Opioid Therapy Management includes criteria for ALL of the following:

- Immediate-release opioid analgesic (refer to Appendix 1 for products)
- Extended-release opioid analgesic (refer to Appendix 2 for products)
- Opioid analgesic morphine milligram equivalent risk assessment

Note: The Center for Disease Control and Prevention (CDC), recommends healthcare professionals consider naloxone education and provision when factors that increase risk for opioid overdose, such as history of overdose, history of substance use disorder, opioid dosages equal to or greater than 50 morphine milligram equivalents per day, or concurrent benzodiazepine use, are present. (refer to the Pharmacy Prior Authorization - (1407) coverage policy for specific criteria)

Note: Individuals with a documented diagnosis of active cancer treatment (defined as receiving antineoplastic or antitumor therapy) requiring treatment for cancer-related pain, end-of-life care (including hospice or palliative care), sickle cell disease, or receiving medication-assisted treatment for opioid addiction (methadone only) are exempt from these criteria except where request is for a non-preferred brand or a drug not covered.

Cigna covers immediate-release opioid analgesics exceeding a 7 day supply in an opioid naïve individual when ONE of the following criteria are documented:

- For the management of acute pain (for example, pain lasting less than 90 days) when the following criteria are documented
  - Attestation that an initial treatment regimen exceeding 7 days is medically necessary (for example, the individual is not a candidate for less than 7 days of therapy)
• For the management chronic pain (for example, pain lasting more than 90 days) when ALL of the following criteria are documented:
  o Failure / inadequate response, contraindication per FDA label, intolerance or not a candidate for nonopioid pharmacologic therapies intended to treat pain
  o Attestation that opioids will be prescribed in accordance with current clinical practice guidelines AND that an assessment of risks, harms, and goals consistent with an opioid agreement (or similar agreement) has been undertaken
• For Levorphanol or Roxicodone only: In addition to the criteria detailed above, Levorphanol and Roxicodone will only be covered when there is a documented contraindication per FDA label, intolerance, or not a candidate for FIVE of the following short acting narcotics: hydromorphone, morphine, oxycodone, oxymorphone, hydrocodone / acetaminophen, oxycodone/acetaminophen

Cigna covers extended-release opioid analgesics when ALL of the following criteria are documented:
• ALL of the following:
  o Diagnosis of pain severe enough to require daily, around-the-clock, long-term opioid treatment
  o Failure / inadequate response, contraindication per FDA label, intolerance, or not a candidate for a minimum one week trial of immediate-release opioids
  o Opioid therapy management agreement signed by BOTH the individual and prescribing clinician
• For methadone and fentanyl transdermal patches only, ALL of the following are met:
  o Prescriber of therapy is (or prescribed in coordination with) a board certified pain management specialist.
  o Individual is opioid tolerant (required daily dosage for pain management exceeds 60 morphine milligram equivalents (MME)
  o Alternative treatment options are ineffective, not tolerated, or would be otherwise inadequate to provide sufficient management of pain
• Requests for a non-preferred brand or a drug not covered (unless approved under medical necessity review) will require a documentation of ONE of the following:
  o Failure, contraindication per FDA label or intolerance to ALL preferred brands as shown below
  o Established therapy for an individual in hospice or end of life care

Extended-release opioid analgesic products:

<table>
<thead>
<tr>
<th>Preferred Brands</th>
<th>Non-preferred Brands or Drugs Not Covered**</th>
</tr>
</thead>
<tbody>
<tr>
<td>Embeda®</td>
<td>Arymo™ ER</td>
</tr>
<tr>
<td>Hysingla® ER</td>
<td>Exalgo® (brand only)</td>
</tr>
<tr>
<td>Xtampza® ER</td>
<td>Kadian® (brand only)</td>
</tr>
<tr>
<td></td>
<td>**Levorphanol</td>
</tr>
<tr>
<td></td>
<td>Morphabond ER™</td>
</tr>
<tr>
<td></td>
<td>MS Contin® (brand only)</td>
</tr>
<tr>
<td></td>
<td>Nucynta ER®</td>
</tr>
<tr>
<td></td>
<td>Opana ER® (brand only)</td>
</tr>
<tr>
<td></td>
<td>**Oxycontin®</td>
</tr>
<tr>
<td></td>
<td>Zohydro® ER</td>
</tr>
</tbody>
</table>

(Note: hydromorphone ER, methadone, morphine ER, and oxymorphone ER are available generically)

Note: Receipt of sample product does not satisfy any criteria requirements for coverage

**Employer group plans may adopt a Prescription Drug List that does not cover certain drugs or biologics unless those products are approved based on a medical necessity review.

