# EFFICACY AND SAFETY OF TAPENTADOL EXTENDED RELEASE FOR THE MANAGEMENT OF CHRONIC LOW BACK PAIN:

## Results of a prospective, randomized, double-blind, placebo- and active-controlled Phase III study.

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*Expert Opinion on Pharmacotherapy*. 2010;11(11):1787-1804. doi:10.1517/14656566.2010.497720.

### INDICATIONS AND USAGE

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

- Pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate
- Neuropathic pain associated with diabetic peripheral neuropathy (DPN) severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate

Limitations of Use

- Because of the risks of addiction, abuse, and misuse with opioids, even at recommended doses, and because of the greater risks of overdose and death with extended-release opioid formulations, reserve NUCYNTA ER for use in patients for whom alternative treatment options (eg, non-opioid analgesics or immediate-release opioids) are ineffective, not tolerated, or would be otherwise inadequate to provide sufficient management of pain
- NUCYNTA ER is not indicated as an as-needed (prn) analgesic

### IMPORTANT SAFETY INFORMATION

**WARNING: ADDICTION, ABUSE, AND MISUSE; RISK EVALUATION AND MITIGATION STRATEGY (REMS); LIFE-THREATENING RESPIRATORY DEPRESSION; ACCIDENTAL INGESTION; NEONATAL OPIOID WITHDRAWAL SYNDROME; INTERACTION WITH ALCOHOL and RISKS FROM CONCOMITANT USE WITH BENZODIAZEPINES OR OTHER CNS DEPRESSANTS**

**Addiction, Abuse, and Misuse**

**NUCYNTA ER exposes patients and other users to the risks of opioid addiction, abuse, and misuse, which can lead to overdose and death. Assess each patient's risk prior to prescribing NUCYNTA ER, and monitor all patients regularly for the development of these behaviors and conditions.**

**Opioid Analgesic Risk Evaluation and Mitigation Strategy (REMS)**

**To ensure that the benefits of opioid analgesics outweigh the risks of addiction, abuse, and misuse, the Food and Drug Administration (FDA) has required a REMS for these products. Under the requirements of the REMS, drug companies with approved opioid analgesic products must make REMS-compliant education programs available to healthcare providers. Healthcare providers are strongly encouraged to**

- **complete a REMS-compliant education program,**
- **counsel patients and/or their caregivers, with every prescription, on safe use, serious risks, storage, and disposal of these products,**
- **emphasize to patients and their caregivers the importance of reading the Medication Guide every time it is provided by their pharmacist, and**
- **consider other tools to improve patient, household, and community safety.**

**Life-Threatening Respiratory Depression**

**Serious, life-threatening, or fatal respiratory depression may occur with use of NUCYNTA ER. Monitor for respiratory depression, especially during initiation of NUCYNTA ER or following a dose increase. Instruct patients to swallow NUCYNTA ER tablets whole; crushing, chewing, or dissolving NUCYNTA ER tablets can cause rapid release and absorption of a potentially fatal dose of tapentadol.**

**Accidental Ingestion**

**Accidental ingestion of even one dose of NUCYNTA ER, especially by children, can result in a fatal overdose of tapentadol.**

**Neonatal Opioid Withdrawal Syndrome**

**Prolonged use of NUCYNTA ER during pregnancy can result in neonatal opioid withdrawal syndrome, which may be life-threatening if not recognized and treated, and requires management according to protocols developed by neonatology experts. If opioid use is required for a prolonged period in a pregnant woman, advise the patient of the risk of neonatal opioid withdrawal syndrome and ensure that appropriate treatment will be available.**

**Interaction With Alcohol**

**Instruct patients not to consume alcoholic beverages or use prescription or non-prescription products that contain alcohol while taking NUCYNTA ER. The co-ingestion of alcohol with NUCYNTA ER may result in increased plasma tapentadol levels and a potentially fatal overdose of tapentadol.**

**Risks From Concomitant Use With Benzodiazepines or Other CNS Depressants**

**Concomitant use of opioids with benzodiazepines or other central nervous system (CNS) depressants, including alcohol, may result in profound sedation, respiratory depression, coma, and death.**

- **Reserve concomitant prescribing of NUCYNTA ER and benzodiazepines or other CNS depressants for use in patients for whom alternative treatment options are inadequate.**
- **Limit dosages and durations to the minimum required.**
- **Follow patients for signs and symptoms of respiratory depression and sedation.**

