedarone (antiarrhythmic)
- antihistamine (H1-receptor antagonists)
  - chlorphenamine
  - diphenhydramine
- antipsychotic
  - haloperidol
  - perphenazine
  - thioridazine
  - zuclopenthixol
  - risperidone
- celecoxib (NSAID)
- cimetidine (H2-receptor antagonist)
- clomipramine (tricyclic antidepressant)
- chloramphenicol (laevomycetin)
- **cocaine** (stimulant)
- doxorubicin (chemotherapeutic)

Inducers

Strong:

- Piperidines and derivatives (pharmacokinetics modifiers)
  - glutethimide (piperidinedione derivative)

Moderate:

- carbamazepine

Unspecified:

- dexamethasone (glucocorticoid)
- rifampicin (bactericidal)

antidepressant) • phenformin (antidiabetic) • tropisetron (5-HT3 receptor antagonist) • amphetamine (in ADHD, narcolepsy) • chlorphenamine (antihistamine) • metoclopramide (dopamine antagonist) • tamoxifen (SERM) • vinca alkaloids (anti-mitotic, anti-microtubule) ○ vincristine	• metoclopramide (antiemetic, prokinetic) • **methadone** (analgesic and anti-addictive) • moclobemide (antidepressant) • quinidine (Class I antiarrhythmic) • ranitidine (H2-receptor antagonist) • ranolazine (antianginal) • ritonavir (antiretroviral) • doxepin (tricyclic antidepressant, anxiolytic) • halofantrine (in malaria) • imipramine (tricyclic antidepressant) • levomepromazine (antipsychotic) • pimozide (antipsychotic) • thioridazine (antipsychotic)	

PHARMACOKINETIC INTERACTIONS: CYP3A4 LIGANDS

Selected inducers, inhibitors and substrates of CYP3A4

Effects: Cytochrome P_{450} 3A4 (abbreviated **CYP3A4**), is an important enzymes involved in the metabolism of certain opioids/opiates. **Inhibitors** will lead to the accumulation of the opioid/opiate, possibly leading to overdosage, while **inducers** will cause the rapid elimination of the medication, with subsequent decreased effects. A **substrate** is a molecule upon which an enzyme acts, thereby, when present, competing against other substrates. Opioid/opiate "pro-drugs" would act differently.

Substrates

Major:

- immunosuppressants
  - ciclosporin
  - sirolimus
  - tacrolimus
- Chemotherapeutic
  - anastrazole
  - cyclophosphamide
  - docetaxel
  - doxorubicin
  - erlotinib
  - etoposide
  - ifosfamide
  - paclitaxel
  - tamoxifen
  - teniposide
  - vinblastine
  - vindesine
  - gefitinib
- azole antifungals
  - clotrimazole
  - ketoconazole
  - itraconazole
- macrolide
  - clarithromycin
  - erythromycin
- tricyclic antidepressants
  - amitriptyline
  - clomipramine
  - imipramine
- SSRIs
  - citalopram
  - escitalopram
  - fluoxetine and norfluoxetine
  - sertraline
- buspirone (anxiolytic)
- venlafaxine (SNRI)
- antipsychotics
  - Aripiprazole
  - haloperidol
  - Risperidone
  - Ziprasidone
- **opiate analgesics**
  - alfentanil
  - codeine

Inhibitors

Strong / moderate:

- protease inhibitors
  - ritonavir
  - indinavir
  - nelfinavir
- macrolide antibiotics
  - erythromycin
  - telithromycin
  - clarithromycin
- chloramphenicol (antibiotic)
- azole antifungals
  - fluconazole
  - ketoconazole
  - itraconazole
- nefazodone (antidepressant)
- bergamottin (constituent of **grapefruit juice**)
- aprepitant (antiemetic)
- verapamil (calcium channel blocker)

Weak:

- cimetidine (H2-receptor antagonist)
- buprenorphine (analgesic)
- cafestol (in **unfiltered coffee**)

Unspecified:

