OPIATES / COMBINATION

OPIATES

Codeine
Fentanyl
Hydrocodone
Hydromorphone (Dilaudid ®)
Levorphanol (Levo-Dromoran ®)
Meperidine (Demerol ®)
Methadone (Dolophine ®)
Morphine sulfate
Oxycodone (Roxicodone®)
Propoxyphene (Darvon ®)
tapentadol- NUCYNTA®

NON-NARCOTIC ANALGESICS

Fioricet ®(apap 325mg + butalbital 50mg + caffeine 40mg)
Fiorinal ®(ASA 325mg + butalbital 50mg + caffeine 40mg)
Soma compound ®(Carisoprodol 200mg + ASA 325mg)
Tramadol (Ultram®)

AGONIST-ANTAGONISTS

Buprenorphine (Buprenex®)	
Butorphanol (Stadol®)	
Dezo	
Nalbu	
Penta	

Naltr

Nalox

OTHER

Subo and naloxone)

Zicon

Addit

Pleas r additional information and possible updates. The authors make no claims of the accuracy of the information contained herein doses are not a substitute for clinical judgment. Neither GlobalRPh Inc. nor any other party involved in the preparation of this progr y special, consequential, or exemplary damages resulting in whole or part from any user's use of or reliance upon this mater ISCLAIMER CAREFULLY BEFORE ACCESSING OR USING THIS SITE. BY ACCESSING OR USING THIS SITE, YOU AGREE TO BE BOUN CONDITIONS SET FORTH IN THE DISCLAIMER. [Read the disclaimer | <<Back]

OPIATES

CODEINE

CLINICAL PHARMACOLOGY
The major effects of codeine are on the central nervous system and the bowel. Opioids act as agonists, interacting with stereospecific and saturable binding sites or receptors in the brain and other tissues.

Codeine is readily absorbed from the gastrointestinal tract with the maximum analgesic effect occurring 60 minutes post administration. Codeine retains at least one half its analgesic activity when administered orally.

Dosing (Adult):
Pain: Oral, M, IV, SC: 30 mg (15-60mg) q4-6h prn. (Max 360mg/day).
Cough (non-productive): 10-20mg q4-6h prn (Max: 120 mg/day).

Analgesic: Oral: 30 mg every 4-6 hours as needed; patients with prior opiate exposure may require higher initial doses. Usual range: 15-120 mg every 4-6 hours as needed

I.M., SubQ: 30 mg every 4-6 hours as needed; patients with prior opiate exposure may require higher initial doses. Usual range: 15-120 mg every 4-6 hours as needed; more frequent dosing may be needed

Antitussive: Oral (for nonproductive cough):
Adults: 10-20 mg/dose every 4-6 hours as needed; maximum: 120 mg/day
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COMBINATION:
Tylenol with Codeine
(APAP/codeine)
#2: 300/15,
#3: 300/30mg,
#4: 300/60 mg: 1-2 tabs orally every 4 to 6 hours as needed.

Antitussive: Based on codeine (15-30 mg/dose) every 4-6 hours (maximum: 360 mg/24 hours based on codeine component)

Analgesic: Based on codeine (30-60 mg/dose) every 4-6 hours (maximum: 4000 mg/24 hours based on acetaminophen component)

Dosing adjustment in renal impairment:
Clcr 10-50 mL/minute: Administer 75% of dose
Clcr<10 mL/minute: Administer 50% of dose

Comments: Oral dose = 2/3 effectiveness of IV route when converting. Adult doses > 60mg fail to give commensurate relief of pain but merely prolong analgesia and are associated with an appreciably increased incidence of side effects.

Supplied:
Injection, as phosphate: 15 mg/mL (2 mL); 30 mg/mL (2 mL)
Solution, oral, as phosphate: 15 mg/5 mL (5 mL, 500 mL)
Tablet, as phosphate: 30 mg, 60 mg
Tablet, as sulfate: 15 mg, 30 mg, 60 mg

X

every 4 hours as needed.
[Supplied: Suspension: 120 mg-12 mg/5 ml. Tablets: 300/15 mg, 300/30mg, 300/60mg, 650/30 mg]

FENTANYL

Doses should be titrated to pain relief/prevention. Monitor vital signs routinely. Single I.M. doses have a duration of 1-2 hours, single I.V. doses last 0.5-1 hour.

Dosing (Adults):
Sedation for minor procedures/analgesia: I.M., I.V.: 0.5-1 mcg/kg/dose; higher doses are used for major procedures
Premedication: I.M., slow I.V.: 50-100 mcg/dose 30-60 minutes prior to surgery.
Adjunct to regional anesthesia: I.M., slow I.V.: 50-100 mcg/dose; if I.V. used, give over 1-2 minutes.
Severe pain: I.M.: 50-100 mcg/dose every 1-2 hours as needed; patients with prior opiate exposure may tolerate higher initial doses.
Adjunct to general anesthesia: Slow I.V.:
Low dose: Initial: 2 mcg/kg/dose; Maintenance: Additional doses infrequently needed
Moderate dose: Initial: 2-20 mcg/kg/dose; Maintenance: 25-100 mcg/dose may be given slow I.V. or I.M. as needed
High dose: Initial: 20-50 mcg/kg/dose; Maintenance: 25 mcg to one-half the initial loading dose may be given as needed

General anesthesia without additional anesthetic agents: Slow I.V.: 50-100 mcg/kg with O2 and skeletal muscle relaxant

Mechanically-ventilated patients (based on 70 kg patient): Slow I.V.: 0.35-1.5 mcg/kg every 30-60 minutes as needed; infusion: 0.7-10 mcg/kg/hour

Patient-controlled analgesia (PCA): I.V.: Usual concentration: 50 mcg/mL
Demand dose: Usual: 10 mcg; range: 10-50 mcg
Lockout interval: 5-8 minutes.

Pain management: Transdermal:
Initial: To convert patients from oral or parenteral opioids to transdermal formulation, a 24-hour analgesic requirement should be calculated (based on prior opiate use). This analgesic requirement should be converted to the equianalgesic oral morphine dose. The initial fentanyl dosage may be approximated from the 24-hour morphine dosage and titrated to minimize adverse effects and provide analgesia. Change patch every 72 hours.
Titration: Short-acting agents may be required until analgesic efficacy is established and/or as supplements for "breakthrough" pain. The amount of supplemental doses should be closely monitored. Appropriate dosage increases may be based on daily supplemental dosage using the ratio of 45 mg/24 hours of oral morphine to a 12.5 mcg/hour increase in fentanyl dosage. **Frequency of adjustment**: The dosage should not be titrated more frequently than every 3 days after the initial dose or every 6 days thereafter. Patients should wear a consistent fentanyl dosage through two applications (6 days) before dosage increase based on supplemental opiate dosages can be estimated. **Frequency of application**: The majority of patients may be controlled on every 72-hour administration; however, a small number of patients require every 48-hour administration.

Note:
Muscular rigidity may occur with rapid I.V. administration. During prolonged administration, dosage requirements may decrease.

SUPPLIED:
Infusion [premixed in NS]: 0.05 mg (10 mL); 1 mg (100 mL); 1.25 mg (250 mL); 2 mg (100 mL); 2.5 mg (250 mL)
Injection, solution, as citrate [preservative free]: 0.05 mg/mL (2 mL, 5 mL, 10 mL, 20 mL, 30 mL, 50 mL)
Lozenge, oral transmucosal, as citrate (Actiq®): 200 mcg, 400 mcg, 600 mcg, 800 mcg, 1200 mcg, 1600 mcg,
Transdermal system: 25 mcg/hour [6.25 cm 2] (5s); 50 mcg/hour [12.5 cm 2] (5s); 75 mcg/hour [18.75 cm 2]; 100 mcg/hour [25 cm 2] (5s)

HYDROCODONE

Maximum: 60 mg hydrocodone/day.

DOSING (Adults): >/= 50 kg: Average starting dose in opioid naive patients: Hydrocodone 5-10 mg 4 times/day; the dosage of acetaminophen should be limited to </= 4 g/day (and possibly less in patients with hepatic impairment or ethanol use).

