

Clinical Policy: Extended Release Opioids, Levorphanol

Reference Number: CP.HNMC.259

Effective Date: 11.16.16

Last Review Date: 11.17

Line of Business: Medicaid – Medi-Cal

[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 (Xtampza ER)

Levorphanol tartrate is an opioid agonist.

FDA approved indication

- Arymo ER, Hysingla ER, Zohydro ER, Morphabond ER, 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.
- Levorphanol tartrate is indicated for the management of pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate.

Limitations 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, 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, Xtampza ER are not indicated as an as-needed (prn) analgesic.
- 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 (which may include office chart notes and lab results) 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, Xtampza ER, Levorphanol tartrate are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Diagnosis of Cancer Pain (must meet all):

1. Diagnosis of cancer pain;
2. Failure of one of the following unless contraindicated or clinically significant adverse effects are experienced: controlled-release morphine sulfate (MS Contin), morphine sulfate sustained-release beads (Avinza), or sustained-release morphine sulfate (Kadian);

Approval duration: Length of Benefit

B. End-Stage Medical Conditions Accompanied by Significant Pain (must meet all):

1. Diagnosis of end-stage medical conditions accompanied by significant pain;
2. Failure of one of the following unless contraindicated or clinically significant adverse effects are experienced: controlled-release morphine sulfate (MS Contin), morphine sulfate sustained-release beads (Avinza), or sustained-release morphine sulfate (Kadian);

Approval duration: Length of Benefit

C. Chronic Pain for Which There is a Documented, Objective Etiology (must meet all):

1. Diagnosis of chronic pain for which there is a documented, objective etiology;
2. One of the following (a or b):
 - a. Documentation that the patient is being managed under a pain medication contract signed and dated within the year;
 - b. Member resides in a Long Term Care (LTC) facility;
3. Failure of one of the following unless contraindicated or clinically significant adverse effects are experienced: controlled-release morphine sulfate (MS Contin), morphine sulfate sustained-release beads (Avinza), or sustained-release morphine sulfate (Kadian);

Approval duration:

LTC Facility Residence: Length of benefit

All other diagnoses: Up to 1 year

D. Other diagnoses/indications

1. Refer to CP.PMN.53 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized)

II. Continued Therapy

A. Diagnosis of Cancer Pain (must meet all):

1. Currently receiving medication via a health plan affiliated with Centene Corporation or member has previously met initial approval criteria.

Approval duration: Length of Benefit

B. End-Stage Medical Conditions Accompanied by Significant Pain (must meet all):

1. Currently receiving medication via a health plan affiliated with Centene Corporation or member has previously met initial approval criteria.

Approval duration: Length of Benefit

C. Chronic Pain for Which There is a Documented, Objective Etiology (must meet all):

1. Currently receiving medication via a health plan affiliated with Centene Corporation or member has previously met initial approval criteria;
2. A new pain medication contract is required every year.

Approval duration:

LTC Facility Residence: Length of benefit

All other diagnoses: Up to 1 year

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

1. Currently receiving medication via a health plan affiliated with Centene Corporation and documentation supports positive response to therapy.

Approval duration: Duration of request or 12 months (whichever is less); or

2. Refer to CP.PMN.53 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized)

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.PMN.53 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 pain relief.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

FDA: food and drug administration

LTC: long term care facility

Appendix B: General Information

- Zohydro ER and Hysingla ER are Schedule II controlled substance under the Controlled Substances Act. These products are single-entity (not combined with an analgesic such as acetaminophen) and extended-release hydrocodone products. Zohydro ER and Hysingla ER will be part of the ER/ LA (Long-Acting) Opioid Analgesics Risk Evaluation and Mitigation Strategy (REMS).
- Zohydro ER and Hysingla ER should be reserved for use in patients for whom alternative treatment options are ineffective, not tolerated, or would be otherwise inadequate to provide sufficient management of pain. Zohydro ER and Hysingla ER are not FDA approved for as needed pain relief.
- 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 onehalf 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.