**Please see additional Important Safety Information throughout and accompanying full Prescribing Information, including Boxed Warning, or at Nucynta.com/ERpi.**

NUCYNTA® ER (tapentadol) EXTENDED-RELEASE TABLETS

# A RANDOMIZED, DOUBLE-BLIND STUDY COMPARING THE EFFICACY OF NUCYNTA® ER WITH PLACEBO FOR MANAGEMENT OF MODERATE TO SEVERE CHRONIC LOW BACK PAIN

## OBJECTIVE

- To evaluate the efficacy and safety of NUCYNTA ER for the management of moderate to severe chronic low back pain (cLBP)

## STUDY DESIGN

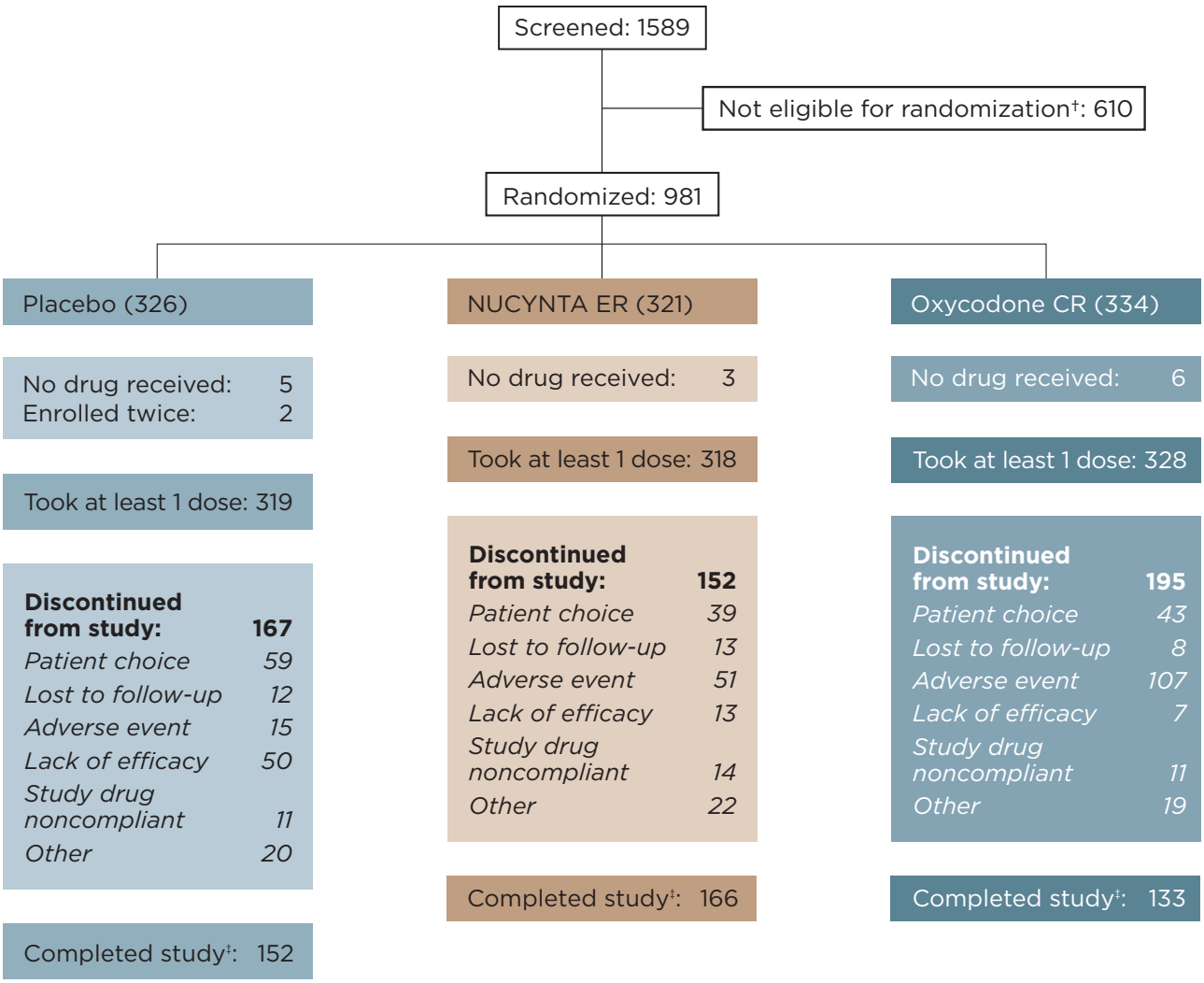
- Prospective, randomized, double-blind, active- and placebo-controlled, multicenter, Phase III study in patients with moderate to severe cLBP in the United States, Canada, and Australia
- Patients were randomized in a 1:1:1 ratio to receive NUCYNTA ER, oxycodone CR, or placebo
- Oxycodone CR was included in the study as an active control

