Oxycodone

Description

Oxycodone IR, Oxycodone ER, OxyContin, Xtampza ER

Background

Oxycodone hydrochloride, a pure opioid agonist, is used in the treatment of moderate to severe pain (1-4). The precise mechanism of action is unknown; however, specific opioid receptors in the CNS have been identified and are considered to play a role in the therapeutic effects of the drug. Chronic opioids are most appropriate for patients with moderate to severe pain unresponsive to non-opioids (5).

Oxycodone is a Schedule II controlled substance and can be abused in a manner similar to other opioid agonists, legal or illicit. This should be considered when prescribing or dispensing oxycodone in a situation where misuse, abuse, or diversion are a concern (1).

Regulatory Status

FDA-approved indications:

1. OxyContin and Xtampza ER are opioid agonists 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 (1, 4).

Limitations of use: (1, 4)

- 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 formulations, reserve 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.

- OxyContin and Xtampza ER are not indicated as an as-needed (prn) analgesic.

2. Oxycodone hydrochloride tablets and capsules are immediate-release oral formulations of oxycodone hydrochloride indicated for the management of moderate to severe pain where the use of an opioid analgesic is appropriate (2). Oxycodone hydrochloride oral solution 100 mg/5 mL (20 mg/mL) is an opioid analgesic indicated for the management of moderate to severe acute and chronic pain in opioid-tolerant patients (3).

The OxyContin, Xtampza ER and oxycodone immediate release have boxed warnings for the following (1-2,4):

- Respiratory depression is the chief hazard of opioid agonists, including morphine sulfate, 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. The risk for opioid abuse increases in patients with a personal or family history of substance abuse or mental illness. Patients should be assessed for the risk of developing abuse prior to the start of treatment and should be routinely monitored during therapy

- Prolonged use of opioid agonists during pregnancy can result in neonatal opioid withdrawal syndrome, which may be life-threatening.

- Patients should not consume alcohol or any products containing alcohol while taking.

OxyContin and Xtampza ER are contraindicated in patients who have significant respiratory depression, paralytic ileus, acute or severe bronchial asthma and hypersensitivity to any of its components or the active ingredient, oxycodone (1). Usual therapeutic doses of immediate-release oxycodone hydrochloride may decrease respiratory drive to the point of apnea. In these patients, alternative non-opioid analgesics should be considered, and opioids should be employed only under careful medical supervision at the lowest effective dose (2).
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 (6).

CDC guidelines finds that given uncertain benefits and substantial risks that opioids should not be considered first-line or routine therapy for chronic pain (i.e., pain continuing or expected to continue longer than 3 months or past the time of normal tissue healing) outside of active cancer, palliative, and end-of-life care (6).

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) (7).

The FDA requires healthcare providers to go through the REMS program before prescribing OxyContin / long acting opioids (1).

Related policies
Abstral, Actiq, Duragesic, Embeda, Fentanyl Powder, Fentora, Hysingla ER, Lazanda, Meperidine, Methadone, Morphine, Nucynta, Onsolis, Subsys, Xartemis ER, Zohydro ER

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

Oxycodone IR may be considered medically necessary in patients that are 18 years of age and older with moderate to severe pain and if the conditions below are met.

Oxycodone ER may be considered medically necessary in patients that are 18 years of age and older with pain severe enough to require daily, around-the-clock long term opioid treatment and if the conditions below are met.

Oxycodone IR and ER are considered investigational in patients below 18 years of age and for all other indications.