Cigna covers opioid analgesics when the daily dose of all opioid analgesics exceed 120 morphine milligram equivalents (120 MME) when ALL of the following criteria are documented
• Quarterly reassessment of opioid therapy benefits and risks specific to the individuals diagnosis and treatment goals
• Consideration of additional precautions intended to reduce the risk of serious harm associated with high dose opioids (for example, education and provision of naloxone)
• Prescriber of therapy is (or prescribed in coordination with) a board certified pain management specialist.
Cigna covers opioid analgesics when the daily dose of all opioid analgesics exceed 200 morphine milligram equivalents (200 MME) when ALL of the following criteria are documented

- Quarterly reassessment of opioid therapy benefits and risks specific to the individuals diagnosis and treatment goals
- Consideration of additional precautions intended to reduce the risk of serious harm associated with high dose opioids (for example, education and provision of naloxone)
- Prescriber of therapy is (or prescribed in coordination with) a board certified pain management specialist
- The provider has performed an individualized behavioral health screening to assess the risks and benefits of the opioid dose (for example, PHQ-9, GAD-7, PC-PTSD)
- The provider has screened for substance abuse risk to assess the risks and benefits of the opioid dose (for example, DIRE, ORT, PDUQ, PMQ)

Note: Resources for calculating morphine milligram equivalents can be found in the Appendix 3.

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to Opioid Therapy Management.

Note: Receipt of sample product does not satisfy any criteria requirements for coverage

### FDA Indication Summary

<table>
<thead>
<tr>
<th>Therapeutic Category</th>
<th>FDA Indication Summary</th>
</tr>
</thead>
</table>
| Immediate-release opioid analgesics | For product specific indications, please refer to the corresponding FDA product label. In general, immediate-release opioid analgesics are 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 reserve for use in patients for whom alternative treatment options [e.g., nonopioid 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 |
| Extended-release opioid analgesics | For product specific indications, please refer to the corresponding FDA product label. In general, extended-release opioid analgesics 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. 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 extended-release opioids 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. Extended-release opioids are not indicated as an as-needed (prn) analgesic |

### FDA Dosing Summary

<table>
<thead>
<tr>
<th>Therapeutic Category</th>
<th>FDA Dosing Summary</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Immediate-release opioid analgesics

For product specific dosing, please refer to the corresponding FDA product label.

In general, immediate-release opioid analgesics share the following statements from the dosing section of their prescribing information:

Use the lowest effective dosage for the shortest duration consistent with individual patient treatment goals.

Initiate the dosing regimen for each patient individually, taking into account the patient’s severity of pain, patient response, prior analgesic treatment experience, and risk factors for addiction, abuse, and misuse.

Monitor patients closely for respiratory depression, especially within the first 24-72 hours of initiating therapy and following dosage increases and adjust the dosage accordingly.

Extended-release opioid analgesics

For product specific dosing, please refer to the corresponding FDA product label.

In general, extended-release opioid analgesics share the following statements from the dosing section of their prescribing information:

Extended-release opioids should be prescribed only by healthcare professionals who are knowledgeable in the use of potent opioids for the management of chronic pain.

High dose opioid analgesics are only for use in patients in whom tolerance to an opioid of comparable potency has been established. 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, 60 mg oral hydrocodone per day, or an equianalgesic dose of another opioid.

• Use the lowest effective dosage for the shortest duration consistent with individual patient treatment goals.
• Initiate the dosing regimen for each patient individually, taking into account the patient’s severity of pain, patient response, prior analgesic treatment experience, and risk factors for addiction, abuse, and misuse.
• Monitor patients closely for respiratory depression, especially within the first 24-72 hours of initiating therapy and following dosage increases and adjust the dosage accordingly.

Other FDA Information
On June 8, 2017, the FDA announced its request for the manufacturer of Opana ER (oxymorphone hydrochloride) to voluntarily remove the product from the market. The request is based on concerns that the benefits of the drug no longer outweigh the risks. In 2012 Opana ER was reformulated with the intent of reducing abuse. While the reformulated product met regulatory standards for approval, it did not meet the FDA’s standards to include labeling describing potentially abuse-deterrent properties. The FDA notes that an outbreak of HIV and hepatitis C and thrombotic microangiopathy have been associated with injection abuse of Opana ER. (FDA, 2017)

General Background Guidelines

• Center for Disease Control and Prevention (CDC)
In 2016 the Centers for Disease Control and Prevention (CDC) published clinical guidelines titled Prescribing Opioids for Chronic Pain. The guideline recommendations are largely addressed to primary care clinicians who prescribe opioids in an outpatient setting for conditions unrelated to active cancer treatment, palliative care, and end-of-life care. The scope of this coverage policy similarly excludes these diagnoses, as well as sickle cell disease, due to the complex nature of pain management in these conditions. For more information pertaining to pain management in these conditions please refer to the following resources: for cancer related pain
management refer to the National Comprehensive Cancer Network Clinical Practice Guidelines, for palliative and end-of-life care please refer to the American Family Physician or National Institutes of Health, for pain management related to sickle cell disease refer to the National Heart, Lung, and Blood Institute division of the National Institutes of Health.

