



5.70.61

| | | | |
|--------------------|-------------------------------|------------------------------|-----------------|
| Section: | Prescription Drugs | Effective Date: | April 1, 2021 |
| Subsection: | Analgesics and Anesthetics | Original Policy Date: | January 1, 2018 |
| Subject: | Extended Release Opioid Drugs | Page: | 1 of 15 |

Last Review Date: March 12, 2021

Extended Release Opioid Drugs

Description

Belbuca (buprenorphine), Hysingla ER, Zohydro ER (hydrocodone ER), Exalgo (hydromorphone ER), Arymo ER, Avinza, Kadian, MorphaBond, MS Contin (morphine sulfate ER), Embeda (morphine sulfate/naltrexone ER), OxyContin, Xtampza ER (oxycodone ER), Opana ER (oxymorphone ER) Nucynta ER (tapentadol ER), Conzip*, Ultram ER (tramadol ER)

*Prior authorization for certain non-covered formulations applies only to formulary exceptions

Background

Hydrocodone (Hysingla ER, Zohydro ER), hydromorphone (Exalgo), morphine sulfate (Arymo ER, Avinza, Embeda, Kadian, MorphaBond, MS Contin), oxycodone (OxyContin, Xartemis XR), Opana ER (oxymorphone ER) and tapentadol (Nucynta ER) are Schedule II narcotics. Buprenorphine (Belbuca) is a Schedule III narcotic. Tramadol ER (Ultram ER, Conzip) is a Schedule IV narcotic. Extended-release opioids are drugs that are indicated for the management of severe pain when a continuous, around-the-clock opioid analgesic is needed for an extended period of time (1-20).

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Extended-release opioids are indicated for the management of pain in opioid-tolerant patients severe enough to require daily, around-the-clock, long-term opioid treatment in a patient who has been taking an opioid. 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 extended-release opioids for use in patients for whom alternative treatment options (e.g., non-opioid analgesics or immediate-release opioids) are

5.70.61

| | | | |
|--------------------|-------------------------------|------------------------------|-----------------|
| Section: | Prescription Drugs | Effective Date: | April 1, 2021 |
| Subsection: | Analgesics and Anesthetics | Original Policy Date: | January 1, 2018 |
| Subject: | Extended-Release Opioid Drugs | Page: | 2 of 15 |

ineffective, not tolerated, or would be otherwise inadequate to provide sufficient management of pain. Extended-release opioids are not indicated as as-needed (prn) analgesics (1-15).

Regulatory Status

FDA-approved indications:

Extended-release opioids are indicated for the management of severe pain when a continuous, around-the-clock opioid analgesic is needed for an extended period of time (1-20).

Patients considered opioid-tolerant are those taking, 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, 60 mg oral hydrocodone per day, or an equianalgesic dose of another opioid (1-17).

Extended-release opioids have boxed warnings for the following (1-15):

- Respiratory depression is the chief hazard of opioid agonists, which if not immediately recognized and treated, may lead to respiratory arrest and death. Risk is increased in patients receiving concurrent CNS depressants (including alcohol), patients with chronic obstructive pulmonary disease, orthostatic hypotension, increased intracranial pressure, biliary tract diseases, and seizure disorders. To reduce the risk of respiratory depression, proper dosing, titration, and monitoring are essential.
- All patients treated with opioids require careful monitoring for signs of abuse and addiction, since use of opioid analgesic products carries the risk of addiction even under appropriate medical use.
- Accidental ingestion of extended-release opioids, especially in children, can result in fatal opioid overdose.
- Prolonged use of opioid agonists during pregnancy can result in neonatal opioid withdrawal syndrome, which may be life-threatening.
- Concomitant use of opioids with benzodiazepines or other central nervous system (CNS) depressants, including alcohol, may result in profound sedation, respiratory depression, coma, and death.

Other boxed warnings include the following:

5.70.61

| | | | |
|--------------------|-------------------------------|------------------------------|-----------------|
| Section: | Prescription Drugs | Effective Date: | April 1, 2021 |
| Subsection: | Analgesics and Anesthetics | Original Policy Date: | January 1, 2018 |
| Subject: | Extended-Release Opioid Drugs | Page: | 3 of 15 |

- Concomitant use with CYP 3A4 inhibitors (or discontinuation of CYP 3A4 inducers) can result in a fatal overdose of hydrocodone and oxycodone (5, 11-13).