## TREATMENT SCHEDULE

- During the titration period, active treatment started with NUCYNTA ER 50 mg BID or oxycodone CR 10 mg BID
- After 3 days, patients were titrated to NUCYNTA ER 100 mg BID or oxycodone CR 20 mg BID
- At a minimum of 3-day intervals, patients could be titrated in increments of NUCYNTA ER 50 mg BID or oxycodone CR 10 mg BID
- Patients could be titrated downward in decrements of NUCYNTA ER 50 mg BID or oxycodone CR 10 mg BID until minimum doses were reached
- The highest tested doses were NUCYNTA ER 250 mg BID or oxycodone CR 50 mg BID

**IMPORTANT SAFETY INFORMATION continued**
**CONTRAINDICATIONS:**
NUCYNTA ER is contraindicated in patients with:
- Significant respiratory depression
- Acute or severe bronchial asthma or hypercarbia in an unmonitored setting or in the absence of resuscitative equipment
- Known or suspected gastrointestinal obstruction, including paralytic ileus
- Hypersensitivity (eg, anaphylaxis, angioedema) to tapentadol or to any other ingredients of the product
- Concurrent use of monoamine oxidase inhibitors (MAOIs) or use of MAOIs within the last 14 days

# PATIENT DISPOSITION




†Includes patients who were randomized in error, but did not take study drug.
‡Includes all patients who were enrolled in an open-label extension study or completed all follow-up visits for the current study.

**ARTICLE HIGHLIGHT:** Demographic and baseline characteristics were similar between treatment groups; most patients in the safety population were white (73.3%), female (57.9%), and aged <65 years (84.6%). The mean age of the study population was 50 years (range, 18-89 years). The mean baseline pain intensity score was 7.5 with 88.5% of patients reporting severe pain (a score of ≥6) at baseline. The time that patients experienced cLBP prior to the study ranged from 6 months to 66 years.

**IMPORTANT SAFETY INFORMATION continued**
**WARNINGS AND PRECAUTIONS:**

**Addiction, Abuse, and Misuse**
NUCYNTA ER contains tapentadol, a Schedule II controlled substance. As an opioid, NUCYNTA ER exposes users to the risks of addiction, abuse, and misuse. Because extended-release products such as NUCYNTA ER deliver the opioid over an extended period of time, there is a greater risk for overdose and death due to the larger amount of tapentadol present.



**Please see additional Important Safety Information throughout and accompanying full Prescribing Information, including Boxed Warning, or at Nucynta.com/ERpi.**

