Medical Policy

BlueCross BlueShield of Kansas
An independent licensee of the Blue Cross Blue Shield Association

Title: Opioids, Extended Release (ER)

- **Prime Therapeutics will review Prior Authorization requests**
  Prior Authorization Form:
  https://www.bcbsks.com/CustomerService/Forms/pdf/PriorAuth-6202KS-OPIO.pdf

  Link to Drug List (Formulary):
  http://www.bcbsks.com/CustomerService/PrescriptionDrugs/drug_list.shtml

Professional	**Institutional**
Original Effective Date: July 1, 2017	Original Effective Date: July 1, 2017
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Current Effective Date: May 1, 2018	Current Effective Date: May 1, 2018

State and Federal mandates and health plan member contract language, including specific provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage. To verify a member's benefits, contact Blue Cross and Blue Shield of Kansas Customer Service.

The BCBSKS Medical Policies contained herein are for informational purposes and apply only to members who have health insurance through BCBSKS or who are covered by a self-insured group plan administered by BCBSKS. Medical Policy for FEP members is subject to FEP medical policy which may differ from BCBSKS Medical Policy.

The medical policies do not constitute medical advice or medical care. Treating health care providers are independent contractors and are neither employees nor agents of Blue Cross and Blue Shield of Kansas and are solely responsible for diagnosis, treatment and medical advice.

If your patient is covered under a different Blue Cross and Blue Shield plan, please refer to the Medical Policies of that plan.

DESCRIPTION

The intent of the quantity limit for opioids extended-release (ER) is to allow for quantities that permit dose choices that individualize the treatment plan for chronic pain to the needs of the patient. Requests for larger quantities will be reviewed if the prescriber provides evidence that the requested dose is appropriate for the patient

FDA-Approved Indications and Dosage

FDA Approved Indications:[1-6,10,14-16,18-22,24,25]

Narcotic analgesics are indicated for relief of moderate to severe pain.

Brand/Generic Name	Strength	Dosing frequency (maximum labeled dose[a])
Narcotics		
Arymo ER™ (morphine sulfate ER)	15, 30, 60 mg	Two to three time daily
Avinza® morphine sulfate ER	30, 45, 60, 75, 90, 120 mg	Once daily (not to exceed 1600 mg daily)
Belbuca™ (buprenorphine buccal film)	75, 150, 300, 450, 600, 750, 900 mcg	Twice daily (not to exceed 900 mcg twice daily)
Butrans® (buprenorphine transdermal)	5, 7.5, 10, 15, 20 mcg/hour system	1 transdermal system weekly (maximum dose 20 mcg/hr)
Duragesic® (fentanyl transdermal patch ER)	12, 25, 50, 75, 100 mcg/hour	15 patches / month
Embeda® (morphine/naltrexone ER)	20-0.8, 30-1.2, 50-2, 60-2.4, 80-3.2, 100-4 mg	Once or twice daily
Exalgo® (hydromorphone ER)	8, 12, 16, 32 mg	Once daily
Fentanyl transdermal patch	37.5, 62.5, 87.5 mcg/hour	15 patches / month
Hysingla ER® (hydrocodone ER)	20, 30, 40, 60, 80, 100, 120 mg	Once daily
Kadian® (morphine ER)	10, 20, 30, 40, 50, 60, 70, 80,100, 130, 150, 200 mg	Once or twice daily
Morphabond ER (morphine ER)	15, 30, 60, 100 mg	Twice daily
MS Contin® (morphine sulfate ER)	15, 30, 60, 100, 200 mg	Twice daily (some patients may require three times daily)
Opana ER® (oxymorphone ER)	5, 7.5, 10, 15, 20, 30, 40 mg	Twice daily
Opana ER® crush-resistant (oxymorphone ER)	5, 7.5, 10, 15, 20, 30, 40 mg	Twice daily
Oramorph SR® (morphine ER)	15, 30, 60, 100 mg	Twice daily (some patients may require three times daily)
OxyContin® (oxycodone ER)	10, 15, 20, 30, 40, 60, 80 mg	Twice daily
Xartemis™ XR (oxycodone and acetaminophen ER)	7.5/325 mg	Twice daily
Xtampza ER™ (oxycodone ER)	9, 13.5, 18, 27, 36 mg	Twice daily (288 mg)

