Olinvyk® (oliceridine) injection

Dosing and administration.

IMPORTANT SAFETY INFORMATION

WARNING: ADDICTION, ABUSE, AND MISUSE; LIFE-THREATENING RESPIRATORY DEPRESSION; NEONATAL OPIOID WITHDRAWAL SYNDROME; and RISKS FROM CONCOMITANT USE WITH BENZODIAZEPINES OR OTHER CENTRAL NERVOUS SYSTEM (CNS) DEPRESSANTS

ADDICTION, ABUSE, AND MISUSE
OLINVYK 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 before prescribing OLINVYK, and monitor all patients regularly for the development of behaviors or conditions.

LIFE-THREATENING RESPIRATORY DEPRESSION
Serious, life-threatening, or fatal respiratory depression may occur with use of OLINVYK. Monitor for respiratory depression, especially during initiation of OLINVYK or following a dose increase.

NEONATAL OPIOID WITHDRAWAL SYNDROME
Prolonged use of OLINVYK 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.

RISK FROM CONCOMITANT USE WITH BENZODIAZEPINES OR OTHER CNS DEPRESSANTS
Concomitant use of opioids with benzodiazepines or other CNS depressants, including alcohol, may result in profound sedation, respiratory depression, coma, and death. Reserve concomitant prescribing for use in patients for whom alternative treatment options are inadequate; limit dosages and durations to the minimum required; and follow patients for signs and symptoms of respiratory depression and sedation.

INDICATIONS AND USAGE
OLINVYK is an opioid agonist indicated in adults for the management of acute pain severe enough to require an intravenous opioid analgesic and for whom alternative treatments are inadequate.

Please see Full Prescribing Information in pocket, and Important Safety Information, including Boxed Warning, on pages 5-7.

Simple flexible dosing.

Olinvyk® (oliceridine) injection

INITIAL DOSING CONVERSION[1]

1 mg OLINVYK ≈ 5 mg IV morphine

BOLUS DOSING[1*]

- **1-2 mg loading dose**
- **1-3 mg supplemental dose every 1-3 hours as needed**

1 mg/1 mL (single dose)

2 mg/2 mL (single dose)

*In an open-label safety study in patients with moderate to severe acute postoperative pain, OLINVYK was administered via clinician-administered bolus dosing, PCA, or a combination of the two (N=768).
†In 2 randomized, double-blind, placebo- and morphine-controlled studies in patients with moderate to severe acute pain following either bunionectomy or abdominoplasty, patients received 1 of 3 OLINVYK dosing regimens, a morphine-control regimen, or a volume-matched placebo-control regimen and all dosing regimens were administered via PCA (N=389).
IV=intravenous; PCA=patient-controlled analgesia.

30 mg/30 mL (single-patient use, PCA use only)

PREDICTABLE ANALGESIA[1-3]

- **No active metabolites—reduces dose stacking concerns**

PCA DOSING[1*†]

- **1.5 mg loading dose**
- **0.35 mg or 0.5 mg demand dose as needed**
- **6 min lockout interval**

- **Do not administer single doses greater than 3 mg[1]**
- **Cumulative total daily dose should not exceed 27 mg[1]**
- **Refrigeration and reconstitution not required[1]**

Limitations of Use

Because of the risks of addiction, abuse, and misuse with opioids, even at recommended doses, reserve OLINVYK for use in patients for whom alternative treatment options [e.g., non-opioid analgesics or opioid combination products]:

- Have not been tolerated, or are not expected to be tolerated
- 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.

CONTRAINDICATIONS

OLINVYK 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
- Known hypersensitivity to oliceridine (e.g., anaphylaxis)

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Important dosing and administration instructions.

IV ONLY[1]

For intravenous administration only.

PCA USAGE[1]

30 mg/30 mL single-patient use vial is intended for PCA use only. Draw OLINVYK directly from the vial into the PCA syringe or IV bag without diluting.

INDIVIDUALIZE DOSING[1]

Use the lowest effective dose for the shortest duration consistent with individual patient treatment goals.

DOSING REGIMEN[1]

Initiate the dosing regimen 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.

USE IN SPECIFIC POPULATIONS[1]

Elderly patients (aged ≥65 years) may have increased sensitivity to OLINVYK. In general, use caution when selecting a dosage for an elderly patient, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function and of concomitant disease or other drug therapy. Respiratory depression is the chief risk for elderly patients treated with opioids. Titrate the dosage of OLINVYK slowly in geriatric patients and monitor for signs of central nervous system and respiratory depression.

INSPECT PRODUCT[1]

Visually inspect parenteral drug products for particulate matter and discoloration prior to administration. The solution is a clear, colorless, preservative-free solution for intravenous use. If visibly opaque particles, discoloration, or other foreign particles are observed, do not use.