- amiodarone (antiarrhythmic)
- ciprofloxacin (antibiotic)
- ciclosporin (immunosuppressant)
- diltiazem (calcium channel blocker)
- imatinib (anticancer)
- echinacea (immunostimulator)
- enoxacin (antibacterial)
- ergotamine (in migraine)
- metronidazole (antibacterial)
- mifepristone (abortifacient)
- norfloxacin (antibiotic)
- tofisopam (anxiolytic)
- non-nucleoside reverse

Inducers

Strong:

- anticonvulsants, mood stabilizers
  - phenytoin (anticonvulsant)
  - carbamazepine
  - oxcarbazepine
- barbiturates
  - phenobarbital
- non-nucleoside reverse transcriptase inhibitors
  - efavirenz
  - nevirapine
  - etravirine
- rifampicin (bactericidal)
- modafinil (stimulant)
- hyperforin (constituent of St John's Wort)
- cyproterone (antiandrogen, progestin)

Weak:

- dexamethasone (anti-inflammatory, immunosuppressant)
- felbamate (anticonvulsant)
- glucocorticoids (blood glucose increase, immunosuppressive)
- griseofulvin (antifungal)
- pioglitazone (hypoglycemic)
- primidone (anticonvulsant)
- topiramate (anticonvulsant)
- troglitazone (hypoglycemic)

(analgesic, antitussive, antidiarrheal)
    - fentanyl
    - methadone (analgesic, anti-addictive)
- **benzodiazepines**
    - alprazolam
    - clonazepam
    - flunitrazepam
    - midazolam
    - triazolam
    - pimozide
- statins
    - atorvastatin
    - lovastatin
    - simvastatin
- calcium channel blockers
    - amlodipine
    - diltiazem
    - felodipine
    - nifedipine
    - verapamil
- amiodarone (antiarrhythmic)
- PDE5 inhibitors
    - sildenafil
- kinins (vasodilators, smooth muscle contractors)
- sex hormones agonists and antagonists
    - estradiol (estrogen)
    - ethinylestradiol (hormonal contraceptive)
    - finasteride (antiandrogen)
    - levonorgestrel (female sex hormone, oral contraceptive)
    - mifepristone (antiprogesterone, anti-implantation agent)
    - testosterone (androgen)
    - toremifene (SERM)
- Astemizole (H1 antagonist, antipruritic)
- warfarin (anticoagulant)

transcriptase inhibitors
    - delavirdine
    - efavirenz
    - nevirapine
- gestodene (hormonal contraceptive)
- mibefradil (in angina pectoris)
- protease inhibitors
    - saquinavir
- SSRIs
    - fluoxetine/norfluoxetine
    - fluvoxamine
- star fruit
- piperine
- milk thistle

- rifabutin (in tuberculosis

PHARMACOKINETIC INTERACTIONS: CYP3A4 LIGANDS

Minor:
 	
• protease inhibitors
  ○ indinavir
  ○ ritonavir
  ○ saquinavir
  ○ nelfinavir
• Mirtazapine (NaSSA)
• nefazodone (antidepressant)
• pimozide (antipsychotic)
• reboxetine (antidepressant)
• zopiclone (hypnotic)
• non-nucleoside reverse transcriptase inhibitors
  ○ nevirapine
• budesonide (glucocorticoid)
• donepezil (acetylcholinesterase inhibitor)
• proton pump inhibitors
  ○ omeprazole and esomeprazole
• glibenclamide (antidiabetic)
• cisapride (5-HT4 receptor agonist)
• terfenadine (H1-receptor antagonist)
• barbiturates
  ○ phenobarbital
• carbamazepine (anticonvulsant, mood stabilizing)
• dextromethorphan (antitussive)
• digoxin (Antiarrhythmic)
• ergot alkaloids (circulation, neurotransmission)
• ivabradine (in angina pectoris)
• lidocaine (local anesthetic, antiarrhythmic)
• montelukast (leukotriene receptor antagonist)
• ondansetron (5-HT3 antagonist)
• paracetamol (analgesic, antipyretic)
• quinidine (class I antiarrhythmic)
• quinine (antipyretic, anti-smallpox, analgesic)		

• theophylline (stimulant) • valproate (anticonvulsant, mood-stabilizing) • tetrahydrocannabinol (psychoactive)		

NC PAIN MANAGEMENT SERVICES, PA
FRANCISCO A. NAVEIRA, MD

911 OPIOID SAFETY

Opioid Pain Reliever Side Effects

What they are. What to know. What you can do.