Brand/Generic Name	Strength	Dosing frequency (maximum labeled dose[a])
Zohydro® ER Abuse Deterrent (hydrocodone ER)	10, 15, 20, 30, 40, 50 mg	Twice daily
Tramadol, Tapentadol		
ConZip™ (tramadol SR biphasic)	100, 200, 300 mg	Once daily
Nucynta ER® (tapentadol ER)	50, 100, 150, 200, 250 mg	Twice daily
tramadol extended-release	100, 200, 300 mg	Once daily
Tramadol SR Biphasic (tramadol SR biphasic)	150 mg	Once daily
Ultram ER® (tramadol extended-release)	100, 200, 300 mg	Once daily

a - Maximum dosage units in FDA-approved labeling where available. In addition, daily doses should not exceed the following limits for individual ingredients: tramadol ER - 300 mg, tapentadol ER - 500 mg

POLICY

Prior Authorization and Quantity Limits Criteria for Approval

A. Quantities of **Opioids ER** which are above the program set limit but **less than or equal to the Program Maximum Daily Dose** (maximum mg allowed with highest dosage strength) will be approved when BOTH of the following are met:
   1. The quantity (dose) requested cannot be achieved using a lesser quantity of a higher strength
      AND
   2. The prescriber has submitted documentation in support of therapy with a higher dose (quantity) for the intended diagnosis which has been reviewed and approved by the Clinical Review pharmacist

B. Quantities of **Opioids ER** which are **greater than the Program Maximum Daily Dose** (maximum mg allowed with highest dosage strength) will be approved when ALL of the following are met:
   1. The quantity (dose) requested cannot be achieved using a lesser quantity of a higher strength
      AND
   2. ONE of the following:
      a. The member has a diagnosis of active cancer pain due to an active malignancy
         OR
      b. The member is eligible for hospice care
         OR

c. The member is undergoing treatment of chronic non-cancer pain and ALL of the following are met:
   i. The prescriber provides documentation of a formal, consultative evaluation including:
      a. Diagnosis
      AND
      b. A complete medical history which includes previous and current pharmacological and non-pharmacological therapy
   AND
   ii. The prescriber has confirmed that a patient-specific pain management plan is on file for the patient
   AND
   iii. The prescriber has confirmed that the patient is not diverting the requested medication, according to the patient's records in the state's prescription drug monitoring program (PDMP), if applicable

AND

3. The prescriber has submitted documentation in support of therapy with a higher dose (quantity) for the intended diagnosis which has been reviewed and approved by the Clinical Review pharmacist.

Length of Approval: 1 month for dose titration requests
Up to 6 months for all other requests

Quantity Limit Target Drugs – Recommended Limits	
Brand (generic)	**Quantity Per Day Limit**
Narcotic Analgesics	
Arymo ER™ (morphine sulfate)	
15 mg extended release tablet	3 tablets
30 mg extended release tablet	3 tablets
60 mg extended release tablet	3 tablets
Avinza, morphine sulfate ER	
30 mg sustained-release capsule	1 capsule
45 mg sustained-release capsule	1 capsule
60 mg sustained-release capsule	1 capsule
75 mg sustained-release capsule	1 capsule
90 mg sustained-release capsule	1 capsule
120 mg sustained-release capsule	1 capsule
Belbuca (buprenorphine buccal film)	
75 mcg buccal film	2 films
150 mcg buccal film	2 films
300 mcg buccal film	2 films
450 mcg buccal film	2 films
600 mcg buccal film	2 films
750 mcg buccal film	2 films
900 mcg buccal film	2 films