Dosage ranges (based on specific product labeling): Hydrocodone 2.5-10 mg every 4-6 hours; maximum: 60 mg hydrocodone/day (maximum dose of hydrocodone may be limited by the acetaminophen content of specific product)

Drug UPDATES : ZOHYDRO ® ER (hydrocodone bitartrate) extended-release capsules, for oral use, CII [Drug information / PDF] **- See link for dosing info.**

Mechanism of Action: Hydrocodone is a semi-synthetic opioid agonist with relative selectivity for the mu-opioid (μ) receptor, although it can interact with other opioid receptors at higher doses. Hydrocodone acts as a full agonist, binding to and activating opioid receptors at sites in the peri-aquaductal and

INDICATIONS AND USAGE: ZOHYDRO ER is an opioid agonist indicated for the management of pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate. (1)

Drug UPDATES : **HYSINGLA™ ER** (hydrocodone bitartrate) extended-release tablets, for oral use, CII
[Drug information / PDF]
Dosing: Click (+) next to Dosage and Administration section (drug info link)

Initial U.S. Approval: 2014

Mechanism of Action: Hydrocodone is a semi-synthetic opioid agonist with relative selectivity for the mu-opioid receptor, although it can interact with other opioid receptors at higher doses. Hydrocodone acts as an agonist binding to and activating opioid receptors in the brain and spinal cord, which are coupled to G-protein complexes and modulate synaptic transmission through adenylate cyclase. The pharmacological effects of hydrocodone including analgesia, euphoria, respiratory depression and physiological dependence are believed to be primarily mediated via μ opioid receptors.

INDICATIONS AND USAGE:
HYSINGLA ER is an opioid agonist indicated for the management of pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate.

Limitations of Use:
Because of the risks of addiction, abuse, and misuse with opioids, even at recommended doses, and because of the greater risks of overdose and death with extended-release opioid formulations, reserve HYSINGLA ER for use in patients for whom alternative treatment options (e.g., non-opioid analgesics or immediate-release opioids) are ineffective, not tolerated, or would be otherwise inadequate to provide sufficient management of pain.
HYSINGLA ER is not indicated as an as-needed (prn) analgesic.

HOW SUPPLIED: Extended-release Tablets: 20, 30, 40, 60, 80, 100, and 120 mg

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Elderly: Doses should be titrated to appropriate analgesic effect; 2.5-5 mg of the hydrocodone component every 4-6 hours. Do not exceed 4 g/day of acetaminophen.

Dosage adjustment in hepatic impairment: Use with caution. Limited, low-dose therapy usually well tolerated in hepatic disease/cirrhosis; however, cases of hepatotoxicity at daily acetaminophen dosages <4 g/day have been reported. Avoid chronic use in hepatic impairment.

SUPPLIED:
Elixir, oral:
hycet®: Hydrocodone bitartrate 7.5 mg and acetaminophen 325 mg per 15 mL (473 mL)

Zamicet™: Hydrocodone bitartrate 10 mg and acetaminophen 325 mg per 15 mL (7.5 mL, 15 mL, 473 mL)

Tablet, oral:
Hydrocodone bitartrate 2.5 mg and acetaminophen 325 mg
Hydrocodone bitartrate 5 mg and acetaminophen 300 mg
Hydrocodone bitartrate 5 mg and acetaminophen 325 mg
Hydrocodone bitartrate 7.5 mg and acetaminophen 300 mg
Hydrocodone bitartrate 7.5 mg and acetaminophen 325 mg
Hydrocodone bitartrate 10 mg and acetaminophen 300 mg
Hydrocodone bitartrate 10 mg and acetaminophen 325 mg

Norco®:
Hydrocodone bitartrate 5 mg and acetaminophen 325 mg
Hydrocodone bitartrate 7.5 mg and acetaminophen 325 mg
Hydrocodone bitartrate 10 mg and acetaminophen 325 mg

Vicodin®: Hydrocodone bitartrate 5 mg and acetaminophen 300 mg

Vicodin ES®: Hydrocodone bitartrate 7.5 mg and acetaminophen 300 mg

Vicodin HP®: Hydrocodone bitartrate 10 mg and acetaminophen 300 mg

Xodol®:
5/300: Hydrocodone bitartrate 5 mg and acetaminophen 300 mg
7.5/300: Hydrocodone bitartrate 7.5 mg and acetaminophen 300 mg
10/300: Hydrocodone bitartrate 10 mg and acetaminophen 300 mg

HYDROMORPHONE (DILAUDID ®)

Dosing (Adults):
Give 2 to 4 mg orally every 4 to 6 hours as needed.
1-4 mg IM/SC/IV every 4 to 6 hours as needed.
3 mg rectally every 6 to 8 hours as needed.

(Higher doses/more frequent administration may be required in opiate tolerant patients).

Oral: (opiate naive) Start 2-4 mg q3-4h prn. Usual range: 2-8 mg q3-4h prn.
IV: (opiate naive) Start: 0.2 - 0.6 mg q2-3h prn. Pain, acute: 1-2 mg IV (slow - over 2-3 min) q3h prn.

Mechanically-ventilated pts: 0.7 - 2 mg q1-2h prn or start infusion: 0.5 - 1 mg/hr.
PCA: Usual concentration: 0.2 mg/ml. Demand dose (usual): 0.1 - 0.2 mg (range: 0.05 - 0.5mg). Lockout: 5-15 min. 4 hour limit: 4-6 mg.
Epidural: Bolus: 1-1.5 mg. Infusion conc: 0.05 - 0.075 mg/ml. Infusion rate: 0.04 - 0.4 mg/hr. Demand dose: 0.15mg. Lockout: 30 minutes.
IM/SC: (opiate naive) Start: 0.8 - 1 mg q4-6h prn. Usual range: 1-2 mg q3-6h prn.
Acute pain: 1-2 mg IM/SC q4-6h prn.
Rectal: 3 - 6mg q3-8h prn.
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INDIVIDUALIZATION OF DOSAGE
The dosage of opioid analgesics like hydromorphone hydrochloride should be individualized for any given patient, since adverse events can occur at doses that may not provide complete freedom from pain.

Safe and effective administration of opioid analgesics to patients with acute or chronic pain depends upon a comprehensive assessment of the patient. The nature of the pain (severity, frequency, etiology, and pathophysiology) as well as the concurrent medical status of the patient will affect selection of the starting dosage.

In non-opioid-tolerant patients, therapy with hydromorphone is typically initiated at an oral dose of 2-4 mg every four hours, but elderly patients may require lower doses.

In patients receiving opioids, both the dose and duration of analgesia will vary substantially depending on the patient's opioid tolerance. The dose should be selected and adjusted so that at least 3-4 hours of pain relief may be achieved. In patients taking opioid analgesics, the starting dose of DILAUDID should be based on prior opioid usage. This should be done by converting the total daily usage of the previous opioid to an equivalent total daily dosage of oral DILAUDID using an equianalgesic table.

Once the total daily dosage of DILAUDID has been estimated, it should be divided into the desired number of doses. Since there is individual variation in response to different opioid drugs, only 1/2 to 2/3 of the estimated dose of DILAUDID calculated from equivalence tables should be given for the first few doses, then increased as needed according to the patient's response.

Since the pharmacokinetics of hydromorphone are affected in hepatic and renal impairment with a consequent increase in exposure, patients with hepatic and renal impairment should be started on a lower starting dose.

In chronic pain, doses should be administered around-the-clock. A supplemental dose of 5-15% of the total daily usage may be administered every two hours on an "as-needed" basis.

Periodic reassessment after the initial dosing is always required. If pain management is not satisfactory and in the absence of significant opioid-induced adverse events, the hydromorphone dose may be increased gradually. If excessive opioid side effects are observed early in the dosing interval, the hydromorphone dose should be reduced. If this results in breakthrough pain at the end of the dosing interval, the dosing interval may need to be shortened. Dose titration should be guided more by the need for analgesia than the absolute dose of opioid employed.
Acute pain (moderate to severe): Note: These are guidelines and do not represent the maximum doses that may be required in all patients. Doses should be titrated to pain relief/prevention.

Oral: Initial: Opiate-naive: 2-4 mg every 3-4 hours as needed; patients with prior opiate exposure may require higher initial doses; usual dosage range: 2-8 mg every 3-4 hours as needed.

I.V.: Initial: Opiate-naive: 0.2-0.6 mg every 2-3 hours as needed; patients with prior opiate exposure may tolerate higher initial doses.

Note: More frequent dosing may be needed.

Mechanically-ventilated patients (based on 70 kg patient): 0.7-2 mg every 1-2 hours as needed; infusion (based on 70 kg patient): 0.5-1 mg/hour

I.M., SubQ: Note: I.M. use may result in variable absorption and a lag time to peak effect.
Initial: Opiate-naive: 0.8-1 mg every 4-6 hours as needed; patients with prior opiate exposure may require higher initial doses; usual dosage range: 1-2 mg every 3-6 hours as needed

Controlled release formulation (Hydromorph Contin®, not available in U.S.): 3-30 mg every 12 hours. Note: A patient's hydromorphone requirement should be established using prompt release formulations; conversion to long acting products may be considered when chronic, continuous treatment is required. Higher dosages should be reserved for use only in opioid-tolerant patients.

