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FDA Approves TROXYCA® ER (oxycodone hydrochloride and naltrexone hydrochloride) Extended-Release Capsules CII with Abuse-Deterrent Properties for the Management of Pain

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Pfizer Inc. (NYSE:PFE) announced today that the U.S. Food and Drug Administration (FDA) has approved TROXYCA® ER (oxycodone hydrochloride and naltrexone hydrochloride) extended-release capsules, for oral use, CII 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. TROXYCA ER has properties that are expected to reduce abuse when crushed and administered by the oral and intranasal routes. However, abuse of TROXYCA ER by these routes is still possible. It is the only oxycodone with oral abuse-deterrent features described in the labeling.

“Public health authorities and regulators have encouraged the development of treatments that are more difficult to abuse, yet offer pain relief to appropriate patients when used as indicated,” said Rory O’Connor, MD, Chief Medical Officer, Internal Medicine, Pfizer Inc. “The development of this medication with abuse-deterrent properties is another example of our ongoing commitment to advancing science and the treatment of patients with pain conditions.”

TROXYCA ER extended-release capsules contain pellets that consist of oxycodone hydrochloride, an opioid agonist, which surround sequestered naltrexone hydrochloride, an opioid antagonist. When taken as directed, the naltrexone is intended to remain sequestered and patients receive oxycodone in an extended-release manner. Studies demonstrated that when the pellets are crushed the sequestered naltrexone is released and is available to counteract the effects of oxycodone.

The abuse-deterrent features of TROXYCA ER were demonstrated in a battery of in vitro laboratory studies and three clinical abuse-potential studies utilizing crushed TROXYCA ER by oral and intranasal routes of administration and the IV route (with simulated TROXYCA ER).

Indication

TROXYCA ER® (oxycodone hydrochloride and naltrexone hydrochloride) Extended-Release capsules, for oral use, CII is a combination opioid agonist/opioid antagonist product 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.

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 TROXYCA ER for use in patients for whom alternative treatment options (e.g., non-opioid analgesics or immediate-release opioids) are ineffective, not tolerated, or would be otherwise inadequate to provide sufficient management of pain
- TROXYCA ER is not indicated as an as-needed (prn) analgesic

IMPORTANT SAFETY INFORMATION

WARNING: ADDICTION, ABUSE, and MISUSE; LIFE-THREATENING RESPIRATORY DEPRESSION; ACCIDENTAL INGESTION; NEONATAL OPIOID WITHDRAWAL SYNDROME; and CYTOCHROME P450 3A4 INTERACTION.

Addiction, Abuse, and Misuse: TROXYCA 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 TROXYCA ER, and monitor all patients regularly for the development of these behaviors or conditions.

Life-threatening Respiratory Depression: Serious, life-threatening, or fatal respiratory depression may occur with use of TROXYCA ER. Monitor for respiratory depression, especially during initiation of TROXYCA ER or following a dose increase. Instruct patients to swallow TROXYCA ER capsules whole or to sprinkle the contents of the capsule on applesauce and swallow immediately without chewing. Crushing, chewing, or dissolving TROXYCA ER can cause rapid release and absorption of a potentially fatal dose of oxycodone.

Accidental Ingestion: Accidental ingestion of even one dose of TROXYCA ER, especially by children, can result in respiratory depression and death due to an overdose of oxycodone.

Neonatal Opioid Withdrawal Syndrome: Prolonged use of TROXYCA ER (oxycodone hydrochloride and naltrexone hydrochloride) Extended-Release capsules, for oral use, CII 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.

Cytochrome P450 3A4 Interaction: The concomitant use of TROXYCA ER with all cytochrome P450 3A4 inhibitors may result in an increase in oxycodone plasma concentrations, which could increase or prolong adverse drug effects and may cause potentially fatal respiratory depression. In addition, discontinuation of a concomitantly used cytochrome P450 3A4 inducer may result in an increase in oxycodone plasma concentrations. Monitor patients receiving TROXYCA ER and any CYP3A4 inhibitor or inducer.

CONTRAINDICATIONS

TROXYCA ER is contraindicated in patients with:

- Significant respiratory depression
- Acute or severe bronchial asthma in an unmonitored setting or in the absence of resuscitative equipment
- Known or suspected gastrointestinal obstruction, including paralytic ileus
- Hypersensitivity (e.g., anaphylaxis) to oxycodone or naltrexone or any other components of the TROXYCA ER formulation

WARNINGS AND PRECAUTIONS

Addiction, Abuse, and Misuse: TROXYCA ER contains oxycodone, a Schedule II controlled substance. As an opioid, TROXYCA ER exposes users to the risks of addiction, abuse, and misuse. As modified-release products such as TROXYCA 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 oxycodone present.

