Vantrela™ ER (hydrocodone bitartrate) – New Drug Approval

- On January 18, 2017, Teva announced the FDA approval of Vantrela ER (hydrocodone bitartrate) extended-release (ER) tablets, 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.

    — Vantrela ER is a Schedule II controlled substance.
    — 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 ER opioid formulations, reserve Vantrela 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.
    — Vantrela ER is not indicated as an as-needed (prn) analgesic.

- The safety and efficacy of Vantrela ER were evaluated in a placebo-controlled study of patients with moderate to severe chronic low back pain who required continuous opioid treatment.

    — Vantrela ER provided greater relief of low back pain than placebo as measured by the weekly average of daily worst pain intensity scores ($p < 0.001$).

- Vantrela ER administered orally or intranasally was associated with a lower risk of abuse compared to hydrocodone, as measured by Drug Liking and Take Drug Again scores ($p < 0.001$). In addition, Vantrela ER has physical and chemical properties that are expected to make intravenous abuse difficult and to reduce abuse via the oral and the intranasal route. However, abuse of Vantrela ER by the intravenous, nasal, and oral routes is still possible.

- Additional data, when available, may provide further information on the impact of the current formulation of Vantrela ER on the abuse liability of the drug.

- Vantrela ER carries a boxed warning for addiction, abuse, and misuse; life-threatening respiratory depression; accidental ingestion; neonatal opioid withdrawal syndrome; cytochrome P450 3A4 interaction; and risks from concomitant use with benzodiazepines or other central nervous system depressants.

- Vantrela 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; and hypersensitivity to hydrocodone bitrate or any other ingredients in Vantrela ER.

- Other warnings and precautions of Vantrela ER include risk of life-threatening respiratory depression in patients with chronic pulmonary disease and in elderly, cachectic, or debilitated patients; adrenal insufficiency; severe hypotension; risks of use in patients with increased intracranial pressure, brain tumors, head injury or impaired consciousness; risks of use in patients with gastrointestinal conditions; increased risk of seizures in patients with seizure disorders; withdrawal; risks of driving and operating machinery; and risk of QTc interval prolongation.

- The most common adverse events (≥ 2%) with Vantrela ER use were nausea, constipation, headache, somnolence, vomiting, dizziness, pruritus, fatigue, dry mouth, diarrhea, insomnia, and anxiety.

- The dosing regimen for each patient should be individualized, taking into account the patient's severity of pain, patient response, prior analgesic treatment experience, and risk factors for

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addiction, abuse, and misuse. The recommended dose of Vantrela ER in opioid-naïve and opioid non-tolerant patients is 15 mg orally every 12 hours.

  - Vantrela ER 90 mg tablets, a single dose greater than 60 mg, or a total daily dose greater than 120 mg, are only for use in patients in whom tolerance to an opioid of comparable potency has been established.
  - A dose of 90 mg every 12 hours (180 mg per day) should not be exceeded.
  - Consult product information for dosing recommendations for patients converting from other opioids to Vantrela ER.

- Teva's launch plans for Vantrela ER are pending. Vantrela ER will be available as 15 mg, 30 mg, 45 mg, 60 mg and 90 mg ER tablets.