



## **FDA Issues Complete Response Letter to Johnson & Johnson Pharmaceutical Research & Development Regarding New Drug Application for Tapentadol Extended Release**

RARITAN, N.J., Oct 04, 2010 /PRNewswire via COMTEX News Network/ -- Johnson & Johnson Pharmaceutical Research & Development, L.L.C. (J&JPRD) announced today that it received a Complete Response letter from the U.S. Food and Drug Administration (FDA) regarding its New Drug Application (NDA) for tapentadol extended release tablets. The application, filed by J&JPRD in late 2009 [see press release at [http://www.jnj.com/connect/news/product/20091201\\_200000](http://www.jnj.com/connect/news/product/20091201_200000)], seeks approval to market tapentadol extended release as an oral analgesic for the management of moderate to severe chronic pain in patients 18 years of age or older.

The FDA has not requested any new clinical studies evaluating the efficacy or safety of tapentadol extended release. The agency is, however, requesting data regarding the conversion of the extended release formulation used in the clinical efficacy and safety trials to a different extended release formulation that is designed to increase mechanical resistance to breaking or crushing.

"We will engage FDA in active discussions as quickly as possible so that we can address the requests in the Complete Response letter," said Juergen Haeussler, MD, Therapeutic Area Head, Analgesia, J&JPRD. "We remain fully committed to bringing tapentadol ER to patients experiencing chronic pain as quickly as possible."

The NDA filing is part of the ongoing commitment of J&JPRD to bring new and innovative products to patients and physicians for the treatment and management of pain.

### **About Chronic Pain**

According to the National Institutes of Health, an estimated 100 million Americans suffer from chronic pain. Osteoarthritis and low back pain are particularly prevalent, with osteoarthritis affecting 16 million Americans and low back pain affecting four out of five Americans at some point in their lives. Chronic pain is complex and there are many different types of pain, which can make it difficult to manage.

### **About tapentadol**

Tapentadol is a centrally acting oral analgesic that binds to mu-opioid receptors and inhibits norepinephrine reuptake. Although the exact mechanism of action is not known, these two mechanisms, which affect established pain pathways, are thought to be responsible for pain relief with tapentadol. The tapentadol molecule is classified as Schedule II of the Controlled Substances Act.

NUCYNTA(R) (tapentadol) CII Immediate Release Formulation was approved by the FDA on November 20, 2008, and is available by prescription only for the relief of moderate to severe acute pain in patients 18 years of age or older. PriCara(R), Division of Ortho-McNeil-Janssen Pharmaceuticals, Inc., markets NUCYNTA in the United States. To date, more than 450,000 total prescriptions for NUCYNTA have been written since the launch of the medication in June 2009.

## **IMPORTANT SAFETY INFORMATION FOR NUCYNTA(R) (tapentadol) CII IMMEDIATE RELEASE TABLET FORMULATION**

### Contraindications

Like other drugs with mu-opioid agonist activity, NUCYNTA(R) 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(R) is contraindicated in patients who have or are suspected to have paralytic ileus. NUCYNTA(R) is also contraindicated in patients currently using or within 14 days of using monoamine oxidase inhibitors (MAOIs) due to potential additive effects on norepinephrine levels, which may result in adverse cardiovascular events.

### Warnings & Precautions

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. NUCYNTA(R) should be administered with caution to the elderly, debilitated patients, and 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, CNS depression, or coma. In such patients, even usual therapeutic doses of NUCYNTA(R) may increase airway resistance and decrease respiratory drive to the point of apnea. Alternative non-mu-opioid agonist analgesics should be considered and NUCYNTA(R) 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 mu-opioid agonist analgesics, general anesthetics, phenothiazines, other tranquilizers, sedatives, hypnotics, or other CNS depressants (including alcohol) concomitantly with NUCYNTA(R) 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(R). 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(R) should not be used in patients susceptible to the effects of raised cerebrospinal fluid pressure such as those with 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(R) should be used with caution in patients with head injury, intracranial lesions, or other sources of preexisting increased intracranial pressure.

NUCYNTA(R) 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. NUCYNTA(R) can be abused in a manner similar to other mu-opioid agonists, legal or illicit. This should be considered when prescribing or dispensing NUCYNTA(R) in situations where the physician or pharmacist is concerned about an increased risk of misuse and abuse. All patients treated with mu-opioid agonists require careful monitoring for signs of abuse and addiction. NUCYNTA(R) may be abused by crushing, chewing, snorting or injecting the product. These practices pose a significant risk to the abuser that could result in overdose and death.

