# Clinical Policy: Extended Release Opioids, Levorphanol

Reference Number: CP.CPA.259
Effective Date: 11.16.16
Last Review Date: 02.20
Line of Business: Commercial

Revision Log

**See Important Reminder at the end of this policy for important regulatory and legal information.**

## Description

The following are extended release opioid agonist products requiring prior authorization: hydrocodone bitartrate extended-release (Hysingla™ ER, Zohydro® ER), morphine sulfate extended-release (Arymo® ER, Morphabond ER™), oxycodone extended-release (OxyContin®, Xtampza® ER).

Levorphanol tartrate is an opioid agonist.

## FDA Approved Indication(s)

- Arymo ER, Hysingla ER, Zohydro ER, Morphabond ER, and Xtampza ER 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, in adults.
- Oxycontin 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, in adults and in opioid-tolerant pediatric patients 11 years of age and older who are already receiving and tolerate a minimum daily opioid dose of at least 20 mg oxycodone orally or its equivalent.
- Levorphanol tartrate is indicated for the management of pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate.

Limitation(s) 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, Zohydro ER, Arymo ER, Morphabond ER, OxyContin, and 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.
- Hysingla ER, Zohydro ER, Arymo ER, Morphabond ER, OxyContin, and Xtampza ER are not indicated as as-needed (prn) analgesics.
- Because of the risks of addiction, abuse, and misuse, with opioids, even at recommended doses, reserve levorphanol tartrate tablets for use in patients for whom alternative treatment options (e.g., non-opioid analgesics or opioid combination products):
  - Have not been tolerated, or are not expected to be tolerated,
  - Have not provided adequate analgesia, or are not expected to provide adequate analgesia.

**Policy/Criteria**
*Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.*

It is the policy of health plans affiliated with Centene Corporation® that Arymo ER, Hysingla ER, Zohydro ER, Morphabond ER, OxyContin, Xtampza ER, and levorphanol tartrate are **medically necessary** when the following criteria are met:

**I. Initial Approval Criteria**

**A. Chronic Pain** (must meet all)**:**

1. Diagnosis of chronic pain;
2. Member's age is one of the following:
   a. For Oxycontin: ≥ 11 years;
   b. All other agents: ≥ 18 years;
3. Failure of two of the following unless contraindicated or clinically significant adverse effects are experienced: controlled-release morphine sulfate (MS Contin), morphine sulfate sustained-release beads (Kadian), transdermal fentanyl patches, extended release oxymorphone, or extended-release morphine sulfate (Avinza).
4. A treatment plan is required, including all of the following (a-i):
   a. Diagnosis or conditions that are contributing to the pain;
   b. Pain intensity (scales or ratings);
   c. Functional status (physical and psychosocial);
   d. Patient's goal of therapy (level of pain acceptable and/or functional status);
   e. Current analgesic (opioid and adjuvant) regimen;
   f. Current non-pharmacological treatment;
   g. Opioid-related side effects;
   h. Indications of medical misuse;
   i. Action plan if analgesic failure occurs.

**Approval duration: 12 months**

**B. Other diagnoses/indications**

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial.

**II. Continued Therapy**

**A. Chronic Pain** (must meet all)**:**

1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Member is responding positively to therapy.

**Approval duration: 12 months**

**B. Other diagnoses/indications** (must meet 1 or 2)**:**

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
   **Approval duration: Duration of request or 12 months (whichever is less)**; or

2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial.

**III. Diagnoses/Indications for which coverage is NOT authorized:**

**A.** Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off-label use policy – CP.CPA.09 or evidence of coverage documents;
**B.** Acute or intermittent pain;
**C.** Immediate post-surgical pain;
**D.** Use in patients who require opioid analgesia for a short period of time or as-needed (prn) for pain relief.

