## Morphine Sulfate ER Capsules (Avinza)
Capsules 30 mg, 45 mg, 60 mg, 75 mg, 90 mg, and 120 mg

<table>
<thead>
<tr>
<th>Dosing interval</th>
<th>• Once a day</th>
</tr>
</thead>
</table>
| Key instructions | • Initial dose in opioid non-tolerant patients is 30 mg  
|                 | • Titrate in increments of not greater than 30 mg using a minimum of 3-4 d intervals  
|                 | • Swallow capsule whole (do not chew, crush, or dissolve)  
|                 | • May open capsule & sprinkle pellets on applesauce for patients who can reliably swallow without chewing; use immediately  
|                 | • MDD:* 1600 mg (renal toxicity of excipient, fumaric acid) |
| Drug interactions | • Alcoholic beverages or medications w/ alcohol may result in rapid release & absorption of potentially fatal dose  
|                 | • P-gp* inhibitors (e.g., quinidine) may increase absorption/exposure of morphine by ~2-fold |
| Opioid-tolerant | • 90 mg & 120 mg capsules for use in opioid-tolerant patients only |
| Product-specific safety concerns | • None |

* MDD=maximum daily dose; P-gp= P-glycoprotein
## Buprenorphine Buccal Film (Belbuca)

### 75 mcg, 150 mcg, 300 mcg, 450 mcg, 600 mcg, 750 mcg, and 900 mcg

**Dosing interval**

- Every 12 h (or once every 24 h for initiation in opioid naïve patients & patients taking less than 30 mg oral morphine sulfate eq

**Key instructions**

- Opioid-naïve pts or pts taking <30 mg oral morphine sulfate eq: Initiate treatment with a 75 mcg buccal film, once daily, or if tolerated, every 12 h
  - Titrate to 150 mcg every 12 h no earlier than 4 d after initiation
  - Individual titration to a dose that provides adequate analgesia and minimizes adverse reaction should proceed in increments of 150 mcg every 12 h, no more frequently than every 4 d

- When converting from another opioid, first taper the current opioid to no more than 30 mg oral morphine sulfate eq/day prior to initiating Belbuca
  - If prior daily dose before taper was 30 mg to 89 mg oral morphine sulfate eq, initiate with 150 mcg dose every 12 h
  - If prior daily dose before taper was 90 mg to 160 mg oral morphine sulfate eq, initiate with 300 mcg dose every 12 h
  - Titration of the dose should proceed in increments of 150 mcg every 12 h, no more frequently than every 4 d
**Buprenorphine Buccal Film (Belbuca) cont’d**

### Key instructions
- **Maximum dose:** 900 mcg every 12 h due to the potential for QTc prolongation
- **Severe Hepatic Impairment:** Reduce the starting and incremental dose by half that of patients with normal liver function
- **Oral Mucositis:** Reduce the starting and incremental dose by half that of patients without mucositis
- **Do not use** if the package seal is broken or the film is cut, damaged, or changed in any way

### Specific Drug Interactions
- CYP3A4 inhibitors may increase buprenorphine levels
- CYP3A4 inducers may decrease buprenorphine levels
- Benzodiazepines may increase respiratory depression
- Class IA and III antiarrhythmics, other potentially arrhythmogenic agents, may increase risk for QTc prolongation and torsade de pointes

### Use in Opioid-Tolerant Patients
- Belbuca 600 mcg, 750 mcg, and 900 mcg are for use following titration from lower doses of Belbuca

### Product-Specific Safety Concerns
- QTc prolongation and torsade de pointes
- Hepatotoxicity

### Relative Potency: Oral Morphine
- Equipotency to oral morphine has not been established.
## Buprenorphine Transdermal System (Butrans)