# EFFICACY RESULTS

**PRIMARY EFFICACY ANALYSIS**

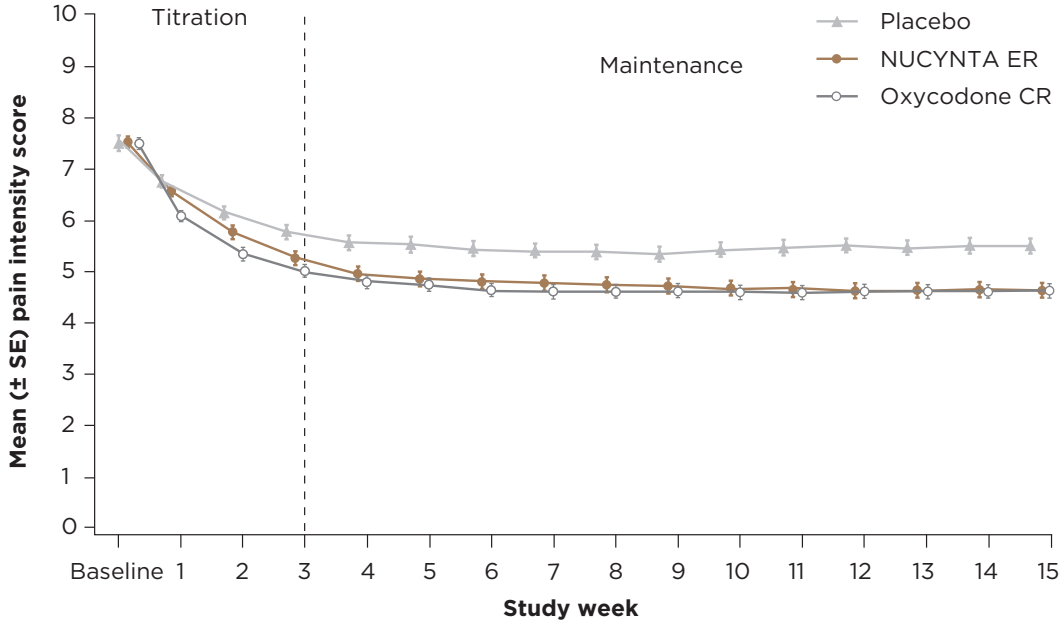
- Based on the last observation carried forward (LOCF) imputation method
- Treatment comparisons used the ANCOVA model and were based on least squares (LS) mean difference from placebo

**PRIMARY ENDPOINT**

- Change from baseline in mean pain intensity at week 12 of the maintenance period (United States)
- Improvement in mean cLBP pain intensity at week 15 from baseline as measured by numerical rating scale (NRS):
  - NUCYNTA ER: -2.9
  - Placebo: -2.1

**NUCYNTA® ER ACHIEVED ENDPOINT BY SIGNIFICANTLY REDUCING MEAN PAIN INTENSITY COMPARED WITH PLACEBO AT WEEK 12 AND THROUGHOUT THE ENTIRE MAINTENANCE PERIOD**

**IMPROVEMENT IN MEAN cLBP PAIN INTENSITY (N=965)**




Average daily dose in the maintenance period:

- NUCYNTA ER: 357 mg to 393 mg
- Oxycodone CR: 67 mg to 75 mg

**OXYCODONE CR WAS INCLUDED AS ACTIVE CONTROL**

**ARTICLE HIGHLIGHT:** Treatment with NUCYNTA ER 100 mg to 250 mg BID resulted in significantly greater relief of cLBP over 15 weeks than placebo.

**IMPORTANT SAFETY INFORMATION continued**
**WARNINGS AND PRECAUTIONS continued**
**Addiction, Abuse, and Misuse continued**

Although the risk of addiction in any individual is unknown, it can occur in patients appropriately prescribed NUCYNTA ER. Addiction can occur at recommended doses and if the drug is misused or abused.

Assess each patient's risk for opioid addiction, abuse, or misuse prior to prescribing NUCYNTA ER, and monitor all patients receiving NUCYNTA ER for the development of these behaviors and conditions.



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# SAFETY AND TOLERABILITY

- Safety was assessed throughout the study using adverse event reporting, findings from clinical laboratory testing, physical examinations, vital signs, and 12-lead electrocardiograms