The guidelines provide statistical information related to the utilization of opioid medications for the treatment of pain in the United States. In 2012, a total of 259 million prescriptions for opioid analgesics were written, a 7% increase per person since 2007. As the numbers of opioid prescriptions have increased, so have the individual and societal consequences. In 2013, approximately 1.9 million individuals met diagnostic criteria for having abused or being dependent on prescription opioid medications. More than 165,000 individuals died from an overdose involving a prescription opioid in the United States from 1999 to 2014. Opioids are increasingly relied upon for pain management however many other treatment modalities exist. (Dowell, 2016)

For the treatment of chronic pain (defined by the guideline as pain that typically lasts greater than 3 months or past the time of normal tissue healing), a preference is given to nonpharmacologic and nonopioid pharmacologic therapy. Several nonpharmacologic therapies (including physical therapy, multidisciplinary biopsychosocial rehabilitation, and weight loss) are identified as being beneficial for a number of pain sources including osteoarthritis, low back pain, and fibromyalgia. For individuals whose pain persists despite the use of nonpharmacologic therapies, several specific nonopioid pharmacologic medications are available. Based on individual characteristics and diagnoses, the guidelines recognize non-steroidal anti-inflammatory drugs, acetaminophen, and select antidepressants and anticonvulsants as first line agents for many common sources of pain. Nonopioid therapies have proven efficacy and are associated with less severe risks than opioid therapies. (Dowell, 2016)

Opioids are associated with significant risks necessitating their judicious use. In addition to common adverse events, opioids are associated with severe risks including dependence, addiction, respiratory depression, overdose, and death. The CDC guidelines offer multiple strategies intended to mitigate the risks associated with opioid therapy. They recommend treating pain at the lowest possible dose and only for the expected duration of the pain. The guidelines state most cases of acute pain requiring opioids will rarely require treatment longer than seven days and should be treated with immediate-release opioids. (Dowell, 2016)

The risk of overdose and death can be reduced by avoiding dose escalations. Doses greater than fifty morphine milligram equivalents (50 MME) per day have been associated with at least a two time increase in the risk of overdose and have not shown to be more efficacious in reducing pain or restoring function. The guidelines recommend clinicians incorporate into the management plan strategies to mitigate risk, including considering offering naloxone when factors that increase risk for opioid overdose, such as history of overdose, history of substance use disorder, higher opioid dosages (≥50 MME/day), or concurrent benzodiazepine use, are present. A tool to assist with calculating morphine milligram equivalent dosages can be found in Appendix 3. When doses exceed 50 MME the guidelines recommend implementing additional precautions including providing educational resources for individuals and household members intended to reduce the risk of overdose, prescribing naloxone, and increasing the frequency of appointments. (Dowell, 2016)

The guidelines advocate for frequent appointments for all individuals on opioid therapy. Benefits and risks of therapy should be discussed at least every three months. Shorter intervals, or more frequent appointments, should occur in the presence of dose adjustments or when doses exceed 50 MME per day. Clinicians are recommended to communicate all expectations of therapy, including responsibilities of both the prescriber and patient, to the individual. (Dowell, 2016) A commonly used tool to aid in this communication is a medication use agreement.

