Oxymorphone Tablets SA 12 Hour C-II
Criteria for Use
January, 2018

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 *Oxymorphone 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. The Veteran and a VHA health care prescriber have determined the Veteran is to continue oxymorphone SA.

Exclusion Criteria *If the answer to ANY item below is met, then the patient should NOT receive oxymorphone 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 moderate or severe hepatic impairment
☐ Patient has hypersensitivity to oxymorphone or other tablet contents
☐ Patient is unable to swallow whole tablets/requires tablets to be crushed before administration
☐ Patient has intent to consume or likelihood of consuming alcoholic beverages or prescription or non-prescription products containing alcohol while on oxymorphone SA therapy

Inclusion Criteria *The following criteria must be fulfilled for provision of oxymorphone 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, history of intolerable medication-related adverse effects (to IR or SA forms), or inadequate analgesia despite appropriate upwards titration of dosage, in separate trials of morphine SA tabs and oxycodone SA tabs.

Therapeutic Options

Methadone oral tablet is a long acting opioid alternative to oxymorphone 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 longterm 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 prvision of naloxone rescue, and exercise of other strategies to mitigate risk of chronic opioid therapy. See *Provider-Related Guidance* below.

Dosage and Administration

- Oxymorphone SA is available in the following strengths: 5, 7.5, 10, 15, 20, 30, 40mg
- Food can increase oxymorphone C_{MAX}; patients should take oxymorphone SA on an empty stomach, 1 hour before or 2 hours after eating.
- Tablets should not be wetted before placing in mouth (see *Safety*).
- Oxymorphone is contraindicated in patients with moderate or severe hepatic impairment. See *Safety* for information regarding reduced oxymorphone clearance in patients with impaired renal function.

- **Opioid naïve patients:** a reasonable initial dose of oxymorphone SA in patients who are opioid naïve is 5 mg q 12 h; use of higher starting doses in patients who are not opioid tolerant may cause fatal respiratory depression.
- **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 oxymorphone through use of standard equianalgesic dosage estimates such as those suggested by the 2016 CDC Opioid Prescribing Guidelines (adapted, see below).[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.
    - In opioid-tolerant patients with mild hepatic impairment, impaired renal function (creatinine clearance < 50 ml/min), or when age is ≥ 65 years, initiate treatment with oxymorphone at 50% lower than the usual doses and titrate slowly.
    - Steady-state plasma concentrations of oxymorphone are reached within 3 days; dosage adjustments of oxymorphone SA, preferably at increments of 5-10 mg every 12 hours, may be performed every 3 to 7 days.
- Conversion from fentanyl TDS: There are no FDA-approved dosing instructions on how to convert patients from fentanyl to oxymorphone. Treatment with oxymorphone may be initiated 18 hours after removal of the fentanyl TDS (which will allow an approximate 50% fall in serum fentanyl concentration). A conservative oxymorphone dose, 5 or 7.5 mg every 12 hours, can be initially substituted for each 25 mcg of fentanyl TDS; oxymorphone dose may then be titrated according to the patient's level of pain relief and tolerability.
- Conversion from methadone: The FDA-approved dosing instructions for oxymorphone SA contain a 0.5 conversion factor for oral methadone to oral oxymorphone (10 mg oral methadone/day ≈ 5 mg oral oxymorphone/day). It is recommended that a clinician with expertise in methadone dosing be consulted in converting methadone to an alternate opioid [also see the VA PBM-MAP-VPE document *Oral Methadone Dosing Recommendations for the Treatment of Chronic Pain*].

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	

- 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.
- When converting to oxymorphone SA, rescue doses of oxymorphone IR or other short-acting analgesic, either alone or in combination with acetaminophen, aspirin, or NSAIDs, may be administered for breakthrough pain as needed or about 1 h before anticipated incident pain.
- 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 *See Product Information for additional safety information*

- The adverse effect profile of oxymorphone SA is similar to that of morphine SA and other opioid analgesics in the management of patients with moderate to severe pain; oxymorphone 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.
- The co-ingestion of alcohol with oxymorphone SA may result in increased plasma levels and a potentially fatal overdose of oxymorphone.Patients must not consume alcoholic beverages or prescription or non-prescription products containing alcohol while on oxymorphone SA therapy.
- The concomitant use of oxymorphone SA with other CNS depressants including other opioids, sedative hypnotics, tranquilizers, general anesthetics, and phenothiazines can increase the risk of respiratory depression, profound sedation,

coma and death. When combined therapy with any of these medications is considered, the dose of one or both agents should be reduced.

- 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.
- In a study of oxymorphone SA, oxymorphone bioavailability was increased 26%, 57%, and 65% in patients with mild (CrCl 51 to 80 mL/min), moderate (CrCl 30 to 50 mL/min), and severe renal impairment (CrCl <30 mL/min), respectively, compared to healthy controls.
- Oxymorphone SA contains tablet component(s) which causes tablets to swell and become sticky when wetted. This can result in tablets sticking in the GI tract, choking, and possible GI obstruction, particularly in patients who have had a prior GI surgery or who have a structural abnormality resulting in a small gastrointestinal lumen. Patients should be instructed not to pre-soak, lick, or otherwise wet oxymorphone SA prior to placing in the mouth and to take one tablet at a time with adequate water to ensure complete swallowing immediately after placing in the mouth.
- Oxymorphone SA potential to cause hypotensive effects warrants monitoring of blood pressure during dose initiation and titration.
- Avoid use of oxymorphone 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.
- Oxymorphone is Pregnancy Category C; it should be used during pregnancy only if the potential benefit to the mother justifies the potential risk to the fetus.
- Oxymorphone should not be used in women during or immediately prior to labor; use of opioids during pregnancy can prolong labor and result in respiratory depression, physical dependence and withdrawal syndrome in the neonate.
- It is unknown whether oxymorphone is excreted in breast milk; infants who may be exposed to oxymorphone SA through breast milk should be monitored for excess sedation and respiratory depression.
- Similar to long-acting morphine products, oxymorphone 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 oxymorphone, 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.

Provider-Related Guidance

Implement Risk Mitigation Strategies. Ensure risk mitigation strategies are in place when starting oxymorphone 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: January, 2018. 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.