Extended release formulation (Palladone™): For use only in opioid-tolerant patients requiring extended treatment of pain. Initial Palladone™ dose should be calculated using standard conversion estimates based on previous total daily opioid dose, rounding off to the most appropriate strength available. Doses should be administered once every 24 hours. Discontinue all previous around-the-clock opioids when treatment is initiated. Dose may be adjusted every 2 days as needed.
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SUPPLIED:
Capsule, extended release, as hydrochloride (Palladone™): 12 mg, 16 mg, 24 mg, 32 mg

Injection, powder for reconstitution, as hydrochloride (Dilaudid-HP®): 250 mg.
Injection, solution, as hydrochloride: 1 mg/mL (1 mL); 2 mg/mL (1 mL, 20 mL); 4 mg/mL (1 mL); 10 mg/mL (1 mL, 5 mL, 10 mL)

Dilaudid®: 1 mg/mL (1 mL); 2 mg/mL (1 mL, 20 mL); 4 mg/mL (1 mL)
Dilaudid-HP®: 10 mg/mL (1 mL, 5 mL, 50 mL)

Liquid, oral, as hydrochloride (Dilaudid®): 1 mg/mL (480 mL)

Suppository, rectal, as hydrochloride (Dilaudid®): 3 mg (6s)
Tablet, as hydrochloride (Dilaudid®): 2 mg, 4 mg, 8 mg

LEVORPHANOL (LEVO-DROMORAN ®)

Dosing (Adults):
Acute pain (moderate to severe):
Oral: Initial: Opiate-naive: 2 mg every 6-8 hours as needed; patients with prior opiate exposure may require higher initial doses; usual dosage range: 2-4 mg every 6-8 hours as needed

I.M., SubQ: Initial: Opiate-naive: 1 mg every 6-8 hours as needed; patients with prior opiate exposure may require higher initial doses; usual dosage range: 1-2 mg every 6-8 hours as needed

Slow I.V.: Initial: Opiate-naive: Up to 1 mg/dose every 3-6 hours as needed; patients with prior opiate exposure may require higher initial doses

Chronic pain: Patients taking opioids chronically may become tolerant and require doses higher than the usual dosage range to maintain the desired effect. Tolerance can be managed by appropriate dose titration. There is no optimal or maximal dose for levorphanol in chronic pain. The appropriate dose is one that relieves pain throughout its dosing interval without causing unmanageable side effects.

Premedication: I.M., SubQ: 1-2 mg/dose 60-90 minutes prior to surgery; older or debilitated patients usually require less drug

Dosing adjustment in hepatic disease: Reduction is necessary in patients with liver disease

SUPPLIED:
Injection, solution, as tartrate: 2 mg/mL (1 mL, 10 mL)
Tablet, as tartrate: 2 mg

MEPERIDINE (DEMEROL ®)

Note: Doses should be titrated to necessary analgesic effect. When changing route of administration, note that oral doses are about half as effective as parenteral dose. Oral route not recommended for chronic pain. These are guidelines and do not represent the maximum doses that may be required in all patients.

Dosing (Adults):
Pain:
Oral: Initial: Opiate-naive: 50 mg every 3-4 hours as needed; usual dosage range: 50-150 mg every 2-4 hours as needed.
I.M., SubQ: Initial: Opiate-naive: 50-75 mg every 3-4 hours as needed; patients with prior opiate exposure may require higher initial doses; usual dosage range: 50-150 mg every 2-4 hours as needed

Preoperatively: 50-100 mg given 30-90 minutes before the beginning of anesthesia
Slow I.V.: Initial: 5-10 mg every 5 minutes as needed

Patient-controlled analgesia (PCA): Usual concentration: 10 mg/mL
Initial dose: 10

Elderly:
Oral: 50 mg every 4 hours
I.M.: 25 mg every 4 hours

Dosing adjustment in renal impairment: Avoid repeated administration of meperidine in renal dysfunction:
Clcr 10-50 mL/minute: Administer at 75% of normal dose
Clcr<10 mL/minute: Administer at 50% of normal dose

Dosing adjustment/comments in hepatic disease: Increased narcotic effect in cirrhosis; reduction in dose more important for oral than I.V. route

Administration
Meperidine may be administered I.M. (preferably), SubQ, or I.V.; I.V. push should be administered slowly, use of a 10 mg/mL concentration has been recommended. For continuous I.V. infusions, a more dilute solution (eg, 1 mg/mL) should be used.

SUPPLIED:
Injection, solution, as hydrochloride [**ampul**]: 25 mg/0.5 mL (0.5 mL); 25 mg/mL (1 mL); 50 mg/mL (1 mL, 1.5 mL, 2 mL); 75 mg/mL (1 mL); 100 mg/mL (1 mL)
Injection, solution, as hydrochloride [prefilled **syringe**]: 25 mg/mL (1 mL); 50 mg/mL (1 mL); 75 mg/mL (1 mL); 100 mg/mL (1 mL)
Injection, solution, as hydrochloride [for **PCA** pump]: 10 mg/mL (30 mL, 50 mL, 60 mL)

Injection, solution, as hydrochloride [**vial**]: 25 mg/mL (1 mL); 50 mg/mL (1 mL, 30 mL); 75 mg/mL (1 mL); 100 mg/mL (1 mL, 20 mL)

Syrup, as hydrochloride: 50 mg/5 mL (480 mL)
Tablet, as hydrochloride (Demerol®, Meperitab®): 50 mg, 100 mg

METHADONE (DOLOPHINE ®)

Important Note: Methadone accumulates with repeated doses and dosage may need to be adjusted downward after 3-5 days to prevent toxic effects. Some patients may benefit from q8-12h dosing intervals.

Dosing (Adults):
Pain:
Oral: Initial: 5-10 mg; dosing interval may range from 4-12 hours during initial therapy; decrease in dose or frequency may be required (~days 2-5) due to accumulation with repeated doses

Manufacturer's labeling: 2.5-10 mg every 3-4 hours as needed

I.V.: Manufacturers labeling: Initial: 2.5-10 mg every 8-12 hours in opioid-naive patients; titrate slowly to effect; may also be administered by SubQ or I.M. injection

Detoxification: Oral: 15-40 mg/day
Maintenance treatment of opiate dependence: Oral: 20-120 mg/day

Dosage adjustment in renal impairment: Clcr<10 mL/minute: Administer 50% to 75% of normal dose
Dosage adjustment in hepatic impairment: Avoid in severe liver disease

SUPPLIED:
Injection, solution, as hydrochloride: 10 mg/mL (20 mL)
Solution, oral, as hydrochloride: 5 mg/5 mL (500 mL); 10 mg/5 mL (500 mL)
Solution, oral concentrate, as hydrochloride: 10 mg/mL (30 mL)
Methadone Intensol™: 10 mg/mL (30 mL)
Methadose®: 10 mg/mL (30 mL) [cherry flavor]
Tablet, as hydrochloride (Dolophine®, Methadose®): 5 mg, 10 mg
Tablet, dispersible, as hydrochloride:
Methadose®: 40 mg
Methadone Diskets®: 40 mg

MORPHINE SULFATE

Dosing (Adults):
(**Regular release**): 10-30mg orally every 4 hours.
(**MS Contin**): 15 to 60mg orally every 8 to 12 hours.
(**Oral solution**-Roxanol): 10-30 mg orally every 4 hours.
((**Injection**): usual range: 2-15 mg IM/SC/IV every 4 hours as needed.

Extended release (Avinza®): 30 - 120mg qd. The daily dose must be limited to a maximum of 1600 mg/day. Doses over 1600 mg/day contain a quantity of fumaric acid that has not been demonstrated to be safe, and which may result in serious renal toxicity. Patients receiving other oral morphine formulations may be converted to Avinza® by administering the patient's total daily oral morphine dose as Avinza® once-daily. Should not be given more frequently than every 24 hours.

Rectal: 10-30 mg PR q4h prn.
IM, IV, SC: 2.5 to 20 mg q2-6h prn. Usual: 10mg q4h prn.

IV/SC continuous infusion: 0.8 - 10 mg/hr. Titrate to response. Usual range: up to 80mg/hr.

Epidural: Start 5 mg in lumbar region. If inadequate relief c/in 1 hr, give 1-2 mg. Max: 10 mg/24 hours.
Intrathecal (1/10th epidural dose): 0.2 - 1 mg. Repeat doses are not recommended.