In addition to overall guidance regarding opioid therapy, the CDC guidelines also make recommendations for opioid selection. It is recommended to initiate opioid therapy with an immediate-release opioid for a minimum one week trial. Initiating opioid therapy with an extended-release opioid is associated with greater risks of overdose. Additionally, specific concerns regarding methadone and fentanyl are acknowledged by the guidelines. It is stated that methadone should not be the first choice for an extended-release opioid in pain management due to risks of overdose and QT prolongation. Fentanyl is also specifically recognized as a complex extended-release opioid due to dosing, absorption, and pharmacodynamics factors. (Dowell, 2016)
The use of a behavioral health evaluation and substance abuse risk screening, to assess risks and benefits of opioid therapy, is supported by guidelines from several professional organizations. The American Academy of Neurology (AAN) lists screening for past and current substance abuse and for severe depression, anxiety, and posttraumatic stress disorder prior to initiation of chronic opioid analgesic therapy as a most crucial best practice. (Franklin, 2014) The American Pain Society (APS) and American Academy of Pain Medicine (AAPM) state that prior to initiating chronic opioid therapy, clinicians should conduct a history, physical examination and appropriate testing, including an assessment of risk of substance abuse, misuse, or addiction. (Chou, 2009) The American Society of Interventional Pain Physicians (ASIPP) guidelines recommend establishing an appropriate physical diagnosis and psychological diagnosis if available prior to initiating opioid therapy, and to screen for opioid abuse. (Manchikanti, 2017) The Oregon Pain Guidance Group recommends a psychosocial and risk assessment, to assess the risk of medication abuse, psychiatric co-morbidity (for example, depression, bipolar disorder, ADD and PSTD) as part of the initial patient assessment. (Shames, 2014) The Utah Department of Health states the provider should screen for risk of abuse or addiction before initiating chronic opioid treatment. (Utah, 2009) The Washington State Agency Medical Directors’ Group state to screen for depression using the Patient Health Questionnaire (PHQ-9) and for anxiety using the Generalized Anxiety Disorder 7-item (GAD-7) or other validated tools. Administer the 4-item Primary Care PTSD Screen (PC-PTSD) screen or other validated tools if the patient’s history suggests PTSD, or if PHQ-9 or GAD-7 remains elevated after treatment. And, to screen for opioid misuse risk using the Opioid Risk Tool, Screener and Opioid Assessment for Patients with Pain-Revised (SOAPP-R), the Diagnosis, Intractability, Risk, Efficacy (DIRE), CAGE-AID or other validated tools. (Washington, 2015)

Other organizations, such as the American College of Occupational and Environmental Medicine (Hegmann, 2014) and the Centers for Disease Control and Prevention (Dowell, 2016), are silent on the use of behavioral health screenings with opioid therapy.

Medication Use Agreements
A medication use agreement is a tool used by clinicians to clearly communicate roles and responsibilities of the individual patient and prescribing clinician in relation to controlled substance prescriptions. The agreement outlines clinician expectations of the patient including circumstances of treatment discontinuation. Several national organizations, including National Institutes of Health and American Academy of Family Physicians, have published such agreements and allow for their use by prescribing clinicians.

- The National Institute on Drug Abuse division of the National Institutes of Health provides two sample medication use agreement forms for public use. One form provided by the National Institute on Drug Abuse is adapted from the American Academy of Pain Medicine. Both medication use agreements can be found online at the following URL or by following the provided web navigation.
    - www.nih.gov > Institutes at NIH > NIDA > Medical & Health Professionals > Other Opioid Prescribing Resources > Sample Patient Agreement Forms
- The American Academy of Family Physicians has also published a medication use agreement for public use. The medication use agreement can be found online at the following URL or by following the provided web navigation.
    - www.aafp.org > Family Practice Management > Toolbox > Patient Handouts > Medication Use Agreement

Appendix 1
Immediate-release opioid analgesics include the following:

<table>
<thead>
<tr>
<th>Immediate-release opioid analgesics</th>
<th>Brand Names</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetaminophen/codeine tablet</td>
<td></td>
</tr>
<tr>
<td>Butalbital/acetaminophen/caffeine/ codeine</td>
<td></td>
</tr>
<tr>
<td>Butalbital/aspirin/caffeine/codeine</td>
<td></td>
</tr>
<tr>
<td>Butorphanol tartrate spray</td>
<td></td>
</tr>
<tr>
<td>Codeine sulfate tablets and solution</td>
<td></td>
</tr>
<tr>
<td>Codeine/carisoprodol/aspirin</td>
<td></td>
</tr>
<tr>
<td>Dihydrocodeine/acetaminophen/caffeine; Trezix™</td>
<td></td>
</tr>
<tr>
<td>Dihydrocodeine/aspirin/caffeine</td>
<td></td>
</tr>
<tr>
<td>Hydrocodone/acetaminophen; Lorcet® HD, Lortab®, Stagesic-10, Zamicet®, Zydone®</td>
<td></td>
</tr>
<tr>
<td>Hydrocodone/ibuprofen; Reprexain™</td>
<td></td>
</tr>
<tr>
<td>Hydromorphone tablets, solution, suppositories</td>
<td></td>
</tr>
</tbody>
</table>
Levorphanol tablets
Meperidine tablets and solution
Morphine sulfate tablets, solution, suppositories
Nucynta® (tapentadol)
Opium Tincture
Opium/Belladonna alkaloids (Belladonna-Opium)
Oxycodone hydrochloride tablets, capsules, solution; Oxecta™
Oxycodone/acetaminophen; Magnacet®; Primlev™; Roxicet™; Xolox
Oxycodone/aspirin
Oxycodone/ibuprofen
Oxymorphone tablets; Numorphan® suppository
Pentazocine/acetaminophen
Pentazocine/naloxone
Roxicodone tablets