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IMPORTANT SAFETY INFORMATION

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NEONATAL OPIOID WITHDRAWAL SYNDROME
Prolonged use of OLINVYK 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.

RISK FROM CONCOMITANT USE WITH BENZODIAZEPINES OR OTHER CNS DEPRESSANTS
Concomitant use of opioids with benzodiazepines or other CNS depressants, including alcohol, may result in profound sedation, respiratory depression, coma, and death. Reserve concomitant prescribing for use in patients for whom alternative treatment options are inadequate; limit dosages and durations to the minimum required; and follow patients for signs and symptoms of respiratory depression and sedation.

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OLINVYK is an opioid agonist indicated in adults for the management of acute pain severe enough to require an intravenous opioid analgesic and for whom alternative treatments are inadequate.

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- Significant respiratory depression
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- Known or suspected gastrointestinal obstruction, including paralytic ileus
- Known hypersensitivity to oliceridine (e.g., anaphylaxis)

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS

- OLINVYK contains oliceridine, a Schedule II controlled substance, that exposes users to the risks of addiction, abuse, and misuse. Although the risk of addiction in any individual is unknown, it can occur in patients appropriately prescribed OLINVYK. Assess risk, counsel, and monitor all patients receiving opioids.
- Serious, life-threatening respiratory depression has been reported with the use of opioids, even when used as recommended, especially in patients with chronic pulmonary disease, or in elderly, cachectic and debilitated patients. The risk is greatest during initiation of OLINVYK therapy, following a dose increase, or when used with other drugs that depress respiration. Proper dosing of OLINVYK is essential, especially when converting patients from another opioid product to avoid overdose. Management of respiratory depression may include close observation, supportive measures, and use of opioid antagonists, depending on the patient's clinical status.
- Opioids can cause sleep-related breathing disorders including central sleep apnea (CSA) and sleep-related hypoxemia with risk increasing in a dose-dependent fashion. In patients who present with CSA, consider decreasing the dose of opioid using best practices for opioid taper.
- Prolonged use of opioids during pregnancy can result in withdrawal in the neonate that may be life-threatening. Observe newborns for signs of neonatal opioid withdrawal syndrome and manage accordingly. Advise pregnant women using OLINVYK for a prolonged period of the risk of neonatal opioid withdrawal syndrome and ensure that appropriate treatment will be available.
- Profound sedation, respiratory depression, coma, and death may result from the concomitant use of OLINVYK with benzodiazepines or other CNS depressants (e.g., non-benzodiazepine sedatives/hypnotics, anxiolytics, tranquilizers, muscle relaxants, general anesthetics, antipsychotics, other opioids, or alcohol). Because of these risks, reserve concomitant prescribing of these drugs for use in patients for whom alternative treatment options are inadequate, prescribe the lowest effective dose, and minimize the duration.
- OLINVYK was shown to have mild QTc interval prolongation in thorough QT studies where patients were dosed up to 27 mg. Total cumulative daily doses exceeding 27 mg per day were not studied and may increase the risk for QTc interval prolongation. Therefore, the cumulative total daily dose of OLINVYK should not exceed 27 mg.
- Increased plasma concentrations of OLINVYK may occur in patients with decreased Cytochrome P450 (CYP) 2D6 function or normal metabolizers taking moderate or strong CYP2D6 inhibitors; also in patients taking a moderate or strong CYP3A4 inhibitor, in patients with decreased CYP2D6 function who are also receiving a moderate or strong CYP3A4 inhibitor, or with discontinuation of a CYP3A4 inducer. These patients may require less frequent dosing and should be closely monitored for respiratory depression and sedation at frequent intervals. Concomitant use of OLINVYK with CYP3A4 inducers or discontinuation of a moderate or strong CYP3A4 inhibitor can lower the expected concentration, which may decrease efficacy, and may require supplemental doses.
- Cases of adrenal insufficiency have been reported with opioid use (usually greater than one month). Presentation and symptoms may be nonspecific and include nausea, vomiting, anorexia, fatigue, weakness, dizziness, and low blood pressure. If confirmed, treat with physiologic replacement doses of corticosteroids and wean patient from the opioid.
- OLINVYK may cause severe hypotension, including orthostatic hypotension and syncope in ambulatory patients. There is 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 (e.g., phenothiazines or general anesthetics). Monitor these patients for signs of hypotension. In patients with circulatory shock, avoid the use of OLINVYK as it may cause vasodilation that can further reduce cardiac output and blood pressure.
- Avoid the use of OLINVYK in patients with impaired consciousness or coma. OLINVYK should be used with caution in patients who may be susceptible to the intracranial effects of CO_2 retention, such as those with evidence of increased intracranial pressure or brain tumors, as a reduction in 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.
- As with all opioids, OLINVYK may cause spasm of the sphincter of Oddi, and may cause increases in serum amylase. Monitor patients with biliary tract disease, including acute pancreatitis, for worsening symptoms.
- OLINVYK may increase the frequency of seizures in patients with seizure disorders and may increase the risk of seizures in vulnerable patients. Monitor patients with a history of seizure disorders for worsened seizure control.
- Do not abruptly discontinue OLINVYK in a patient physically dependent on opioids. Gradually taper the dosage to avoid a withdrawal syndrome and return of pain. Avoid the use of mixed agonist/antagonist (e.g., pentazocine, nalbuphine, and butorphanol) or partial agonist (e.g., buprenorphine) analgesics in patients who are receiving OLINVYK, as they may reduce the analgesic effect and/or precipitate withdrawal symptoms.
- OLINVYK may impair the mental or physical abilities needed to perform potentially hazardous activities such as driving a car or operating machinery.
- Although self-administration of opioids by patient-controlled analgesia (PCA) may allow each patient to individually titrate to an acceptable level of analgesia, PCA administration has resulted in adverse outcomes and episodes of respiratory depression. Health care providers and family members monitoring patients receiving PCA analgesia should be instructed in the need for appropriate monitoring for excessive sedation, respiratory depression, or other adverse effects of opioid medications.