The Centers for Disease Control and Prevention (CDC) Guideline for Prescribing Opioids for Chronic Pain recommends that when opioids are started, clinicians should prescribe the lowest effective dosage. Clinicians should use caution when prescribing opioids at any dosage, should carefully reassess evidence of individual benefits and risks when increasing dosage to ≥ 50 morphine milligram equivalents (MME)/day, and should avoid increasing dosage to ≥ 90 MME/day or carefully justify a decision to titrate dosage to ≥ 90 MME/day. The extended-release opioid drug initial quantity limits are set to encompass the usual/starting dosage and frequency range recommendations in labeling without exceeding 90 MME per day (16).

CDC guidelines find that concurrent use of benzodiazepines and opioids might put patients at greater risk for potentially fatal overdose. Three studies of fatal overdose deaths found evidence of concurrent benzodiazepine use in 31%–61% of decedents (16). The FDA also states that benzodiazepines “are also commonly abused and misused, often together with opioid pain relievers and other medicines” (22).

The CDC Guideline for Prescribing Opioids for Chronic Pain states that when starting opioid therapy for chronic pain, clinicians should prescribe immediate-release opioids instead of extended-release/long-acting opioids. Clinicians should evaluate benefits and harms with patients within 1 to 4 weeks of starting opioid therapy for chronic pain or of dose escalation. Clinicians should evaluate benefits and harms of continued therapy with patients every 3 months or more frequently. If benefits do not outweigh harms of continued opioid therapy, clinicians should optimize other therapies and work with patients to taper opioids to lower dosages or to taper and discontinue opioids (16).

The American Pain Society Opioid Treatment Guidelines state that a reasonable definition for high dose opioid therapy is >200 mg daily of oral morphine (or equivalent). The Institute for Clinical Systems Improvement Chronic Pain Guideline states that among patients receiving opioids for non-malignant pain, the daily dose is strongly associated with opioid-related mortality. An average dose of 200 mg or more morphine (or equivalent) was associated with a nearly nine-fold increase in the risk of overdose relative to low doses (<20 mg of morphine or equivalent) (15-18).

The extended-release opioid drug post quantity limits are set to encompass the usual/starting dosage range recommendations in labeling, or up to one additional dose per day above the initial quantity limit without exceeding 200 MME per day (unless minimum FDA-labeled

5.70.61

| | | | |
|--------------------|-------------------------------|------------------------------|-----------------|
| Section: | Prescription Drugs | Effective Date: | April 1, 2021 |
| Subsection: | Analgesics and Anesthetics | Original Policy Date: | January 1, 2018 |
| Subject: | Extended-Release Opioid Drugs | Page: | 4 of 15 |

strength/dose/frequency exceeds 200 MME/day) to promote optimization of pain management, safe and effective use, and to reduce misuse, abuse, and overdose (17-19).

FDA warns that opioids can interact with antidepressants and migraine medicines to cause a serious central nervous system reaction called serotonin syndrome, in which high levels of the chemical serotonin build up in the brain and cause toxicity (see Appendix 1 for list of drugs) (17).

Centers for Medicare and Medicaid Services have a chart that includes buprenorphine MME conversion factors (21).

The FDA has determined that a REMS is necessary for all opioid analgesics intended for outpatient use to ensure that the benefits of these drugs continue to outweigh the risks. The Opioid Analgesic REMS is a strategy to reduce the risk of abuse, misuse, addiction, overdose, and deaths due to prescription opioid analgesics (21).

The safety and effectiveness of extended-release opioids in pediatric patients below the age of 18 have not been established (1-15).

Related policies

Abstral, Actiq, Butrans, Duragesic, Fentanyl Powder, Fentora, Immediate Release Opioid Drugs, IR Opioid Combo Drugs, Methadone, Opioid Injectables, Opioid Powders, Suboxone Drug Class, Subsys

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Extended-release opioids may be considered **medically necessary** for patients 18 years of age or older for the management of severe pain when a continuous, around-the-clock opioid analgesic is needed for an extended period of time and if the conditions indicated below are met.

Extended-release opioids may be considered **investigational** in patients less than 18 years of age and for all other indications.