Appendix 2
Extended-release opioid analgesics include the following:
Arymo™ ER (morphine sulfate)
Avinza® (morphine sulfate)
Embeda® (morphine sulfate)
Exalgo® (hydromorphone hydrochloride)
Fentanyl patches
Hysingla™ ER (hydrocodone bitartrate)
Kadian® (morphine sulfate)
Levorphanol tablets
Morphabond ER™ (morphine sulfate)
Morphine sulfate ER capsules; MS Contin®
Nucynta® ER (tapentadol)
Opana® ER (oxymorphone hydrochloride)
Oxycodone hydrochloride ER tablets
Oxycontin® (oxycodone HCl)
Oxymorphone hydrochloride ER tablets
Xtampza® ER (oxycodone myristate)
Zohydro® ER (hydrocodone bitartrate)

Appendix 3
Morphine Milligram Equivalent (MME) Dose Calculation
A commonly used method to compare opioid analgesic doses is to calculate its dose in terms of morphine milligram equivalents. To calculate the morphine milligram equivalent (MME) dose one starts by adding the total daily milligram amount of each opioid an individual takes. Next, each opioid total dose should be converted to a morphine milligram equivalent by multiplying the total dose by the conversion factor associated with the identity of the patients’ opioid. The conversion factors are shown in the table below. Once all opioid doses have been converted to a morphine milligram equivalent dose, they should be added together to calculate a total MME dose per day. It is important to note that this calculation should only be used as an approximation for comparative purposes. If using a similar conversion to switch an individual to a different opioid, a dose reduction must be made to account for incomplete tolerance and prevent an overdose.

<table>
<thead>
<tr>
<th>Opioid</th>
<th>Conversion Factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Codeine</td>
<td>0.15</td>
</tr>
<tr>
<td>Fentanyl (transdermal) in mcg / hr</td>
<td>2.4</td>
</tr>
<tr>
<td>Hydrocodone</td>
<td>1</td>
</tr>
<tr>
<td>Hydromorphone</td>
<td>4</td>
</tr>
<tr>
<td>Methadone</td>
<td>4</td>
</tr>
<tr>
<td>1 – 20 mg / day</td>
<td></td>
</tr>
<tr>
<td>Dosage Range</td>
<td>Conversion Factor</td>
</tr>
<tr>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>21 – 40 mg / day</td>
<td>8</td>
</tr>
<tr>
<td>41 – 60 mg / day</td>
<td>10</td>
</tr>
<tr>
<td>≥ 61 – 80 mg / day</td>
<td>12</td>
</tr>
<tr>
<td>Morphine</td>
<td>1</td>
</tr>
<tr>
<td>Oxycodone Hydrochloride</td>
<td>1.5</td>
</tr>
<tr>
<td>Oxycodone Myristate (Xtampza ER)</td>
<td>1.67</td>
</tr>
<tr>
<td>Oxymorphone</td>
<td>3</td>
</tr>
<tr>
<td>Tapentadol</td>
<td>0.4</td>
</tr>
</tbody>
</table>

**Source:** Adapted from CDC Guideline for Prescribing Opioids for Chronic Pain

Example: An individual is using 20 mg of extended-release oxycodone twice daily and 5 mg / 300 mg of immediate-release hydrocodone / acetaminophen three times daily.

1. **Calculate the total daily dose of each opioid**
   a. 20 mg oxycodone twice daily = 40 mg oxycodone
   b. 5 mg hydrocodone three times daily = 15 mg hydrocodone

2. **Convert to a morphine milligram equivalent dose by multiplying the total daily dose of each opioid by the conversion factor**
   a. 40 mg oxycodone x 1.5 = 60 morphine milligram equivalents
   b. 15 mg hydrocodone x 1 = 15 morphine milligram equivalents

3. **Add the morphine milligram equivalent doses to calculate the total morphine milligram equivalent dose per day**
   a. 60 + 15 = 75 morphine milligram equivalents per day

**Coding/Billing Information**

Note: Opioid Therapy Management is typically covered under pharmacy benefit plans. Certain prescription drugs require an authorization for coverage to ensure that appropriate treatment regimens are followed. Medical drug coding and diagnosis codes, however, are generally not required for pharmacy claims submissions, therefore, this section is not in use.

**References**