HIGHLIGHTS OF PRESCRIBING INFORMATION

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

NUCYNTA® ER (tapentadol) extended-release oral tablets C-II

Initial U.S. Approval: 2008

WARNING: ABUSE POTENTIAL, LIFE-THREATENING RESPIRATORY DEPRESSION, ACCIDENTAL EXPOSURE, and INTERACTION WITH ALCOHOL

See full prescribing information for complete boxed warning.

- **NUCYNTA® ER contains tapentadol, a Schedule II controlled substance. Monitor for signs of misuse, abuse, and addiction during NUCYNTA® ER therapy. (5.1)**
- **Fatal respiratory depression may occur, with highest risk at initiation and with dose increases. Instruct patients on proper administration of NUCYNTA® ER tablets to reduce the risk. (5.2)**
- **Accidental ingestion of NUCYNTA® ER can result in fatal overdose of tapentadol, especially in children. (5.3)**
- **Instruct patients not to consume alcoholic beverages or use prescription or non-prescription products containing alcohol while taking NUCYNTA® ER because of the risk of increased and potentially fatal plasma tapentadol levels. (5.4)**

----------RECENT MAJOR CHANGES----------

Boxed Warning	7/2012
Indications and Usage (1)	7/2012
Indications and Usage, Neuropathic pain associated with diabetic peripheral neuropathy (1)	8/2012
Dosage and Administration (2)	8/2012
Contraindications (4)	7/2012
Warnings and Precautions (5)	7/2012

——————INDICATIONS AND USAGE——————

NUCYNTA® ER is an opioid agonist indicated for the management of:

- moderate to severe chronic pain in adults (1)
- neuropathic pain associated with diabetic peripheral neuropathy (DPN) in adults (1)

when a continuous, around-the-clock opioid analgesic is needed for an extended period of time.

Limitations of Use

- NUCYNTA® ER is not for use:
  - As an as-needed (prn) analgesic (1)
  - For pain that is mild or not expected to persist for an extended period of time (1)
  - For acute pain (1)
  - For postoperative pain, unless the patient is already receiving chronic opioid therapy prior to surgery, or if the postoperative pain is expected to be moderate to severe and persist for an extended period of time. (1)

——————DOSAGE AND ADMINISTRATION——————

- Individualize dosing based on patient's prior analgesic treatment experience, and titrate as needed to provide adequate analgesia and minimize adverse reactions. (2.1, 2.2)
- The initial dose in patients not currently taking opioid analgesics is 50 mg twice a day. (2.1).
- Instruct patients to swallow NUCYNTA® ER tablets whole. (2.7)
- Use a gradual downward titration when NUCYNTA® ER is discontinued in a physically dependent patient. (2.3, 5.13)
- Reduce the dose of NUCYNTA® ER in patients with moderate hepatic impairment. (2.4)
- NUCYNTA® ER use in patients with severe renal impairment is not recommended. (2.5)
- Conservative initial dosing of NUCYNTA® ER in elderly patients is recommended due to possible decreased renal and hepatic function. (2.6)

——————DOSAGE FORMS AND STRENGTHS——————

- Extended-Release Tablets: 50 mg, 100 mg, 150 mg, 200 mg, 250 mg (3)

——————CONTRAINDICATIONS——————

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

——————WARNINGS AND PRECAUTIONS——————

See Boxed WARNINGS

- Elderly, cachectic, and debilitated patients and patients with chronic pulmonary disease: Monitor closely because of increased risk of respiratory depression. (5.5, 5.6)
- Interaction with CNS depressants: Consider dose reduction of one or both drugs because of additive effects. (5.7, 7.3)
- Hypotensive effect: Monitor during dose initiation and titration. (5.8)
- Patients with head injury or increased intracranial pressure: Monitor for sedation and respiratory depression. Avoid use of NUCYNTA® ER 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 administration of drugs with serotonergic activity. (5.11)

——————ADVERSE REACTIONS——————

The most common (≥10%) adverse reactions were nausea, constipation, dizziness, headache, 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® ER 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® ER. (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 MEDICATION GUIDE.

Revised: 8/2012

FULL PRESCRIBING INFORMATION: CONTENTS*

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

FULL PRESCRIBING INFORMATION

WARNING: ABUSE POTENTIAL, LIFE-THREATENING RESPIRATORY DEPRESSION, ACCIDENTAL EXPOSURE, and INTERACTION WITH ALCOHOL

Abuse Potential

NUCYNTA® ER contains tapentadol, an opioid agonist and Schedule II controlled substance with an abuse liability similar to other opioid agonists, legal or illicit *[see Warnings and Precautions (5.1)]*. Assess each patient's risk for opioid abuse or addiction prior to prescribing NUCYNTA® ER. The risk for opioid abuse is increased in patients with a personal or family history of substance abuse (including drug or alcohol abuse or addiction) or mental illness (e.g., major depressive disorder). Routinely monitor all patients receiving NUCYNTA® ER for signs of misuse, abuse, and addiction during treatment *[see Drug Abuse and Dependence (9)]*.

