HIGHLIGHTS OF PRESCRIBING INFORMATION[1]

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 CO_2 retention. (5.9)
- 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)
- Impaired mental/physical abilities: Caution must be used with potentially hazardous activities. (5.14)

----------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: 11/2014

FULL PRESCRIBING INFORMATION: CONTENTS*

*Sections or subsections omitted from the full prescribing information are not listed

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. Monitor the patient for signs of respiratory or central nervous system depression.

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

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

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

2.4 Hepatic Impairment

The safety and efficacy of NUCYNTA® has not been studied in patients with severe hepatic impairment (Child-Pugh Score 10-15) and use in this population is not recommended *[see Warnings and Precautions (5.15)]*.

Initiate treatment of patients with moderate hepatic impairment (Child-Pugh Score 7 to 9) with 50 mg 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)]*.

No dosage adjustment is recommended in patients with mild hepatic impairment (Child-Pugh Score 5 to 6) *[see Clinical Pharmacology (12.3)]*.

2.5 Elderly Patients

In general, recommended dosing for elderly patients with normal renal and hepatic function is the same as for younger adult patients with normal renal and hepatic function. Because elderly patients are more likely to have decreased renal and hepatic function, consideration should be given to starting elderly patients with the lower range of recommended doses.

2.6 Cessation of Therapy

When the patient no longer requires therapy with tapentadol, gradually taper the dose to prevent signs and symptoms of withdrawal in the physically dependent patient *[see Warnings and Precautions (5.13)]*.

2.7 Instructions for Use

Concentration and Dispensing: The oral solution contains 20 mg tapentadol per milliliter (mL) and prescriptions should be written in milliliters (mL) and milligrams (mg). An oral syringe is supplied with dose marks corresponding directly to 2.5 mL (equals 50 mg) oral solution, 3.75 mL (equals 75 mg) oral solution, and 5 mL (equals 100 mg) oral solution.

Inform patients of the availability of FDA-approved patient labeling, Instructions for Use, for step-by-step instructions for patients on how to use the medicine bottle and the oral syringe.

3 DOSAGE FORMS AND STRENGTHS

NUCYNTA® oral solution: 20 mg/mL oral solution in 100 mL and 200 mL fill bottles with child-resistant closure *[see Description (11)* and *How Supplied/Storage and Handling (16)]*.

4 CONTRAINDICATIONS

NUCYNTA® is contraindicated in:

- Patients with significant respiratory depression
- Patients with acute or severe bronchial asthma or hypercarbia in an unmonitored setting or in the absence of resuscitative equipment
- Patients with known or suspected paralytic ileus
- Patients with hypersensitivity (e.g. anaphylaxis, angioedema) to tapentadol or to any other ingredients of the product *[see Adverse Reactions (6.2)]*.
- Patients who are receiving monoamine oxidase (MAO) inhibitors or who have taken them within the last 14 days due to potential additive effects on norepinephrine levels which may result in adverse cardiovascular events *[see Drug Interactions (7.2)]*.

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