**IV. Appendices/General Information**

*Appendix A: Abbreviation/Acronym Key*
ER: extended release
FDA: Food and Drug Administration
MAOI: monoamine oxidase inhibitor

*Appendix B: Therapeutic Alternatives*
*This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.*

| Drug Name | Dosing Regimen | Dose Limit/ Maximum Dose |
|---|---|---|
| morphine sulfate controlled-release tablet (MS Contin®) | Opioid naïve patients: 15 mg PO Q12 hours<br>Conversion to MS Contin: Dosing is individualized based on previous analgesic therapy.<br>Administer at ½ the total daily requirement PO Q12 hours or 1/3 the total daily requirement PO Q8 hours | Varies |
| morphine sulfate sustained-release capsule (Kadian®) | Opioid naïve patients: 10 mg or 20 mg PO, may adjust dosage at 20mg increment QOD<br>Conversion to Kadian: Dosing is individualized based on previous analgesic therapy.<br>Administer patient's total daily requirement PO Q24 hours or administer ½ patient's total daily requirement PO Q12 hours. | Varies |
| morphine sulfate beads sustained release (Avinza®) | Opioid naïve patients: 30 mg PO Q24 hours, with dosage adjustments of not > 30 mg every 4 days<br>Conversion to Avinza: Dosing is individualized based on previous analgesic therapy<br>Administer patient`s total daily morphine requirement PO Q24 hours | Varies |

| Drug Name | Dosing Regimen | Dose Limit/ Maximum Dose |
|---|---|---|
| fentanyl transdermal system (Duragesic®) | Dosing is individualized based on previous analgesic therapy. Initiate dose at one patch TD Q 72 hours. May increase following 3 days of therapy. Some patients may require dosing Q 48 hours | Varies |
| oxymorphone extended release (Opana® ER) | One tablet PO twice daily; individualized dosing may require multiple tablets dosing | Varies |

*Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.*

*Appendix C: Contraindications/Boxed Warnings*

- Contraindication(s):
  - Opioid non-tolerant patients;
  - Significant respiratory depression;
  - Acute or severe bronchial asthma in an unmonitored setting or in absence of resuscitative equipment;
  - Known or suspected gastrointestinal obstruction, including paralytic ileus;
  - Narrowed or obstructed gastrointestinal tract;
  - Known hypersensitivity to the active ingredient or to any components;
  - Arymo ER, Morphabond ER only: concurrent use of monoamine oxidase inhibitors (MAOIs) or use within 14 days.
- Boxed warning(s):
  - Addiction, abuse, and misuse;
  - Opioid analgesic Risk Evaluation and Mitigation Strategy (REMS) program;
  - Life-threatening respiratory depression;
  - Accidental ingestion;
  - Neonatal opioid withdrawal syndrome;
  - Risks from concomitant use with benzodiazepines or other CNS depressants;
  - Oxycontin only: concomitant use with CYP3A4 inhibitors (or discontinuation of CYP3A4 inducers) can result in a fatal overdose of oxycodone.

*Appendix D: General Information*

- Patients who are 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 per day, 8 mg oral hydromorphone per day, 25 mg oral oxymorphone per day, or an equianalgesic dose of another opioid.
- Initial dose for Morphabond in patients as the first opioid analgesic or not opioid tolerant is 15 mg PO every 12 hours. Conversion from other oral morphine products by administering one-half of the patient's 24-hour requirement as Morphabond on an every 12 hour schedule. Conversion from other opioids to Morphabond by using 15 mg every 12 hours and discontinuation of other opioids.
- Use of higher starting doses in patients who are not opioid tolerant may cause fatal respiratory depression. A single dose of Zohydro ER greater than 40 mg, Zohydro ER 50

mg capsules, or a total daily dose greater than 80 mg are only for patients in whom tolerance to an opioid of comparable potency is established. Daily doses of Hysingla ER greater than 80 mg are only for use in opioid tolerant patients.