Prior-Approval Requirements
Prior authorization is not required if prescribed by an oncologist
Age 18 years of age or older

Diagnosis

Oxycodone IR
Patient must have the following:

1. Moderate to Severe Pain

AND ALL of the following:
   a. NO dual therapy with other immediate release opioid analgesic(s)
   b. NO dual therapy with opioid addiction treatment or methadone
   c. Alternative treatment options have been ineffective, not tolerated or inadequate for controlling the pain
      i. These include: non-opioid analgesics
   d. Prescriber agrees to assess the benefits of pain control (i.e. Care Plan signs of abuse, severity of pain) after 3 months of therapy
   e. Prescriber agrees to assess patient for serotonin syndrome
   f. 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. Chloralhydrate (Librium)
      vii. Clorazepate dipotassium (Tranxene)

Oxycodone ER (OxyContin / Xampza ER):
Patient must have the following:

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

AND ALL of the following:
   a. NO dual therapy with other extended release opioid analgesic(s)
   b. NO dual therapy with opioid addiction treatment or methadone
   c. Alternative treatment options have been ineffective, not tolerated or inadequate for controlling the pain
      i. These include: non-opioid analgesics and opioid immediate release analgesics
d. Patient must have been on a previous immediate-release opioid therapy for at least 10 days in the last 90 days

e. Prescriber agrees to assess the benefits of pain control (i.e. Care Plan signs of abuse, severity of pain) after 3 months of therapy

f. Prescriber agrees to assess patient for serotonin syndrome

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)

Prior – Approval Renewal Requirements

Age 18 years of age or older

Diagnosis

Oxycodone IR:
   Patient must have the following:

1. Moderate to Severe Pain

   AND ALL of the following:

   a. NO dual therapy with other immediate release opioid analgesic(s)
   b. Prescriber agrees to assess the benefits of pain control (i.e. Care Plan signs of abuse, severity of pain) after 3 months of therapy
   c. Prescriber agrees to assess patient for serotonin syndrome
   d. NO dual therapy with opioid addiction treatment or methadone
   e. 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)
Oxycodone ER (OxyContin / Xtampza ER):
Patient must have the following:

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

AND ALL of the following:
   a. NO dual therapy with other extended release opioid analgesic(s)
   b. Prescriber agrees to assess the benefits of pain control after 3 months of therapy
   c. Prescriber agrees to assess patient for serotonin syndrome
   d. NO dual therapy with opioid addiction treatment or methadone
   e. 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)

Policy Guidelines

Pre - PA Allowance

<table>
<thead>
<tr>
<th>Quantity</th>
<th>Oxycodone IR: Immediate Release (IR): 4 per day (360 per 90 days) OR 6ml per day (540ml per 90 days)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Oxycodone 20mg/ml (IR):</td>
</tr>
<tr>
<td></td>
<td>**OxyContin /oxycodone ER: 4 per day (360 per 90 days) OR</td>
</tr>
<tr>
<td>**Xtampza ER:</td>
<td>30ml per day (2700ml per 90 days)</td>
</tr>
<tr>
<td></td>
<td>**Xtampza ER: 30ml per day (2700ml per 90 days)</td>
</tr>
<tr>
<td></td>
<td>Oxycodone 1mg/ml (IR):</td>
</tr>
</tbody>
</table>

**Patients will be eligible for a Pre-PA Allowance for Extended Release (ER) if the patient has been on a previous immediate-release opioid therapy for at least 10 days in the last 90 days or they are switching from another extended release opioid
### Prior - Approval Limits

#### Quantity

<table>
<thead>
<tr>
<th>Drug Formulation</th>
<th>Immediate Release (IR)</th>
<th>Oxycodone 20mg/ml (IR)</th>
<th>Oxycodone 1mg/ml (IR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oxycodone IR</td>
<td>6 per day (540 per 90 days)</td>
<td>9ml per day (810ml per 90 days)</td>
<td>67ml per day (6030ml per 90 days)</td>
</tr>
<tr>
<td>Oxycodone ER</td>
<td>OxyContin /oxycodone ER: 6 per day (540 per 90 days)</td>
<td>8 per day (720 per 90 days)</td>
<td></td>
</tr>
</tbody>
</table>

#### Duration

180 days

### Prior – Approval Renewal Limits

#### Quantity

<table>
<thead>
<tr>
<th>Drug Formulation</th>
<th>Immediate Release (IR)</th>
<th>Oxycodone 20mg/ml (IR)</th>
<th>Oxycodone 1mg/ml (IR)</th>
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</thead>
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<tr>
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<td></td>
</tr>
</tbody>
</table>

