Long-Acting Oral Opioids

Policy # 00323
Original Effective Date: 11/16/2011
Current Effective Date: 06/21/2017

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the “Company”), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services May Be Eligible for Coverage
Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- Benefits are available in the member’s contract/certificate, and
- Medical necessity criteria and guidelines are met.

Based on a review of the available data, brand name oral long-acting opioid products including, but not limited to Avinza™‡ (morphine), Embeda™‡ (morphine/naltrexone), Exalgo™‡ (hydromorphone), Kadian™‡ (morphine), MS Contin™ (morphine), Nucynta™‡ ER (tapentadol), Opana™‡ ER (oxymorphone), Oramorph SR™ (morphine), Zohydro™‡ ER (hydrocodone), Hysingla™‡ ER (hydrocodone), Xtampza™‡ ER (oxycodone), branded oxycodone extended release tablets, Arymo™‡ ER (morphine sulfate), and OxyContin®‡ (oxycodone) may be considered eligible for coverage when one of the below patient selection criteria is met:

Patient Selection Criteria:
Coverage eligibility will be considered for brand name oral long-acting opioid products when ONE of the following criteria is met:

- Requested drug is any of the brand name long-acting oral opioids and patient has tried and failed generic hydromorphone HCl extended release tablets, generic morphine sulfate controlled-release tablets, generic morphine sulfate extended-release capsules or generic oxymorphone extended-release tablets; OR
- Requested drug is OxyContin, Xtampza ER, branded oxycodone extended release tablets, Nucynta ER, Exalgo, Zohydro ER, or Hysingla ER and patient is unable to tolerate morphine sulfate or has a drug allergy to morphine sulfate; OR
- Requested drug is OxyContin, Xtampza ER, branded oxycodone extended release tablets, Nucynta ER, Exalgo, Zohydro ER, or Hysingla ER and patient has renal insufficiency; OR
- Requested drug is OxyContin and the patient is 11 years to 18 years of age; OR
- There is clinical evidence or patient history that suggests the generically available products will be ineffective or cause an adverse reaction to the patient.

When Services Are Considered Not Medically Necessary
Based on review of available data, the Company considers the use of brand name oral long-acting opioids when patient selection criteria are not met or for usage not included in the above patient selection criteria to be not medically necessary.

Background/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, tapentadol extended-release 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. All of the available long-acting oral opioids share the same general indication. Although there are differences noted in some studies, it is generally accepted that these drugs are equally safe and effective when administered at equipotent doses.

Morphine undergoes conjugation in the liver to two primary metabolites. Significant concentrations of these metabolites result from morphine’s extensive first-pass metabolism. Accumulation of these metabolites, primarily in renally impaired patients, may be associated with adverse effects such as hyperalgesia, myoclonus, and prolonged respiratory depression. Although a dosage reduction of morphine for renally impaired patients has been proposed, this recommendation has not been firmly established. When other safer opioids are available, it is recommended to avoid the use of morphine in patients with renal dysfunction. Oxycodone is extensively metabolized to noroxycodone, oxymorphone, and their glucuronides. Noroxycodone is a much weaker analgesic than oxycodone, and oxymorphone is present in low concentrations in the plasma. Therefore, the parent compound is primarily responsible for the opioid activity. In the presence of renal dysfunction, the elimination half-life of the parent compound is lengthened and the excretion of metabolites is severely impaired, so that accumulation can occur. Oxycodone should be given cautiously in the setting of renal impairment, and use of oxycodone in patients with a creatinine clearance of < 60 mL/min should be avoided. Oxymorphone is highly metabolized and has two major metabolites. Oxymorphone accumulates in renal failure. Hydromorphone is minimally metabolized by P450 enzymes. There is no evidence that hydromorphone inhibits or induces any enzymes. The dosage of hydromorphone should be adjusted in renal failure. Tapentadol is minimally metabolized by CYP enzymes. The major pathway of metabolism is conjugation with glucuronic acid to produce glucuronides. None of the metabolites contribute to the analgesic activity.

Oxycontin is the only long acting oral opioid product that has an indication specifically for pediatric patients ages 11 to 18 years of age.

Rationale/Source
The patient selection criteria presented in this policy takes into consideration multiple factors, including drug allergies, renal insufficiency, age, and clinical evidence or patient history that suggests the generically available products will be ineffective or cause an adverse reaction to the patient. Based on a review of the data, in the absence of the above mentioned caveats, there is no advantage of using a brand name oral long-acting opioid over the available generic oral long-acting opioids. Generic drugs are considered to have equal bioavailability and efficacy in comparison to brand name drugs.

References
Policy # 00323  
Original Effective Date: 11/16/2011  
Current Effective Date: 06/21/2017


10. MS Contin tablets [package insert]. Stamford, CT: Purdue Frederick; August 2013.


Long-Acting Oral Opioids

Policy # 00323
Original Effective Date: 11/16/2011
Current Effective Date: 06/21/2017

Policy History

<table>
<thead>
<tr>
<th>Date</th>
<th>Action Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>11/03/2011</td>
<td>Medical Policy Committee review</td>
</tr>
<tr>
<td>02/02/2012</td>
<td>Medical Policy Committee review</td>
</tr>
<tr>
<td>02/15/2012</td>
<td>Medical Policy Implementation Committee approval. Nucynta ER added to the policy. “Patient has tried and failed generic morphine sulfate extended-release capsules or generic oxymorphone extended-release tablets” added to the patient selection criteria. “There is clinical evidence or patient history that suggests the generically available products will be ineffective or cause an adverse reaction to the patient” was added to the criteria of the policy.</td>
</tr>
<tr>
<td>02/07/2013</td>
<td>Medical Policy Committee review</td>
</tr>
<tr>
<td>02/20/2013</td>
<td>Medical Policy Implementation Committee approval. Changed “the following” to “including, but not limited to” in the eligible for coverage statement and added “name” to the not medically necessary statement for clarification. Coverage eligibility unchanged.</td>
</tr>
<tr>
<td>05/01/2014</td>
<td>Medical Policy Committee review</td>
</tr>
<tr>
<td>05/21/2014</td>
<td>Medical Policy Implementation Committee approval. Added Zohydro to the step therapy policy.</td>
</tr>
<tr>
<td>05/07/2015</td>
<td>Medical Policy Committee review</td>
</tr>
<tr>
<td>05/20/2015</td>
<td>Medical Policy Implementation Committee approval. Added Hysingla ER to the policy.</td>
</tr>
<tr>
<td>06/02/2016</td>
<td>Medical Policy Committee review</td>
</tr>
<tr>
<td>06/20/2016</td>
<td>Medical Policy Implementation Committee approval. Added new products: Xtampza ER and branded oxycodone extended release. Added to step 1: hydromorphone extended release tablets. Removed the opt out for pregnancy. Added an opt out for patients aged 11-18</td>
</tr>
<tr>
<td>06/01/2017</td>
<td>Medical Policy Committee review</td>
</tr>
<tr>
<td>06/21/2017</td>
<td>Medical Policy Implementation Committee approval. Added a new product (Arymo ER) to step 2.</td>
</tr>
</tbody>
</table>

Next Scheduled Review Date: 06/2018

**Medically Necessary (or “Medical Necessity”) - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:
A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient’s illness, injury or disease; and
C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient’s illness, injury or disease.

For these purposes, “nationally accepted standards of medical practice” means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.