Experience with NUCYNTA(R) overdose is very limited. Management of overdose should be focused on treating symptoms of mu-opioid agonism. Primary attention should be given to reestablishment of a patent airway and institution of assisted or controlled ventilation when overdose of NUCYNTA(R) is suspected. Supportive measures (including oxygen and vasopressors) should be employed in the management of circulatory shock and pulmonary edema accompanying overdose as indicated. Cardiac arrest or arrhythmias may require cardiac massage or defibrillation.

Patients should be cautioned that NUCYNTA(R) 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(R) has not been systematically evaluated in patients with a seizure disorder, and such patients were excluded from clinical studies. NUCYNTA(R) 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.

The development of a potentially life-threatening serotonin syndrome may occur with use of SNRI products, including NUCYNTA(R), particularly with concomitant use of serotonergic drugs such as SSRIs, SNRIs, TCAs, MAOIs and triptans, and with drugs which impair metabolism of serotonin (including MAOIs). Serotonin syndrome may include mental-status changes (e.g., agitation, hallucinations, coma), autonomic instability (e.g., tachycardia, labile blood pressure, hyperthermia), neuromuscular aberrations (e.g., hyperreflexia, incoordination) and/or gastrointestinal symptoms (e.g., nausea, vomiting, diarrhea).

Withdrawal symptoms may occur if NUCYNTA(R) 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(R).

Pregnancy Category C. There are no adequate and well-controlled studies of NUCYNTA(R) in pregnant women. NUCYNTA(R) should be used during pregnancy ONLY if the potential benefit justifies the potential risk to the fetus. NUCYNTA(R) is not recommended for use in women during and immediately prior to labor and delivery. Neonates whose mothers have been taking NUCYNTA(R) should be monitored for respiratory depression. NUCYNTA(R) should not be used during breastfeeding.

NUCYNTA(R) is not recommended in patients with severe renal or hepatic impairment. NUCYNTA(R) should be used with caution in patients with moderate hepatic impairment. Like other drugs with mu-opioid agonist activity, NUCYNTA(R) may cause spasm of the sphincter of Oddi and should be used with caution in patients with biliary tract disease, including acute pancreatitis.

### Adverse Events

The most common adverse events are nausea, dizziness, vomiting, somnolence and headache. To see the NUCYNTA(R) full

prescribing information, go to <http://www.nucynta.com/nucynta/assets/Nucynta-PI.pdf>.

**About Johnson & Johnson Pharmaceutical Research & Development, L.L.C.**

Johnson & Johnson Pharmaceutical Research & Development, L.L.C., (J&JPRD) is a wholly owned subsidiary of Johnson & Johnson, the world's most broadly based producer of health care products. J&JPRD is headquartered in Raritan, N.J., and has facilities throughout Europe, the United States and Asia. J&JPRD is leveraging drug discovery and drug development in a variety of therapeutic areas, including CNS, Internal Medicine and Oncology, to address unmet medical needs worldwide. More information can be found at [www.jnjpharmarnd.com](http://www.jnjpharmarnd.com).

**PriCara(R), Division of Ortho-McNeil-Janssen Pharmaceuticals, Inc.**

PriCara(R), Division of Ortho-McNeil-Janssen Pharmaceuticals, Inc., is a major health care company in the United States dedicated to the needs of primary care providers who serve a vital role on the frontline of medicine. For more information about the company, please visit [www.PriCara.com](http://www.PriCara.com).

(This press release contains "forward-looking statements" as defined in the Private Securities Litigation Reform Act of 1995. These statements are based on current expectations of future events. If underlying assumptions prove inaccurate or unknown risks or uncertainties materialize, actual results could vary materially from Johnson & Johnson Pharmaceutical Research & Development, L.L.C., and/or Johnson & Johnson's expectations and projections. Risks and uncertainties include general industry conditions and competition; economic conditions, such as interest rate and currency exchange rate fluctuations; technological advances and patents attained by competitors; challenges inherent in new product development, including obtaining regulatory approvals; domestic and foreign health care reforms and governmental laws and regulations; and trends toward health care cost containment. A further list and description of these risks, uncertainties and other factors can be found in Exhibit 99 of Johnson & Johnson's Annual Report on Form 10-K for the fiscal year ended January 3, 2010. Copies of this Form 10-K, as well as subsequent filings, are available online at [www.sec.gov](http://www.sec.gov), [www.jnj.com](http://www.jnj.com) or on request from Johnson & Johnson. Neither Johnson & Johnson Pharmaceutical Research & Development, L.L.C., nor Johnson & Johnson undertake to update any forward-looking statements as a result of new information or future events or developments).

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