**Transdermal System** 5 mcg/hr, 7.5 mcg/hr, 10 mcg/hr, 15 mcg/hr, 20 mcg/hr

### Key Instructions
- **Initial dose** in opioid non-tolerant patients on <30 mg morphine equivalents & in mild-moderate hepatic impairment: 5 mcg/h
- When converting from 30 mg-80 mg morphine equivalents, first taper to 30 mg morphine equivalent, then initiate w/ 10 mcg/h
- Titrate in 5 or 10 mcg/h increments by using no more than 2 patches of the 5 or 10 mcg/h system(s) w/ minimum of 72 h prior between dose adjustments. Total dose from all patches should be ≤20 mcg/h
- **Maximum dose:** 20 mcg/h due to risk of QTc prolongation
- **Application**
  - Apply only to sites indicated in PI
  - Apply to intact/non-irritated skin
  - Prep skin by clipping hair; wash site w/ water only
  - Rotate application site (min 3 wks before reapply to same site)
  - Do not cut
- **Avoid exposure to heat**
- Dispose of patches: fold adhesive side together & flush down toilet

### Dosing Interval
- One transdermal system every 7 d
Buprenorphine Transdermal System (Butrans) cont’d

<table>
<thead>
<tr>
<th>Drug Interactions</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>• CYP3A4 inhibitors may increase buprenorphine levels</td>
<td>• CYP3A4 inducers may decrease buprenorphine levels</td>
</tr>
<tr>
<td>• Benzodiazepines may increase respiratory depression</td>
<td>• Class IA &amp; III antiarrythmics, other potentially arrhythmogenic agents, may increase risk of QTc prolongation &amp; torsade de pointe</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Opioid-tolerant</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>• 7.5 mcg/h, 10 mcg/h, 15 mcg/h, &amp; 20 mcg/h for use in opioid-tolerant patients only</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Product-specific safety concerns</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>• QTc prolongation &amp; torsade de pointe</td>
<td>• Hepatotoxicity</td>
</tr>
<tr>
<td>• Application site skin reactions</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Relative potency: oral morphine</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>• Equipotency to oral morphine not established</td>
<td></td>
</tr>
</tbody>
</table>
# Methadone Hydrochloride Tablets (Dolophine)

## Dosing interval
- Every 8 to 12 h

## Key instructions
- Initial dose in opioid non-tolerant patients: 2.5 – 10 mg
- Conversion of opioid-tolerant patients using equianalgesic tables can result in overdose & death. Use low doses according to table in full PI
- Titrate slowly with dose increases no more frequent than every 3-5 d. Because of high variability in methadone metabolism, some patients may require substantially longer periods between dose increases (up to 12 d).
- High inter-patient variability in absorption, metabolism, & relative analgesic potency
- Opioid detoxification or maintenance treatment only provided in a federally certified opioid (addiction) treatment program (CFR, Title 42, Sec 8)

## Drug interactions
- Pharmacokinetic drug-drug interactions w/ methadone are complex
  - CYP 450 inducers may decrease methadone levels
  - CYP 450 inhibitors may increase methadone levels
  - Anti-retroviral agents have mixed effects on methadone levels
- Potentially arrhythmogenic agents may increase risk for QTc prolongation & torsade de pointe
- Benzodiazepines may increase respiratory depression

---

**FDA. Blueprint for Prescriber Education for Extended-Release and Long-Acting Opioid Analgesics. 08/2014.**

© CO*RE 2013
Methadone Hydrochloride Tablets (Dolophine) cont’d

<table>
<thead>
<tr>
<th>Opioid-tolerant</th>
<th>Product-specific safety concerns</th>
<th>Relative potency: oral morphine</th>
</tr>
</thead>
</table>
| • Refer to full PI | • QTc prolongation & torsade de pointe  
• Peak respiratory depression occurs later & persists longer than analgesic effect  
• Clearance may increase during pregnancy  
• False-positive UDT possible | • Varies depending on patient’s prior opioid experience |

Relative potency:

- Oral morphine

- Varies depending on patient’s prior opioid experience
Fentanyl Transdermal System (Duragesic)

12, 25, 37.5*, 50, 62.5*, 75, 87.5*, and 100 mcg/hr
(*These strengths are available only in generic form)

Dosing interval

- Every 72 h (3 d)

Key instructions

- Use product-specific information for dose conversion from prior opioid
- Hepatic or renal impairment: use 50% of dose if mild/moderate, avoid use if severe
- Application
  - Apply to intact/non-irritated/non-irradiated skin on a flat surface
  - Prep skin by clipping hair, washing site w/ water only
  - Rotate site of application
  - Titrate using a minimum of 72 h intervals between dose adjustments
  - Do not cut
- Avoid exposure to heat
- Avoid accidental contact when holding or caring for children
- Dispose of used/unused patches: fold adhesive side together & flush down toilet
### Key instructions