[**Supplied**:
Capsule - immediate release (MSIR®): 15, 30mg.
Capsule - extended release (Avinza®): 30, 60, 90, 120mg.
Capsule - sustained release (Kadian®): 20,30, 50, 60, 100mg.
Infusion (premixed in D5W): 0.2 mg/ml (250, 500ml); 1 mg/ml (100, 250, 500ml)
Injection: 0.5 mg/ml (10 ml); 1 mg/ml (10, 30, 50 ml); 2 mg/ml (1 ml); 4 mg/ml (1 ml); 5 mg/ml (1, 30, 50 ml); 8 mg/ml (1 ml); 10 mg/ml (1, 2, 10 ml); 15 mg/ml (1 , 20 ml); 25 mg/ml (4, 10, 20, 40, 50ml); 50 mg/ml (10, 20, 40, 50ml).
Preservative free (Inj) Astramorph®: 0.5 mg/ml (2, 10ml); 1 mg/ml (2, 10 ml). Infumorph®: 10 mg/ml (20 ml); 25 mg/ml (20ml). Duramorph®: 0.5 and1 mg/ml (10 ml)
Oral solution: 10 mg/5ml (5, 100, 500 ml); 20 mg/ml(30, 120, 240ml); 20mg/5ml(30, 120 ml). Roxanol®: 20 mg/ml(30, 120 ml). Roxanol 100®: 100mg/5ml (240 ml).
Suppository: 5, 10, 20, 30mg.
Tablet (MSIR®): 15, 30mg.
Tablet - Controlled release (MS Contin®): 15, 30, 60, 100, 200mg. (Oramorph®): 15, 30, 60, 100mg.]

Kadian® Conversion from Other Oral Morphine Formulations to Kadian® Patients on other oral morphine formulations may be converted to Kadian® by administering one-half of the patient's total daily oral morphine dose as Kadian® capsules every 12 hours (twice-a-day) or by administering the total daily oral morphine dose as Kadian® capsules every 24 hours (once-a-day). Kadian® should not be given more frequently than every 12 hours.
[Supplied: capsule: 20, 30, 50, 60, 100mg]

OXYCODONE (ROXICODONE®)

Dosing (Adults): 5 mg orally every 6 hours as needed. [5 mg tab]
(OxyContin- Extended release): 10-40 mg orally every 12 hours. [10, 20, 40, 80, 160mg]

Pain: (Regular release)- 2.5 - 5 mg po q6h prn.
(Controlled release): 10 - 40 mg po q12h (Much higher doses possible in opiate tolerant patients).

COMBINATIONS:
Percocet (oxycodone 5 mg/APAP 325 mg): 1 tab orally every 6 hours as needed.
Percodan (Oxycodone 5 mg/ ASA 325mg): 1 tab orally every 6 hours as needed.
Roxicet (oxycodone/APAP 5/325, 5/500): 1 tablet orally every 6 hours as needed.
Tylox (oxycodone 5mg /APAP 500mg): 1 tab orally every 6 hours as needed.

[**Supplied**: (oxycodone hydrochloride)
Capsule - immediate release: OxyIR®: 5 mg.
Oral solution (Roxicodone®): 5 mg/5ml (5 ml, 500ml).
Oral solution concentrate (Oxydose®, Oxyfast®, Roxicodone Intensol®): 20mg/ml (30ml)
Tablet: Precolone®: 5 mg. Roxicodone®: 5, 15, 30mg.
Tablet - controlled release (Oxycontin®): 10, 20, 40, 80, 160mg]

Combinations:
Initial dose based on oxycodone content. Max dose based on APAP content. Dosing: 1 tab q4-6h prn.
[**Supplied**: Caplet: (Roxicet®): 5/500mg.
Capsule: Tylox®: 5/500mg
Oral Solution: Roxicet®: 5 mg-325mg/5 ml (5ml, 500ml).
Tablet: Endocet®: 5/325 mg. Perocet®: 2.5/325mg, 5/325mg, 7.5/325mg, 7.5/500mg, 10/325mg, 10/650mg. Roxicet®: 5/325mg. Percodan: 5/325mg - 1 tab q6h prn.

BOXED WARNING:
WARNING: ADDICTION, ABUSE, AND MISUSE; LIFE-THREATENING RESPIRATORY DEPRESSION; ACCIDENTAL INGESTION; NEONATAL OPIOID WITHDRAWAL SYNDROME; CYTOCHROME P450 3A4 INTERACTION; and RISKS FROM CONCOMITANT USE WITH BENZODIAZEPINES OR OTHER CNS DEPRESSANTS

[REVIEW PACKAGE INSERT]

Initial U.S. Approval: 2016

Mechanism of Action:
Oxycodone is a full opioid agonist and is relatively selective for the mu receptor, although it can bind to other opioid receptors at higher doses. The principal therapeutic action of oxycodone is analgesia. Like all full opioid agonists, there is no ceiling effect to analgesia for oxycodone. Clinically, dosage is titrated to provide adequate analgesia and may be limited by adverse reactions, including respiratory and CNS depression.

The precise mechanism of the analgesic action is unknown. However, specific CNS opioid receptors for endogenous compounds with opioid-like activity have been identified throughout the brain and spinal cord and are thought to play a role in the analgesic effects of this drug. In addition, when oxycodone binds to mu-opioid receptors, it results in positive subjective effects, such as drug liking, euphoria, and high.

INDICATIONS AND USAGE:
XTAMPZA ER is an opioid agonist product indicated for the management of pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate. (1)

Limitations of Use
Because of the risks of addiction, abuse, and misuse with opioids, even at recommended doses, and because of the greater risks of overdose and death with extended-release opioid formulations, reserve XTAMPZA ER for use in patients for whom alternative treatment options (e.g., non-opioid analgesics or immediate-release opioids) are ineffective, not tolerated, or would be otherwise inadequate to provide sufficient management of pain. (1)
XTAMPZA ER is not indicated as an as-needed (prn) analgesic. (1)

DOSAGE AND ADMINISTRATION:

- XTAMPZA ER at a total daily dose greater than 72 mg (equivalent to 80 mg oxycodone hydrochloride [HCl]) or a single dose greater than 36 mg (equivalent to 40 mg oxycodone HCl) is only for use in patients in whom tolerance to an opioid of comparable potency has been established. (2.1)
- Patients considered opioid tolerant are those receiving, for one week or longer, at least 60 mg oral morphine per day, 25 mcg transdermal fentanyl per hour, 30 mg oral oxycodone HCl per day, 8 mg oral hydromorphone per day, 25 mg oral oxymorphone per day, 60 mg oral hydrocodone per day, or an equianalgesic dose of another opioid. (2.1)
- Use the lowest effective dose for the shortest duration consistent with individual patient treatment goals (2.1)
- For opioid-naïve and opioid non-tolerant patients, initiate with 9 mg (equivalent to 10 mg oxycodone HCl) capsules orally every 12 hours with food. (2.2)
- The daily dose of XTAMPZA ER must be limited to a maximum of 288 mg per day (equivalent to 320 mg oxycodone HCl per day) (2.1)
- Hepatic impairment: Initiate therapy at 1/3 to 1/2 the usual dosage and titrate carefully. Monitor carefully. Use alternate analgesia for patients requiring less than 9 mg. (2.3, 8.6)
- Do not abruptly discontinue XTAMPZA ER in a physically dependent patient. (2.5)
- Instruct patients to take XTAMPZA ER capsules with food in order to ensure consistent plasma levels are achieved. For patients who have difficulty swallowing, XTAMPZA ER can also be taken by sprinkling the capsule contents on soft foods or into a cup and then administering directly into the mouth, or through a gastrostomy or nasogastric feeding tube. (2.6)

HOW SUPPLIED:
DOSAGE FORMS AND STRENGTHS
Extended-release capsules:
9 mg (equivalent to 10 mg oxycodone HCl)
13.5 mg (equivalent to 15 mg oxycodone HCl)
18 mg (equivalent to 20 mg oxycodone HCl)
27 mg (equivalent to 30 mg oxycodone HCl)
36 mg (equivalent to 40 mg oxycodone HCl).

PROPOXYPHENE (DARVON ®)

Dosing (Adults):
Propoxyphene Hydrochloride: 65 mg every 3-4 hours as needed for pain; maximum: 390 mg/day
Propoxyphene Napsylate: 100 mg every 4 hours as needed for pain; maximum: 600 mg/day

Darvocet-N® 100: 1 tablet every 4 hours as needed; maximum: 600 mg propoxyphene napsylate/day

Darvocet-N® 50: 1-2 tablets every 4 hours as needed; maximum: 600 mg propoxyphene napsylate/day

Napsylate: 100 mg every 4-6 hours as needed for pain

Dosing adjustment in renal impairment: Serum concentrations of propoxyphene may be increased or elimination may be delayed. Avoid use in Clcr<10 mL/minute. Specific dosing recommendations not available for less severe impairment.