Prior-Approval Requirements

5.70.61

| | | | |
|--------------------|-------------------------------|------------------------------|-----------------|
| Section: | Prescription Drugs | Effective Date: | April 1, 2021 |
| Subsection: | Analgesics and Anesthetics | Original Policy Date: | January 1, 2018 |
| Subject: | Extended-Release Opioid Drugs | Page: | 5 of 15 |

Prior authorization is not required if prescribed by an oncologist and/or the member has paid pharmacy claims for an oncology medication(s) in the past 6 months

Age 18 years of age or older

Diagnosis

Patient must have the following:

Pain, severe enough to require daily, around-the-clock long term opioid treatment

AND ALL of the following:

- a. **NO** dual therapy with other long acting opioid analgesic(s)
- b. Alternative treatment options have been ineffective, not tolerated or inadequate for controlling the pain
 - i. These include: non-opioid analgesics and immediate release analgesics
- c. Prescriber agrees to assess the benefits of pain control (i.e. care plan, signs of abuse, severity of pain) after 3 months of therapy
- d. Prescriber agrees to assess patient for signs and symptoms of serotonin syndrome
- e. Prescriber agrees to participate in the Opioid Analgesic REMS program and to monitor for abuse, misuse, addiction, and overdose and discontinue if necessary
(<https://opioidanalgesicrems.com>)
- f. Patient must have **ONE** of the following:
 - i. Previous immediate-release opioid therapy for at least 10 days in the last 90 days
 - ii. Previous extended-release opioid therapy in the past 180 days
- g. **NO** other opioid at prior authorization limits
- h. **NO** dual therapy with opioid addiction treatment or methadone
- i. **NO** dual therapy with an anti-anxiety benzodiazepine(s)
 - i. Alprazolam (Xanax)
 - ii. Clonazepam (Klonopin)
 - iii. Diazepam (Valium)
 - iv. Lorazepam (Ativan)
 - v. Oxazepam (Serax)
 - vi. Chlordiazepoxide (Librium)
 - vii. Clorazepate dipotassium (Tranxene)

5.70.61

| | | | |
|--------------------|-------------------------------|------------------------------|-----------------|
| Section: | Prescription Drugs | Effective Date: | April 1, 2021 |
| Subsection: | Analgesics and Anesthetics | Original Policy Date: | January 1, 2018 |
| Subject: | Extended-Release Opioid Drugs | Page: | 6 of 15 |

- j. **NO** cumulative morphine milligram equivalent (MME) over 300 MME

Prior – Approval *Renewal* Requirements

Age 18 years of age or older

Diagnosis

Patient must have the following:

Pain, severe enough to require daily, around-the-clock long term opioid treatment

AND ALL of the following:

- a. **NO** dual therapy with other long acting opioid analgesic(s)
- b. Prescriber agrees to continue to assess the benefits of pain control (i.e. care plan signs of abuse, severity of pain)
- c. Prescriber agrees to assess patient for signs and symptoms of serotonin syndrome
- d. Prescriber agrees to participate in the Opioid Analgesic REMS program and to monitor for abuse, misuse, addiction, and overdose and discontinue if necessary
(<https://opioidanalgesicrems.com>)
- e. **NO** other opioid at prior authorization limits
- f. **NO** dual therapy with opioid addiction treatment or methadone
- g. **NO** dual therapy with an anti-anxiety benzodiazepine(s)
 - i. Alprazolam (Xanax)
 - ii. Clonazepam (Klonopin)
 - iii. Diazepam (Valium)
 - iv. Lorazepam (Ativan)
 - v. Oxazepam (Serax)
 - vi. Chlordiazepoxide (Librium)
 - vii. Clorazepate dipotassium (Tranxene)
- h. **NO** cumulative morphine milligram equivalent (MME) over 300 MME

Policy Guidelines

Pre - PA Allowance

Age 12 years of age or older – Conzip/Ultram ER (tramadol ER) **ONLY**

5.70.61

| | | | |
|--------------------|-------------------------------|------------------------------|-----------------|
| Section: | Prescription Drugs | Effective Date: | April 1, 2021 |
| Subsection: | Analgesics and Anesthetics | Original Policy Date: | January 1, 2018 |
| Subject: | Extended-Release Opioid Drugs | Page: | 7 of 15 |

No age limit for all other products available for Pre-PA (see chart)

Quantity

Extended Release Tablets or Capsules ≤ 90 MME/day

| Medication | Strength | Quantity Limit per 90 days |
|-------------------------------|----------------------------|----------------------------|
| Avinza (morphine) | 60mg, 75mg, 90mg | 90 units per 90 days |
| Embeda (morphine /naltrexone) | 50/2mg, 60/2.4mg, 80/3.2mg | |
| Exalgo (hydromorphone) | 8mg, 12mg, 16mg | |
| Kadian (morphine) | 50mg, 60mg, 80mg | |
| Avinza (morphine) | 45mg | 180 units per 90 days |
| Embeda (morphine /naltrexone) | 20/0.8mg, 30/1.2mg, | |
| Kadian (morphine) | 10mg, 20mg, 30mg, 40mg | |
| MorphaBond (morphine) | 15mg, 30mg | |
| Nucynta ER (tapentadol) | 50mg, 100mg | |
| Opana ER (oxymorphone) | 5mg, 7.5mg, 10mg, 15mg | |
| OxyContin (oxycodone) | 10mg, 15mg, 20mg, 30mg | |
| Xtampza ER (oxycodone) | 9mg, 13.5mg, 18mg, 27mg | |
| Avinza (morphine) | 30mg | |
| Arymo ER (morphine) | 15mg, 30mg | |
| MS Contin (morphine) | 15mg, 30mg | 270 units per 90 days |