**Specific contraindications:**
- Patients who are not opioid-tolerant
- Management of
  - Acute or intermittent pain, or patients who require opioid analgesia for a short time
  - Post-operative pain, out-patient, or day surgery
  - Mild pain

### Drug interactions

- CYP3A4 inhibitors may increase fentanyl exposure
- CYP3A4 inducers may decrease fentanyl exposure
- Discontinuation of concomitant CYP P450 3A4 inducer may increase fentanyl plasma concentration

### Opioid-tolerant

- All doses indicated for opioid-tolerant patients only

### Product-specific safety concerns

- Accidental exposure due to secondary exposure to unwashed/unclothed application site
- Increased drug exposure w/ increased core body temp or fever
- Bradycardia
- Application site skin reactions

### Relative potency: oral morphine

- See individual PI for conversion recommendations from prior opioid
# Morphine Sulfate ER-Naltrexone (Embeda)

Capsules 20 mg/0.8 mg, 30 mg/1.2 mg, 50 mg/2 mg, 60 mg/2.4 mg, 80 mg, 3.2 mg, 100 mg/4 mg

## Dosing interval
- Once a day or every 12 h

## Key instructions
- Initial dose as first opioid: 20 mg/0.8 mg
- Titrate using a minimum of 1-2 d intervals
- Swallow capsules whole (do not chew, crush, or dissolve)
- Crushing or chewing will release morphine, possibly resulting in fatal overdose, & naltrexone, possibly resulting in withdrawal symptoms
- May open capsule & sprinkle pellets on applesauce for patients who can reliably swallow without chewing, use immediately

## Drug interactions
- Alcoholic beverages or medications w/ alcohol may result in rapid release & absorption of potentially fatal dose
- P-gp inhibitors (e.g., quinidine) may increase absorption/exposure of morphine by ~2-fold

## Opioid-tolerant
- 100 mg/4 mg capsule for use in opioid-tolerant patients only

## Product-specific safety concerns
- None
# Hydromorphone Hydrochloride (Exalgo)

**ER Tablets 8 mg, 12 mg, 16 mg, 32 mg**

<table>
<thead>
<tr>
<th>Dosing interval</th>
<th>• Once a day</th>
</tr>
</thead>
</table>
| **Key instructions** | • Use conversion ratios in individual PI  
• Start patients w/ moderate hepatic impairment on 25% dose prescribed for patient w/ normal function  
• Renal impairment: start patients w/ moderate on 50% & patients w/ severe on 25% dose prescribed for patient w/ normal function  
• Titrate in increments of 4-8 mg using a minimum of 3-4 d intervals  
• Swallow tablets whole (do not chew, crush, or dissolve)  
• Do not use in patients w/ sulfite allergy (contains sodium metabisulfite) |
| **Drug interactions** | • None |
| **Opioid-tolerant** | • All doses are indicated for opioid-tolerant patients only |
| **Product-specific adverse reactions** | • Allergic manifestations to sulfite component |
| **Relative potency: oral morphine** | • ~5:1 oral morphine to hydromorphone oral dose ratio, use conversion recommendations in individual product information |
Hydrocodone Bitartrate (Hysingla ER)
ER Tablets, 20 mg, 30 mg, 40 mg, 60 mg, 80 mg, 100 mg, 120 mg

Dosing interval
• Once a day

Key instructions
• Opioid-naïve patients: initiate treatment with 20 mg orally once daily.
• During titration, adjust the dose in increments of 10 mg to 20 mg every 3 to 5 days until adequate analgesia is achieved.
• Swallow tablets whole (do not chew, crush, or dissolve).
• Consider use of an alternative analgesic in patients who have difficulty swallowing or have underlying gastrointestinal disorders that may predispose them to obstruction.
• Take one tablet at a time, with enough water to ensure complete swallowing immediately after placing in the mouth.
• Use 1/2 of the initial dose and monitor closely for adverse events, such as respiratory depression and sedation, when administering Hysingla ER to patients with severe hepatic impairment or patients with moderate to severe renal impairment.
### Drug interactions

- CYP3A4 inhibitors may increase hydrocodone exposure.
- CYP3A4 inducers may decrease hydrocodone exposure.
- Concomitant use of Hysingla ER with strong laxatives (e.g., Lactulose) that rapidly increase GI motility may decrease hydrocodone absorption and result in decreased hydrocodone plasma levels.
- The use of MAO inhibitors or tricyclic antidepressants with Hysingla ER may increase the effect of either the antidepressant or Hysingla ER.