Not dialyzable (0% to 5%)

Dosing adjustment in hepatic impairment: Serum concentrations of propoxyphene may be increased or elimination may be delayed; specific dosing recommendations not available.

SUPPLIED:
Tablet: Propoxyphene hydrochloride 65 mg and acetaminophen 650 mg, propoxyphene napsylate 100 mg, and acetaminophen 650 mg
Darvocet A500™: Propoxyphene napsylate 100 mg and acetaminophen 500 mg [contains lactose]

Darvocet-N® 50: Propoxyphene napsylate 50 mg and acetaminophen 325 mg

Darvocet-N® 100, Pronap-100®: Propoxyphene napsylate 100 mg and acetaminophen 650 mg

Capsule, as hydrochloride (Darvon®): 65 mg
Tablet, as napsylate (Darvon-N®): 100 mg

TAPENTADOL- NUCYNTA®

NUCYNTA (TAPENTADOL HYDROCHLORIDE) TABLET, FILM COATED

INDICATIONS AND USAGE:
NUCYNTA® is an opioid analgesic indicated for the relief of moderate to severe acute pain in patients 18 years of age or older.

DOSAGE AND ADMINISTRATION:
As with many centrally-acting analgesic medications, the dosing regimen of NUCYNTA® should be individualized according to the severity of pain being treated, the previous experience with similar drugs and the ability to monitor the patient.
Initiate NUCYNTA® with or without food at a dose of 50 mg, 75 mg, or 100 mg every 4 to 6 hours depending upon pain intensity. On the first day of dosing, the second dose may be administered as soon as one hour after the first dose, if adequate pain relief is not attained with the first dose.
Subsequent dosing is 50 mg, 75 mg, or 100 mg every 4 to 6 hours and should be adjusted to maintain adequate analgesia with acceptable tolerability.
Daily doses greater than 700 mg on the first day of therapy and 600 mg on subsequent days have not been studied and are, therefore, not recommended

DOSAGE FORMS AND STRENGTHS:
Tablets: 50 mg, 75 mg, 100 mg

CONTRAINDICATIONS:
1] Impaired pulmonary function (significant respiratory depression, acute or severe bronchial asthma or hypercapnia in unmonitored settings or the absence of resuscitative equipment)
2] Paralytic ileus
3] Concomitant use with monoamine oxidase inhibitors (MAOI) or use within 14 days

WARNINGS AND PRECAUTIONS
1] Respiratory depression: Increased risk in elderly, debilitated patients, those suffering from conditions accompanied by hypoxia, hypercapnia, or upper airway obstruction.
2] CNS effects: Additive CNS depressive effects when used in conjunction with alcohol, other opioids, or illicit drugs.
3] Elevation of intracranial pressure: May be markedly exaggerated in the presence of head injury, other intracranial lesions.
4] Abuse potential may occur. Monitor patients closely for signs of abuse and addiction.
5] Impaired mental/physical abilities: Caution must be used with potentially hazardous activities.
6] Seizures: Use with caution in patients with a history of seizures.
7] Serotonin Syndrome: Potentially life-threatening condition could result from concomitant serotonergic administration.

ADVERSE REACTIONS
The most common adverse events were nausea, dizziness, vomiting and somnolence.

To report SUSPECTED ADVERSE REACTIONS, contact PriCara, Division of Ortho-McNeil-Janssen Pharmaceuticals, Inc. at 1-800-526-7736 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch

DRUG INTERACTIONS
-Use NUCYNTA® with caution in patients currently using specified centrally-acting drugs or alcohol.
-Do not use NUCYNTA® in patients currently using or within 14 days of using a monoamine oxidase inhibitor (MAOI).

Nursing mothers: should not breast-feed.

Pediatric use: safety and effectiveness not established in patients less than 18 years of age.

Renal or hepatic impairment: not recommended in patients with severe renal or hepatic impairment. Use with caution in patients with moderate hepatic impairment.

Elderly: care should be taken when selecting an initial dose.

NUCYNTA® ER (TAPENTADOL) EXTENDED-RELEASE ORAL TABLETS C-II

INDICATIONS AND USAGE
NUCYNTA® ER is an opioid agonist indicated for the management of:

-moderate to severe chronic pain in adults.
-neuropathic pain associated with diabetic peripheral neuropathy (DPN) in adults.
-when a continuous, around-the-clock opioid analgesic is needed for an extended period of time.

Limitations of Use
NUCYNTA® ER is not for use:
– As an as-needed (prn) analgesic
– For pain that is mild or not expected to persist for an extended period of time
– For acute pain
– For postoperative pain, unless the patient is already receiving chronic opioid therapy prior to surgery, or if the postoperative pain is expected to be moderate to severe and persist for an extended period of time.

DOSAGE AND ADMINISTRATION
Individualize dosing based on patient's prior analgesic treatment experience, and titrate as needed to provide adequate analgesia and minimize adverse reactions.
The initial dose in patients not currently taking opioid analgesics is 50 mg twice a day.
Instruct patients to swallow NUCYNTA® ER tablets whole.
Use a gradual downward titration when NUCYNTA® ER is discontinued in a physically dependent patient.
Reduce the dose of NUCYNTA® ER in patients with moderate hepatic impairment.
NUCYNTA® ER use in patients with severe renal impairment is not recommended.
Conservative initial dosing of NUCYNTA® ER in elderly patients is recommended due to possible decreased renal and hepatic function.

DOSAGE FORMS AND STRENGTHS
Extended-Release Tablets: 50 mg, 100 mg, 150 mg, 200 mg, 250 mg

CONTRAINDICATIONS
Significant respiratory depression.
Acute or severe bronchial asthma .
Known or suspected paralytic ileus .
Hypersensitivity to tapentadol or to any other ingredients of the product.
Concurrent use of monoamine oxidase inhibitors (MAOI) or use within the last 14 days.

NON-NARCOTIC ANALGESICS

FIORICET ®(APAP 325MG + BUTALBITAL 50MG + CAFFEINE 40MG)

Dosing (Adults): Oral: 1-2 tablets or capsules (or 15-30 mL elixir) every 4 hours; not to exceed 6 tablets or capsules (or 180 mL elixir) daily.

Dosing interval in renal or hepatic impairment: Should be reduced

SUPPLIED:
Capsule:
Anolor 300, Esgic®, Medigesic®: Butalbital 50 mg, caffeine 40 mg, and acetaminophen 325 mg
Dolgic® Plus: Butalbital 50 mg, caffeine 40 mg, and acetaminophen 750 mg
Esgic-Plus™, Zebutal™: Butalbital 50 mg, caffeine 40 mg, and acetaminophen 500 mg

Elixir (Dolgic® LQ): Butalbital 50 mg, caffeine 40 mg, and acetaminophen 325 mg per 15 mL (480 mL)

Tablet: Butalbital 50 mg, caffeine 40 mg, and acetaminophen 325 mg;

FIORINAL ®(ASA 325MG + BUTALBITAL 50MG + CAFFEINE 40MG)

Dosing (Adults):
Oral: 1-2 tablets or capsules every 4 hours; not to exceed 6/day

Dosing interval in renal or hepatic impairment: Should be reduced

SUPPLIED:
Capsule (Fiorinal®): Butalbital 50 mg, caffeine 40 mg, and aspirin 325 mg

SOMA COMPOUND ®(CARISOPRODOL 200MG + ASA 325MG)

Dosing (Adults): 1-2 tabs orally four times daily.

SUPPLIED:
Tablet: Carisoprodol 200 mg and aspirin 325 mg

TRAMADOL (ULTRAM®)

Pharmacodynamics
ULTRAM® contains tramadol, a centrally acting synthetic opioid analgesic. Although its mode of action is not completely understood, from animal tests, at least two complementary mechanisms appear applicable: binding of parent and M1 metabolite to μ-opioid receptors and weak inhibition of reuptake of norepinephrine and serotonin.

Opioid activity is due to both low affinity binding of the parent compound and higher affinity binding of the O-demethylated metabolite M1 to μ-opioid receptors. In animal models, M1 is up to 6 times more potent than tramadol in producing analgesia and 200 times more potent in μ-opioid binding. Tramadol-induced analgesia is only partially antagonized by the opiate antagonist naloxone in several animal tests. The relative contribution of both tramadol and M1 to human analgesia is dependent upon the plasma concentrations of each compound.