Common Opioid Side Effects

CAUTION: Drinking alcohol with opioids can make side effects worse. Never change your opioid dose, or take any other medicine or drug with opioids, unless your opioid prescriber has told you to do so.

Problem	What to Know & Do
Constipation	Having less frequent or more difficult bowel movements than usual may commonly occur if opioids are taken for more than a few days. All opioids slow down natural muscle movements in the bowels (intestines and colon). The resulting "irregularity" or constipation may continue for as long as opioids are taken, but it is more of a problem in some persons than others — and it can be effectively managed. **DO NOT** take products called "bulk-producing laxatives" (such as, Metamucil, FiberCon, Citrucel, or others), unless you take them with plenty of water (8oz. glass of water 8x/day), otherwise they will make the constipation worse. **Recommendations:** Drinking plenty of fluids, some exercise (if possible and safe), and a diet rich in natural fiber (grains, fruits, vegetables) may be of help. You also should talk to your opioid prescriber or pharmacist about medicines called "stool softeners" and "stimulant laxatives." Some of these are available without prescription: Take **Dulcolax** (Bisacodyl) two (2) tablets by mouth at bedtime + **Miralax** (Polyethylene Glycol 3350, 17 g) one capful mixed with 8oz. of water or juice, one (1) to three (3) times a day. Add *General Mill's* "**Fiber One**" cereal or *Kellog's* "**All-Bran**" cereal to your daily diet.
Nausea	This is a sensation of discomfort in the upper stomach with an urge to vomit ("throw up"). Any nausea due to opioids usually goes away within a few days. If this continues, or if you have vomiting and cannot keep down the opioid medicine, call your opioid prescriber. There is medicine that can help with nausea. Also, try sitting calmly and breathing through your mouth. Drinking small amounts of **"ginger ale"** helps some persons to combat nausea, as does sips of **ginger, chamomile, or peppermint tea**.
Sedation	Mild feelings of being drowsy, sleepy, "light-headed," or "cloudy-headed" can be common when first starting opioids or after a dose increase. Some persons experience these feelings much more than others. It can take days or weeks for this to completely go away. Until any sedation goes away, you will need to avoid activities that may be dangerous if you are not fully alert, such as driving a car or operating machinery (including power tools and lawn mowers at home). If sedation continues to be a problem there are medicines that can be prescribed to help. If you cannot stay awake and are repeatedly nodding off to sleep this may be a more serious indication of opioid overmedication — *stay awake* and call your opioid prescriber right away.
Respiratory Failure	Medication overdose can lead to profound sedation which if unattended can lead to respiratory failure and death. If the patient is found unconscious or it is difficult to arise, stimulate them to try to keep them awake. If unresponsive, call 911 and continue to stimulate until help arrives.

Less Common Opioid Side Effects

CAUTION: Drinking alcohol with opioids can make side effects worse. Never change your opioid dose, or take any other medicine or drug with opioids, unless your opioid prescriber has told you to do so.

Problem	What to Know & Do
Itching, Dry Skin	Itchy, dry skin can be bothersome if it occurs, but it is usually temporary and is not the same as being allergic to opioids. If you develop a rash and/or hives along with