Life-threatening Respiratory Depression

Respiratory depression, including fatal cases, may occur with use of NUCYNTA® ER, even when the drug has been used as recommended and not misused or abused *[see Warnings and Precautions (5.2)]*. Proper dosing and titration are essential and NUCYNTA® ER should only be prescribed by healthcare professionals who are knowledgeable in the use of potent opioids for the management of chronic pain. Monitor for respiratory depression, especially during initiation of NUCYNTA® ER or following a dose increase. Instruct patients to swallow NUCYNTA® ER tablets whole. Crushing, dissolving, or chewing NUCYNTA® ER can cause rapid release and absorption of a potentially fatal dose of tapentadol.

Accidental Exposure

Accidental ingestion of NUCYNTA® ER, especially in children, can result in a fatal overdose of tapentadol *[see Warnings and Precautions (5.3)]*.

Interaction with Alcohol

The co-ingestion of alcohol with NUCYNTA® ER may result in an increase of plasma levels and potentially fatal overdose of tapentadol *[see Warnings and Precautions (5.4)]*. Instruct patients not to consume alcoholic beverages or use prescription or non-prescription products that contain alcohol while on NUCYNTA® ER.

1 INDICATIONS AND USAGE

NUCYNTA® ER (tapentadol) is indicated for the management of:

- moderate to severe chronic pain in adults
- neuropathic pain associated with diabetic peripheral neuropathy (DPN) in adults

when a continuous, around-the-clock opioid analgesic is needed for an extended period of time *[see Clinical Studies (14.1, 14.2)]*.

Limitations of Usage

NUCYNTA® ER is not intended for use:

- As an as-needed (prn) analgesic
- For pain that is mild or not expected to persist for an extended period of time
- For acute pain
- For postoperative pain unless the patient is already receiving chronic opioid therapy prior to surgery or if the postoperative pain is expected to be moderate to severe and persist for an extended period of time.

2 DOSAGE AND ADMINISTRATION

2.1 Initial Dosing

Initiate the dosing regimen for each patient individually, taking into account the patient's prior analgesic treatment experience. Monitor patients closely for respiratory depression, especially within the first 72 hours of initiating therapy with NUCYNTA® ER *[see Warnings and Precautions (5.2)]*.

Consider the following factors when selecting an initial dose of NUCYNTA® ER:

- Total daily dose, potency, and kind of any prior analgesic the patient has been taking previously;
- Reliability of the relative potency estimate used to calculate the equivalent dose of tapentadol needed (Note: potency estimates may vary with the route of administration);
- Patient's degree of opioid experience and opioid tolerance;
- General condition and medical status of the patient;
- Concurrent medication;
- Type and severity of the patient's pain.

NUCYNTA® ER tablets must be taken whole, one tablet at a time, with enough water to ensure complete swallowing immediately after placing in the mouth *[see Patient Counseling Information (17)]*.

NUCYNTA® ER is administered at a frequency of twice daily (every 12 hours).

Discontinue all other tapentadol and tramadol products when beginning and while taking NUCYNTA® ER *[see Serotonin Syndrome Risk (5.11)]*. Although the maximum approved total daily dose of NUCYNTA® immediate-release formulation is 600 mg per day, the maximum total daily dose of NUCYNTA® ER is 500 mg. Do not exceed a total daily dose of NUCYNTA® ER of 500 mg.

Use of NUCYNTA® ER as the First Opioid Analgesic

Initiate NUCYNTA® ER therapy with the 50 mg tablet twice daily (at 12 hour intervals).

Conversion from NUCYNTA® to NUCYNTA® ER

Patients can be converted from NUCYNTA® to NUCYNTA® ER using the equivalent total daily dose of NUCYNTA® and dividing it into two equal doses of NUCYNTA® ER separated by approximately 12-hour intervals. As an example, a patient receiving 50 mg of NUCYNTA® four times per day (200 mg/day) may be converted to 100 mg NUCYNTA® ER twice a day.

Conversion from other Opioids to NUCYNTA® ER

While there are useful tables of oral and parenteral equivalents, there is substantial inter-patient variation in the relative potency of different opioid drugs and formulations. Specific recommendations are not available because of a lack of systematic evidence for these types of analgesic substitutions. As such, it is safer to underestimate a patient's 24-hour NUCYNTA® ER requirement and provide rescue medication (e.g., immediate-release opioid or non-opioid) than to overestimate and manage an adverse reaction. In general, begin with half of the estimated daily tapentadol requirement as the initial dose, managing inadequate analgesia by supplementation with immediate-release rescue medication.

Published relative potency/equianalgesia data are available and may be referred to in clinical practice guidelines such as those published by authorities in the field of pain medicine, but such ratios are approximations. Consider contacting your specific state medical or pharmacy professional societies for further information on how to safely convert patients from one opioid to another.

2.2 Titration and Maintenance of Therapy

Individually titrate NUCYNTA® ER to a dose that provides adequate analgesia and minimizes adverse reactions. Continually reevaluate patients receiving NUCYNTA® ER to assess the maintenance of pain control and the relative incidence of adverse reactions. During chronic therapy, especially for non-cancer-related pain (or pain associated with other terminal illnesses), periodically reassess the continued need for the use of opioid analgesics.

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