## INCIDENCE OF TREATMENT-EMERGENT ADVERSE EVENTS IN ≥5% OF PATIENTS IN ANY TREATMENT GROUP (SAFETY POPULATION), NO. (%)

| | Placebo (n=319) | NUCYNTA ER (n=318) | Oxycodone CR (n=328) |
|---|---|---|---|
| Patients with ≥1 TEAE | 190 (59.6) | 240 (75.5) | 278 (84.8) |
| GASTROINTESTINAL DISORDERS | 84 (26.3) | 139 (43.7) | 203 (61.9) |
| Nausea | 29 (9.1) | 64 (20.1) | 113 (34.5) |
| Constipation | 16 (5.0) | 44 (13.8) | 88 (26.8) |
| Vomiting | 5 (1.6) | 29 (9.1) | 63 (19.2) |
| Dry mouth | 7 (2.2) | 26 (8.2) | 12 (3.7) |
| Diarrhea | 23 (7.2) | 19 (6.0) | 8 (2.4) |
| Dyspepsia | 8 (2.5) | 16 (5.0) | 6 (1.8) |
| NERVOUS SYSTEM DISORDERS | 72 (22.6) | 126 (39.6) | 147 (44.8) |
| Headache | 44 (13.8) | 63 (19.8) | 55 (16.8) |
| Dizziness | 18 (5.6) | 38 (11.9) | 56 (17.1) |
| Somnolence | 8 (2.5) | 42 (13.2) | 53 (16.2) |
| GENERAL DISORDERS | 32 (10.0) | 50 (15.7) | 62 (18.9) |
| Fatigue | 13 (4.1) | 21 (6.6) | 24 (7.3) |
| PSYCHIATRIC DISORDERS | 30 (9.4) | 47 (14.8) | 59 (18.0) |
| Insomnia | 9 (2.8) | 13 (4.1) | 25 (7.6) |
| SKIN AND SUBCUTANEOUS TISSUE DISORDERS | 17 (5.3) | 45 (14.2) | 91 (27.7) |
| Pruritus | 6 (1.9) | 23 (7.2) | 55 (16.8) |
| Hyperhidrosis | 0 | 12 (3.8) | 17 (5.2) |

CR, controlled release; ER, extended release; TEAE, treatment-emergent adverse event.

## OXYCODONE CR WAS INCLUDED AS ACTIVE CONTROL

**KEY TAKEAWAY:** NUCYNTA ER demonstrated a well-defined tolerability profile.

**IMPORTANT SAFETY INFORMATION continued**
**WARNINGS AND PRECAUTIONS continued**
**Addiction, Abuse, and Misuse continued**

Risks are increased in patients with a personal or family history of substance abuse (including drug or alcohol abuse or addiction) or mental illness (eg, major depression). The potential for these risks should not, however, prevent the prescribing of NUCYNTA ER for the proper management of pain in any given



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**IMPORTANT SAFETY INFORMATION continued**
**WARNINGS AND PRECAUTIONS continued**
**Addiction, Abuse, and Misuse continued**

patient. Patients at increased risk may be prescribed opioids such as NUCYNTA ER, but use in such patients necessitates intensive counseling about the risks and proper use of NUCYNTA ER along with intensive monitoring for signs of addiction, abuse, and misuse.

Abuse or misuse of NUCYNTA ER by crushing, chewing, snorting, or injecting the dissolved product will result in the uncontrolled delivery of tapentadol and can result in overdose and death.

Opioids are sought by drug abusers and people with addiction disorders and are subject to criminal diversion. Consider these risks when prescribing or dispensing NUCYNTA ER. Strategies to reduce these risks include prescribing the drug in the smallest appropriate quantity and advising the patient on the proper disposal of unused drug. Contact the local state professional licensing board or state controlled substances authority for information on how to prevent and detect abuse or diversion of this product.

**Opioid Analgesic Risk Evaluation and Mitigation Strategy (REMS)**

To ensure that the benefits of opioid analgesics outweigh the risks of addiction, abuse, and misuse, the Food and Drug Administration (FDA) has required a Risk Evaluation and Mitigation Strategy (REMS) for these products. Under the requirements of the REMS, drug companies with approved opioid analgesic products must make REMS-compliant education programs available to healthcare providers. Healthcare providers are strongly encouraged to do all of the following:

- Complete a REMS-compliant education program offered by an accredited provider of continuing education (CE) or another education program that includes all the elements of the FDA Education Blueprint for Health Care Providers Involved in the Management or Support of Patients with Pain
- Discuss the safe use, serious risks, and proper storage and disposal of opioid analgesics with patients and/or their caregivers every time these medicines are prescribed. The Patient Counseling Guide (PCG) can be obtained at this link: www.fda.gov/OpioidAnalgesicREMSPCG
- Emphasize to patients and their caregivers the importance of reading the Medication Guide that they will receive from their pharmacist every time an opioid analgesic is dispensed to them
- Consider using other tools to improve patient, household, and community safety, such as patient-prescriber agreements that reinforce patient-prescriber responsibilities

To obtain further information on the opioid analgesic REMS and for a list of accredited REMS CME/CE, call 1-800-503-0784, or log on to www.opioidanalgesicrems.com. The FDA Blueprint can be found at www.fda.gov/OpioidAnalgesicREMSBlueprint.

