Oxycodone Tablets SA 12 Hour C-II
Criteria for Use
November, 2017

VA Pharmacy Benefits Management Services, Medical Advisory Panel, and VISN Pharmacist Executives

The following recommendations are based on medical evidence, clinician input, and expert opinion. The content of the document is dynamic and will be revised as new information becomes available. The purpose of this document is to assist practitioners in clinical decision-making, to standardize and improve the quality of patient care, and to promote cost-effective drug prescribing. **THE CLINICIAN SHOULD UTILIZE THIS GUIDANCE AND INTERPRET IT IN THE CLINICAL CONTEXT OF THE INDIVIDUAL PATIENT. INDIVIDUAL CASES THAT ARE EXCEPTIONS TO THE EXCLUSION AND INCLUSION CRITERIA SHOULD BE ADJUDICATED AT THE LOCAL FACILITY ACCORDING TO THE POLICY AND PROCEDURES OF ITS P&T COMMITTEE AND PHARMACY SERVICES.**

The Product Information should be consulted for detailed prescribing information.

Transitioning Veteran *Oxycodone SA is on the DoD VHA Transitional Continuity of Care Drug List; if the criterion is met, the remainder of the criteria for use is not applicable.*

☐ Veteran is transitioning care from the Department of Defense to VHA. A VA prescriber, after assessing and consulting with the Veteran, has determined that continuation of oxycodone SA tablets is safe and clinically appropriate.

Exclusion Criteria *If the answer to ANY item below is met, then the patient should NOT receive oxycodone SA:*

☐ Intended use is for treatment of mild pain
☐ Intended use is for treatment of acute pain
☐ Intended use is for postoperative pain (may be appropriate if patient is already receiving the drug prior to surgery or if the postoperative pain is expected to be moderate to severe and persist for an extended period of time)
☐ Intended use is as an as-needed (prn) analgesic
☐ Patient has significant respiratory depression, condition predisposing to significant respiratory depression such as acute or severe bronchial asthma, or known/suspected paralytic ileus
☐ Patient has hypersensitivity to oxycodone or other tablet contents
☐ Patient is unable to swallow whole tablets/requires tablets to be crushed before administration

Inclusion Criteria *The following criteria must be fulfilled for provision of oxycodone SA:*

☐ Indication is management of moderate to severe chronic pain requiring a continuous, around-the-clock opioid analgesic for an extended period of time
☐ Patient has a documented contraindication to morphine, history of intolerable medication-related adverse effects to morphine, or documentation of inadequate analgesia despite an appropriate upwards titration of morphine SA tablets.

Therapeutic Options

Methadone oral tablet is a long acting opioid alternative to oxycodone SA for management of moderate to severe pain; however, only clinicians who are familiar with methadone's unique pharmacological characteristics, appropriate titration, and risk profile, and who are prepared to educate and closely monitor their patients, should consider initiation or titration of methadone for pain. Similarly, due to safety concerns, including dosing effects of fentanyl TDS that can be easily misunderstood by both clinicians and patients, only clinicians who are familiar with the dosing and absorption properties of fentanyl TDS and are prepared to educate their patients about its use should initiate or titrate fentanyl TDS therapy.[1]

Practice Standards for Provision of Chronic Opioid Therapy

General principles, defined by CDC and VA/DoD Clinical Practice Guidelines for prescribing of opioids for chronic pain, should be utilized to guide management of long-term opioid therapy. Practitioners should obtain informed consent from each patient after explaining the risks, benefits, and obligatory terms of long term treatment with opioids. All federal and state guidelines on prescribing and dispensing opioids should be strictly followed. There should be an initial and periodic checking of the respective State(s) Prescription Drug Monitoring System (if available), consideration of provision of naloxone rescue, and exercise of other strategies to mitigate risk of chronic opioid therapy. See *Provider-Related Guidance* below.

Dosage and Administration

- Oxycodone SA is available in the following strengths: 10, 15, 20, 30, 40, 60, 80, 160mg
- **Opioid naïve patients:** The use of low-dose short-acting as-needed opioids is recommended as a means to establish tolerance/efficacy and as a dose finding method *prior* to the initiation of long-acting opioid therapy.
- **Opioid tolerant patients:**
    - 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, or an equianalgesic dose of another opioid.
    - Patients who are already taking other opioids but who cannot tolerate those agents may have their previous opioid dose converted to the equivalent of oral oxycodone using standard equianalgesic dosage estimates such as those suggested by the 2016 CDC Opioid Prescribing Guidelines (adapted, see Table next page).[1] Practitioners can also

use a 'feature-rich' online opioid dosing calculator as a double-check to avoid mathematical errors and to improve confidence in the dose of the conversion-to drug.

