Long-Acting Opioids (Oral)
Preferred Step Therapy Policy
March 2017

Step 1 Medications
- generic hydromorphone HCl extended-release tablets
- generic morphine sulfate controlled-release tablets
- generic morphine sulfate extended-release capsules
- generic oxymorphone extended-release tablets

Step 2 Medications
- Arymo™ ER (morphine sulfate extended-release tablets)
- Avinza® (morphine sulfate extended-release capsules)
- Embeda® (morphine sulfate and naltrexone hydrochloride extended-release capsules)
- Exalgo® (hydromorphone HCl extended release tablets)
- Hysingla™ ER (hydrocodone bitartrate extended-release tablets – Purdue)
- Kadian® (morphine sulfate extended-release capsules)
- MS Contin® (morphine sulfate controlled-release tablets)
- Nucynta® ER (tapentadol extended-release tablets)
- Opana® ER (oxymorphone extended-release tablets)
- OxyContin® (oxycodone controlled-release tablets)
- Oxycodone extended-release tablets – Par Pharma and Sandoz (brand products)
- Xtampza™ ER (oxycodone extended-release capsules)
- Zohydro® ER (hydrocodone extended-release capsules)

Overview
Opioid analgesics have a central role in the management of moderate to severe pain. These medications produce most of their effects by binding to μ, κ, and δ receptors in the central nervous system (CNS). However, Nucynta ER has a unique dual mechanism of action. It demonstrates μ-opioid agonist activity and inhibition of norepinephrine reuptake. Sustained-release opioid dosage forms offer a long duration of effect, reduce severity of end-of-dose pain, and allow many patients to sleep through the night. Long-acting products should be prescribed with an immediate-release dosage form, to be used as needed for breakthrough pain.

Morphine sulfate, oxycodone, oxymorphone, hydromorphone, tapentadol, and hydrocodone are the currently available oral long-acting opioids. All of the long-acting oral opioids are 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. OxyContin is the only product specifically indicated in pediatric patients 11 years to 18 years of age. Nucynta ER is the only product also indicated for the management of neuropathic pain associated with diabetic peripheral neuropathy (DPN) in adults. Morphine sulfate is available in long-acting forms as
sustained-release capsules (Avinza [generics] or Kadian [generics]) and controlled-release tablets (MS Contin, generics). Previously sustained-release tablets (Oramorph® SR) were also available; however, this product has been discontinued. MS Contin, Kadian, Exalgo, and Avinza are available generically. Morphine sulfate is also available as an extended-release capsule with a sequestered core of naltrexone hydrochloride, an opioid receptor antagonist (Embeda). Hydromorphone is available as an extended-release tablet (Exalgo) which is only indicated for opioid tolerant patients. Tapentadol is available as an extended-release tablet (Nucynta ER).

Avinza (generics), Exalgo, and Hysingla ER should only be taken once daily. Kadian (generics) and Embeda can be dosed once or twice daily. MS Contin (generics) is dosed every 8 to 12 hours. OxyContin, Opana ER, Nucynta ER, Xtampza ER, and Zohydro ER are dosed every 12 hours. Opana ER is the only agent that should be taken on an empty stomach.

All products should be swallowed whole and not broken, crushed, dissolved, or chewed. Alternatively, Kadian (generics), Avinza (generics), and Embeda capsules can be opened and sprinkled on applesauce immediately before ingestion. In addition, Kadian capsules may be opened and the contents sprinkled in water and flushed through a gastrostomy tube (G-tube). Avinza pellets (generics) and Embeda pellets should not be administered through a nasogastric or gastric tube. Xtampza ER capsules can be taken by sprinkling the capsule contents on soft foods or sprinkling the contents into a cup and then administering directly into the mouth or through a gastrostomy or nasogastric feeding tube.

**POLICY STATEMENT**
A step therapy program has been developed to encourage the use of one generic Step1 product prior to the use of a Step 2 product. If the step therapy rule is not met for a Step 2 agent at the point of service, coverage will be determined by the step therapy criteria below. All approvals are provided for 1 year in duration.

**STEP THERAPY CRITERIA**

1. If the patient has tried a Step1 medication, then authorization for a Step 2 medication may be given.

2. Authorization may be given for Hysingla ER, OxyContin, oxycodone extended-release tablets (brand products), Nucynta ER, Xtampza ER, or Zohydro ER if the patient is unable to tolerate or has a drug allergy noted with morphine sulfate.

3. Authorization may be given for Hysingla ER, OxyContin, oxycodone extended-release tablets (brand products), Nucynta ER, Xtampza ER, or Zohydro ER if the patient has renal insufficiency.

4. Authorization may be given for OxyContin in opioid-tolerant pediatric patients 11 years to 18 years of age.

5. No other exceptions are recommended.
REFERENCES

- MS Contin® tablets [prescribing information]. Stamford, CT: Purdue Frederick; April 2014.
- Oramorph® SR tablets [prescribing information]. Columbus, OH: Roxane Laboratories; February 2006.
- OxyContin® tablets [prescribing information]. Stamford, CT: Purdue Pharma LP; December 2016.
- Opana® ER tablets [prescribing information]. Malvern, PA: Endo Pharmaceuticals; April 2014.

OTHER REFERENCES UTILIZED

- Raffa BR. Pergolizzi JV. Opioid formulations designed to resist/deter abuse. Drugs. 2010;70(13):1657-1675.