Oxymorphone Immediate-release (IR) Tablets C-II
Criteria for Use
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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 IR tablets are 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 oxymorphone IR tablets is safe and clinically appropriate.

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

☐ Intended use is for treatment of mild pain
☐ Patient is opioid naïve and initial single dosage is > 20mg (see *Dosage and Administration*)
☐ Patient has significant respiratory depression, condition that predisposes 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

Inclusion Criteria *The following criteria must be fulfilled for provision of oxymorphone IR:*

☐ Intended use is for treatment of moderate to severe acute pain where the use of an opioid is appropriate

AND

☐ Patient has a documented intolerance, contraindication or or lack of sufficient analgesic response to other formulary short-acting immediate-release opioids (tramadol, codeine, codeine/acetaminophen, hydrocodone/acetaminophen, oxycodone/acetaminophen, oxycodone, hydromorphone, and morphine)

OR

☐ Patient is approved for oxymorphone SA tabs and oxymorphone IR is required for breakthrough pain.

Dosage and Administration

- Oxymorphone IR is available in the following strengths: 5 and 10 mg
- C_{MAX} of oxymorphone can be increased by a high-fat meal; oxymorphone IR should be administered on an empty stomach, at least 1 hour before or 2 hours after eating.
- **Opioid naïve patients:** prescribing information indicates opioid naïve patients may initiate oxymorphone IR at doses up to 10-20 mg every 4 to 6 hours. Use of higher starting doses in patients who are not opioid tolerant may cause fatal respiratory depression.
  - Initiate treatment with the 5mg dose in opioid-naïve patients with mild hepatic impairment, impaired renal function (creatinine clearance < 50 ml/min), or when age is ≥ 65 years.
- **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 using standard equianalgesic dosage estimates generated through use of the conversion factor table from 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.
- Oxymorphone is contraindicated in patients with moderate or severe hepatic impairment. See *Safety* for information on the effect of renal impairment on the pharmacokinetics of oxymorphone SA.

Morphine Milligram Equivalent Doses (MME)[1]	
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

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.

Safety *See Product Information for additional safety information*

- The adverse effect profile of oxymorphone IR is similar to that of other IR opioid analgesics in the management of patients with moderate to severe pain and includes nausea, somnolence, vomiting, pruritus, headache, dizziness, constipation and confusion.
- Oxymorphone IR, like all opioid analgesics, may cause severe hypotension in a patient whose ability to maintain blood pressure has been compromised by a depleted blood volume or after concurrent administration of drugs that compromise vasomotor tone.
- 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.
- Co-administration of oxymorphone IR with alcohol has not been studied; however, *in vivo* combination of alcohol and oxymorphone SA has been shown to significantly increase C_{MAX} of oxymorphone. Avoid co-administration of oxymorphone IR and alcohol.
- The concomitant use of oxymorphone IR 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.
- 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.
- The effect of renal impairment on the pharmacokinetics of oxymorphone IR has not been studied. However, 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 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 through breast milk should be monitored for excess sedation and respiratory depression.
- Opioid overdose resulting in respiratory depression, hypotension, and profound sedation, coma and death can result when oxymorphone IR is misused or abused or when patient clinical circumstances predispose to reduced drug clearance or potentiation of effect. Consider provision of a naloxone rescue kit as a risk mitigation strategy.

Provider-Related Guidance

Implement Risk Mitigation Strategies. Ensure risk mitigation strategies are in place when starting oxymorphine IR 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.