Quantity Limit Target Drugs – Recommended Limits	
Brand (generic)	**Quantity Per Day Limit**
Butrans, Buprenorphine Transdermal System	
5 mcg/hour transdermal system	1 system/week
7.5 mcg/hour transdermal system	1 system/week
10 mcg/hour transdermal system	1 system/week
15 mcg/hour transdermal system	1 system/week
20 mcg/hour transdermal system	1 system/week
Duragesic (fentanyl transdermal patch)	
12 mcg/hr transdermal patch	15 patches/month
25 mcg/hr transdermal patch	15 patches/month
50 mcg/hr transdermal patch	15 patches/month
75 mcg/hr transdermal patch	15 patches/month
100 mcg/hr transdermal patch	15 patches/month
Embeda (morphine/naltrexone)	
20 mg/0.8 mg controlled-release capsule	2 capsules
30 mg/1.2 mg controlled-release capsule	2 capsules
50 mg/2 mg controlled-release capsule	2 capsules
60 mg/2.4 mg controlled-release capsule	2 capsules
80 mg/3.2 mg controlled-release capsule	2 capsules
100 mg/4 mg controlled-release capsule	2 capsules
Exalgo (hydromorphone)	
8 mg extended-release tablet[a]	1 tablet
12 mg extended-release tablet[a]	1 tablet
16 mg extended-release tablet[a]	1 tablet
32 mg extended-release tablet	1 tablet
Fentanyl transdermal patch	
37.5 mcg/hr transdermal patch	15 patches/month
62.5 mcg/hr transdermal patch	15 patches/month
87.5 mcg/hr transdermal patch	15 patches/month
Hysingla ER (hydrocodone)	
20 mg extended-release tablet	1 tablet
30 mg extended-release tablet	1 tablet
40 mg extended-release tablet	1 tablet
60 mg extended-release tablet	1 tablet
80 mg extended-release tablet	1 tablet
100 mg extended-release tablet	1 tablet
120 mg extended-release tablet	1 tablet
Kadian (morphine sulfate)	
10 mg sustained-release capsule[a]	2 capsules
20 mg sustained-release capsule[a]	2 capsules
30 mg sustained-release capsule[a]	2 capsules
40 mg sustained-release capsule	2 capsules
50 mg sustained-release capsule[a]	2 capsules
60 mg sustained-release capsule[a]	2 capsules
70 mg sustained-release capsule[b]	2 capsules
80 mg sustained-release capsule[a]	2 capsules
100 mg sustained-release capsule[a]	2 capsules
130 mg sustained-release capsule[b]	2 capsules
150 mg sustained-release capsule[b]	2 capsules
200 mg sustained-release capsule	2 capsules

Quantity Limit Target Drugs – Recommended Limits	
Brand (generic)	**Quantity Per Day Limit**
Morphabond ER™ (morphine ER)	
15 mg ER tablet	2 tablets
30 mg ER tablet	2 tablets
60 mg ER tablet	2 tablets
100 mg ER tablet	2 tablets
MS Contin (morphine sulfate)	
15 mg sustained-release tablet[a]	3 tablets
30 mg sustained-release tablet[a]	3 tablets
60 mg sustained-release tablet[a]	3 tablets
100 mg sustained-release tablet[a]	3 tablets
200 mg sustained-release tablet[a]	3 tablets
Opana ER /oxymorphone SR	
5 mg sustained-release tablet[a]	2 tablets
7.5 mg sustained-release tablet[a]	2 tablets
10 mg sustained-release tablet[a]	2 tablets
15 mg sustained-release tablet[a]	2 tablets
20 mg sustained-release tablet[a]	2 tablets
30 mg sustained-release tablet[a]	2 tablets
40 mg sustained-release tablet[a]	2 tablets
Opana ER (oxymorphone SR, crush resistant)	
5 mg sustained-release tablet	2 tablets
7.5 mg sustained-release tablet	2 tablets
10 mg sustained-release tablet	2 tablets
15 mg sustained-release tablet	2 tablets
20 mg sustained-release tablet	2 tablets
30 mg sustained-release tablet	2 tablets
40 mg sustained-release tablet	2 tablets
Oramorph SR (morphine sulfate)	
15 mg sustained-release tablet[b]	3 tablets
30 mg sustained-release tablet[b]	3 tablets
60 mg sustained-release tablet[b]	3 tablets
100 mg sustained-release tablet[b]	3 tablets
OxyContin (oxycodone ER)	
10 mg tablet	2 tablets
15 mg tablet	2 tablets
20 mg tablet	2 tablets
30 mg tablet	2 tablets
40 mg tablet	2 tablets
60 mg tablet	4 tablets
80 mg tablet	4 tablets
Xartemis XR (oxycodone/acetaminophen)	
7.5/325 mg tablet	4 tablets
Xtampza ER (oxycodone ER)	
9 mg capsule	2 capsules
13.5 mg capsule	2 capsules
18 mg capsule	2 capsules
27 mg capsule	2 capsules
36 mg capsule	2 capsules

