

## Tapentadol Immediate Release (IR) Tablets 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<sup>1</sup> should be consulted for detailed prescribing information.*

**Transitioning Veteran** *Tapentadol IR tablets are on the DoD VHA Transitional Continuity of Care Drug List; if this 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 tapentadol IR tablets is safe and clinically appropriate.

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

- Intended use is for treatment of mild pain
- Patient is opioid naïve and initial single dosage is > 100 mg (see *Dosage and Administration*)
- Patient has significant respiratory depression, conditions that predisposes to significant respiratory depression (such as acute or severe bronchial asthma), or known/suspected gastrointestinal obstruction including paralytic ileus
- Patient has severe renal or hepatic impairment
- Patient is receiving a monoamine oxidase inhibitor (MAOI) or has taken an MAOI within 14 days
- Patient has hypersensitivity to tapentadol

**Inclusion Criteria** *The following criteria must be fulfilled for provision of tapentadol 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 lack of sufficient analgesic response to at least 4 other formulary short-acting immediate-release opioids (grouping includes tramadol, codeine, codeine/acetaminophen, hydrocodone/acetaminophen, oxycodone/acetaminophen, oxycodone, hydromorphone, and morphine)

**OR**

- Patient is approved for tapentadol SA tabs and tapentadol IR is required for breakthrough pain.

**Dosage and Administration** *See Product Information<sup>1</sup> for additional dosing information*

- Tapentadol IR is available in the following strengths: 50, 75 and 100 mg
- On the first day of dosing, the second dose may be administered as soon as one hour after the first dose, if adequate pain relief is not attained with the first dose. Subsequent dosing is 50 mg, 75 mg, or 100 mg up to every 4 to 6 hours and should be adjusted to maintain adequate analgesia with acceptable tolerability.
- Daily doses greater than 700 mg on the first day of therapy and 600 mg on subsequent days have not been studied and are not recommended.
- Tapentadol IR is not recommended in patients with severe renal impairment (CrCl < 30 ml/min) or severe hepatic impairment (Child-Pugh score 10 to 15).
- Consider giving elderly patients starting doses in the lower range of recommended dosages.
- There are no FDA-approved dosing instructions that indicate how to convert patients from another opioid to tapentadol IR. See the Table (page 2) for conversion factors that can be used to calculate an estimated tapentadol IR dose from another opioid.

**Safety** *See Product Information<sup>1</sup> for additional safety information*

- Tapentadol IR does not offer any consistent advantages over morphine IR in terms of safety or tolerability. Serious adverse reactions include potentially life-threatening respiratory depression, profound sedation, and hypotension. Non-serious adverse events include nausea, vomiting, constipation, dry mouth, fatigue, dizziness, somnolence, and pruritus.
- The concomitant use of tapentadol IR with other CNS depressants including other opioids, alcohol, sedative hypnotics, tranquilizers, general anesthetics, and phenothiazines can increase the risk of respiratory depression, profound sedation, coma and death.

- Avoid use of tapentadol IR 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.
- Potentially life-threatening serotonin syndrome may occur with recommended doses of tapentadol IR when combined with drugs that have serotonergic activity including SSRIs, SNRIs, tricyclic antidepressants, triptans, mirtazepine, trazodone, tramadol, and MAOIs.
- Seizure disorders may be aggravated or induced by tapentadol; monitoring is recommended and this agent should be used with caution in patients with a history of seizures.
- Tapentadol IR is not recommended in patients with severe renal impairment (CrCl < 30 ml/min) or severe hepatic impairment (Child-Pugh score 10 to 15).
- Tapentadol 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.
- Tapentadol IR 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.
- There is insufficient information on the excretion of tapentadol in breast milk; infants who may be exposed to tapentadol through breast milk should be monitored for excess sedation and respiratory depression during therapy and withdrawal symptoms when tapentadol is stopped.
- Tapentadol IR may be abused by crushing, chewing, snorting or injecting the product; these practices pose a significant risk of overdose and death. Opioid overdose may also result 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.
- The concomitant use of tapentadol 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.

**Table:** Morphine milligram equivalent doses for commonly prescribed opioids. Adapted from Reference 2.

<b>Morphine Milligram Equivalent Doses (MME)<sup>1</sup></b>	
<b>Opioid Agent</b>	<b>Conversion Factor</b>
Codeine	0.15
<b>Tapentadol</b>	<b>0.4</b>
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/day 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 (reduction to 50-67% of the calculated MME) 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.

**Provider-Related Guidance**

**Implement Risk Mitigation Strategies.** Ensure risk mitigation strategies are in place when starting tapentadol 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

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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](#).

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Updated: January 2018. Revised September, 2016 (original prepared September 2010). Contact: Mitchell Nazario, PharmD, National Clinical Pharmacy Program Manager, VA Pharmacy Benefits Management Services

1. Nucynta™ [package insert]. Janssen Pharmaceuticals, Inc, Titusville, NJ, Sept 2013.
2. Dowell D, Haegerich TM, Chou R. CDC Guideline for Prescribing Opioids for Chronic Pain – United States, 2016. JAMA 2016; 315: 1624-45.