### Opioid-tolerant

- A single dose ≥ 80 mg is only for use in opioid tolerant patients.

### Product-specific safety concerns

- Use with caution in patients with difficulty swallowing the tablet or underlying gastrointestinal disorders that may predispose patients to obstruction.
- Esophageal obstruction, dysphagia, and choking have been reported with Hysingla ER.
- In nursing mothers, discontinue nursing or discontinue drug. QTc prolongation has been observed with Hysingla ER following daily doses of 160 mg.
- Avoid use in patients with congenital long QTc syndrome. This observation should be considered in making clinical decisions regarding patient monitoring when prescribing Hysingla ER in patients with congestive heart failure, bradyarrhythmias, electrolyte abnormalities, or who are taking medications that are known to prolong the QTc interval.
- In patients who develop QTc prolongation, consider reducing the dose.

### Relative potency: oral morphine

- See individual PI for conversion recommendations from prior opioid
Morphine Sulfate (Kadian)

ER Capsules 10 mg, 20 mg, 30 mg, 40 mg, 50 mg, 60 mg, 70 mg, 80 mg, 100 mg, 130mg, 150 mg, 200 mg

<table>
<thead>
<tr>
<th><strong>Dosing interval</strong></th>
<th>• Once a day or every 12 h</th>
</tr>
</thead>
</table>
| **Key instructions** | • PI recommends not using as first opioid  
• Titrate using minimum of 2-d intervals  
• Swallow capsules whole (do not chew, crush, or dissolve)  
• May open capsule & sprinkle pellets on applesauce for patients who can reliably swallow without chewing, use immediately |
| **Drug interactions** | • Alcoholic beverages or medications w/ alcohol may result in rapid release & absorption of potentially fatal dose of morphine  
• P-gp inhibitors (e.g., quinidine) may increase absorption/exposure of morphine by ~2-fold |
| **Opioid-tolerant** | • 100 mg, 130 mg, 150 mg, 200 mg capsules for use in opioid-tolerant patients only |
| **Product-specific safety concerns** | • None |
# Morphine Sulfate (MorphaBond)

**ER Tablets 15 mg, 30 mg, 60 mg, 100 mg**

## Dosing interval
- Every 8 h or every 12 h

## Key instructions
- Product information recommends not using as first opioid
- Titrate using a minimum of 1 – 2 d intervals
- Swallow tablets whole (do not chew, crush, or dissolve)

## Specific Drug interactions
- P-gp inhibitors (e.g. quinidine) may increase the absorption/exposure of morphine sulfate by about two-fold

## Opioid-tolerant
- MorphaBond 100 mg tablets are for use in opioid-tolerant patients only

## Product-specific safety concerns
- None
# Morphine Sulfate (MS Contin)

**ER Tablets 15 mg, 30 mg, 60 mg, 100 mg, 200mg**

<table>
<thead>
<tr>
<th>Dosing interval</th>
<th>• Every 8 h or every 12 h</th>
</tr>
</thead>
</table>
| **Key instructions** | • Product information recommends not using as first opioid.  
• Titrate using a minimum of 1-2 d intervals  
• Swallow tablets whole (do not chew, crush, or dissolve) |
| **Drug interactions** | • P-gp inhibitors (e.g., quinidine) may increase absorption/exposure of morphine by ~2-fold |
| **Opioid-tolerant** | • 100 mg & 200 mg tablet strengths for use in opioid-tolerant patients only |
| **Product-specific safety concerns** | • None |
# Tapentadol (Nucynta ER)