Morphine Milligram Equivalent Doses (MME)[1]		All doses in mg/d except for fentanyl. Multiply the daily dosage for each opioid by the conversion factor to determine the equianalgesic dose in MME. Equianalgesic dose conversions are only estimates and cannot account for individual variability in genetics and pharmacokinetics. **Do not use the calculated dose in morphine milligram equivalents (MME) to determine the doses to use when converting one opioid to another.** When converting opioids, the new opioid is typically dosed at substantially lower than the calculated MME dose (33 to 50% less) to avoid accidental overdose due to incomplete cross-tolerance and individual variability in opioid pharmacokinetics. Use particular caution with fentanyl because it is dosed in µg/h instead of mg/d, and absorption is affected by heat and other factors.
Opioid Agent	**Conversion Factor**	
Codeine	0.15	
Tapentadol	0.4	
Morphine	1	
Hydrocodone	1	
Oxycodone	**1.5**	
Fentanyl TD, µg/h	2.4	
Oxymorphone	3	
Hydromorphone	4	
Methadone	Consult with provider with detailed knowledge of methadone pharmacology and expertise in dosing	

- Conversion from fentanyl TDS: Initiate treatment with oxycodone SA 18 hours after removal of the transdermal fentanyl patch. A conservative oxycodone dose, approximately 10 mg every 12 hours of oxycodone SA, should be initially substituted for each 25 mcg/hr of fentanyl TDS.
- Conversion from methadone: There is no widely accepted conversion strategy for switching from methadone to another opioid. It is recommended that a clinician with expertise in methadone dosing be consulted in converting methadone to an alternate opioid [see the VA PBM-MAP-VPE document *Oral Methadone Dosing Recommendations for the Treatment of Chronic Pain*].
- When titrating opioids or converting between drug formulations or opioid agents, dosing requirements should be monitored and individualized to patient response. Lower initial doses may be indicated in special patient populations (age > 65, hepatic impaired, renal impaired, and in patients taking other CNS depressants). Patients should be followed closely during the conversion and dose titration process.
- When converting to oxycodone SA, rescue doses of oxycodone IR or other short-acting analgesic, either alone or in combination with acetaminophen, aspirin, or NSAIDs, may be given for breakthrough pain as needed or about 1 h before anticipated incident pain. The dose of supplemental oxycodone IR may be about one fourth to one third of the 12-h dose of oxycodone SA.
- Co-therapy using a long-duration opioid and a nonopioid analgesic (acetaminophen or nonsteroidal anti-inflammatory drug [NSAID]) should be considered for opioid-sparing effects or additive analgesia.

Safety

- The adverse effect profile of oxycodone SA is similar to that of morphine SA and other opioid analgesics in the management of patients with moderate to severe pain; oxycodone SA does not offer any consistent advantages over morphine SA in terms of safety or tolerability. Serious adverse reactions include respiratory depression, apnea, respiratory arrest, circulatory depression, hypotension, or shock. Non-serious adverse events are typically seen on initiation of therapy and decrease over time; they include commonly encountered opioid side effects such as constipation, nausea, and somnolence.
- Oxycodone SA potential to cause hypotensive effects warrants monitoring of blood pressure during dose initiation and titration.
- Avoid use of oxycodone in patients with impaired consciousness or coma, head injury or increased intracranial pressure, as the respiratory depressant effects of the drug may be magnified in these clinical scenarios.
- Initiating or discontinuing CYP3A4 inducers may result in alteration of oxycodone plasma concentrations
- Oxycodone is Pregnancy Category B; as there are no adequate and well-controlled studies in pregnant women the drug should be used during pregnancy only if clearly indicated. Use of opioids during pregnancy can prolong labor and result in respiratory depression, physical dependence and withdrawal syndrome in the neonate.
- Oxycodone is excreted in breast milk and opioid withdrawal symptoms can occur in infants when mothers discontinue oxycodone therapy. Discontinue nursing or discontinue the drug while nursing because of the possibility of sedation or respiratory depression in the infant.
- Similar to extended-release morphine products, oxycodone SA tablets cannot be crushed for patients who have difficulty swallowing or require administration of medications through nasogastric or gastrostomy tubes; crushing the SA tablet results in immediate release of the full dose of oxycodone, which may lead to a potentially fatal overdose.
- Abuse of the crushed tablets poses a hazard of overdose and death. This risk is increased with concurrent abuse of alcohol and other substances. With parenteral abuse, the tablet excipients, especially talc, can be expected to result in local tissue necrosis, infection, pulmonary granulomas, and increased risk of endocarditis and valvular heart injury.

