Clinical Policy: Morphine Sulfate/Naltrexone Extended-Release (Embeda)

Reference Number: CP.CPA.254
Effective Date: 11.16.16
Last Review Date: 08.19
Line of Business: Commercial

Revision Log

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

Description

Morphine sulfate/naltrexone hydrochloride extended-release (Embeda®) is an extended release combination opioid agonist and opioid antagonist product.

FDA Approved Indication(s)

Embeda 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.

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 Embeda 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.
- Embeda is not indicated as an as-needed (prn) analgesic.

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 Embeda is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

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

1. Diagnosis of severe chronic pain for which there is a documented, objective etiology;
2. Age ≥ 18 years;
3. Provider submits a treatment plan that includes all the following:
   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;
4. Failure of two formulary long-acting opioid analgesics, unless all are contraindicated or clinically significant adverse effects are experienced.

Approval duration: 3 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: 3 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 3 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.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
FDA: Food and Drug Administration
MAOI: monoamine oxidase inhibitor
REMS: Risk Evaluation and Mitigation Strategy

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 Q8-12 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	Not applicable
Morphine sulfate sustained-release capsule (Kadian®)	Opioid naïve patients: 10 mg or 20 mg PO, may adjust dosage at 20 mg 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
Morphine sulfate beads sustained-release (Avinza®)	Opioid naïve patients: 30 mg PO Q24 hours, with dosage adjustments of not more than 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	1,600 mg/day
Fentanyl transdermal system (Duragesic®)	Initiate dose at one patch topically Q 72 hours. May increase following 3 days of therapy.	Not applicable
Oxymorphone extended-release (Opana® ER)	One tablet PO BID; individualized dosing may require multiple tablets dosing	Not applicable
Hydromorphone (Exalgo®)	Initiate dose equal to total daily hydromorphone dose PO once daily; may titrate by increments of 4 to 8 mg every 3 to 4 days as needed	Not applicable
Nucynta® ER (tapentadol)	Initiate treatment with 50 mg PO BID	500 mg/day

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): significant respiratory depression, acute or severe bronchial asthma in an unmonitored setting or in absence of resuscitative equipment, concurrent use of monoamine oxidase inhibitors (MAOIs) or use of MAOIs within the last 14 days, known or suspected gastrointestinal obstruction, including paralytic ileus, hypersensitivity to morphine or naltrexone
- Boxed warning(s): addiction, abuse, and misuse, life-threatening respiratory depression, accidental ingestion, neonatal opioid withdrawal syndrome, interaction with alcohol, hepatotoxicity, risks from concomitant use with benzodiazepines or other central nervous system depressants, risk evaluation and mitigation strategy (REMS)

Appendix D: General Information

- Embeda 100 mg/4 mg capsules are for use in opioid-tolerant patients only.
- Opioid-tolerant patients are those receiving for one week or longer, at least 60 mg oral morphine/day, 30 mg oral oxycodone/day, 8 mg oral hydromorphone/day or an equianalgesic dose of another opioid.

Equianalgesic Opioid Chart		
Analgesic	**IM (mg)**	**Oral (mg)**
Fentanyl	0.1	-
Oxycodone	-	20
Methadone	10	20
Oxymorphone	1	-
Hydromorphone	1.5	7.5
Morphine*	10	30
Levorphanol	2	4
Meperidine*	75	300

*Adjust dose for renal impairment

V. Dosage and Administration

Drug Name	Dosing Regimen	Maximum Dose
Morphine sulfate/naltrexone hydrochloride extended-release (Embeda)	For opioid naïve and opioid non-tolerant, initiate with 20 mg/0.8 mg PO Q24H	Not applicable

VI. Product Availability

Extended-release 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

VII. References

1. Embeda Prescribing Information New York, NY: Pfizer, Inc; September 2018. Available at: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=a7658a2d-b7a9-4fb5-8d65-a20ca1b9ad1f. Accessed May 20, 2019.
2. DRUGDEX® System [Internet database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Accessed May 20, 2019.
3. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2016. Available at: http://www.clinicalpharmacology-ip.com/. Accessed May 20, 2019.

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
3Q 2018 annual review: no significant changes; added the requirement that other formulary long acting is trialed; changed	05.23.18	08.18

Reviews, Revisions, and Approvals	Date	P&T Approval Date
approval durations from 12 months to 3 months. References reviewed and updated.		
3Q 2019 annual review: no significant changes; references reviewed and updated.	05.20.19	08.19

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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