



## **NUCYNTA<sup>®</sup> ER (tapentadol extended-release tablets) Fact Sheet**

### **What is NUCYNTA<sup>®</sup> ER (pronounced 'new-sinn-tah')?**

- NUCYNTA<sup>®</sup> ER (tapentadol extended-release tablets), an oral analgesic taken twice daily, is now approved by the U.S. Food and Drug Administration (FDA) for the management of moderate to severe chronic pain in adults when a continuous, around-the-clock opioid analgesic is needed for an extended period of time.
  - NUCYNTA<sup>®</sup> ER is available in 50 mg, 100 mg, 150 mg, 200 mg and 250 mg doses by prescription only.
- NUCYNTA<sup>®</sup> ER has demonstrated proven efficacy in moderate to severe chronic pain models.
  - The New Drug Application (NDA) for NUCYNTA<sup>®</sup> ER is based on data from double-blind, randomized, active- and/or placebo-controlled Phase 3 studies that evaluated the efficacy and safety of NUCYNTA<sup>®</sup> ER for the treatment of moderate to severe chronic low back pain and painful diabetic peripheral neuropathy (DPN).
- In addition to the Phase 3 studies on chronic low back pain and painful diabetic peripheral neuropathy, safety was also evaluated in more than 1,100 patients with moderate to severe chronic pain over a 1-year period. NUCYNTA<sup>®</sup> ER demonstrated:
  - A favorable tolerability profile.
  - Favorable discontinuation rates.
  - That its most common ( $\geq 10\%$ ) adverse events were nausea, constipation, headache, dizziness, and somnolence.

### **Additional Information about NUCYNTA<sup>®</sup> ER**

- To help ensure the risks of NUCYNTA<sup>®</sup> ER are communicated accurately, Janssen Pharmaceuticals has developed a Risk Evaluation and Mitigation Strategy (REMS) for the medication, in collaboration with the FDA. This REMS, which is in line with similar programs for other medicines in this category, educates prescribers about the potentials for abuse, misuse, overdose and addiction from exposure to NUCYNTA<sup>®</sup> ER.
- To supplement the REMS, Janssen Pharmaceuticals also utilizes surveillance methodologies to monitor for inappropriate use of its products.
- The U.S. Drug Enforcement Agency has placed NUCYNTA<sup>®</sup> ER into Schedule II of the Controlled Substances Act.

- Janssen Pharmaceuticals, Inc. markets NUCYNTA<sup>®</sup> ER in the United States.

## **IMPORTANT SAFETY INFORMATION**

### **WARNING: POTENTIAL FOR ABUSE, PROPER PATIENT SELECTION, AND LIMITATIONS OF USE**

#### **Potential for Abuse**

NUCYNTA<sup>®</sup> ER contains tapentadol, a mu-opioid agonist and a Schedule II controlled substance with an abuse liability similar to other opioid analgesics.

NUCYNTA<sup>®</sup> ER can be abused in a manner similar to other opioid agonists, legal or illicit. These risks should be considered when prescribing or dispensing NUCYNTA<sup>®</sup> ER in situations where the physician or pharmacist is concerned about an increased risk of misuse, abuse, or diversion. Schedule II opioid substances, which include hydromorphone, morphine, oxycodone, fentanyl, oxymorphone, and methadone, have the highest potential for abuse and risk of fatal overdose due to respiratory depression.

#### **Proper Patient Selection**

NUCYNTA<sup>®</sup> ER is an extended-release formulation of tapentadol indicated for the management of moderate to severe chronic pain in adults when a continuous, around-the-clock opioid analgesic is needed for an extended period of time.

#### **Limitations of Use**

NUCYNTA<sup>®</sup> ER is not intended for use as an as-needed analgesic.

NUCYNTA<sup>®</sup> ER is not intended for the management of acute or postoperative pain.

NUCYNTA<sup>®</sup> ER tablets are to be swallowed whole and are not to be split, broken, chewed, dissolved, or crushed. Taking split, broken, chewed, dissolved, or crushed NUCYNTA<sup>®</sup> ER tablets could lead to rapid release and absorption of a potentially fatal dose of tapentadol.