Appendix C: Therapeutic Alternatives

Drug	Dosing Regimen	Dose Limit/ Maximum Dose
MS Contin® (morphine sulfate controlled-release tablet)	Opioid naïve patients: 15 mg PO Q12 hours Conversion to MS Contin: Dosing is individualized based on previous analgesic therapy. Administer at ½ the total daily requirement PO Q12 hours or 1/3 the total daily requirement PO Q8 hours	The 100 mg and 200 mg tablets are reserved only for opioid tolerant individuals who require morphine equivalent doses of 200 mg or more for the 100 mg tablet and 400 mg or more for the 200 mg tablet
Kadian® (morphine sulfate sustained-release capsule)	Opioid naïve patients: 10mg or 20mg PO, may adjust dosage at 20mg increment QOD Conversion to Kadian: Dosing is individualized based on previous analgesic therapy. Administer patient's total daily requirement PO Q24 hours or administer ½ patient's total daily requirement PO Q12 hours.	Should not be given more frequently than every 12 hours
Avinza® (morphine sulfate beads sustained release)	Opioid naïve patients: 30 mg PO Q24 hours, with dosage adjustments of not > 30 mg every 4 days Conversion to Avinza: Dosing is individualized based on previous analgesic therapy. Administer patient's total daily morphine requirement PO Q24 hours	1600 mg/day Should not be given more frequently than every 24 hours

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.

V. Dosage and Administration

Drug Name	Dosing Regimen	Maximum Dose
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Hydrocodone bitartrate extended release (Zohydro ER)	For opioid-naïve and opioid non-tolerant patients, initiate with 10 mg PO every 12 hours. 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. 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. 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. Individualize treatment; titrate to effective and tolerable dose.	
Levorphanol tartrate	Initial: 1 to 2 mg PO q6-8h, may increase up to 3 mg q6-8h	
Morphine sulfate extended release (Arymo ER)	For opioid-naïve and opioid non-tolerant patients, initiate with 15 mg PO Q 8-12 hours. Increase the dose to achieve adequate analgesia every 1 to 2 days. Individualize treatment; titrate to effective and tolerable dose.	
Morphine sulfate extended release (Morphabond ER)	For opioid-naïve and opioid non-tolerant patients, initiate with 15 mg PO every 12 hours. Increase the dose to achieve adequate analgesia every 1 to 2 days.	

	Individualize treatment; titrate to effective and tolerable dose.	
Oxycodone extended release (Xtampza ER)	For opioid-naïve and opioid non-tolerant patients, initiate with 9 mg PO every 12 hours. Limit daily dose to a maximum of 288 mg per day.	

VI. Product Availability

Drug	Availability
Morphine sulfate extended release (Arymo ER)	Extended-release tablets: 15 mg, 30 mg, 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: 2 mg
Morphine sulfate extended release (Morphabond ER)	Extended-release tablets: 15 mg, 30 mg, 60 mg, 100 mg
Oxycodone extended release (Xtampza ER)	Extended-release capsules: 9 mg, 13.5 mg, 18 mg, 27 mg, 36 mg

VII. References

1. Zohydro ER [Prescribing Information] Morristown, NJ: Pernix Therapeutics; December 2016.
2. Hysingla ER [Prescribing Information] Stamford, CT: Purdue Pharma L.P.; December 2016.
3. Chronic Pain. American Chronic Pain Association. Accessed June 7, 2016. Available at: <http://theacpa.org/conditionDetail.aspx?id=74>.
4. Farrell, SE. Acetaminophen Toxicity. Medscape. Accessed June 7, 2016. Available at: <http://emedicine.medscape.com/article/820200-overview>
5. Morphabond ER [Prescribing Information] Basking Ridge, NJ: Inspirion Delivery Sciences, LLC; December 2016.
6. Xtampza ER [Prescribing Information] Cincinnati, OH: Patheon Pharmaceuticals; November 2016
7. Levorphanol Tartrate [Prescribing Information] Solana Beach, CA: Sentynl Therapeutics, Inc; December 2016.
8. Arymo ER [Prescribing Information] Wayne, PA: Egalet US Inc.; January 2017.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Converted to new template. Minor changes to verbiage and grammar. References updated.	05.17	11.17

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.

CLINICAL POLICY

Extended Release Opioids, Levorphanol



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Note: For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

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