	the itching it could be an allergic reaction and you should stop taking the medicine and call your opioid prescriber about this right away.
Confusion	When first starting opioid therapy some, but not all, persons find it more difficult to concentrate and think clearly. Some persons may have difficulty remembering things for awhile. Similar to the more common sedation, this may last from several days to a week or two. If confusion continues, or gets worse, talk to your opioid prescriber about it as soon as possible.
Muscle Twitching	Opioids may sometimes cause uncontrollable muscle twitching, jerking, or shaking - usually of the arms or legs - that can be bothersome. It is not harmful but, in some cases, may make pain worse due to the quick movements. Usually, the twitches are mild and do not happen very often. If this is an ongoing problem, your opioid prescriber may reduce the opioid dose or switch you to a different opioid, and there also are certain medicines that can be prescribed to ease this condition.
Hormonal Disturbances	Taking opioids for a long time and/or at higher doses may decrease normal levels of certain hormones in the body. Hormones are chemicals that regulate organ function, body growth, and tissue repair. The hormone disturbances due to opioids may reduce sexual desire and performance in men and women. They also may influence weight gain and depression ("feeling blue"), weaken bones, and cause menstrual period irregularities. Certain medicines may help to control or reduce the problems, but it also may be necessary to decrease the opioid dose, switch to a different opioid or, eventually, discontinue taking opioids. A simple blood test can be done to measure hormone levels. Each person is different and, if hormonal problems occur, you will need to work closely with your opioid prescriber in finding the best solution.
Others	When starting opioid therapy, some persons are bothered by dry mouth, sweating, fatigue or weakness, or mild headaches. Almost always, these are temporary problems and will go away as your body gets used to the opioid medicine. Your opioid prescriber or pharmacist can prescribe or recommend medicines to help ease these effects.

Rare Opioid Side Effects

CAUTION: Drinking alcohol with opioids can make side effects worse. Never change your opioid dose, or take any other medicine or drug with opioids, unless your opioid prescriber has told you to do so.

Problem	What to Know & Do
Allergic Reaction	Few people have a true allergy to opioids. However, if after starting an opioid medicine you develop a rash, hives, swelling (of lips, tongue, hands, or other body part), or tightening in the throat stop taking the medicine and seek medical attention right away.
Urine Retention	Having difficulty passing urine (peeing) when starting opioid therapy is uncommon, but happens more often in elderly men. It usually goes away fairly quickly, but it may be necessary to insert a tube into the bladder to temporarily allow the flow of urine (this is called "catheterization"). Call your opioid prescriber right away if this problem occurs — do not delay.
Heart Problems	There have been rare reports of certain opioids upsetting normal heartbeat, a condition called "arrhythmia." Call your opioid prescriber right away if your heart is sometimes pounding, or if it is beating either oddly, rapidly, or extremely slowly; also call if you are feeling faint or actually have a fainting spell. This is especially important if you are taking methadone or using the buprenorphine patch.
Increased Pain Sensitivity	In some persons opioids help greatly in reducing pain at first but, after awhile, taking opioids may seem to actually make the pain worse. This is not the same as opioid tolerance (this is, getting used to the usual dose and needing more opioid).

	Increasing the opioid dose does not help, and the reasons for this condition - called “hyperalgesia” - are not completely understood. Fortunately, it happens in few persons taking opioids. It may be necessary to reduce the opioid dose, switch to another opioid, or discontinue taking opioids at least for a period of time. In some cases, pain may normally increase because of opioid tolerance, or due to increased physical activity, or from worsening of a condition causing the pain. Talk to your opioid prescriber if the pain worsens at any time while taking opioids.
Brand names mentioned above are registered trademarks of their respective manufacturers, and are presented above for information purposes only. Brand names are for products available in the United States; different brands may be available in other countries.	

NC PAIN MANAGEMENT SERVICES, PA
FRANCISCO A. NAVEIRA, MD

911 OPIOID SAFETY

Signs to Watch For - Overmedication or Overdose?

Share this with your family caregivers.

Overmedication Warning - Call Healthcare Provider

U.S. residents also can call the National Poison Hotline at 1-800-222-1222.

Intoxicated behavior - confusion, slurred speech, stumbling.
Feeling dizzy or faint.
Feeling or acting very drowsy or groggy, or nodding off to sleep.
Unusual snoring, gasping, or snorting during sleep.
Difficulty waking-up from sleep and becoming alert or staying awake.