Patients must not consume alcoholic beverages, or prescription or nonprescription medications containing alcohol. Co-ingestion of alcohol with NUCYNTA<sup>®</sup> ER may result in a potentially fatal overdose of tapentadol.

## **CONTRAINDICATIONS**

- NUCYNTA<sup>®</sup> ER is contraindicated in patients with significant respiratory depression, acute or severe bronchial asthma or hypercapnia in unmonitored settings or in the absence of resuscitative equipment.
- NUCYNTA<sup>®</sup> ER is contraindicated in any patient who has or is suspected of having a paralytic ileus.
- NUCYNTA<sup>®</sup> ER is contraindicated in patients who are receiving monoamine oxidase inhibitors (MAOIs) 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.

- NUCYNTA<sup>®</sup> ER is contraindicated in patients with a known hypersensitivity to the active substance, tapentadol, or any component of the product. Angioedema has been reported in association with use of tapentadol.

## **WARNINGS and PRECAUTIONS**

- **NUCYNTA<sup>®</sup> ER tablets are to be swallowed whole and are not to be split, broken, chewed, dissolved, or crushed.** Taking split, broken, chewed, crushed, or dissolved NUCYNTA<sup>®</sup> ER tablets leads to the rapid release and absorption of a potentially fatal dose of tapentadol.
- NUCYNTA<sup>®</sup> ER tablets must be kept in a secure place out of the reach of children. Accidental consumption of NUCYNTA<sup>®</sup> ER, especially in children, can result in a fatal overdose of tapentadol.
- Respiratory depression is the primary risk of mu-opioid agonists. Respiratory depression occurs more frequently in elderly or debilitated patients and in those suffering from conditions accompanied by hypoxia, hypercapnia, or upper airway obstruction, in whom even moderate therapeutic doses may significantly decrease pulmonary ventilation.
- Use NUCYNTA<sup>®</sup> ER with caution in patients with conditions accompanied by hypoxia, hypercapnia, or decreased respiratory reserve, such as: asthma, chronic obstructive pulmonary disease or cor pulmonale, severe obesity, sleep apnea syndrome, myxedema, kyphoscoliosis, central nervous system (CNS) depression, or coma. In such patients, even usual therapeutic doses of NUCYNTA<sup>®</sup> ER may increase airway resistance and decrease respiratory drive to the point of apnea. Alternative non-mu-opioid agonist analgesics should be considered, and NUCYNTA<sup>®</sup> ER should be employed only under careful medical supervision at the lowest effective dose in such patients. If respiratory depression occurs, it should be treated as any mu-opioid agonist-induced respiratory depression.
- Patients receiving other opioid agonist analgesics, general anesthetics, phenothiazines, other tranquilizers, sedatives, hypnotics, centrally acting muscle relaxants, or other CNS depressants (including alcohol) concomitantly with NUCYNTA<sup>®</sup> ER may exhibit additive CNS depression. Interactive effects resulting in respiratory depression, hypotension, profound sedation, coma, or death may result if these drugs are taken in combination with NUCYNTA<sup>®</sup> ER. When such combined therapy is contemplated, a dose reduction of one or both agents should be considered.
- Opioid analgesics can raise cerebrospinal fluid pressure as a result of respiratory depression with carbon dioxide retention. Therefore, NUCYNTA<sup>®</sup> ER should not be used in patients who may be susceptible to the effects of raised cerebrospinal fluid pressure, such as those with evidence of head injury and increased intracranial pressure. Opioid analgesics may obscure the clinical course of patients with head injury due to effects on pupillary response and consciousness. NUCYNTA<sup>®</sup> ER should be used with caution in patients with head injury, intracranial lesions, or other sources of preexisting increased intracranial pressure.