Tramadol ER ≤ 30 MME/day

| | | |
|----------------------|----------------------------|----------------------|
| Ultram ER (tramadol) | 100mg, 150mg, 200mg, 300mg | 90 units per 90 days |
|----------------------|----------------------------|----------------------|

****Maximum daily limit of any combination: 300 mg**

Films ≤ 90 MME/day

| | | |
|-------------------------|-------------------------------|----------------------|
| Belbuca (buprenorphine) | 75mcg, 150mcg, 300mcg, 450mcg | 90 units per 90 days |
|-------------------------|-------------------------------|----------------------|

The following drugs/strengths require PA for any quantity:

| | |
|--|--------------------------------|
| Arymo ER 60mg | Morphabond 60mg, 100mg |
| Avinza 120mg | MS Contin 60mg, 100mg, 200mg |
| Belbuca 600mcg, 750mcg, 900mcg | Nucynta ER 150mg, 200mg, 250mg |
| Embeda 100/4mg | Opana ER 20mg, 30mg, 40mg |
| Exalgo 32mg | OxyContin 40mg, 60mg, 80mg |
| Hysingla ER 20mg, 30mg, 40mg, 60mg, 80mg, 100mg, 120mg | Xtampza ER 36mg |

5.70.61

| | |
|---|--|
| Section: Prescription Drugs | Effective Date: April 1, 2021 |
| Subsection: Analgesics and Anesthetics | Original Policy Date: January 1, 2018 |
| Subject: Extended-Release Opioid Drugs | Page: 8 of 15 |

| | |
|---------------------|---|
| Kadian 100mg, 200mg | Zohydro ER 10mg, 15mg, 20mg, 30mg, 40mg, 50mg |
|---------------------|---|

*Patients will not be eligible for a Pre-PA Allowance for Extended Release (ER) if patients have **NOT** been on a previous immediate-release opioid therapy for at least 10 days in the last 90 days unless switching from another extended release opioid. Members using dual therapy with opioid addiction treatment or methadone in the last 30 days will not be eligible for Pre-PA Allowance.

**Patients are only eligible for a combination of opioids not exceeding 300 MME

***Utilizing the highest strengths available to achieve the dosage is recommended to minimize dosing errors and improve compliance

Prior - Approval Limits

Quantity

Extended Release Tablets or Capsules ≤200 MME/day

| Medication / Strength | Quantity Limit per 90 days | Morphine Milligram Equivalent Daily Dosing |
|----------------------------------|------------------------------------|--|
| Arymo ER 15mg (morphine sulfate) | 360 tablets per 90 days OR | 60 MME/day |
| Arymo ER 30mg (morphine sulfate) | 360 tablets per 90 days OR | 120 MME/day |
| Arymo ER 60mg (morphine sulfate) | 270 tablets per 90 days | 180 MME/day |
| Avinza 30mg (morphine sulfate) | 360 capsules per 90 days OR | 120 MME/day |
| Avinza 45mg (morphine sulfate) | 360 capsules per 90 days OR | 180 MME/day |
| Avinza 60mg (morphine sulfate) | 270 capsules per 90 days OR | 180 MME/day |
| Avinza 75mg (morphine sulfate) | 180 capsules per 90 days OR | 150 MME/day |
| Avinza 90mg (morphine sulfate) | 180 capsules per 90 days OR | 180 MME/day |
| Avinza 120mg (morphine sulfate) | 90 capsules per 90 days | 120 MME/day |
| Belbuca 75mcg (buprenorphine) | 180 films per 90 days OR | 4.5 MME/day |
| Belbuca 150mcg (buprenorphine) | 180 films per 90 days OR | 9 MME/day |
| Belbuca 300mcg (buprenorphine) | 180 films per 90 days OR | 18 MME/day |
| Belbuca 450mcg (buprenorphine) | 180 films per 90 days OR | 27 MME/day |
| Belbuca 600mcg (buprenorphine) | 180 films per 90 days OR | 36 MME/day |
| Belbuca 750mcg (buprenorphine) | 180 films per 90 days OR | 45 MME/day |