#### Duration

180 days

### Rationale

**Summary**

Oxycodone hydrochloride is used in the treatment of moderate to severe pain. OxyContin is used for continuous around the clock pain relief, and oxycodone is used for immediate as needed pain relief. Both formulations have the potential for developing substance abuse and addiction. It is necessary to monitor the patient for these behaviors. Patients should be assessed for their risk of developing substance abuse prior to being prescribed oxycodone. They should be routinely monitored for signs of misuse, abuse and addiction during therapy (1-5).
Prior approval is required to ensure the safe, clinically appropriate and cost effective use of oxycodone while maintaining optimal therapeutic outcomes.

References
3. Oxycodone HCl oral solution (oxycodone) [prescribing information]. Greenville, NC: Mayne Pharma; August 2015.

Policy History

<table>
<thead>
<tr>
<th>Date</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>October 2013</td>
<td>Addition to PA</td>
</tr>
</tbody>
</table>
| June 2014   | Annual editorial review and reference update  
Addition of the verbiage “opioid” to the immediate release analgesic example in criteria per PMPC.                                                                                   |
| February 2015 | Addition of oxycodone solution                                                                                                                                                                        |
| June 2015   | Annual editorial review and reference update                                                                                                                                                            |
| March 2016  | Annual editorial review and reference update  
Addition of no dual therapy with other long acting opioid analgesic(s) and Opioid naïve patient must have been on a previous oxycodone IR therapy for at least 10 days in the last 90 days  
Policy number changed from 5.02.25 to 5.70.25                                                                                                                                                            |
| May 2016    | Addition of Xtampza ER and prescriber agrees to assess the benefits of pain control (i.e. Care Plan signs of abuse, severity of pain) after 3 months of therapy; prescriber agrees to assess patient for serotonin syndrome; no dual therapy with the following anti-anxiety benzodiazepine(s): alprazolam (Xanax), clonazepam (Klonopin), diazepam (Valium), lorazepam (Ativan), oxazepam (Serax), chlordiazepoxide (Librium), Clorazepate dipotassium (Tranxene), Also addition of no dual therapy with other immediate release opioid analgesic(s). Removal of data questions |
This policy was approved by the FEP® Pharmacy and Medical Policy Committee on September 15, 2017 and is effective on October 1, 2017.
### Appendix 1 - List of Serotonergic Medications

**Selective Serotonin Reuptake Inhibitors (SSRIs)**

<table>
<thead>
<tr>
<th>Medication</th>
<th>Brand Names</th>
</tr>
</thead>
<tbody>
<tr>
<td>paroxetine</td>
<td>Paxil, Paxil CR, Pexeva, Brisdelle</td>
</tr>
<tr>
<td>fluvoxamine</td>
<td>Luvox, Luvox CR</td>
</tr>
<tr>
<td>fluoxetine</td>
<td>Prozac, Prozac Weekly, Sarafem, Selfemra, Symbyax</td>
</tr>
<tr>
<td>sertraline</td>
<td>Zoloft</td>
</tr>
<tr>
<td>citalopram</td>
<td>Celexa</td>
</tr>
<tr>
<td>escitalopram</td>
<td>Lexapro</td>
</tr>
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</table>

**Serotonin-Norepinephrine Reuptake Inhibitors (SNRIs)**

<table>
<thead>
<tr>
<th>Medication</th>
<th>Brand Names</th>
</tr>
</thead>
<tbody>
<tr>
<td>venlafaxine</td>
<td>Effexor XR</td>
</tr>
<tr>
<td>desvenlafaxine</td>
<td>Pristiq, Khedezla</td>
</tr>
<tr>
<td>duloxetine</td>
<td>Cymbalta</td>
</tr>
<tr>
<td>milnacipran</td>
<td>Savella</td>
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</table>

