

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) immediate-release oral tablets C-II
Initial U.S. Approval: 2008

RECENT MAJOR CHANGES

Contraindications (4) 07/2013
Warnings and Precautions (5) 07/2013

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 50 mg, 75 mg, or 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 50 mg, 75 mg, or 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)

DOSAGE FORMS AND STRENGTHS

Tablets: 50 mg, 75 mg, 100 mg (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)

- 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

Revised: 10/2013

FULL PRESCRIBING INFORMATION: CONTENTS*

- 1 INDICATIONS AND USAGE**
- 2 DOSAGE AND ADMINISTRATION**
 - 2.1 Individualization of Dosage
 - 2.2 Initiation of Therapy
 - 2.3 Renal Impairment
 - 2.4 Hepatic Impairment
 - 2.5 Elderly Patients
 - 2.6 Cessation of Therapy
- 3 DOSAGE FORMS AND STRENGTHS**
- 4 CONTRAINDICATIONS**
- 5 WARNINGS AND PRECAUTIONS**
 - 5.1 Abuse Potential
 - 5.2 Life Threatening Respiratory Depression
 - 5.3 Accidental Exposure
 - 5.4 Interactions with Alcohol, Other Opioids, and Drugs of Abuse
 - 5.5 Elderly, Cachectic, and Debilitated Patients
 - 5.6 Use in Patients with Chronic Pulmonary Disease
 - 5.7 Interactions with CNS Depressants and Illicit Drugs
 - 5.8 Hypotensive Effect
 - 5.9 Use in Patients with Head Injury or Increased Intracranial Pressure
 - 5.10 Seizures
 - 5.11 Serotonin Syndrome Risk
 - 5.12 Use in Patients with Gastrointestinal Conditions
 - 5.13 Withdrawal
 - 5.14 Driving and Operating Heavy Machinery
 - 5.15 Hepatic Impairment
 - 5.16 Renal Impairment
- 6 ADVERSE REACTIONS**
 - 6.1 Clinical Studies Experience
 - 6.2 Post-marketing Experience
- 7 DRUG INTERACTIONS**
 - 7.1 Alcohol, Other Opioids, and Drugs of Abuse
 - 7.2 Monoamine Oxidase Inhibitors
 - 7.3 CNS Depressants
 - 7.4 Serotonergic Drugs
 - 7.5 Mixed Agonist/Antagonist Opioid Analgesics
 - 7.6 Anticholinergics
- 8 USE IN SPECIFIC POPULATIONS**
 - 8.1 Pregnancy
 - 8.2 Labor and Delivery
 - 8.3 Nursing Mothers
 - 8.4 Pediatric Use
 - 8.5 Geriatric Use
 - 8.6 Neonatal Withdrawal Syndrome
 - 8.7 Renal Impairment
 - 8.8 Hepatic Impairment
- 9 DRUG ABUSE AND DEPENDENCE**
 - 9.1 Controlled Substance
 - 9.2 Abuse
 - 9.3 Dependence
- 10 OVERDOSAGE**
 - 10.1 Clinical Presentation
 - 10.2 Management
- 11 DESCRIPTION**
- 12 CLINICAL PHARMACOLOGY**
 - 12.1 Mechanism of Action
 - 12.2 Pharmacodynamics
 - 12.3 Pharmacokinetics
- 13 NON-CLINICAL TOXICOLOGY**
 - 13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility
 - 13.2 Animal Toxicology and/or Pharmacology
- 14 CLINICAL STUDIES**
 - 14.1 Orthopedic Surgery – Bunionectomy
 - 14.2 End-Stage Degenerative Joint Disease
- 16 HOW SUPPLIED/STORAGE AND HANDLING**
- 17 PATIENT COUNSELING INFORMATION**

*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

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 50 mg, 75 mg, or 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 50 mg, 75 mg, or 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)*].

3 DOSAGE FORMS AND STRENGTHS

NUCYNTA[®] Tablets are round, biconvex and film-coated and are available in the following strengths, colors, and debossings: 50 mg of tapentadol (yellow with “O-M” on one side and “50” on the other side), 75 mg of tapentadol (yellow-orange with “O-M” on one side and “75” on the other side), and 100 mg of tapentadol (orange with “O-M” on one side and “100” on the other side) [*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)*].

5 WARNINGS AND PRECAUTIONS

5.1 Abuse Potential

NUCYNTA[®] contains tapentadol, an opioid agonist and a Schedule II controlled substance. Tapentadol can be abused in a manner similar to other opioid agonists legal or illicit. Opioid agonists are sought by drug abusers and people with addiction disorders and are subject to criminal diversion. Consider these risks when prescribing or dispensing NUCYNTA[®] in situations where there is concern about increased risks of misuse, abuse, or diversion. Concerns about abuse, addiction, and diversion should not, however, prevent the proper management of pain.

Assess each patient’s risk for opioid abuse or addiction prior to prescribing NUCYNTA[®]. 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 depression). Patients at increased risk may still be appropriately treated with opioids; however these patients will require intensive monitoring for signs of misuse, abuse, or addiction. Routinely monitor all patients receiving opioids for signs of misuse, abuse, and addiction because these drugs carry a risk for addiction even under appropriate medical use.

Explore Litigation Insights

Docket Alarm provides insights to develop a more informed litigation strategy and the peace of mind of knowing you're on top of things.

Real-Time Litigation Alerts



Keep your litigation team up-to-date with **real-time alerts** and advanced team management tools built for the enterprise, all while greatly reducing PACER spend.

Our comprehensive service means we can handle Federal, State, and Administrative courts across the country.

Advanced Docket Research



With over 230 million records, Docket Alarm's cloud-native docket research platform finds what other services can't. Coverage includes Federal, State, plus PTAB, TTAB, ITC and NLRB decisions, all in one place.

Identify arguments that have been successful in the past with full text, pinpoint searching. Link to case law cited within any court document via Fastcase.

Analytics At Your Fingertips



Learn what happened the last time a particular judge, opposing counsel or company faced cases similar to yours.

Advanced out-of-the-box PTAB and TTAB analytics are always at your fingertips.

API

Docket Alarm offers a powerful API (application programming interface) to developers that want to integrate case filings into their apps.

LAW FIRMS

Build custom dashboards for your attorneys and clients with live data direct from the court.

Automate many repetitive legal tasks like conflict checks, document management, and marketing.

FINANCIAL INSTITUTIONS

Litigation and bankruptcy checks for companies and debtors.

E-DISCOVERY AND LEGAL VENDORS

Sync your system to PACER to automate legal marketing.