5.70.61

| | | | |
|--------------------|-------------------------------|------------------------------|-----------------|
| Section: | Prescription Drugs | Effective Date: | April 1, 2021 |
| Subsection: | Analgesics and Anesthetics | Original Policy Date: | January 1, 2018 |
| Subject: | Extended-Release Opioid Drugs | Page: | 9 of 15 |

| | | |
|---------------------------------------|------------------------------------|-------------|
| Belbuca 900mcg (buprenorphine) | 180 films per 90 days | 54 MME/day |
| Conzip*/Ultram ER 100mg (tramadol) | 270 units per 90 days OR | 30 MME/day |
| Conzip*/Ultram ER 150mg (tramadol) | 180 units per 90 days OR | 30 MME/day |
| Conzip*/Ultram ER 200mg (tramadol) | 90 units per 90 days OR | 20 MME/day |
| Conzip*/Ultram ER 300mg (tramadol) | 90 units per 90 days | 30 MME/day |
| Embeda 20/0.8mg (morphine/naltrexone) | 270 capsules per 90 days OR | 60 MME/day |
| Embeda 30/1.2mg (morphine/naltrexone) | 270 capsules per 90 days OR | 90 MME/day |
| Embeda 50/2mg (morphine/naltrexone) | 180 capsules per 90 days OR | 100 MME/day |
| Embeda 60/2.4mg (morphine/naltrexone) | 180 capsules per 90 days OR | 120 MME/day |
| Embeda 80/3.2mg (morphine/naltrexone) | 180 capsules per 90 days OR | 160 MME/day |
| Embeda 100/4mg (morphine/naltrexone) | 180 capsules per 90 days | 200 MME/day |
| Exalgo 8mg (hydromorphone) | 180 tablets per 90 days OR | 64 MME/day |
| Exalgo 12mg (hydromorphone) | 180 tablets per 90 days OR | 96 MME/day |
| Exalgo 16mg (hydromorphone) | 180 tablets per 90 days OR | 128 MME/day |
| Exalgo 32mg (hydromorphone) | 90 tablets per 90 days | 128 MME/day |
| Hysingla ER 20mg (hydrocodone) | 90 tablets per 90 days OR | 20 MME/day |
| Hysingla ER 30mg (hydrocodone) | 90 tablets per 90 days OR | 30 MME/day |
| Hysingla ER 40mg (hydrocodone) | 90 tablets per 90 days OR | 40 MME/day |
| Hysingla ER 60mg (hydrocodone) | 90 tablets per 90 days OR | 60 MME/day |
| Hysingla ER 80mg (hydrocodone) | 90 tablets per 90 days OR | 80 MME/day |
| Hysingla ER 100mg (hydrocodone) | 90 tablets per 90 days OR | 100 MME/day |
| Hysingla ER 120mg (hydrocodone) | 90 tablets per 90 days | 120 MME/day |
| Kadian 10mg (morphine sulfate) | 270 capsules per 90 days OR | 30 MME/day |
| Kadian 20mg (morphine sulfate) | 270 capsules per 90 days OR | 60 MME/day |
| Kadian 30mg (morphine sulfate) | 270 capsules per 90 days OR | 90 MME/day |
| Kadian 40mg (morphine sulfate) | 270 capsules per 90 days OR | 120 MME/day |
| Kadian 50mg (morphine sulfate) | 270 capsules per 90 days OR | 150 MME/day |
| Kadian 60mg (morphine sulfate) | 270 capsules per 90 days OR | 180 MME/day |
| Kadian 80mg (morphine sulfate) | 180 capsules per 90 days OR | 160 MME/day |
| Kadian 100mg (morphine sulfate) | 180 capsules per 90 days OR | 200 MME/day |
| Kadian 200mg (morphine sulfate) | 90 capsules per 90 days | 200 MME/day |
| MorphaBond 15mg (morphine sulfate) | 270 tablets per 90 days OR | 45 MME/day |