- The tables below are only to be used for the conversion from current opioid therapy to Zohydro ER or Hysingla ER. The tables cannot be used to convert from Zohydro ER or Hysingla ER to another opioid. Doing so will result in an overestimation of the dose of the new opioid and may result in fatal overdose.

| Conversion Factors to Zohydro ER (not equianalgesic doses) | | |
|---|---|---|
| **Prior Oral Opioid** | **Oral Dose (mg)** | **Approximate Oral Conversion Factor** |
| Hydrocodone | 10 | 1 |
| Oxycodone | 10 | 1 |
| Methadone | 10 | 1 |
| Oxymorphone | 5 | 2 |
| Hydromorphone | 3.75 | 2.67 |
| Morphine | 15 | 0.67 |
| Codeine | 100 | 0.10 |

| Conversion Factors to Hysingla ER (not equianalgesic doses) | | |
|---|---|---|
| **Prior Oral Opioid** | **Oral Dose (mg)** | **Approximate Oral Conversion Factor** |
| Tramadol | 200 | 0.1 |
| Oxycodone | 20 | 1 |
| Methadone | 13.3 | 1.5 |
| Oxymorphone | 10 | 2 |
| Hydromorphone | 5 | 4 |
| Morphine | 40 | 0.5 |
| Codeine | 133 | 0.15 |

- The following table describes the equivalent amount of oxycodone HCl present in Xtampza ER compared to other oxycodone products.

| Oxycodone Hydrochloride | Oxycodone base (Xtampza ER) |
|---|---|
| 10 mg | 9 mg |
| 15 mg | 13.5 mg |
| 20 mg | 18 mg |
| 30 mg | 27 mg |
| 40 mg | 36 mg |

- Patients receiving other oral oxycodone formulations may be converted to Xtampza ER, using the same total daily dose of oxycodone, by administering one-half of the patient's total daily oral oxycodone dose as Xtampza ER every 12 hours with food. Because Xtampza ER is not bioequivalent to other oxycodone extended-release products, monitor patients for possible dosage adjustment.
- There are no established conversion ratios for conversion from other opioids to Xtampza ER defined by clinical trials. Discontinue all other around-the-clock opioid drugs when Xtampza ER therapy is initiated. Initiate dosing using Xtampza ER 9 mg orally every 12 hours with food.

## V. Dosage and Administration

| Drug Name | Dosing Regimen | Maximum Dose |
|---|---|---|
| Hydrocodone bitartrate extended release (Zohydro ER) | For opioid-naïve and opioid non-tolerant patients, initiate with 10 mg PO every 12 hours.<br>Increase the dose of Zohydro ER in increments of 10 mg every 12 hours every 3 to 7 days as needed to achieve adequate analgesia.<br>Individualize treatment; titrate to effective and tolerable dose. | Varies |
| Hydrocodone bitartrate extended release (Hysingla ER) | For opioid-naïve and opioid non-tolerant patients, initiate with 20 mg PO every 24 hours.<br>Increase the dose of Hysingla ER in increments of 10 mg to 20 mg every 3 to 5 days as needed to achieve adequate analgesia.<br>Individualize treatment; titrate to effective and tolerable dose. | Varies |
| Levorphanol tartrate | Initial: 1 to 2 mg PO q6-8h, may increase up to 3 mg q6-8h | Varies |
| Morphine sulfate extended release (Arymo ER) | For opioid-naïve and opioid non-tolerant patients, initiate with 15 mg PO Q 8-12 hours.<br>Increase the dose to achieve adequate analgesia every 1 to 2 days.<br>Individualize treatment; titrate to effective and tolerable dose. | Varies |
| Morphine sulfate extended release (Morphabond ER) | For opioid-naïve and opioid non-tolerant patients, initiate with 15 mg PO every 8 or 12 hours.<br>Increase the dose to achieve adequate analgesia every 1 to 2 days.<br>Individualize treatment; titrate to effective and tolerable dose. | Varies |
| Oxycodone extended release (Xtampza ER) | For opioid-naïve and opioid non-tolerant patients, initiate with 9 mg PO every 12 hours. | 288 mg/day |
| Oxycodone extended release (OxyContin) | One tablet PO twice daily; individualized dosing may require multiple tablets and three times daily dosing | Varies |