**Life-Threatening Respiratory Depression**

Serious, life-threatening, or fatal respiratory depression has been reported with the use of opioids, even when used as recommended. Respiratory depression, if not immediately recognized and treated, may lead to respiratory arrest and death. Management of respiratory depression may include close observation, supportive measures, and use of opioid antagonists, depending on the patient's clinical status. Carbon dioxide ($CO_2$) retention from opioid-induced respiratory depression can exacerbate the sedating effects of opioids.

**IMPORTANT SAFETY INFORMATION continued**
**WARNINGS AND PRECAUTIONS continued**
**Life-Threatening Respiratory Depression continued**

While serious, life-threatening, or fatal respiratory depression can occur at any time during the use of NUCYNTA ER, the risk is greatest during the initiation of therapy or following a dosage increase. Monitor patients closely for respiratory depression especially within the first 24-72 hours of initiating therapy with and following dosage increases of NUCYNTA ER.

To reduce the risk of respiratory depression, proper dosing and titration of NUCYNTA ER are essential. Overestimating the NUCYNTA ER dosage when converting patients from another opioid product can result in fatal overdose with the first dose.

Accidental ingestion of even one dose of NUCYNTA ER, especially by children, can result in respiratory depression and death due to an overdose of tapentadol.

Opioids can cause sleep-related breathing disorders, including central sleep apnea (CSA) and sleep-related hypoxemia. Opioid use increases the risk of CSA in a dose-dependent fashion. In patients who present with CSA, consider decreasing the opioid dosage using best practices for opioid taper.

**Neonatal Opioid Withdrawal Syndrome**

Prolonged use of NUCYNTA ER during pregnancy can result in withdrawal in the neonate. Neonatal opioid withdrawal syndrome, unlike opioid withdrawal syndrome in adults, may be life-threatening if not recognized and treated, and requires management according to protocols developed by neonatology experts. Observe newborns for signs of neonatal opioid withdrawal syndrome and manage accordingly. Advise pregnant women using opioids for a prolonged period of the risk of neonatal opioid withdrawal syndrome and ensure that appropriate treatment will be available.

**Risk From Concomitant Use With Benzodiazepines or Other CNS Depressants**

Patients must not consume alcoholic beverages or prescription or non-prescription products containing alcohol while on NUCYNTA ER therapy. The co-ingestion of alcohol with NUCYNTA ER may result in increased plasma tapentadol levels and a potentially fatal overdose of tapentadol.

Profound sedation, respiratory depression, coma, and death may result from the concomitant use of NUCYNTA ER with benzodiazepines or other CNS depressants (eg, non-benzodiazepine sedatives/hypnotics, anxiolytics, tranquilizers, muscle relaxants, general anesthetics, antipsychotics, other opioids, alcohol). Because of these risks, reserve concomitant prescribing of these drugs for use in patients for whom alternative treatment options are inadequate.

Observational studies have demonstrated that concomitant use of opioid analgesics and benzodiazepines increases the risk of drug-related mortality compared to use of opioid analgesics alone. Because of similar pharmacological properties, it is reasonable to expect similar risk with the concomitant use of other CNS depressant drugs with opioid analgesics.

If the decision is made to prescribe a benzodiazepine or other CNS depressant concomitantly with an opioid analgesic, prescribe the lowest effective dosages and minimum durations of concomitant use. In patients already receiving an opioid analgesic, prescribe a lower initial dose of the benzodiazepine or other CNS depressant than indicated in the absence of an opioid, and titrate based on clinical response. If an opioid analgesic is initiated in a patient already taking a benzodiazepine or other CNS depressant, prescribe a lower initial dose of the opioid analgesic, and titrate based on clinical response. Follow patients closely for signs and symptoms of respiratory depression and sedation.

**IMPORTANT SAFETY INFORMATION continued**
**WARNINGS AND PRECAUTIONS continued**

**Risk From Concomitant Use With Benzodiazepines or Other CNS Depressants continued**

Advise both patients and caregivers about the risks of respiratory depression and sedation when NUCYNTA ER is used with benzodiazepines or other CNS depressants (including alcohol and illicit drugs). Advise patients not to drive or operate heavy machinery until the effects of concomitant use of the benzodiazepine or other CNS depressants have been determined. Screen patients for risk of substance use disorders, including opioid abuse and misuse, and warn them of the risk for overdose and death associated with the use of additional CNS depressants including alcohol and illicit drugs.