ER Tablets 50 mg, 100 mg, 150 mg, 200 mg, 250 mg

## Dosing interval

- Every 12 h

## Key instructions

- 50 mg every 12 h is initial dose in opioid non-tolerant patients
- Titrate by 50 mg increments using minimum of 3-d intervals
- MDD: 500 mg
- Swallow tablets whole (do not chew, crush, or dissolve)
- Take 1 tablet at a time w/ enough water to ensure complete swallowing immediately after placing in mouth
- Dose once/d in moderate hepatic impairment (100 mg/d max)
- Avoid use in severe hepatic & renal impairment

## Drug interactions

- Alcoholic beverages or medications w/ alcohol may result in rapid release & absorption of a potentially fatal dose of tapentadol
- Contraindicated in patients taking MAOIs

## Opioid-tolerant

- No product-specific considerations

## Product-specific safety concerns

- Risk of serotonin syndrome
- Angio-edema

## Relative potency: oral morphine

- Equipotency to oral morphine has not been established
### Dosing interval

- Every 12 h dosing, some may benefit from asymmetric (different dose given in AM than in PM) dosing

### Key instructions

- Use 5 mg every 12 h as initial dose in opioid non-tolerant patients & patients w/ mild hepatic impairment & renal impairment (creatinine clearance <50 mL/min) & patients >65 yrs
- Swallow tablets whole (do not chew, crush, or dissolve)
- Take 1 tablet at a time, w/ enough water to ensure complete swallowing immediately after placing in mouth
- Titrate in increments of 5-10 mg using a minimum of 3-7 d intervals
- Contraindicated in moderate & severe hepatic impairment

### Drug interactions

- Alcoholic beverages or medications w/ alcohol may result in absorption of a potentially fatal dose of oxymorphone

### Opioid-tolerant

- No product-specific considerations

### Product-specific safety concerns

- Use with caution in patients who have difficulty swallowing or underlying GI disorders that may predispose to obstruction (e.g. small gastrointestinal lumen)

### Relative potency: oral morphine

- Approximately 3:1 oral morphine to oxymorphone oral dose ratio
### Oxycodone Hydrochloride (OxyContin)

**ER Tablets 10mg, 15mg, 20mg, 30mg, 40mg, 60mg and 80 mg**

<table>
<thead>
<tr>
<th><strong>Dosing interval</strong></th>
<th>• Every 12 h</th>
</tr>
</thead>
</table>
| **Key instructions** | • Initial dose in opioid-naïve and non-tolerant patients: 10 mg every 12 h  
  • Titrate using a minimum of 1-2 d intervals  
  • Hepatic impairment: start w/ ⅓-½ usual dosage  
  • Renal impairment (creatinine clearance <60 mL/min): start w/ ½ usual dosage  
  • Consider other analgesics in patients w/ difficulty swallowing or underlying GI disorders that predispose to obstruction. Swallow tablets whole (do not chew, crush, or dissolve)  
  • Take 1 tablet at a time, w/ enough water to ensure complete swallowing immediately after placing in mouth |
| **Drug interactions** | • CYP3A4 inhibitors may increase oxycodone exposure  
  • CYP3A4 inducers may decrease oxycodone exposure |
| **Opioid-tolerant** | • Single dose >40 mg or total daily dose >80 mg for use in opioid-tolerant patients only |
| **Product-specific safety concerns** | • Choking, gagging, regurgitation, tablets stuck in throat, difficulty swallowing tablet  
  • Contraindicated in patients w/ GI obstruction |
| **Relative potency: oral morphine** | • Approximately 2:1 oral morphine to oxycodone oral dose ratio |
Oxycodone Hydrochloride (OxyContin) con’t
ER Tablets 10mg, 15mg, 20mg, 30mg, 40mg, 60mg and 80 mg

Key instructions

For Adults:
• Single dose greater than 40 mg or total daily dose greater than 80 mg are for use in adult patients in whom tolerance to an opioid of comparable tolerance has been established.
• When a dose increase is clinically indicated, the total daily oxycodone dose usually can be increased by 25% to 50% of the current dose.