Although the risk of addiction in any individual is unknown, it can occur in patients appropriately prescribed TROXYCA ER and in those who obtain the drug illicitly. 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 TROXYCA ER, and monitor all patients receiving TROXYCA ER for the development of these behaviors or conditions. Risks are increased in patients with a personal or family history of substance abuse (including drug or alcohol addiction or abuse) or mental illness (e.g., major depression). The potential for these risks should not, however, prevent the prescribing of TROXYCA ER for the proper management of pain in any given patient. Patients at increased risk may be prescribed modified-release opioid formulations such as TROXYCA ER, but use in such patients necessitates intensive counseling about the risks and proper use of TROXYCA ER along with intensive monitoring for signs of addiction, abuse, and misuse.

Abuse or misuse of TROXYCA ER by cutting, breaking, chewing, crushing, or dissolving the pellets in TROXYCA ER and then swallowing, snorting or injecting will result in the uncontrolled delivery of the oxycodone and can result in overdose and death. Misuse or abuse of TROXYCA ER by these methods may also release sufficient naltrexone to precipitate withdrawal in opioid-dependent individuals.

Opioids are sought by drug abusers and people with addiction disorders and are subject to criminal diversion. Consider these risks when prescribing or dispensing TROXYCA 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.

Life-Threatening Respiratory Depression: Serious, life-threatening, or fatal respiratory depression has been reported with the use of modified-release opioids, even when used as recommended. Respiratory depression from opioid use, 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 (CO2) retention from opioid-induced respiratory depression can exacerbate the sedating effects of opioids.

While serious, life-threatening, or fatal respiratory depression can occur at any time during the use of TROXYCA ER, the risk is greatest during the initiation of therapy or following a dose increase. Monitor patients closely for respiratory depression when initiating therapy with TROXYCA ER and following dose increases.

Neonatal Opioid Withdrawal Syndrome: Prolonged use of TROXYCA 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.

Use in Elderly, Cachectic, and Debilitated Patients: Life-threatening respiratory depression is more likely to occur in elderly, cachectic, or debilitated patients as they may have altered pharmacokinetics or altered clearance compared to younger, healthier patients. Monitor such patients closely, particularly when initiating and titrating TROXYCA ER and when TROXYCA ER is given concomitantly with other drugs that depress respiration. Alternatively, consider the use of non-opioid analgesics in these patients.

Use in Patients with Chronic Pulmonary Disease: TROXYCA ER-treated patients with significant chronic obstructive pulmonary disease or corpulmonale, 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 TROXYCA ER.

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.

Hypotensive Effect: TROXYCA 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 (i.e., phenothiazines or general anesthetics. Monitor these patients for signs of hypotension after initiating or titrating the dose of TROXYCA ER. In patients with circulatory shock, TROXYCA ER may cause vasodilation that can further reduce cardiac output and blood pressure. Avoid the use of TROXYCA ER in patients with circulatory shock.

Use in Patients with Head Injury or Increased Intracranial Pressure:

In patients who may be susceptible to the intracranial effects of CO2 retention (e.g., those with evidence of increased intracranial pressure or brain tumors), TROXYCA ER may reduce respiratory drive, and the resultant CO2 retention can further increase intracranial pressure. Monitor such patients for signs of sedation and respiratory depression, particularly when initiating therapy with TROXYCA ER.

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

Adverse Reactions: Most common adverse reactions with TROXYCA ER therapy were: nausea, constipation, vomiting, somnolence, headache, and dizziness.

Please see full prescribing information here.

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emerging markets to advance wellness, prevention, treatments and cures that challenge the most feared diseases of our time. Consistent with our responsibility as one of the world's premier innovative biopharmaceutical companies, we collaborate with health care providers, governments and local communities to support and expand access to reliable, affordable health care around the world. For more than 150 years, Pfizer has worked to make a difference for all who rely on us. For more information, please visit us at www.pfizer.com. In addition, to learn more, follow us on Twitter at @Pfizerand @Pfizer_News, LinkedIn, YouTube and like us on Facebook at Facebook.com/Pfizer.

DISCLOSURE NOTICE: *The information contained in this release is as of August 19, 2016. Pfizer assumes no obligation to update forward-looking statements contained in this release as the result of new information or future events or developments.*

This release contains forward-looking information about TROXYCA ER*, including its potential benefits, that involves substantial risks and uncertainties that could cause actual results to differ materially from those expressed or implied by such statements. Risks and uncertainties include, among other things, the uncertainties inherent in research and development; uncertainties regarding the commercial success of TROXYCA ER; and competitive developments.*

A further description of risks and uncertainties can be found in Pfizer's Annual Report on Form 10-K for the fiscal year ended December 31, 2015 and in its subsequent reports on Form 10-Q, including in the sections thereof captioned "Risk Factors" and "Forward-Looking Information and Factors That May Affect Future Results", as well as in its subsequent reports on Form 8-K, all of which are filed with the U.S. Securities and Exchange Commission and available at www.sec.gov and www.pfizer.com.

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