**Risk of Life-Threatening Respiratory Depression in Patients With Chronic Pulmonary Disease or in Elderly, Cachectic, or Debilitated Patients**

The use of NUCYNTA ER in patients with acute or severe bronchial asthma in an unmonitored setting or in the absence of resuscitative equipment is contraindicated.

***Patients with Chronic Pulmonary Disease:*** NUCYNTA ER-treated patients with significant chronic obstructive pulmonary disease or cor pulmonale, and those with a substantially decreased respiratory reserve, hypoxia, hypercapnia, or pre-existing respiratory depression are at increased risk of decreased respiratory drive including apnea, even at recommended dosages of NUCYNTA ER.

***Elderly, Cachectic, or Debilitated Patients:*** Life-threatening respiratory depression is more likely to occur in elderly, cachectic, or debilitated patients because they may have altered pharmacokinetics or altered clearance compared to younger, healthier patients. Alternatively, consider the use of non-opioid analgesics in these patients.

Monitor such patients closely, particularly when initiating and titrating NUCYNTA ER and when NUCYNTA ER is given concomitantly with other drugs that depress respiration.

**Serotonin Syndrome With Concomitant Use of Serotonergic Drugs**

Cases of serotonin syndrome, a potentially life-threatening condition, have been reported during concomitant use of tapentadol with serotonergic drugs. Serotonergic drugs include selective serotonin reuptake inhibitors (SSRIs), serotonin and norepinephrine reuptake inhibitors (SNRIs), tricyclic antidepressants (TCAs), triptans, 5-HT3 receptor antagonists, drugs that affect the serotonergic neurotransmitter system (eg, mirtazapine, trazodone, tramadol), certain muscle relaxants (ie, cyclobenzaprine, metaxalone), and drugs that impair metabolism of serotonin (including MAO inhibitors, both those intended to treat psychiatric disorders and also others, such as linezolid and intravenous methylene blue). This may occur within the recommended dosage range.

Serotonin syndrome symptoms may include mental status changes (eg, agitation, hallucinations, coma), autonomic instability (eg, tachycardia, labile blood pressure, hyperthermia), neuromuscular aberrations (eg, hyperreflexia, incoordination, rigidity), and/or gastrointestinal symptoms (eg, nausea, vomiting, diarrhea). The onset of symptoms generally occurs within several hours to a few days of concomitant use, but may occur later than that. Discontinue NUCYNTA ER if serotonin syndrome is suspected.

**IMPORTANT SAFETY INFORMATION continued**
**WARNINGS AND PRECAUTIONS continued**

**Adrenal Insufficiency**

Cases of adrenal insufficiency have been reported with opioid use, more often following greater than one month of use. Presentation of adrenal insufficiency may include non-specific symptoms and signs including nausea, vomiting, anorexia, fatigue, weakness, dizziness, and low blood pressure. If adrenal insufficiency is suspected, confirm the diagnosis with diagnostic testing as soon as possible. If adrenal insufficiency is diagnosed, treat with physiologic replacement doses of corticosteroids. Wean the patient off of the opioid to allow adrenal function to recover and continue corticosteroid treatment until adrenal function recovers. Other opioids may be tried as some cases reported use of a different opioid without recurrence of adrenal insufficiency. The information available does not identify any particular opioids as being more likely to be associated with adrenal insufficiency.

**Severe Hypotension**

NUCYNTA ER may cause severe hypotension including orthostatic hypotension and syncope in ambulatory patients. There is an increased risk in patients whose ability to maintain blood pressure has already been compromised by a reduced blood volume or concurrent administration of certain CNS depressant drugs (eg, phenothiazines or general anesthetics). Monitor these patients for signs of hypotension after initiating or titrating the dosage of NUCYNTA ER. In patients with circulatory shock, NUCYNTA ER may cause vasodilation that can further reduce cardiac output and blood pressure. Avoid the use of NUCYNTA ER in patients with circulatory shock.

**Risks of Use in Patients With Increased Intracranial Pressure, Brain Tumors, Head Injury, or Impaired Consciousness**

In patients who may be susceptible to the intracranial effects of $CO_2$ retention (eg, those with evidence of increased intracranial pressure or brain tumors), NUCYNTA ER may reduce respiratory drive, and the resultant $CO_2$ retention can further increase intracranial pressure. Monitor such patients for signs of sedation and respiratory depression, particularly when initiating therapy with NUCYNTA ER.