For Pediatric Patients (11 years and older)
• For use only in opioid tolerant pediatric patients already receiving and tolerating opioids for at least five (5) consecutive days with a minimum of 20 mg per day of oxycodone or its equivalent for at least 2 days immediately preceding dosing with Oxycodon ER. Renal impairment (creatinine clearance <60 mL/min): start w/ ½ usual dosage
• If needed, pediatric dose may be adjusted in 1 to 2 day intervals.
• When a dose increase is clinically indicated, the total daily oxycodone dose usually can be increased by 25% of the current daily dose.

IMPORTANT:
• Opioids are rarely indicated or used to treat pediatric patients with chronic pain.
• The recent FDA approval for this oxycodone formulation was NOT intended to increase prescribing or use of this drug in pediatric pain treatment. Review the product information and adhere to best practices in the literature.
# Oxycodone Hydrochloride/Naloxone Hydrochloride (Targiniq ER)

**ER Tablets 10 mg/5mg, 20 mg/10 mg, 40 mg/20 mg**

## Dosing interval
- Every 12 h

## Key instructions
- Opioid-naïve patients: initiate treatment w/ 10mg/5mg every 12 h
- Titrate using min of 1-2 d intervals
- Do not exceed 80 mg/40 mg total daily dose (40 mg/20 mg q12h)
- May be taken w/ or without food
- Swallow whole. Do not chew, crush, split, or dissolve: this will release oxycodone (possible fatal overdose) & naloxone (possible withdrawal)
- Hepatic impairment: contraindicated in moderate-severe impairment. In patients w/ mild impairment, start w/ ⅓-½ usual dosage
- Renal impairment (creatinine clearance <60 mL/min): start w/ ½ usual dosage

## Drug interactions
- CYP3A4 inhibitors may increase oxycodone exposure
- CYP3A4 inducers may decrease oxycodone exposure

## Opioid-tolerant
- Single dose >40 mg/20 mg or total daily dose of 80 mg/40 mg for opioid-tolerant patients only

## Product-specific safety concerns
- Contraindicated in patients w/ moderate-severe hepatic impairment

## Relative potency: oral morphine
- See individual PI for conversion recommendations from prior opioids
# Hydrocodone Bitartrate (Zohydro ER)

ER Capsules 10 mg, 15 mg, 20 mg, 30 mg, 40 mg, 50 mg

<table>
<thead>
<tr>
<th>Dosing interval</th>
<th>• Every 12 h</th>
</tr>
</thead>
</table>
| Key instructions | • Initial dose in opioid non-tolerant patient is 10 mg  
                   • Titrate in increments of 10 mg using a min of 3-7 d intervals  
                   • Swallow capsules whole (do not chew, crush, or dissolve) |
| Drug interactions | • Alcoholic beverages or medications containing alcohol may result in rapid release & absorption of a potentially fatal dose of hydrocodone  
                      • CYP3A4 inhibitors may increase hydrocodone exposure  
                      • CYP3A4 inducers may decrease hydrocodone exposure |
| Opioid-tolerant | • Single dose >40 mg or total daily dose >80 mg for use in opioid-tolerant patients only |
| Product-specific safety concerns | • None |
| Relative potency: oral morphine | • Approximately 1.5:1 oral morphine to hydrocodone oral dose ratio |
# Naloxone (Narcan)

| **Dosing interval** | IM or SQ: onset 2-5 minutes, duration >45 min  
|                     | IV: onset 1-2 min, duration 45 minutes  
|                     | IN: onset 2-3 min, duration ~ 2 hours  |
| **Key instructions** | Monitor respiratory rate  
|                     | Monitor level of consciousness for 3-4 hours after expected peak of blood concentrations  
|                     | Note that reversal of analgesia will occur  |
| **Drug interactions** | Larger doses required to reverse effects of buprenorphine, butorphanol, nalbuphine, or pentazocine  |
| **Opioid-tolerant** | Assess signs and symptoms of opioid withdrawal, may occur w-i 2 min – 2 hrs  
|                     | Vomiting, restlessness, abdominal cramps, increased BP, temperature  
|                     | Severity depends on naloxone dose, opioid involved & degree of dependence  |
| **Product-specific safety concerns** | Ventricular arrhythmias, hypertension, hypotension, nausea & vomiting  
|                                 | As naloxone plasma levels decrease, sedation from opioid overdose may increase  |