Tramadol has been shown to inhibit reuptake of norepinephrine and serotonin in vitro, as have some other opioid analgesics. These mechanisms may contribute independently to the overall analgesic profile of ULTRAM®. Analgesia in humans begins approximately within one hour after administration and reaches a peak in approximately two to three hours.

Dosing (Adults):
Oral: Moderate to severe chronic pain: 50-100 mg every 4-6 hours, not to exceed 400 mg/day

For patients not requiring rapid onset of effect, tolerability may be improved by starting dose at 25 mg/day and titrating dose by 25 mg every 3 days, until reaching 25 mg 4 times/day. Dose may then be increased by 50 mg every 3 days as tolerated, to reach dose of 50 mg 4 times/day.

Elderly: >75 years: 50-100 mg every 4-6 hours (not to exceed 300 mg/day); see dosing adjustments for renal and hepatic impairment

Dosing adjustment in renal impairment: Clcr<30 mL/minute: Administer 50-100 mg dose every 12 hours (maximum: 200 mg/day)

Dosing adjustment in hepatic impairment: Cirrhosis: Recommended dose: 50 mg every 12 hours

SUPPLIED::
Tablet, as hydrochloride: 50 mg

AGONIST-ANTAGONISTS

BUPRENORPHINE (BUPRENEX®)

Dosing (Adults):
Long-term use is not recommended
Note: These are guidelines and do not represent the maximum doses that may be required in all patients. Doses should be titrated to pain relief/prevention. In high-risk patients (eg, elderly, debilitated, presence of respiratory disease) and/or concurrent CNS depressant use, reduce dose by one-half. Buprenorphine has an analgesic ceiling.

Acute pain (moderate to severe):

I.M.: Initial: Opiate-naive: 0.3 mg every 6-8 hours as needed; initial dose (up to 0.3 mg) may be repeated once in 30-60 minutes after the initial dose if needed; usual dosage range: 0.15-0.6 mg every 4-8 hours as needed

Slow I.V.: Initial: Opiate-naive: 0.3 mg every 6-8 hours as needed; initial dose (up to 0.3 mg) may be repeated once in 30-60 minutes after the initial dose if

Sublingual: Adults: Opioid dependence:
Induction: Range: 12-16 mg/day (doses during an induction study used 8 mg on day 1, followed by 16 mg on day 2; induction continued over 3-4 days). Treatment should begin at least 4 hours after last use of heroin or short-acting opioid, preferably when first signs of withdrawal appear. Titrating dose to clinical effectiveness should be done as rapidly as possible to prevent undue withdrawal symptoms and patient drop-out during the induction period.

Maintenance: Target dose: 16 mg/day; range: 4-24 mg/day; patients should be switched to the buprenorphine/naloxone combination product for maintenance and unsupervised therapy

Administration
I.V.: Administer slowly, over at least 2 minutes.

SUPPLIED:
Injection, solution (Buprenex®): 0.3 mg/mL (1 mL)
Tablet, sublingual (Subutex®): 2 mg, 8 mg

Drug UPDATES : **BELBUCA ™ (buprenorphine) buccal film CIII**
[Drug information / PDF] **Click link for the latest monograph**
Dosing: Click (+) next to Dosage and Administration section (drug info link)

Initial U.S. Approval: 2015

Mechanism of Action: Buprenorphine is a partial agonist at the mu-opioid receptor and an antagonist at the kappa-opioid receptor.

INDICATIONS AND USAGE: BELBUCA is indicated for the management of pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate.

Limitations of Use
Because of the risks of addiction, abuse, and misuse with opioids, even at recommended doses, and because of the greater risks of overdose and death with long-acting opioid formulations, reserve BELBUCA for use in patients for whom alternative treatment options (e.g., non-opioid analgesics or immediate-release opioids) are ineffective, not tolerated, or would be otherwise inadequate to provide sufficient management of pain.
BELBUCA is not indicated as an as-needed (prn) analgesic.

HOW SUPPLIED: BELBUCA is a buccal film available in 7 dosage strengths: 75 mcg, 150 mcg, 300 mcg, 450 mcg, 600 mcg, 750 mcg, and 900 mcg buprenorphine per film.

Drug UPDATES : **PROBUPHINE ® (buprenorphine) implant for subdermal administration CIII**
[Drug information / PDF]
Package insert - Dosing: Click (+) next to Dosage and Administration section (drug info link)

BOXED WARNING:
Risk Associated with Insertion and Removal Insertion and removal of PROBUPHINE are associated with the risk of implant migration, protrusion, and expulsion resulting from the ...

WARNING: IMPLANT MIGRATION, PROTRUSION, EXPULSION, and NERVE DAMAGE ASSOCIATED WITH INSERTION and REMOVAL

Risk Associated with Insertion and Removal

Insertion and removal of PROBUPHINE are associated with the risk of implant migration, protrusion, and expulsion resulting from the procedure. Rare but serious complications including nerve damage and migration resulting in embolism and death may result from improper insertion of drug implants inserted in the upper arm. Additional complications may include local migration, protrusion and expulsion.

Incomplete insertions or infections may lead to protrusion or expulsion. [see Warnings and Precautions (5.1)].

Because of the risks associated with insertion and removal, PROBUPHINE is available only through a restricted program called the PROBUPHINE REMS Program. All Healthcare Providers must successfully complete a live training program on the insertion and removal procedures and become certified, prior to performing insertions or prescribing PROBUPHINE implants. Patients must be monitored to ensure that PROBUPHINE is removed by a healthcare provider certified to perform insertions. [see Warnings and Precautions (5.2)].

Initial U.S. Approval: 2016

Mechanism of Action:
PROBUPHINE implants contain buprenorphine HCl. Buprenorphine is a partial agonist at the mu- opioid receptor and an antagonist at the kappa-opioid receptor.

PROBUPHINE should be used as part of a complete treatment program to include counseling and psychosocial support. (1)

PROBUPHINE is not appropriate for new entrants to treatment and patients who have not achieved and sustained prolonged clinical stability, while being maintained on buprenorphine 8 mg per day or less of a Subutex or Suboxone sublingual tablet or generic equivalent. (1)

DOSAGE AND ADMINISTRATION:
Prescription use of this product is limited under the Drug Addiction Treatment Act. (2.1)

Four PROBUPHINE implants are inserted subdermally in the upper arm for 6 months of treatment and are removed by the end of the sixth month. (2.2)

PROBUPHINE implants should not be used for additional treatment cycles after one insertion in each upper arm. (2.2)

PROBUPHINE implants must be inserted and removed by trained Healthcare Providers only. (2.3)

PROBUPHINE implants should be administered in patients who have achieved and sustained prolonged clinical stability on transmucosal buprenorphine. (2.4)

Examine the insertion site one week following insertion of PROBUPHINE implants for signs of infection or other problems. (2.5)

HOW SUPPLIED:
DOSAGE FORMS AND STRENGTHS
Each PROBUPHINE implant is an ethylene vinyl acetate (EVA) implant, 26 mm in length and 2.5 mm in diameter, containing 74.2 mg of buprenorphine (equivalent to 80 mg of buprenorphine hydrochloride).

BUTORPHANOL (STADOL®)

Dosing (Adults):
Note: These are guidelines and do not represent the maximum doses that may be required in all patients. Doses should be titrated to pain relief/prevention. Butorphanol has an analgesic ceiling.
Parenteral:
Acute pain (moderate to severe):
I.M.: Initial: 2 mg, may repeat every 3-4 hours as needed; usual range: 1-4 mg every 3-4 hours as needed.
I.V.: Initial: 1 mg, may repeat every 3-4 hours as needed; usual range: 0.5-2 mg every 3-4 hours as needed.