CAUTION: A person who at first seems to be overmedicated may get much worse. **They should be kept awake and watched closely.**

Overdose Poisoning - Call Emergency Services

Dial **911** in the U.S. or Canada; 112 or 999 in England or the European Union; or other numbers depending on your location.

Person cannot be aroused or wakened, or is unable to talk if awakened.
Any trouble with breathing; such as shortness of breath,
slow or light breathing, or stopped breathing.
Gurgling noises coming from mouth or throat.
Body is limp, seems lifeless. Face is pale, clammy.
Fingernails or lips turned blue/purple.
Slow or unusual heartbeat or stopped heartbeat.

WARNING: If a child or pet ever swallows an opioid that was not prescribed for them, it is ***always an emergency***. Call for help immediately.

911 OPIOID SAFETY

Overdose Emergencies - What to Do Until Help Comes

When there are signs of opioid overdose, taking immediate action can be lifesaving. Patients and their close family and friends should know when to call for emergency help and what to do while waiting for help to arrive. Keep the information below in a handy place where you can always find it.

Can you wake up the person?
Shout their name, pinch their ear, or rub your knuckles on the middle of their chest.

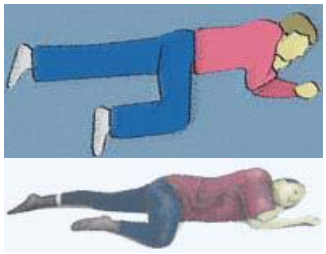
If the person does not respond at all, **call for emergency help right away!**
While you are waiting for help to come...
If the person is breathing, put them in the *Recovery Position*.
If they are not breathing, start *Rescue Breathing*.
If there is no heartbeat, start *CPR*.

Recovery Position

Gently tilt the person's head back so they can breath easier.
Straighten their legs and roll the person to face you.
Pull the bottom arm to be at a right angle to their body, and bend the arm upward at the elbow.
Pull the other arm across the person's chest and place their hand against their
cheek to help support the head.

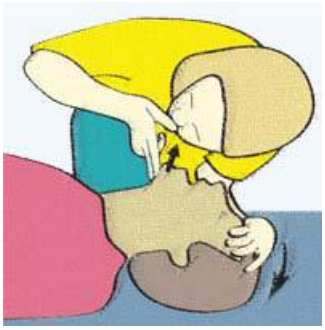
Grabbing just above the knee, pull the person's upper leg toward you until they are on their side.

Finally, place upper leg at a right angle to keep the person from rolling over further.
Be sure their hand is supporting the cheek and the head is tilted back for easier breathing.
Check that their mouth is clear of any chewing gum, food, or vomit.
Stay with the person until help comes.
<*Practice putting a friend or relative into the Recovery Position.*>

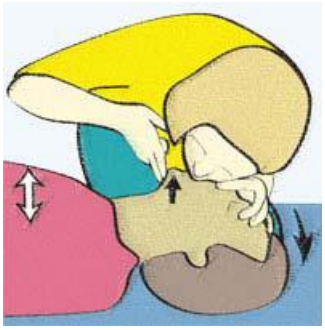


CAUTION: The lifesaving steps below are for your information. You should get training to do them properly. This is available from Red Cross chapters around the world. Look in the phone book for the nearest Red Cross chapter, or to find locations in the USA . The American Heart Association also offers classes; to find one near you.

Is the person breathing?
Roll the person onto their back.
Gently tilt their head back to open the airway (push down on their forehead and support the chin to keep the head back).
Make sure their mouth is clear of chewing gum, food, or vomit.
Lean close to feel on your cheek and hear if there are breaths.
If there is **no breathing**, you will need to do mouth-to-mouth rescue breathing.
Otherwise, the person may suffer brain damage.

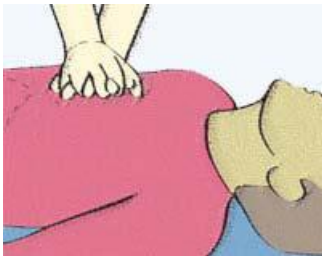


For rescue breathing, first pinch the person's nostrils together between your thumb and first finger.
Make a good seal around the person's lips with your mouth and blow steadily
until their chest rises. Then take your mouth away and let their chest sink back down.
Repeat the breathing, giving 1 breath every 5 seconds. Always keep the person's head tilted back and the airway open.