5.70.61

| | | | |
|--------------------|-------------------------------|------------------------------|-----------------|
| Section: | Prescription Drugs | Effective Date: | April 1, 2021 |
| Subsection: | Analgesics and Anesthetics | Original Policy Date: | January 1, 2018 |
| Subject: | Extended-Release Opioid Drugs | Page: | 10 of 15 |

| | | |
|-------------------------------------|------------------------------------|--------------|
| MorphaBond 30mg (morphine sulfate) | 270 tablets per 90 days OR | 90 MME/day |
| MorphaBond 60mg (morphine sulfate) | 270 tablets per 90 days OR | 180 MME/day |
| MorphaBond 100mg (morphine sulfate) | 180 tablets per 90 days | 200 MME/day |
| MS Contin 15mg (morphine sulfate) | 360 tablets per 90 days OR | 60 MME/day |
| MS Contin 30mg (morphine sulfate) | 360 tablets per 90 days OR | 120 MME/day |
| MS Contin 60mg (morphine sulfate) | 270 tablets per 90 days OR | 180 MME/day |
| MS Contin 100mg (morphine sulfate) | 180 tablets per 90 days OR | 200 MME/day |
| MS Contin 200mg (morphine sulfate) | 90 tablets per 90 days | 200 MME/day |
| Nucynta ER 50mg (tapentadol) | 270 tablets per 90 days OR | 60 MME/day |
| Nucynta ER 100mg (tapentadol) | 270 tablets per 90 days OR | 120 MME/day |
| Nucynta ER 150mg (tapentadol) | 270 tablets per 90 days OR | 180 MME/day |
| Nucynta ER 200mg (tapentadol) | 180 tablets per 90 days OR | 160 MME/day |
| Nucynta ER 250mg (tapentadol) | 180 tablets per 90 days | 200 MME/day |
| Opana ER 5mg (oxymorphone) | 270 tablets per 90 days OR | 45 MME/day |
| Opana ER 7.5mg (oxymorphone) | 270 tablets per 90 days OR | 67.5 MME/day |
| Opana ER 10mg (oxymorphone) | 270 tablets per 90 days OR | 90 MME/day |
| Opana ER 15mg (oxymorphone) | 270 tablets per 90 days OR | 135 MME/day |
| Opana ER 20mg (oxymorphone) | 270 tablets per 90 days OR | 180 MME/day |
| Opana ER 30mg (oxymorphone) | 180 tablets per 90 days OR | 180 MME/day |
| Opana ER 40mg (oxymorphone) | 180 tablets per 90 days OR | 240 MME/day |
| OxyContin 10mg (oxycodone) | 270 tablets per 90 days OR | 45 MME/day |
| OxyContin 15mg (oxycodone) | 270 tablets per 90 days OR | 67.5 MME/day |
| OxyContin 20mg (oxycodone) | 270 tablets per 90 days OR | 90 MME/day |
| OxyContin 30mg (oxycodone) | 270 tablets per 90 days OR | 135 MME/day |
| OxyContin 40mg (oxycodone) | 270 tablets per 90 days OR | 180 MME/day |
| OxyContin 60mg (oxycodone) | 180 tablets per 90 days OR | 180 MME/day |
| OxyContin 80mg (oxycodone) | 180 tablets per 90 days | 240 MME/day |
| Xtampza ER 9mg (oxycodone) | 270 capsules per 90 days OR | 40 MME/day |
| Xtampza ER 13.5mg (oxycodone) | 270 capsules per 90 days OR | 60 MME/day |
| Xtampza ER 18mg (oxycodone) | 270 capsules per 90 days OR | 81 MME/day |
| Xtampza ER 27mg (oxycodone) | 270 capsules per 90 days OR | 121 MME/day |
| Xtampza ER 36mg (oxycodone) | 270 capsules per 90 days | 162 MME/day |

5.70.61

| | | | |
|--------------------|-------------------------------|------------------------------|-----------------|
| Section: | Prescription Drugs | Effective Date: | April 1, 2021 |
| Subsection: | Analgesics and Anesthetics | Original Policy Date: | January 1, 2018 |
| Subject: | Extended-Release Opioid Drugs | Page: | 11 of 15 |

| | | | |
|-------------------------------|--------------------------|-----------|-------------|
| Zohydro ER 10mg (hydrocodone) | 270 capsules per 90 days | OR | 30 MME/day |
| Zohydro ER 15mg (hydrocodone) | 270 capsules per 90 days | OR | 45 MME/day |
| Zohydro ER 20mg (hydrocodone) | 270 capsules per 90 days | OR | 60 MME/day |
| Zohydro ER 30mg (hydrocodone) | 270 capsules per 90 days | OR | 90 MME/day |
| Zohydro ER 40mg (hydrocodone) | 270 capsules per 90 days | OR | 120 MME/day |
| Zohydro ER 50mg (hydrocodone) | 180 capsules per 90 days | | 100 MME/day |

Belbuca ONLY: Maximum daily limit of any combination should NOT exceed 1,800 mcg/day

Tramadol ER ONLY: Maximum daily limit of any combination should NOT exceed 300 mg/day

Maximum daily limit of any other combination should NOT exceed 200 MME/day

*Requires formulary exception + PA

Duration 6 months

Prior – Approval *Renewal* Limits

Same as above

Rationale

Summary

Extended-release opioids are medications that are indicated for the management of severe pain when a continuous, around-the-clock opioid analgesic is needed for an extended period of time (1-20). Safety and effectiveness of extended-release opioids in pediatric patients have not been established (1-15).