- Tapentadol is a mu-opioid agonist and is a Schedule II controlled substance. Such drugs are sought by drug abusers and people with addiction disorders. Diversion of Schedule II products is an act subject to criminal penalty.
- Patients should be assessed for their clinical risks for opioid abuse or addiction prior to being prescribed opioids.
- NUCYNTA<sup>®</sup> ER can be abused in a manner similar to other opioid agonists, legal or illicit. This should be considered when prescribing or dispensing NUCYNTA<sup>®</sup> ER in situations where the physician or pharmacist is concerned about an increased risk of misuse and abuse. Concerns about abuse and addiction should not prevent the proper management of pain. However, all patients treated with mu-opioid agonists require careful monitoring for signs of abuse and addiction, since use of mu-opioid agonist analgesic products carries the risk of addiction even under appropriate medical use.
- Drug abusers may attempt to abuse NUCYNTA<sup>®</sup> ER by crushing, chewing, snorting, or injecting the product. These practices may result in the uncontrolled delivery of NUCYNTA<sup>®</sup> ER and pose a significant risk to the abuser that could result in overdose and death.
- NUCYNTA<sup>®</sup> ER may cause severe hypotension. Patients at higher risk of hypotension include those with hypovolemia or those taking concurrent products that compromise vasomotor tone (eg, phenothiazines, general anesthetics).
- Patients should be cautioned that NUCYNTA<sup>®</sup> ER may impair the mental and/or physical abilities required for the performance of potentially hazardous tasks such as driving a car or operating machinery. This is to be expected, especially at the beginning of treatment, at any change of dosage, as well as in combination with alcohol or tranquilizers.
- NUCYNTA<sup>®</sup> ER may be expected to have additive effects when used in conjunction with alcohol, other opioids, or illicit drugs that cause CNS depression, because respiratory depression, hypotension, hypertension, and profound sedation, coma, or death may result.
- NUCYNTA<sup>®</sup> ER has not been evaluated in patients with a predisposition to a seizure disorder, and such patients were excluded from clinical studies. As with other opioids, NUCYNTA<sup>®</sup> ER should be prescribed with care in patients with a history of a seizure disorder or any condition that would put the patient at risk of seizures.
- Cases of life-threatening serotonin syndrome have been reported with the concurrent use of tapentadol and serotonergic drugs. Serotonergic drugs comprise selective serotonin reuptake inhibitors (SSRIs), serotonin and norepinephrine reuptake inhibitors (SNRIs), tricyclic antidepressants (TCAs), triptans, drugs that affect the serotonergic neurotransmitter system (eg, mirtazapine, trazodone, and tramadol), and drugs that impair metabolism of serotonin (including MAOIs). This may occur within the recommended dose. Serotonin syndrome may include mental-status changes (eg, agitation, hallucinations, coma), autonomic instability (eg, tachycardia, labile blood pressure, hyperthermia), neuromuscular aberrations (eg, hyperreflexia,

incoordination) and/or gastrointestinal symptoms (eg, nausea, vomiting, diarrhea), and can be fatal.

- Withdrawal symptoms may occur if NUCYNTA<sup>®</sup> ER is discontinued abruptly. These symptoms may include: anxiety, sweating, insomnia, rigors, pain, nausea, tremors, diarrhea, upper respiratory symptoms, piloerection, and rarely, hallucinations. Withdrawal symptoms may be reduced by tapering NUCYNTA<sup>®</sup> ER.
- A study with the immediate-release formulation of tapentadol in subjects with hepatic impairment showed higher serum concentrations of tapentadol than in those with normal hepatic function. Tapentadol should be used with caution in patients with moderate hepatic impairment.
- NUCYNTA<sup>®</sup> ER has not been studied in patients with severe hepatic impairment, and use in this population is not recommended.
- Like other drugs with mu-opioid agonist activity, NUCYNTA<sup>®</sup> ER may cause spasm of the sphincter of Oddi and should be used with caution in patients with biliary tract disease, including acute pancreatitis.
- NUCYNTA<sup>®</sup> ER should be used with caution in the following conditions: adrenocortical insufficiency (eg, Addison's disease); delirium tremens; myxedema or hypothyroidism; prostatic hypertrophy or urethral stricture; and toxic psychosis.
- Pregnancy Category C. There are no adequate and well-controlled studies of NUCYNTA<sup>®</sup> ER in pregnant women. NUCYNTA<sup>®</sup> ER should be used during pregnancy ONLY if the potential benefit justifies the potential risk to the fetus.

## **ADVERSE REACTIONS**

- The most common ( $\geq 10\%$ ) adverse reactions were nausea, constipation, headache, dizziness, and somnolence.

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