CPR (Chest Compressions or 'Pumps' & Rescue Breathing) **in Adults**

If both **breathing and heartbeat stop**, there is no pulse and CPR (cardiopulmonary
resuscitation) may keep the person alive until help comes.
First, give 2 rescue breaths (see above).
Place the heel of one hand on the breastbone in the center of the chest and put the other hand on top, locking your fingers together.



Next, keep your shoulders above the center of the person's chest, arms straight, and push down on their chest by about 2 inches. Quickly release the
pressure, but keep your hands where they are.
Do 30 fast down-then-up chest pumps in about 20 seconds, followed by 2 breaths of rescue breathing. Repeat this cycle until help comes.
If the person's heart starts beating, and their normal color returns, stop chest
pumps but still do rescue breathing unless they wake up.

If you have not been trained in rescue breathing, or cannot do it for some reason, you should still do the rapid chest pumps. This is called "Hands-Only CPR".

Opioid Safety Needs YOU!

Always follow these important Safety Tips…

- Never take an opioid pain reliever unless it is prescribed for you.
- Take opioids only as directed. Do not take more opioid or take it more often than is prescribed by your healthcare provider.
- Do not use opioids with alcohol or any other drugs unless approved by the opioid prescriber.
- Protect and lock up your opioids in a safe place at all times, and properly dispose of any leftover medicine.
- Never share opioids with another person, it is illegal and dangerous.
- Be prepared for opioid emergencies. Know signs of trouble and what to do for opioid overmedication or overdose.
- Read instructions that come with your opioid prescription. Contact your opioid prescriber or pharmacist with any questions.

Opioid Medicines Can Have Side Effects

The most common are:

- **Constipation** due to opioids may not go away, so you should ask your opioid prescriber about how to treat this.
- **Nausea** may last several days, and there is medicine that can help with this.
- **Sedation** — feeling mildly tired or groggy — may last a few days after starting opioids or when the dose is increased.

Less common side effects:

- Itching, dry skin, confusion, muscle twitching, dry mouth, sweating, fatigue, weakness, mild headaches – all are usually temporary.
- Allergy and addiction occur rarely to opioids taken as prescribed for pain.

Take Opioid Pain Relievers Safely

- Never chew, cut, crush, or dissolve opioid tablets, or open opioid capsules, unless you are specifically instructed to do so.
- Opioid patches must never be cut or folded, and they need to stick to the skin completely. Follow directions for use carefully.
- Do not drive or operate machinery until you know how opioids will affect you.

Be on the Alert for... Opioid Overmedication or Overdose

(Share this with your family and caregivers.)

Overmedication Warning – Call Healthcare Provider

U.S. residents also can call the National Poison Hotline at 1-800-222-1222 at any time of day or night.

- Intoxicated behavior – confusion, slurred speech, stumbling.
- Feeling dizzy or faint.
- Feeling or acting very drowsy or groggy, or nodding off to sleep.
- Unusual snoring, gasping, or snorting during sleep.
- Difficulty waking up from sleep and becoming alert or staying awake.

CAUTION: A person who at first only seems to be overmedicated may get much worse. **They should be kept awake and watched closely.**

Overdose Poisoning – Call Emergency Services

Dial **911** in the U.S. or Canada.

In England or the European Union dial 112 or 999, or other International numbers depending on your location.

- Person cannot be aroused or wakened, or is unable to talk if awakened.
- Any trouble with breathing; such as shortness of breath, slow or light breathing, or stopped breathing.
- Gurgling noises coming from mouth or throat.
- Body is limp, seems lifeless. Face is pale, clammy.
- Fingernails or lips turned blue/purple.
- Slow or unusual heartbeat or stopped heartbeat.

WARNING: If a child or pet ever swallows an opioid that was not prescribed for them, it is ***always an emergency***. Call for help immediately.