## VI. Product Availability

| Drug | Availability |
|---|---|
| Morphine sulfate extended release (Arymo ER) | Extended-release tablets: 15 mg, 30 mg, and 60 mg |
| Hydrocodone bitartrate extended release (Zohydro ER) | Extended-release capsules: 10 mg, 15 mg, 20 mg, 30 mg, 40 mg, and 50 mg |
| Hydrocodone bitartrate extended release (Hysingla ER) | Extended-release tablets: 20 mg, 30 mg, 40 mg, 60 mg, 80 mg, 100 mg, and 120 mg |
| Levorphanol tartrate | Tablets: 1 mg, 2 mg, 3 mg |
| Morphine sulfate extended release (Morphabond ER) | Extended-release tablets: 15 mg, 30 mg, 60 mg, and 100 mg |
| Oxycodone extended release (Xtampza ER) | Extended-release capsules: 9 mg, 13.5 mg, 18 mg, 27 mg, and 36 mg |
| Oxycodone extended release (OxyContin) | Extended-release tablets: 10 mg, 15 mg, 20 mg, 30 mg, 40 mg, 60 mg, 80 mg |

## VII. References

1. Zohydro ER [Prescribing Information] Morristown, NJ: Pernix Therapeutics; October 2019. Available at: www.zohydroer.com. Accessed November 26, 2019.
2. Hysingla ER [Prescribing Information] Stamford, CT: Purdue Pharma L.P.; October 2019. Available at: www.hysinglaer.com. Accessed November 26, 2019.
3. Morphabond ER [Prescribing Information] Basking Ridge, NJ: Daiichi Sankyo, Inc.; October 2019. Available at: https://morphabondhcp.com/prescribing-information-portlet/getDocument?product=MB&inline=true. Accessed November 26, 2019.
4. Xtampza ER [Prescribing Information] Cincinnati, OH: Patheon Pharmaceuticals; October 2019. Available at: http://www.xtampzaer.com/hcp/assets/pdf/xtampza-pi.pdf. Accessed November 26, 2019.
5. Levorphanol Tartrate [Prescribing Information] Solana Beach, CA: Sentynl Therapeutics, Inc; October 2019. Available at: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=77f4a54a-6901-46d9-93db-ad4be7eae6c3. Accessed November 26, 2019.
6. Arymo ER [Prescribing Information] Wayne, PA: Egalet US Inc.; October 2019. Available at: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=e60552c9-06ce-4790-95e7-aadd4df12b2a. Accessed November 26, 2019.
7. OxyContin [Prescribing Information]. Stamford, CT: Purdue Pharma; October 2019. Available at: www.oxycontin.com. Accessed November 26, 2019.

| Reviews, Revisions, and Approvals | Date | P&T Approval Date |
|---|---|---|
| Converted to new template. Minor changes to verbiage and grammar. References updated. | 05.23.17 | 11.17 |
| 4Q 2018 annual review: no significant changes from previously approved Corporate policies; added age requirement; changed Initial and Continued approval durations from Length of Benefit to 12 months; references reviewed and updated. | 07.26.18 | 11.18 |

| Reviews, Revisions, and Approvals | Date | P&T Approval Date |
|---|---|---|
| No significant changes; per SDC and prior clinical guidance, added Oxycontin to policy and removed from list of redirect options. | 03.04.19 | |
| 4Q 2019 annual review: no significant changes; updated age limit for Oxycontin; references reviewed and updated. | 08.26.19 | 11.19 |
| 1Q 2020 annual review: review is repeated this quarter to bring this policy's review schedule into alignment with that of other existing opioid analgesic policies; no significant changes; references reviewed and updated. | 11.26.19 | 02.20 |

**Important Reminder**

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to

recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

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