**Tricyclic Antidepressants (TCAs)**

<table>
<thead>
<tr>
<th>Medication</th>
<th>Brand Names</th>
</tr>
</thead>
<tbody>
<tr>
<td>amitriptyline</td>
<td>No brand name currently marketed</td>
</tr>
<tr>
<td>desipramine</td>
<td>Norpramin</td>
</tr>
<tr>
<td>clomipramine</td>
<td>Anafranil</td>
</tr>
<tr>
<td>imipramine</td>
<td>Tofranil, Tofranil PM</td>
</tr>
<tr>
<td>nortriptyline</td>
<td>Pamelor, Aventyl</td>
</tr>
<tr>
<td>protriptyline</td>
<td>Vivactil</td>
</tr>
<tr>
<td>doxepin</td>
<td>Zonalon, Silenor</td>
</tr>
<tr>
<td>trimipramine</td>
<td>Surmontil</td>
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</table>

**Monoamine Oxidase Inhibitors (MAOIs)**

<table>
<thead>
<tr>
<th>Medication</th>
<th>Brand Names</th>
</tr>
</thead>
<tbody>
<tr>
<td>isocarboxazid</td>
<td>Marplan</td>
</tr>
<tr>
<td>phenelzine</td>
<td>Nardil</td>
</tr>
<tr>
<td>selegiline</td>
<td>Emsam, Eldepryl, Zelapar</td>
</tr>
<tr>
<td>tranylcypromine</td>
<td>Parnate</td>
</tr>
</tbody>
</table>
### Other Psychiatric Medicines

<table>
<thead>
<tr>
<th>Medication</th>
<th>Brand Names</th>
</tr>
</thead>
<tbody>
<tr>
<td>amoxapine</td>
<td>No brand name currently marketed</td>
</tr>
<tr>
<td>maprotiline</td>
<td>No brand name currently marketed</td>
</tr>
<tr>
<td>nefazodone</td>
<td>No brand name currently marketed</td>
</tr>
<tr>
<td>trazodone</td>
<td>Oleptro</td>
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<tr>
<td>buspirone</td>
<td>No brand name currently marketed</td>
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<tr>
<td>vilazodone</td>
<td>Viibryd</td>
</tr>
<tr>
<td>mirtazapine</td>
<td>Remeron, Remeron Soltab</td>
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<tr>
<td>lithium</td>
<td>Lithobid</td>
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### Migraine Medicines

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<tr>
<th>Medication</th>
<th>Brand Names</th>
</tr>
</thead>
<tbody>
<tr>
<td>almotriptan</td>
<td>Axert</td>
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<tr>
<td>frovatriptan</td>
<td>Frova</td>
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<tr>
<td>naratriptan</td>
<td>Amerge</td>
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<tr>
<td>rizatriptan</td>
<td>Maxalt, Maxalt-MLT</td>
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<tr>
<td>sumatriptan</td>
<td>Imitrex, Imitrex Statdose, Alsuma, Sumavel Dosepro, Zecuity, Treximet</td>
</tr>
<tr>
<td>zolmitriptan</td>
<td>Zomig, Zomig-ZMT</td>
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### Antiemetics

<table>
<thead>
<tr>
<th>Medication</th>
<th>Brand Names</th>
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<tbody>
<tr>
<td>ondansetron</td>
<td>Zofran, Zofran ODT, Zuplenz</td>
</tr>
<tr>
<td>granisetron</td>
<td>Kytril, Sancuso</td>
</tr>
<tr>
<td>dolasetron</td>
<td>Anzemet</td>
</tr>
<tr>
<td>palonosetron</td>
<td>Aloxi</td>
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</table>

### Other Serotonergic Medicines

<table>
<thead>
<tr>
<th>Medication</th>
<th>Brand Names</th>
</tr>
</thead>
<tbody>
<tr>
<td>dextromethorphan</td>
<td>Bromfed-DM, Delsym, Mucinex DM, Nuedexta</td>
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<tr>
<td>linezolid</td>
<td>Zyvox</td>
</tr>
<tr>
<td>cyclobenzaprine</td>
<td>Amrix</td>
</tr>
<tr>
<td>methylene blue</td>
<td></td>
</tr>
<tr>
<td>St. John's wort</td>
<td></td>
</tr>
<tr>
<td>tryptophan</td>
<td></td>
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</table>