- The concomitant use of oxycodone with other central nervous system depressants, including but not limited to other opioids, sedatives, hypnotics, tranquilizers (e.g., benzodiazepines), general anesthetics, phenothiazines, skeletal muscle relaxants, and alcohol, may cause respiratory depression, hypotension, and profound sedation or potentially result in coma. The VA/DOD Clinical Practice Guideline on the Management of Opioid Therapy (OT) for Chronic Pain (2017) https://www.healthquality.va.gov/, recommends against the concurrent use of opioids and benzodiazepines. When such combined therapy is contemplated, consider tapering one or both when risks exceed benefits and obtaining specialty consultation.

Provider-Related Guidance

Implement Risk Mitigation Strategies. Ensure risk mitigation strategies are in place when starting oxycodone SA per the VA/DOD Clinical Practice Guideline on the Management of Opioid Therapy (OT) for Chronic Pain (2017) https://www.healthquality.va.gov/, These strategies include an informed consent conversation covering the risks and benefits of opioid therapy as well as alternative therapies. Other strategies and their frequency should be commensurate with risk factors and include:

- Ongoing, random urine drug testing (including appropriate confirmatory testing)
- Checking state prescription drug monitoring programs
- Monitoring for overdose potential and suicidality
- Providing overdose education
- Prescribing of naloxone rescue and accompanying education

Opioid Initiation/continuation. The VA/DOD Clinical Practice Guideline on the Management of Opioid Therapy (OT) for Chronic Pain (2017) https://www.healthquality.va.gov/, recommends against initiating long-term opioid therapy for chronic pain. For patients already on long-term opioid therapy, the guidelines recommend ongoing risk mitigation strategies, assessment for opioid use disorder, and consideration for tapering when risks exceed benefits.

Opioid Tapering Guidance. If a decision is made to taper the patient off opioids, ensure screening and treatment is offered for conditions that can complicate pain management before initiating an opioid taper. These include mental health disorders (PTSD, anxiety, depression), opioid use disorder (OUD) and other substance use disorders (SUD), medical complications (e.g. lung disease, hepatic disease, renal disease), and sleep disorders including sleep apnea. Most commonly, tapering will involve dose reductions of 5% to 20% every 4 weeks. More specific guidance on opioid tapers is provided in the PBM Academic Detailing Service publication *Opioid Taper Decision Tool*.

Identifying and Managing Opioid Use Disorder. Aberrant behaviors may become more apparent and reveal an opioid use disorder when opioids are tapered or discontinued or as tolerance develops. DSM-5 Diagnostic Criteria for OUD include the following: craving or strong desire or urge to use opioids, tolerance, withdrawal, using a larger amount of opioids or over a longer period than originally intended, spending a lot of time to obtain, use, or recover from opioids, and continued use despite physical or psychological problems related to opioids. If an OUD is suspected, patients should receive addiction focused medical management in PACT or referral to an Interdisciplinary Pain Management Team with Addiction Medicine expertise and access to Medication-Assisted Treatment, or to Primary Care Mental Health or specialty care for evaluation and treatment of OUD/SUD. If they decline, offer treatment that can meet their needs in the setting they feel most comfortable with. Specific guidance on OUD is provided in the PBM Academic Detailing Service publication A VA Clinician's Guide to Identification and Management of Opioid Use Disorder (2016) and the VA/DOD Clinical Practice Guideline for the Management of Substance Use Disorder.

Updated: Novemver, 2017. Original version prepared June, 2016. Contact: Mitchell Nazario, PharmD, National Clinical Pharmacy Program Manager, VA Pharmacy Benefits Management Services

[1] Dowell D, Haegerich TM, Chou R. CDC Guideline for Prescribing Opioids for Chronic Pain – United States, 2016. JAMA 2016; 315: 1624-45.