

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

203794Orig1s000

LABELING

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use NUCYNTA® safely and effectively. See full prescribing information for NUCYNTA®.

NUCYNTA® (tapentadol) oral solution C-II
Initial U.S. Approval: 2008

INDICATIONS AND USAGE

NUCYNTA® is an opioid analgesic indicated for the management of moderate to severe acute pain in adults. (1)

DOSAGE AND ADMINISTRATION

- Individualize dosing according to the severity of pain being treated, the previous experience with similar drugs and the ability to monitor the patient. (2.1)
- Initiate NUCYNTA® with or without food at a dose of 2.5 mL (50 mg), 3.75 mL (75 mg), or 5 mL (100 mg) every 4 to 6 hours depending upon pain intensity. 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 2.5 mL (50 mg), 3.75 mL (75 mg), or 5 mL (100 mg) 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, therefore, not recommended. (2.2)
- Instructions for Use (2.7)

DOSAGE FORMS AND STRENGTHS

Oral Solution: 20 mg/mL (3)

CONTRAINDICATIONS

- Significant respiratory depression (4)
- Acute or severe bronchial asthma, hypercarbia (4)
- Known or suspected paralytic ileus (4)
- Hypersensitivity to tapentadol or to any other ingredients of the product (4)
- Concurrent use of monoamine oxidase (MAO) inhibitors or use within the last 14 days. (4)

WARNINGS AND PRECAUTIONS

- Misuse, Abuse and Diversion: NUCYNTA® is a Schedule II controlled substance with abuse liability similar to other opioids: monitor patients closely for signs of misuse, abuse and addiction. (5.1)
- Elderly, cachectic, and debilitated patients and patients with chronic pulmonary disease: Monitor closely because of increased risk of respiratory depression. (5.5)

- Interaction with CNS depressants including other opioids, sedatives, alcohol, and illicit drugs: Consider dose reduction of one or both drugs because of additive effects. (5.7)
- Hypotensive effect: Monitor for signs of hypotension. (5.8)
- Patients with head injury or increased intracranial pressure: Monitor for sedation and respiratory depression. Avoid use of NUCYNTA® in patients with impaired consciousness or coma susceptible to intracranial effects of CO₂ retention. (5.9)
- Impaired mental/physical abilities: Caution must be used with potentially hazardous activities. (5.14)
- Seizures: Use with caution in patients with a history of seizures. (5.10)
- Serotonin Syndrome: Potentially life-threatening condition could result from concomitant serotonergic administration. (5.11)
- Withdrawal: Withdrawal symptoms may occur if NUCYNTA® is discontinued abruptly. (5.13)

ADVERSE REACTIONS

The most common (≥10%) adverse reactions were nausea, dizziness, vomiting and somnolence. (6)

To report SUSPECTED ADVERSE REACTIONS, contact Janssen Pharmaceuticals, Inc. at 1-800-526-7736 (1-800-JANSSEN) or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch

DRUG INTERACTIONS

- CNS depressants: Increased risk of respiratory depression, hypotension, profound sedation, coma or death. When combined therapy with CNS depressant is contemplated, the dose of one or both agents should be reduced. (7.3)
- Mixed agonist/antagonist opioids (i.e., pentazocine, nalbuphine, and butorphanol): May reduce analgesic effect and/or precipitate withdrawal symptoms. (7.5)
- Monitor for signs of serotonin syndrome when NUCYNTA® is used concurrently with SSRIs, SNRIs, tricyclic antidepressants, or triptans. (7.4)

USE IN SPECIFIC POPULATIONS

- Pregnancy: Based on animal data, may cause fetal harm. (8.1)
- Nursing mothers: Closely monitor infants of nursing women receiving NUCYNTA®. (8.3)
- Renal or hepatic impairment: not recommended in patients with severe renal or hepatic impairment. Reduce dose in patients with moderate hepatic impairment. (8.7, 8.8)

See 17 for PATIENT COUNSELING INFORMATION and the FDA approved Medication Guide

Revised: 10/2012

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FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

NUCYNTA[®] (tapentadol) is indicated for the management of moderate to severe acute pain in adults.

2 DOSAGE AND ADMINISTRATION

NUCYNTA[®] oral solution is available in one concentration: 20 mg/mL.

Take care when prescribing and administering NUCYNTA[®] oral solution to avoid dosing errors, which could result in accidental overdose and death. Take care to ensure the proper dose is communicated and dispensed. Include the dose in milliliters (mL) and milligrams (mg) when writing prescriptions. Always use the enclosed calibrated oral syringe when administering NUCYNTA[®] oral solution to ensure the dose is measured and administered accurately.

2.1 Individualization of Dosage

As with any opioid drug product, adjust the dosing regimen for each patient individually, taking into account the patient's prior analgesic treatment experience. In the selection of the initial dose of tapentadol, give attention to the following:

- the total daily dose, potency and specific characteristics of the opioid the patient has been taking previously;
- the reliability of the relative potency estimate used to calculate the equivalent morphine sulfate dose needed;
- the patient's degree of opioid tolerance;
- the general condition and medical status of the patient;
- concurrent medications;
- the type and severity of the patient's pain;
- risk factors for abuse, addiction or diversion, including a prior history of abuse, addiction or diversion.

The following dosing recommendations, therefore, can only be considered suggested approaches to what is actually a series of clinical decisions over time in the management of the pain of each individual patient. Continual re-evaluation of the patient receiving tapentadol is important, with special attention to the maintenance of pain control and the relative incidence of side effects associated with therapy. During chronic therapy, especially for non-cancer-related pain, periodically re-assess the continued need for the use of opioid analgesics.

During periods of changing analgesic requirements, including initial titration, frequent contact is recommended between physician, other members of the healthcare team, the patient, and the caregiver/family.

2.2 Initiation of Therapy

The dose is 2.5 mL (equivalent to 50 mg), 3.75 mL (equivalent to 75 mg), or 5 mL (equivalent to 100 mg) every 4 to 6 hours depending upon pain intensity.

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 2.5 mL (equivalent to 50 mg), 3.75 mL (equivalent to 75 mg), or 5 mL (equivalent to 100 mg) 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.

NUCYNTA[®] may be given with or without food [*see Clinical Pharmacology (12.3)*].

2.3 Renal Impairment

No dosage adjustment is recommended in patients with mild or moderate renal impairment.

NUCYNTA[®] use in patients with severe renal impairment is not recommended [*see Warnings and Precautions (5.16) and Clinical Pharmacology (12.3)*].

2.4 Hepatic Impairment

No dosage adjustment is recommended in patients with mild hepatic impairment [*see Clinical Pharmacology (12.3)*].

NUCYNTA[®] should be used with caution in patients with moderate hepatic impairment. Treatment in these patients should be initiated at 50 mg administered no more frequently than once every 8 hours (maximum of three doses in 24 hours). Further treatment should reflect maintenance of analgesia with acceptable tolerability, to be achieved by either shortening or lengthening the dosing interval [*see Clinical Pharmacology (12.3)*].

The safety and efficacy of NUCYNTA[®] has not been studied in patients with severe hepatic impairment and use in this population is not recommended [*see Warnings and Precautions (5.15)*].

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