Quantity Limit Target Drugs – Recommended Limits	
Brand (generic)	**Quantity Per Day Limit**
Zohydro ER Abuse Deterrent (hydrocodone ER)	
10 mg sustained-release capsule	2 capsules
15 mg sustained-release capsule	2 capsules
20 mg sustained-release capsule	2 capsules
30 mg sustained-release capsule	2 capsules
40 mg sustained-release capsule	2 capsules
50 mg sustained-release capsule	2 capsules
Tramadol, Tapentadol	
ConZip (tramadol SR biphasic)	
100 mg sustained-release capsule	1 capsule
200 mg sustained-release capsule	1 capsule
300 mg sustained-release capsule	1 capsule
Nucynta ER (tapentadol SR)	
50 mg extended-release tablet	2 tablets
100 mg extended-release tablet	2 tablets
150 mg extended-release tablet	2 tablets
200 mg extended-release tablet	2 tablets
250 mg extended-release tablet	2 tablets
tramadol[a]	
100 mg sustained-release tablet[a]	1 tablet
200 mg sustained-release tablet[a]	1 tablet
300 mg sustained-release tablet[a]	1 tablet
Tramadol ER (tramadol SR biphasic)	
150 mg sustained-release capsule	1 capsule
Ultram ER (tramadol)[a]	
100 mg sustained-release tablet	1 tablet
200 mg sustained-release tablet	1 tablet
300 mg sustained-release tablet	1 tablet

a – generic available, included in quantity limit program
b - discontinued

RATIONALE[1,2]

Narcotic analgesics and combinations are indicated for the treatment of mild to moderate to severe pain. Immediate release products may be administered on an as needed basis whereas extended release agents are used in the treatment of chronic pain. Morphine remains the prototype opioid; as newer agents are introduced, their efficacy and safety are compared to morphine as the gold standard. Morphine is considered the drug of choice for severe pain[3] There is insufficient evidence to recommend any alternative opioid in preference to morphine as the opioid of first choice.[9] Tramadol has been found to be efficacious in several randomized trials for the treatment of neuropathic pain, chronic non-cancer pain, and osteoarthritis pain.[10]

Current Guidelines

Long-term opioid use often begins with treatment of acute pain. When opioids are used for acute pain, clinicians should prescribe the lowest effective dose of immediate-release opioids and should prescribe no greater quantity than needed for the expected duration of pain severe enough to require opioids. Three days or less will often be sufficient; more than seven days will rarely be needed.[23]

When starting opioid therapy for chronic pain, clinicians should prescribe immediate-release opioids instead of extended-release/long-acting (ER/LA) opioids. ER/LA opioids should be reserved for severe, continuous pain and should be considered only for patients who have received immediate-release opioids daily for at least 1 week.[23]

Scientific research has identified high-risk prescribing practices that have contributed to the overdose epidemic (e.g., high-dose prescribing, overlapping opioid and benzodiazepine prescriptions, and extended-release/long-acting [ER/LA] opioids for acute pain).[23]

The National Comprehensive Cancer Network (NCCN) Guidelines: Adult Cancer Pain 2015 include the following recommendations:[5]

- In a patient who has not been exposed to opioids in the past morphine is generally considered the standard starting drug of choice. Oral administration is the preferred route. Patients presenting with severe pain needed urgent relief should be treated with parenteral opioids (Category 1).

Category 1= Recommendation based on high level evidence (ie., randomized trials) and there is uniform NCCN consensus. Category 2A = Recommendation based on lower level evidence and there is uniform NCCN consensus.

The Evidence-based Guideline: Treatment of painful diabetic neuropathy (DPN) from the American Academy of Neurology (AAN), the American Association of Neuromuscular and Electrodiagnostic Medicine, and the American Academy of Physical Medicine and Rehabilitation state the following:[11] Dextromethorphan, morphine, tramadol, and oxycodone should be considered for the treatment of DPN, but data is insufficient to recommend one agent over the other, but are not considered as first line therapy.[11] Tapentadol has a similar mechanism of action as tramadol, with indications for treatment of moderate to severe pain in adults as well as for the treatment of diabetic peripheral neuropathy, but is not recommended by any guidelines.[2,11]

The World Health Organization (WHO) Pain Relief Ladder states:[6]
If pain occurs, there should be prompt oral administration of drugs in the following order: nonopioids (aspirin and acetaminophen); then, as necessary, mild opioids (codeine); then strong opioids such as morphine, until the patient is free of pain.