Prior approval is required to ensure the safe, clinically appropriate and cost-effective use of extended-release opioids while maintaining optimal therapeutic outcomes.

References

1. Arymo ER [package insert]. Wayne, PA: Zyla Life Sciences; October 2019.
2. Belbuca [package insert]. Raleigh, NC: BioDelivery Sciences International, Inc; July 2020.

5.70.61

| | | | |
|--------------------|-------------------------------|------------------------------|-----------------|
| Section: | Prescription Drugs | Effective Date: | April 1, 2021 |
| Subsection: | Analgesics and Anesthetics | Original Policy Date: | January 1, 2018 |
| Subject: | Extended-Release Opioid Drugs | Page: | 12 of 15 |

3. Embeda [package insert]. New York, NY: Pfizer Inc; September 2018.
4. Exalgo [package insert]. Hazelwood, MO: Mallinckrodt Brand Pharmaceuticals, Inc.; December 2016.
5. Hysingla ER [package insert]. Stamford, CT: Purdue Pharma L.P.; October 2019.
6. Kadian [package insert]. Irvine, CA: Allergan USA, Inc.; September 2018.
7. MorphaBond [package insert]. Basking Ridge, NJ: Daiichi Sankyo, Inc.; September 2018.
8. MS Contin [package insert]. Stamford, CT: Purdue Pharma L.P.; December 2016.
9. Nucynta ER [package insert]. Stoughton, MA: Collegium Pharmaceutical, Inc.; September 2018.
10. Opana ER [package insert]. Chadds Ford, PA: Endo Pharmaceuticals; September 2018.
11. OxyContin [package insert]. Stamford, CT: Purdue Pharma L.P.; September 2018.
12. Xtampza ER [package insert]. Cincinnati, OH: Patheon Pharmaceuticals; October 2019.
13. Zohydro ER [package insert]. Morristown, NJ: Persion Pharmaceuticals LLC.; October 2019.
14. Ultram ER [package insert]. Titusville, NJ: Janssen Pharmaceuticals, Inc.; August 2017.
15. Conzip [package insert]. Sayreville, NJ: Vertical Pharmaceuticals LLC. September 2018.
16. Dowell D, Haegerich T, Chou R. CDC Guideline for Prescribing Opioids for Chronic Pain. CDC Guidelines 2016.
17. FDA Safety Release. FDA Drug Safety Communication: FDA warns about several safety issues with opioid pain medicines; requires label changes. March 22, 2016.
18. Chou R, Fanciullo G, Fine P, et al. Clinical Guidelines for the Use of Chronic Opioid Therapy in Chronic Noncancer Pain The Journal of Pain 2009;10:113-130.
19. Hooten W, Timming R, Belgrade M, et al. Institute for Clinical Systems Improvement. Assessment and Management of Chronic Pain. Updated November 2013.
20. Centers for Medicare & Medicaid Services. Opioid Morphine EQ Conversion Factors. August 2017. <https://www.cms.gov/Medicare/Prescription-Drug-Coverage/PrescriptionDrugCovContra/Downloads/Opioid-Morphine-EQ-Conversion-Factors-Aug-2017.pdf>
21. Opioid Analgesic Risk Evaluation and Mitigation Strategy (REMS). Drug Safety and Availability: U.S. Food & Drug Administration. September 19, 2018.
22. FDA News Release. FDA Drug Safety Communication: FDA requiring labeling changes for benzodiazepines. September 23, 2020.

Policy History

| Date | Action |
|------|--------|
|------|--------|

5.70.61

| | | | |
|--------------------|-------------------------------|------------------------------|-----------------|
| Section: | Prescription Drugs | Effective Date: | April 1, 2021 |
| Subsection: | Analgesics and Anesthetics | Original Policy Date: | January 1, 2018 |
| Subject: | Extended-Release Opioid Drugs | Page: | 13 of 15 |