ADVERSE REACTIONS

Adverse reactions are described in greater detail in the Prescribing Information.

The most common (incidence ≥10%) adverse reactions in Phase 3 controlled clinical trials were nausea, vomiting, dizziness, headache, constipation, pruritus, and hypoxia.

MEDICAL INFORMATION

For medical inquiries or to report an adverse event, other safety-related information or product complaints for a company product, please contact the Trevena Medical Information Contact Center at 1-844-465-4686 or email MedInfo@Trevena.com.

You are encouraged to report suspected adverse events of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088.

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Olinvyk® (oliceridine) injection

Olinvyk®
(oliceridine) injection

For your clinically challenging patients

The first IV opioid advancement in decades.[4]

Rapid Relief.

Median onset of pain relief 1-3 minutes after initial dose[1]*

Simple Flexible Dosing.

Bolus dosing 1-3 hours. No dosage adjustment for renal impairment. Bolus and PCA options[1,2†]

Predictable Analgesia.

No active metabolites—reduces dose stacking concerns[1-3]

Clinically Challenging Patients.

Safety established in clinically challenging patients including elderly, obese, and those with comorbidities[1,5†]

*Onset of pain relief was evaluated in a Phase 2, fixed-dose bunionectomy trial in which 192 patients were treated with OLINVYK IV every 3 hours, placebo IV, or morphine IV every 4 hours. Time to onset of analgesia was determined using the 2-stopwatch method, for which patients were given 2 stopwatches and instructed to stop the first for perceptible improvement in pain and the second for meaningful improvement in pain.[6]

†OLINVYK was studied in an open-label safety study in patients with moderate to severe acute postoperative pain (N=768), including obese patients (46%), elderly patients (32%), and patients with comorbidities (all patients had ≥1 comorbid condition), administered using clinician-administered bolus dosing, PCA, or a combination of the two.

IV=intravenous; PCA=patient-controlled analgesia.

Please see Full Prescribing Information in pocket, and Important Safety Information, including Boxed Warning, on pages 5-7.

References: 1. OLINVYK. Prescribing information. Trevena, Inc; 2021. **2.** Gan TJ, Wase L. Oliceridine, a G protein-selective ligand at the μ-opioid receptor, for the management of moderate to severe acute pain. *Drugs Today (Barc)*. 2020;56(4):269-286. **3.** Leiman D, Jové M, Spahn GR, Palmer P. Patient and healthcare professional satisfaction ratings and safety profile of sufentanil sublingual tablets for treatment of acute pain: a pooled demographic analysis. *J Pain Res*. 2021;14:805-813. **4.** Data on file. Trevena, Inc; 2020. **5.** Bergese SD, Brzezinski M, Hammer GB, et al. ATHENA: a phase 3, open-label study of the safety and effectiveness of oliceridine (TRV130), a G-protein selective agonist at the μ-opioid receptor, in patients with moderate to severe acute pain requiring parenteral opioid therapy. *J Pain Res*. 2019;12:3113-3126. **6.** Viscusi ER, Webster L, Kuss M, et al. A randomized, phase 2 study investigating TRV130, a biased ligand of the μ-opioid receptor, for the intravenous treatment of acute pain. *Pain*. 2016;157(1):264-272.

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