Preoperative medication: I.M.: 2 mg 60-90 minutes before surgery

Supplement to balanced anesthesia: I.V.: 2 mg shortly before induction and/or an incremental dose of 0.5-1 mg (up to 0.06 mg/kg), depending on previously administered sedative, analgesic, and hypnotic medications

Pain during labor (fetus >37 weeks gestation and no signs of fetal distress):
I.M., I.V.: 1-2 mg; may repeat in 4 hours. **Note**: Alternative analgesia should be used for pain associated with delivery or if delivery is anticipated within 4 hours
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Nasal spray:
Moderate to severe pain (including migraine headache pain): Initial: 1 spray (~1 mg per spray) in 1 nostril; if adequate pain relief is not achieved within 60-90 minutes, an additional 1 spray in 1 nostril may be given; may repeat initial dose sequence in 3-4 hours after the last dose as needed

Alternatively, 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); additional 2 mg doses should not be given for 3-4 hours

Note: In some clinical trials, an initial dose of 2 mg (as 2 doses 1 hour apart or 2 mg initially - 1 spray in each nostril) has been used, followed by 1 mg in 1 hour; side effects were greater at these dosages

Dosage adjustment in renal impairment:
I.M., I.V.: Initial dosage should generally be 1 /2 of the recommended dose; repeated dosing must be based on initial response rather than fixed intervals, but generally should be at least 6 hours apart

Nasal spray: Initial dose should not exceed 1 mg; a second dose may be given after 90-120 minutes

Dosage adjustment in hepatic impairment:
I.M., I.V.: Initial dosage should generally be 1 /2 of the recommended dose; repeated dosing must be based on initial response rather than fixed intervals, but generally should be at least 6 hours apart

Nasal spray: Initial dose should not exceed 1 mg; a second dose may be given after 90-120 minutes

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but generally should be at least 6 hours apart

Nasal Spray: Initial dose should not exceed 1 mg; a second dose may be given after 90-120 minutes

SUPPLIED:
Injection, solution, as tartrate [preservative free] (Stadol®): 1 mg/mL (1 mL); 2 mg/mL (1 mL, 2 mL)
Injection, solution, as tartrate [with preservative] (Stadol®): 2 mg/mL (10 mL)
Solution, intranasal spray, as tartrate: 10 mg/mL (2.5 mL) [14-15 doses]

DEZOCINE (DALGAN®)

Dosing (Adults):
2.5 to 10 mg IV every 2 to 4 hours or 5-20mg IM every 3 to 6 hours as needed.

NALBUPHINE (NUBAIN®)

Dosing (Adults):
I.M., I.V., SubQ:
10 mg/70 kg every 3-6 hours; maximum single dose: 20 mg; maximum daily dose: 160 mg

Dosing adjustment/comments in hepatic impairment:
Use with caution and reduce dose

SUPPLIED:
Injection, solution, as hydrochloride: 10 mg/mL (10 mL); 20 mg/mL (10 mL)
Injection, solution, as hydrochloride [preservative free]: 10 mg/mL (1 mL); 20 mg/mL (1 mL)

PENTAZOCINE (TALWIN®)

Partial agonist-antagonist.

Dosing (Adults):
Oral: 50 mg every 3-4 hours; may increase to 100 mg/dose if needed, but should not exceed 600 mg/day

I.M., SubQ: 30-60 mg every 3-4 hours, not to exceed total daily dose of 360 mg

I.V.: 30 mg every 3-4 hours (maximum: 360 mg/day)

Elderly: Elderly patients may be more sensitive to the analgesic and sedating effects. The elderly may also have impaired renal function. If needed, dosing should be started at the lower end of dosing range and adjust dose for renal function.

Dosing adjustment in renal impairment:
Clcr 10-50 mL/minute: Administer 75% of normal dose
Clcr<10 mL/minute: Administer 50% of normal dose

Dosing adjustment in hepatic impairment:
Reduce dose or avoid use in patients with liver disease

SUPPLIED:
Injection, solution (Talwin®): 30 mg/mL (1 mL, 10 mL)
Tablet (Talwin® NX): Pentazocine 50 mg and naloxone 0.5 mg

ANTAGONISTS

NALMEFENE (REVEX)

Dosing (Adults):
Reversal of postoperative opioid depression: Blue labeled product (100 mcg/mL): Titrate to reverse the undesired effects of opioids; initial dose for nonopioid dependent patients: 0.25 mcg/kg followed by 0.25 mcg/kg incremental doses at 2- to 5-minute intervals; after a total dose >1 mcg/kg, further therapeutic response is unlikely

Management of known/suspected opioid overdose: Green labeled product (1000 mcg/mL): Initial dose: 0.5 mg/70 kg; may repeat with 1 mg/70 kg in 2-5 minutes; further increase beyond a total dose of 1.5 mg/70 kg will not likely result in improved response and may result in cardiovascular stress and precipitated withdrawal syndrome. (If opioid dependency is suspected, administer a challenge dose of 0.1 mg/70 kg; if no withdrawal symptoms are observed in 2 minutes, the recommended doses can be administered.)

Note: If I.V. access is lost or not readily obtainable, a single SubQ or I.M. dose of 1 mg may be effective in 5-15 minutes.

Dosing adjustment in renal or hepatic impairment: Not necessary with single uses, however, slow administration (over 60 seconds) of incremental doses is recommended to minimize hypertension and dizziness

SUPPLIED:
Injection, solution: 100 mcg/mL (1 mL); 1000 mcg/mL (2 mL)

NALTREXONE (REVIA®)

INDICATIONS:
Treatment of ethanol dependence; blockade of the effects of exogenously administered opioids

Pharmacodynamic Actions: REVIA is a pure opioid antagonist. It markedly attenuates or completely blocks, reversibly, the subjective effects of intravenously administered opioids.

When co-administered with morphine, on a chronic basis, REVIA blocks the physical dependence to morphine, heroin and other opioids.

REVIA has few, if any, intrinsic actions besides its opioid blocking properties. However, it does produce some pupillary constriction, by an unknown mechanism.

The administration of REVIA is not associated with the development of tolerance or dependence. In subjects physically dependent on opioids, REVIA will precipitate withdrawal symptomatology.

Dosing (Adults):
Do not give until patient is opioid-free for 7-10 days as determined by urine analysis
Adults: Oral: 25 mg; if no withdrawal signs within 1 hour give another 25 mg; maintenance regimen is flexible, variable and individualized (50 mg/day to 100-150 mg 3 times/week for 12 weeks); up to 800 mg/day has been tolerated in adults without an adverse effect

Dosing cautions in renal/hepatic impairment: Caution in patients with renal and hepatic impairment. An increase in naltrexone AUC of approximately five- and 10-fold in patients with compensated or decompensated liver cirrhosis respectively, compared with normal liver function has been reported.

Administration
If there is any question of occult opioid dependence, perform a naloxone challenge test; do not attempt treatment until naloxone challenge is negative. Naltrexone is administered orally; to minimize adverse gastrointestinal effects, administer with food or antacids or after meals; advise patient not to self-administer opiates while receiving naltrexone therapy

SUPPLIED:
Tablet, as hydrochloride: 50 mg

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DOSAGE AND ADMINISTRATION
IF THERE IS ANY QUESTION OF OCCULT OPIOID DEPENDENCE, PERFORM A NALOXONE CHALLENGE TEST AND DO NOT INITIATE REVIA THERAPY UNTIL THE NALOXONE CHALLENGE IS NEGATIVE.

Treatment of Alcoholism:
A dose of 50 mg once daily is recommended for most patients (see Individualization of Dosage). The placebo-controlled studies that demonstrated the efficacy of REVIA as an adjunctive treatment of alcoholism used a dose regimen of REVIA 50 mg once daily for up to 12 weeks. Other dose regimens or durations of therapy were not evaluated in these trials.

A patient is a candidate for treatment with REVIA if:
The patient is willing to take a medicine to help with alcohol dependence.
The patient is opioid free for 7-10 days.
The patient does not have severe or active liver or kidney problems (Typical guidelines suggest liver function tests no greater than 3 times the upper limits of normal, and bilirubin normal.)
The patient is not allergic to REVIA , and no other contraindications are present.

REVIA should be considered as only one of many factors determining the success of treatment of alcoholism. Factors associated with a good outcome in the clinical trials with REVIA were the type, intensity, and duration of treatment; appropriate management of comorbid conditions; use of community-based support groups; and good medication compliance. To achieve the best possible treatment outcome, appropriate compliance-enhancing techniques should be implemented for all components of the treatment program, especially medication compliance.

Treatment of Opioid Dependence:
Initiate treatment with REVIA using the following guidelines:

naloxone challenge, treatment with REVIA should not be attempted. The naloxone challenge can be repeated in 24 hours.
3.) Treatment should be initiated carefully, with an initial dose of 25 mg of REVIA. If no withdrawal signs occur, the patient may be started on 50 mg a day thereafter.

Naloxone Challenge Test: The naloxone challenge test should not be performed in a patient showing clinical signs or symptoms of opioid withdrawal, or in a patient whose urine contains opioids. The naloxone challenge test may be administered by either the intravenous or subcutaneous routes.

Intravenous:
Inject 0.2 mg naloxone.
Observe for 30 seconds for signs or symptoms of withdrawal.
If no evidence of withdrawal, inject 0.6 mg of naloxone.
Observe for an additional 20 minutes.

Subcutaneous:
Administer 0.8 mg naloxone.

Observe for 20 minutes for signs or symptoms of withdrawal.

