Olinvyk™ (oliceridine) – New drug approval

- On August 7, 2020, the FDA announced the approval of Trevena's Olinvyk (oliceridine), in adults for the management of in adults for the management of acute pain severe enough to require an intravenous opioid analgesic and for whom alternative treatments are inadequate.

    — Because of the risks of addiction, abuse, and misuse with opioids, even at recommended doses, Olinvyk should be reserved for use in patients for whom alternative treatment options [eg, non-opioid analgesics or opioid combination products] have not been tolerated, or are not expected to be tolerated or have not provided adequate analgesia, or are not expected to provide adequate analgesia.
    — The cumulative total daily dose should not exceed 27 mg, as total daily doses greater than 27 mg may increase the risk for QTc interval prolongation.

- Each year, approximately 45 million hospital patients in the U.S. receive an intravenous (IV) opioid to treat their acute pain.

- Olinvyk is a full opioid agonist and is relatively selective for the mu-opioid receptor. The principal therapeutic action of Olinvyk is analgesia.

- The efficacy of Olinvyk was established in two randomized, double-blind, placebo- and morphine-controlled studies. In study 1, 389 patients with moderate to severe acute pain following orthopedic surgery-bunionectomy were randomized to placebo, 3 different doses of Olinvyk or morphine for up to 48 hours.

    — A statistically significantly greater analgesic effect was observed in both 0.35 mg and 0.5 mg Olinvyk treatment groups vs. the placebo group.

- In study 2, 401 patients with moderate to severe acute pain following plastic surgery-abdominoplasty were randomized to 3 different doses of Olinvyk or morphine for up to 24 hours.

    — A statistically significantly greater analgesic effect was observed in the Olinvyk 0.5 mg and 0.35 mg treatment groups vs. the placebo group.
    — The analgesic effect was not significantly better in the Olinvyk 0.1 mg treatment group vs. the placebo group.

- Olinvyk carries a boxed warning for addiction, abuse and misuse; life-threatening respiratory depression neonatal opioid withdrawal syndrome; and risks from concomitant use with benzodiazepines or other central nervous system depressants.

- Olinvyk is contraindicated in patients with significant respiratory depression; acute or severe bronchial asthma in an unmonitored setting or in absence of resuscitative equipment; known or suspected gastrointestinal obstruction, including paralytic ileus; and known hypersensitivity to Olinvyk.

- Warnings and precautions for Olinvyk include potential for QT prolongation with daily doses exceeding 27 mg; risk of use in patients with decreased cytochrome P450 2D6 function or concomitant use or discontinuation with cytochrome P450 3A4 inhibitors and inducers; life-threatening respiratory depression in patients with chronic pulmonary disease or 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

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use in patients with gastrointestinal conditions; increased risk of seizures in patients with seizure disorders; withdrawal; risks of driving and operating machinery; and patient-controlled analgesia (PCA).

- The most common adverse reactions (≥ 10%) with Olinvyk use were nausea, vomiting, dizziness, headache, constipation, pruritus, and hypoxia.

- The recommended initial dose of Olinvyk is 1.5 mg administered IV by a healthcare provider. For PCA, the initial dose can be followed by access to patient demand doses with a 6-minute lockout. The recommended demand dose is 0.35 mg. A demand dose of 0.5 mg may be considered for some patients if the potential benefit outweighs the risks. Supplemental doses of 0.75 mg can be administered by healthcare providers, beginning 1 hour after the initial dose, and hourly thereafter as needed.

    - Single doses greater than 3 mg should not be administered.
    - The cumulative total daily dose should not exceed 27 mg. If patients reach a 27 mg cumulative daily dose and analgesia is still required, an alternative analgesic regimen should be administered until Olinvyk can be resumed the next day.
    - Alternative analgesia may include multi-modal therapies.
    - The safety of Olinvyk beyond 48 hours of use has not been evaluated in controlled clinical trials.
    - The lowest effective dose should be used for the shortest duration consistent with individual patient treatment goals.
    - The dosing regimen should be initiated for each patient individually, taking into account the patient's severity of pain, patient response, prior analgesic treatment experience, and risk factors for addiction, abuse, and misuse.

- Trevena plans to launch Olinvyk in the fourth quarter of 2020 after the DEA issues its controlled substance schedule in approximately 90 days. Olinvyk will be available as 1 mg/mL and 2 mg/2mL single dose vials, and 30 mg/30 mL single-patient-use vials for PCA.