The American Society for Interventional Pain Physicians (ASIPP) Guidelines for Responsible Opioid Prescribing in Chronic Non-Cancer Pain (2012) states the following: While there is significant short-term evidence available for all opioids, the evidence for long-term effectiveness is inconclusive due to relatively short (3 months) duration of studies and lack of quality studies[13]

Safety
Adverse effects to opioid analgesics include respiratory depression, nausea, vomiting, urinary retention, mental clouding, tolerance and dependence, sedation, ileus, constipation, euphoria, pruritus, and biliary spasms.

Patients should receive FDA approved dosing as excessive narcotic administration may lead to coma or death. Patients that develop opioid tolerance may need increased doses or additional

therapies to manage pain. Tramadol and tramadol containing products have been associated with adverse events including seizures that may be dose related.[1,2]

In September 2013 the FDA issued a safety bulletin. In an effort to combat the rising rate of opioid-related deaths, the FDA will require safety label changes on all extended release and long-acting opioid analgesics (extended-release and long-acting opioids include hydromorphone, morphine, oxycodone, oxymorphone, and tapentadol).[12]

- The new safety information will emphasize that the drugs are only to be used for patients requiring continuous treatment when other treatment options, including non-opioid analgesics or immediate-release opioids, are ineffective or intolerable. The labels will also indicate that the drugs should not be used on an "as-needed" pain relief basis.
- The FDA is also requiring a new boxed warning on ER/LA opioid analgesics to caution that chronic maternal use of these products during pregnancy can result in neonatal opioid withdrawal syndrome (NOWS), which may be life-threatening and require management according to protocols developed by neonatology experts.
- In addition, the FDA is notifying ER/LA opioid analgesic application holders of the need for changes to the following sections of drug labeling: Dosage and Administration; Warnings and Precautions; Drug Interactions; Use in Specific Populations; Patient Counseling Information, and the Medication Guide.[12]
- Once the safety labeling changes are finalized, modifications will also be made to the ER/LA Opioid Analgesics Risk Evaluation and Mitigation Strategy (REMS), to reflect the updated information.
- The FDA will also require drug companies to conduct longer studies and trials of extended-release and long-acting opioid painkillers that are already on the market. The studies will assess known risks associated with the drugs, including increased sensitivity to pain, misuse, abuse, addiction, overdose, and death.[12]

Hydrocodone combination products have been reclassified to Schedule II by the Drug Enforcement Administration (DEA) effective October 2014. This change followed the recommendation out of the FDA Advisory Committee meeting that occurred in January 2013 where the committee voted 19 to 10 to reschedule these products.[17]

Concomitant use of tramadol with MAO inhibitors or selective serotonin reuptake inhibitors (SSRIs) increases the risk of adverse events such as seizures and serotonin syndrome. Withdrawal symptoms may occur if tramadol is discontinued abruptly.[10]

REVISIONS	
07-01-2017	Policy published 05-01-2017. Policy effective 07-01-2017.
07-01-2017	Policy published 07-14-2017. Policy retro-effective to 07-01-2017.
	In Description section: ▪ Added to the FDA Approved Indications chart "Arymo ER™ (morphine sulfate ER)" and "Morphabond ER (morphine ER)"
	In Policy section: ▪ Added to the Quantity Limits Chart "Arymo ER™ (morphine sulfate ER)" and "Morphabond ER (morphine ER)" ▪ Updated Butrans (cuprenorphine)" to "Butrans Buprenorphine Transdermal System"
	References updated

REVISIONS	
05-01-2018	In Description section ▪ Zohydro™ ER (hydrocodone ER) from the Strength and Dosing frequency chart ▪ Removed the brand name "Ryzolt" from the Strength and Dosing frequency chart (the generic drug remains available)
	In Policy section: ▪ Updated the Quantity Limit Chart to reflect discontinued dosages for Kadian (morphine sulfate) 70 mg, 130 mg, 150 mg and Oramorph SR (morphine sulfate) 15 mg, 30 mg, 60 mg 100 mg; removed Zohydre ER (hydrocodone); removed "Ryzolt" brand name (generic drug continues to be available)
	References updated

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