Note: Individual patients, especially those with opioid dependence, may respond to lower doses of naloxone. In some cases, 0.1 mg IV naloxone has produced a diagnostic response.

Interpretation of the Challenge: Monitor vital signs and observe the patient for signs and symptoms of opioid withdrawal. These may include, but are not limited to: nausea, vomiting, dysphoria, yawning, sweating, tearing, rhinorrhea, stuffy nose, craving for opioids, poor appetite, abdominal cramps, sense of fear, skin erythema, disrupted sleep patterns, fidgeting, uneasiness, poor ability to focus, mental lapses, muscle aches or cramps, pupillary dilation, piloerection, fever, changes in blood pressure, pulse or temperature, anxiety, depression, irritability, back ache, bone or joint pains, tremors, sensations of skin crawling or fasciculations. If signs or symptoms of withdrawal appear, the test is positive and no additional naloxone should be administered.

Warning: If the test is positive, do NOT initiate REVIA therapy. Repeat the challenge in 24 hours. If the test is negative, REVIA therapy may be started if no other contraindictions are present. If there is any doubt about the result of the test, hold REVIA and repeat the challenge in 24 hours.

Alternative Dosing Schedules:
Once the patient has been started on REVIA, 50 mg every 24 hours will produce adequate clinical blockade of the actions of parenterally administered opioids (i.e., this dose will block the effects of a 25 mg intravenous heroin challenge). A flexible approach to a dosing regimen may need to be employed in cases of supervised administration. Thus, patients may receive 50 mg of REVIA every weekday with a 100 mg dose on Saturday, 100 mg every other day, or 150 mg every third day. The degree of blockade produced by REVIA may be reduced by these extended dosing intervals.

There may be a higher risk of hepatocellular injury with single doses above 50 mg, and use of higher doses and extended dosing intervals should balance the possible risks against the probable benefits.

NALOXONE (NARCAN®)

CLINICAL PHARMACOLOGY
Complete or Partial Reversal of Opioid Depression
NARCAN prevents or reverses the effects of opioids including respiratory depression, sedation and hypotension. Also, NARCAN can reverse the psychotomimetic and dysphoric effects of agonist-antagonists such as pentazocine.

NARCAN is an essentially pure opioid antagonist, i.e., it does not possess the "agonistic" or morphine-like properties characteristic of other opioid antagonists. When administered in usual doses and in the absence of opioids or agonistic effects of other opioid antagonists, it exhibits essentially no pharmacologic activity.

NARCAN has not been shown to produce tolerance or cause physical or psychological dependence. In the presence of physical dependence on opioids, NARCAN will produce withdrawal symptoms. However, in the presence of opioid dependence, opiate withdrawal symptoms may appear within minutes of NARCAN administration and subside in about 2 hours. The severity and duration of the withdrawal syndrome are related to the dose of NARCAN and to the degree and type of opioid dependence.

While the mechanism of action of NARCAN is not fully understood, in vitro evidence suggests that NARCAN antagonizes opioid effects by competing for the μ, κ and σ opiate receptor sites in the CNS, with the greatest affinity for the μ receptor.

Dosing (Adults):
I.M., I.V. (preferred), intratracheal, SubQ:

Narcotic overdose: Adults: **I.V.**: 0.4-2 mg every 2-3 minutes as needed; may need to repeat doses every 20-60 minutes, if no response is observed after 10 mg, question the diagnosis. Note: Use 0.1-0.2 mg increments in patients who are opioid dependent and in postoperative patients to avoid large cardiovascular changes.

bolus on an hourly basis; add 10 times this dose to each liter of D5W and infuse at a rate of 100 mL/hour; 1 /2 of the initial bolus dose should be readministered 15 minutes after initiation of the continuous infusion to prevent a drop in naloxone levels; increase infusion rate as needed to assure adequate ventilation

SUPPLIED:
Injection, solution, as hydrochloride: 0.4 mg/mL (1 mL, 10 mL)

Drug UPDATES : EVZIO® (naloxone hydrochloride injection) Auto-Injector for intramuscular or subcutaneous use
Initial U.S. Approval: 1971
[Drug information / PDF]
Dosing: Click (+) next to Dosage and Administration section (drug info link)

U.S. Approval: 2014

Mechanism of Action: Naloxone hydrochloride is an opioid antagonist that antagonizes opioid effects by competing for the same receptor sites. Naloxone hydrochloride reverses the effects of opioids, including respiratory depression, sedation, and hypotension. Also, it can reverse the psychotomimetic and dysphoric effects of agonist-antagonists such as pentazocine.

INDICATIONS AND USAGE:
EVZIO is an opioid antagonist indicated for the emergency treatment of known or suspected opioid overdose, as manifested by respiratory and/or central nervous system depression.
EVZIO is intended for immediate administration as emergency therapy in settings where opioids may be present.
EVZIO is not a substitute for emergency medical care.
HOW SUPPLIED: Injection: 0.4 mg/0.4 mL naloxone hydrochloride solution in a pre-filled auto-injector.

OTHER

SUBOXONE ® (BUPRENORPHINE AND NALOXONE)

Dosing (Adults):
Treatment of opioid dependence. Not recommended for use during the induction period. Initial treatment should begin using buprenorphine oral tablets. Patients should be switched to the combination product for maintenance and unsupervised therapy. Maintenance: Target dose (based on buprenorphine content): 16 mg/day - range: 4-24 mg/day.

Supplied: sublingual tablet: Buprenorphine 2 mg and naloxone 0.5 mg; buprenorphine 8 mg and naloxone 2 mg.

ZICONOTIDE (PRIALT ®)

CLINICAL PHARMACOLOGY
Mechanism of Action
Ziconotide binds to N-type calcium channels located on the primary nociceptive (A-δ and C) afferent nerves in the superficial layers (Rexed laminae I and II) of the dorsal horn in the spinal cord. Although the mechanism of action of ziconotide has not been established in humans, results in animals suggest that its binding blocks N-type calcium channels, which leads to a blockade of excitatory neurotransmitter release from the primary afferent nerve terminals and antinociception.

Dosage (adults):
I.T.: Chronic pain: Initial dose: 2.4 mcg/day (0.1 mcg/hour)

Dose may be titrated by </= 2.4 mcg/day (0.1 mcg/hour) at intervals >/= 2-3 times/week to a maximum dose of 19.2 mcg/day (0.8 mcg/hour) by day 21; average dose at day 21: 6.9 mcg/day (0.29 mcg/hour). A faster titration should be used only if the urgent need for analgesia outweighs the possible risk to patient safety.

Administration
Not for I.V. administration. For I.T. administration only using a Medtronic SynchroMed® EL, SynchroMed® II Infusion System or Simms Deltec Cadd Micro® External Microinfusion Device and Catheter.
Medtronic SynchroMed® EL or SynchroMed® II Infusion Systems:

Naive pump priming (first time use with ziconotide): Use 2mL of undiluted ziconotide 25 mcg/mL solution to rinse the internal surfaces of the pump; repeat twice for a total of 3 rinses

Initial pump fill: Use only undiluted 25 mcg/mL solution and fill pump after priming. Following the initial fill only, adsorption on internal device surfaces will occur, requiring the use of the undiluted solution and refill within 14 days.

Pump refills: Contents should be emptied prior to refill. Subsequent pump refills should occur at least every 40 days if using diluted solution or every 60

Elderly: Refer to Adults dosing; use with caution

Dosage adjustment for toxicity: Cognitive impairment: Reduce dose or discontinue; effects are generally reversible within 2 weeks of discontinuation

Supplied: Injection (soln): 100 mcg/ml (1 ml, 2 ml, 5 ml).
25 mcg/ml (20 ml).

ADDITIONAL RESOURCES

DRUG TABLES AND CALCULATORS

- *Muscle Relaxants*
- *NSAIDs (ibuprofen, naproxen, ...) dosing table*
- *Opioids / Combination products*
- *Patient Controlled Analgesia-PCA*
- *Fibromyalgia*
- *Local Anesthetics*
- *Partial opioid agonists and other agents.*

CALCULATORS

1. *NSAID Selection Calculator. Powerful tool help select the most appropriate agent*
2. *Opioid Conversion Calc – original version*

---MEDICAL ARTICLES / NEWS / OTHER---

How does pregabalin compare to gabapentin in the treatment of neuropathic pain?

Pain Management: Its various aspects

REFERENCE(S)

National Institutes of Health, U.S. National Library of Medicine, **DailyMed Database.**
Provides access to the latest drug monographs submitted to the Food and Drug Administration (FDA). Please review the latest applicable package insert for additional information and possible updates. A local search option of this data can be found here.

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