| | |
|----------------|--|
| December 2017 | Annual review Addition to PA for January 1, 2018 Merge of ER opioids from policy numbers 5.70.25, 5.70.30, 5.70.33, 5.70.34, 5.70.35, 5.70.36, 5.70.38, 5.70.39, 5.70.47 |
| January 2018 | Addition of Opana ER and removal of MS Contin 60mg from pre-PA Allowance |
| March 2018 | Annual editorial review Addition of Avinza |
| September 2018 | Addition of Tramadol ER to criteria |
| October 2018 | Addition of Opioid Analgesic REMS requirement. Targiniq ER, Troxyca ER, Vantrela ER, and Xartemis XR removed from market |
| November 2018 | Annual review and reference update. Addition of Opioid Analgesic REMS link per SME |
| February 2019 | Addition of Pre-PA opioids chart |
| March 2019 | Annual review |
| December 2019 | Annual review. Addition of requirement of no cumulative MME over 300. Revised quantity limit for MS Contin 200mg from 180/90 to 90/90 to fall within the MME allowance |
| March 2020 | Annual editorial review. Updated Opioid Analgesic REMS link |
| December 2020 | Annual review. Increased the SA for Belbuca 75mcg, 150mcg, 300mcg, 450mcg to 90/90 from 60/90 per FEP. Conzip requires formulary exception + PA |
| March 2021 | Annual editorial review and reference update |

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on March 12, 2021 and is effective on April 1, 2021.

| | | | |
|--------------------|-------------------------------|------------------------------|-----------------|
| Section: | Prescription Drugs | Effective Date: | April 1, 2021 |
| Subsection: | Analgesics and Anesthetics | Original Policy Date: | January 1, 2018 |
| Subject: | Extended-Release Opioid Drugs | Page: | 14 of 15 |

Appendix 1 - List of Serotonergic Medications

Selective Serotonin Reuptake Inhibitors (SSRIs)

| | |
|--------------|---|
| paroxetine | Paxil, Paxil CR, Pexeva, Brisdelle |
| fluvoxamine | Luvox, Luvox CR |
| fluoxetine | Prozac, Prozac Weekly, Sarafem, Selfemra, Symbyax |
| sertraline | Zoloft |
| citalopram | Celexa |
| escitalopram | Lexapro |

Serotonin-Norepinephrine Reuptake Inhibitors (SNRIs)

| | |
|----------------|-------------------|
| venlafaxine | Effexor XR |
| desvenlafaxine | Pristiq, Khedezla |
| duloxetine | Cymbalta |
| milnacipran | Savella |

Tricyclic Antidepressants (TCAs)

| | |
|---------------|----------------------------------|
| amitriptyline | No brand name currently marketed |
| desipramine | Norpramin |
| clomipramine | Anafranil |
| imipramine | Tofranil, Tofranil PM |
| nortriptyline | Pamelor, Aventyl |
| protriptyline | Vivactil |
| doxepin | Zonalon, Silenor |
| trimipramine | Surmontil |

Monoamine Oxidase Inhibitors (MAOIs)

| | |
|-----------------|--------------------------|
| isocarboxazid | Marplan |
| phenelzine | Nardil |
| selegiline | Emsam, Eldepryl, Zelapar |
| tranylcypromine | Parnate |

5.70.61

| | | | |
|--------------------|-------------------------------|------------------------------|-----------------|
| Section: | Prescription Drugs | Effective Date: | April 1, 2021 |
| Subsection: | Analgesics and Anesthetics | Original Policy Date: | January 1, 2018 |
| Subject: | Extended-Release Opioid Drugs | Page: | 15 of 15 |

Other Psychiatric Medicines

| | |
|-------------|----------------------------------|
| amoxapine | No brand name currently marketed |
| maprotiline | No brand name currently marketed |
| nefazodone | No brand name currently marketed |
| trazodone | Oleptro |
| buspirone | No brand name currently marketed |
| vilazodone | Viiibryd |
| mirtazapine | Remeron, Remeron Soltab |
| lithium | Lithobid |

Migraine Medicines

| | |
|--------------|---|
| almotriptan | Axert |
| frovatriptan | Frova |
| naratriptan | Amerge |
| rizatriptan | Maxalt, Maxalt-MLT |
| sumatriptan | Imitrex, Imitrex Statdose, Alsuma, Sumavel Dosepro, Zecuity, Treximet |
| zolmitriptan | Zomig, Zomig-ZMT |

Antiemetics

| | |
|--------------|-----------------------------|
| ondansetron | Zofran, Zofran ODT, Zuplenz |
| granisetron | Kytril, Sancuso |
| dolasetron | Anzemet |
| palonosetron | Aloxi |

Other Serotonergic Medicines

| | |
|------------------|--|
| dextromethorphan | Bromfed-DM, Delsym, Mucinex DM, Nuedexta |
| linezolid | Zyvox |
| cyclobenzaprine | Amrix |
| methylene blue | |
| St. John's wort | |
| tryptophan | |