Opioids may also obscure the clinical course in a patient with a head injury. Avoid the use of NUCYNTA ER in patients with impaired consciousness or coma.

**Risks of Use in Patients With Gastrointestinal Conditions**

NUCYNTA ER is contraindicated in patients with known or suspected gastrointestinal obstruction, including paralytic ileus.

The tapentadol in NUCYNTA ER may cause spasm of the sphincter of Oddi. Opioids may cause increases in serum amylase. Monitor patients with biliary tract disease, including acute pancreatitis, for worsening symptoms.

**IMPORTANT SAFETY INFORMATION continued**
**WARNINGS AND PRECAUTIONS continued**

**Increased Risk of Seizures in Patients With Seizure Disorders**

The tapentadol in NUCYNTA ER may increase the frequency of seizures in patients with seizure disorders and may increase the risk of seizures in other clinical settings associated with seizures. Monitor patients with a history of seizure disorders for worsened seizure control during NUCYNTA ER therapy.

**Withdrawal**

Do not abruptly discontinue NUCYNTA ER in a patient physically dependent on opioids. When discontinuing NUCYNTA ER in a physically dependent patient, gradually taper the dosage. Rapid tapering of tapentadol in a patient physically dependent on opioids may lead to a withdrawal syndrome and return of pain.

Additionally, avoid the use of mixed agonist/antagonist (eg, pentazocine, nalbuphine, and butorphanol) or partial agonist (eg, buprenorphine) analgesics in patients who have received or are receiving a course of therapy with a full opioid agonist analgesic, including NUCYNTA ER. In these patients, mixed agonists/antagonists and partial agonist analgesics may reduce the analgesic effect and/or may precipitate withdrawal symptoms.

**Risks of Driving and Operating Machinery**

NUCYNTA ER may impair the mental or physical abilities needed to perform potentially hazardous activities such as driving a car or operating machinery. Warn patients not to drive or operate dangerous machinery unless they are tolerant to the effects of NUCYNTA ER and know how they will react to the medication.

**Risk of Toxicity in Patients With Hepatic Impairment**

A study with an immediate-release formulation of tapentadol in subjects with hepatic impairment showed higher serum concentrations of tapentadol than in those with normal hepatic function. Avoid use of NUCYNTA ER in patients with severe hepatic impairment. Reduce the dose of NUCYNTA ER in patients with moderate hepatic impairment. Closely monitor patients with moderate hepatic impairment for respiratory and central nervous system depression when initiating and titrating NUCYNTA ER.

**Risk of Toxicity in Patients With Renal Impairment**

Use of NUCYNTA ER in patients with severe renal impairment is not recommended due to accumulation of a metabolite formed by glucuronidation of tapentadol. The clinical relevance of the elevated metabolite is not known.

# JEREMY

**AGE: 40**
**GENDER: MALE**
**ETHNICITY: AFRICAN AMERICAN**
**OCCUPATION: WAREHOUSE FOREMAN**

## PRESENTATION

- Reports intermittent dullness, tingling, and burning that radiates down to his right toe, in addition to continued sharp pain in his lower back

## PAIN INTENSITY RATING

- Severe: 7 to 8 (on a scale of 0-10)

## PAST MEDICAL HISTORY

- Injured back in a severe fall 1 year ago, which resulted in herniated lumbar discs
- Completed physical therapy twice weekly for 3 months
- Naproxen 500 mg BID ineffective
- Received 1 lumbar epidural steroid injection and still experienced pain
- Currently taking gabapentin and a short-acting opioid, proving to be inadequate

## MEDICAL CONCLUSION

- cLBP with radiculopathy

**For patients like Jeremy, consider NUCYNTA ER.**

Not an actual patient.

**IMPORTANT SAFETY INFORMATION continued**
**ADVERSE REACTIONS:**
In clinical studies, the most common (≥10%) adverse reactions were nausea, constipation, dizziness, headache, and somnolence.

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Collegium PHARMACEUTICAL



NUCYNTA® ER (tapentadol) EXTENDED-RELEASE TABLETS CII