FDA Blueprint Update, Spring 2015

See Attached drug-specific updated pages:

- Hyrdocodone bitartrate ER Tablets (Hysingla) **NEW TO MARKET**
- Additional strength for transdermal fentanyl patch
- ELMINATION of information for hydromorphone hydrochloride ER (Palladone): no longer on the market

Specific Drug Information for Extended-Release and Long-Acting Opioid Analgesics (ER/LA opioid analgesics)	
Dolophine	Methadone Hydrochloride Tablets, 5 mg and 10 mg
Dosing Interval	Every 8 to 12 hours
Key Instructions	Initial dose in opioid non-tolerant patients: 2.5 to 10 mg Conversion of opioid-tolerant patients using equianalgesic tables can result in overdose and death. Use low doses according to the table in the full prescribing information. Dosage adjustments may be done using a minimum of 1 to 2 day intervals. High inter-patient variability in absorption, metabolism, and relative analgesic potency. Opioid detoxification or maintenance treatment shall only be provided in a federally certified opioid (addiction) treatment program (Code of Federal Regulations, Title 42, Sec 8).
Specific Drug Interactions	Pharmacokinetic drug-drug interactions with 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 and torsade de pointe. Benzodiazepines may increase respiratory depression
Use in Opioid-Tolerant Patients	Refer to full prescribing information.
Product-Specific Safety Concerns	QTc prolongation and torsade de pointe. Peak respiratory depression occurs later and persists longer than analgesic effect. Clearance may increase during pregnancy. False positive urine drug screens possible.
Relative Potency To Oral Morphine	Varies depending on patient's prior opioid experience.
Duragesic	Fentanyl Transdermal System, 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 hours (3 days)
Key Instructions	Use product specific information for dose conversion from prior opioid Use 50% of the dose in mild or moderate hepatic or renal impairment, avoid use in severe hepatic or renal impairment Application • Apply to intact/non-irritated/non-irradiated skin on a flat surface. • Skin may be prepped by clipping hair, washing site with water only • Rotate site of application. • Titrate using a minimum of 72 hour 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 by folding the adhesive side together and flushing down the toilet. **Specific contraindications:** Patients who are not opioid-tolerant. Management of acute or intermittent pain, or in patients who require opioid analgesia for a short period of time. Management of post-operative pain, including use after out-patient or day surgery. Management of mild pain.
Specific Drug Interactions	CYP3A4 inhibitors may increase fentanyl exposure. CYP3A4 inducers may decrease fentanyl exposure. Discontinuation of a concomitantly used cytochrome P450 3A4 inducer may result in an increase in fentanyl plasma concentration.

Specific Drug Information for Extended-Release and Long-Acting Opioid Analgesics (ER/LA opioid analgesics)	
Use in Opioid-Tolerant Patients	All doses of Duragesic are indicated for use in opioid-tolerant patients only.
Product-Specific Safety Concerns	Accidental exposure due to secondary exposure to unwashed/unclothed application site. Increased drug exposure with increased core body temperature or fever. Bradycardia Application site skin reactions
Relative Potency To Oral Morphine	See individual product information for conversion recommendations from prior opioid
Embeda	Morphine Sulfate ER-Naltrexone 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 hours
Key Instructions	Initial dose as first opioid: 20 mg/0.8 mg. Titrate using a minimum of 1 to 2 day intervals. Swallow capsules whole (do not chew, crush, or dissolve) Crushing or chewing will release morphine, possibly resulting in fatal overdose, and naltrexone, possibly resulting in withdrawal symptoms. May open capsule and sprinkle pellets on applesauce for patients who can reliably swallow without chewing, use immediately.
Specific Drug Interactions	Alcoholic beverages or medications containing alcohol may result in the rapid release and absorption of a potentially fatal dose of morphine. P-gp inhibitors (e.g. quinidine) may increase the absorption/exposure of morphine sulfate by about two-fold.
Use in Opioid-Tolerant Patients	Embeda 100 mg/4 mg capsule is for use in opioid-tolerant patients only.
Product-Specific Safety Concerns	None
Exalgo	Hydromorphone Hydrochloride Extended-Release Tablets, 8 mg, 12 mg, 16 mg or 32 mg
Dosing Interval	Once a day
Key Instructions	Use the conversion ratios in the individual product information. Start patients with moderate hepatic impairment on 25% dose that would be prescribed for a patient with normal hepatic function. Start patients with moderate renal impairment on 50%, and patients with severe renal impairment on 25% of the dose that would be prescribed for a patient with normal renal function. Titrate in increments of 4 to 8 mg using a minimum of 3 to 4 day intervals. Swallow tablets whole (do not chew, crush, or dissolve). Do not use in patients with sulfite allergy—contains sodium metabisulfite.
Specific Drug Interactions	None
Use in Opioid-Tolerant Patients	All doses of Exalgo are indicated for opioid-tolerant patients only.
Drug-Specific Adverse Reactions	Allergic manifestations to sulfite component.
Relative Potency To Oral Morphine	Approximately 5:1 oral morphine to hydromorphone oral dose ratio, use conversion recommendations in the individual product information.
Hysingla ER	Hydrocodone bitartrate Extended–Release Tablets, 20 mg, 30 mg, 40 mg, 60 mg, 80 mg, 100 mg, and 120 mg
Dosing Interval	Every 24 hours (once-daily)

Specific Drug Information for Extended-Release and Long-Acting Opioid Analgesics (ER/LA opioid analgesics)	
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.
Specific 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.
Use in Opioid-Tolerant Patients	A single dose of Hysingla ER greater than or equal to 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 To Oral Morphine	See individual product information for conversion recommendations from prior opioid.
Kadian	Morphine Sulfate Extended-Release Capsules, 10 mg, 20mg, 30 mg, 40 mg, 50 mg, 60 mg, 70 mg, 80 mg, 100 mg, 130 mg, 150 mg, and 200 mg
Dosing Interval	Once a day or every 12 hours
Key Instructions	Product information recommends not using as first opioid. Titrate using a minimum of 2-day intervals. Swallow capsules whole (do not chew, crush, or dissolve).