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Please see Full Prescribing Information at OLINVYK.com, and Important Safety Information, including Boxed Warning, on pages 15-17.
INTRODUCTION

This guide contains general coding and billing information to consider related to OLINVYK (oliceridine) injection. This guide is provided as general information only and is not intended as coverage or coding advice. Trevena cannot provide specific reimbursement rates, and does not guarantee reimbursement. You should always verify the appropriate reimbursement information for services or items you provide.

INDICATIONS AND USAGE

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

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.

Please see Full Prescribing Information at OLINVYK.com, and Important Safety Information, including Boxed Warning, on pages 15-17.
# CODING QUICK GUIDE

<table>
<thead>
<tr>
<th>Item</th>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>HCPCS¹ Code</td>
<td>J3490*</td>
<td>Unclassified Drugs</td>
</tr>
<tr>
<td>Hospital Outpatient HCPCS¹ Code</td>
<td>C9399</td>
<td>Unclassified Drugs or Biologicals</td>
</tr>
<tr>
<td>CPT² Code</td>
<td>96374</td>
<td>Therapeutic, prophylactic, or diagnostic injection (specify substance or drug); intravenous push, single or initial substance/drug</td>
</tr>
<tr>
<td></td>
<td>96376</td>
<td>Each subsequent IV push of same drug at intervals &gt; 30 minutes</td>
</tr>
<tr>
<td></td>
<td>D25.9</td>
<td>Leiomyoma of uterus, unspecific</td>
</tr>
<tr>
<td></td>
<td>M48.062</td>
<td>Spinal stenosis, lumbar region with neurogenic claudication</td>
</tr>
<tr>
<td></td>
<td>M19.90</td>
<td>Unspecified osteoarthritis, unspecified site</td>
</tr>
<tr>
<td></td>
<td>K40.0</td>
<td>Bilateral inguinal hernia, with obstruction, without gangrene</td>
</tr>
<tr>
<td></td>
<td>K80.80</td>
<td>Other cholelithiasis without obstruction</td>
</tr>
<tr>
<td></td>
<td>M16.31</td>
<td>Unilateral osteoarthritis resulting from hip dysplasia, right hip</td>
</tr>
<tr>
<td>Potential ICD-10-CM³ Codes (Not Exhaustive)²²</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10-Digit NDC⁴</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>71308-011-01</td>
<td>1 mg/1 mL solution in single-dose vials.</td>
</tr>
<tr>
<td></td>
<td>71308-021-01</td>
<td>2 mg/2 mL solution in single-dose vials.</td>
</tr>
<tr>
<td></td>
<td>71308-301-01</td>
<td>30 mg/30 mL solution in single-patient-use vials. For PCA Use Only.</td>
</tr>
<tr>
<td></td>
<td>71308-011-10</td>
<td>Carton of 10 single-dose vials of 1 mg/1 mL solution.</td>
</tr>
<tr>
<td></td>
<td>71308-021-10</td>
<td>Carton of 10 single-dose vials of 2 mg/2 mL solution.</td>
</tr>
<tr>
<td></td>
<td>71308-301-10</td>
<td>Carton of 10 single-patient-use vials of 30 mg/30 mL solution. For PCA Use Only.</td>
</tr>
</tbody>
</table>

*Alternative temporary billing code J9999 can be used in place of J3490.

**Not exclusive list, as many ICD-10-CM codes correspond to possible diagnoses triggering Olinvyk use. Displayed above is sample of diagnoses associated with surgical procedures that may incur OLINVYK use.

Please see Full Prescribing Information at OLINVYK.com, and Important Safety Information, including Boxed Warning, on pages 15-17.
The Drug Listing Act of 1972 requires registered drug establishments to provide the Food and Drug Administration (FDA) with a current list of all drugs manufactured, prepared, propagated, compounded, or processed by it for commercial distribution. (See Section 510 of the Federal Food, Drug, and Cosmetic Act (Act) (21 U.S.C. § 360)). Drug products are identified and reported using a unique, three-segment number, called the National Drug Code (NDC), which serves as a universal product identifier for drugs. FDA publishes the listed NDC numbers and the information submitted as part of the listing information in the NDC Directory which is updated daily.

### 6 NDCs for OLINVYK are:

<table>
<thead>
<tr>
<th>Number</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>71308-011-01</td>
<td>1 mg/mL, sterile solution in single-dose, 1 mL clear glass vial with gray stopper topped with overseal with gray plastic flip-off cap.</td>
</tr>
<tr>
<td>71308-021-01</td>
<td>2 mg/2 mL (1 mg/mL), sterile solution in single-dose, 2 mL clear glass vial with gray stopper topped with overseal with orange plastic flip-off cap.</td>
</tr>
<tr>
<td>71308-301-01</td>
<td>30 mg/30 mL (1 mg/mL), sterile solution in single-patient-use, 30 mL clear glass vial with gray stopper topped with overseal with purple plastic flip-off cap. For PCA Use Only.</td>
</tr>
<tr>
<td>71308-011-10</td>
<td>1 mg/mL, sterile solution in single-dose, 1 mL clear glass vials with gray stoppers topped with overseals with gray plastic flip-off caps (carton of 10 vials).</td>
</tr>
<tr>
<td>71308-021-10</td>
<td>2 mg/2 mL (1 mg/mL), sterile solution in single-dose, 2 mL clear glass vials with gray stoppers topped with overseals with orange plastic flip-off caps (carton of 10 vials).</td>
</tr>
<tr>
<td>71308-301-10</td>
<td>30 mg/30 mL (1 mg/mL), sterile solution in single-patient-use, 30 mL clear glass vials with gray stoppers topped with overseals with purple plastic flip-off caps (carton of 10 vials). For PCA Use Only.</td>
</tr>
</tbody>
</table>

Please see Full Prescribing Information at OLINVYK.com, and Important Safety Information, including Boxed Warning, on pages 15-17.
The HCPCS Level II Code Set is one of the standard code sets used for medical claims processing of office-administered drugs. The HCPCS is divided into two principal subsystems, referred to as level I and level II of the HCPCS. Level I of the HCPCS is comprised of CPT® (Current Procedural Terminology), a numeric coding system maintained by the American Medical Association (AMA). The CPT® is a uniform coding system consisting of descriptive terms and identifying codes that are used primarily to identify medical services and procedures furnished by physicians and other healthcare professionals. These healthcare professionals use the CPT® to identify services and procedures for which they bill public or private health insurance programs. Decisions regarding the addition, deletion, or revision of CPT® codes are made by the AMA. The CPT® codes are republished and updated annually by the AMA. Level I of the HCPCS, the CPT® codes, does not include codes needed to separately report medical items or services that are regularly billed by suppliers other than physicians.

Level II of the HCPCS is a standardized coding system that is used primarily to identify products, supplies, and services not included in the CPT® codes, such as ambulance services and durable medical equipment, prosthetics, orthotics, and supplies (DMEPOS) when used outside a physician’s office. Because Medicare and other insurers cover a variety of services, supplies, and equipment that are not identified by CPT® codes, the level II HCPCS codes were established for submitting claims for these items. The development and use of level II of the HCPCS began in the 1980s. Level II codes are also referred to as alpha-numeric codes because they consist of a single alphabetical letter followed by 4 numeric digits, while CPT® codes are identified using 5 numeric digits.

### Potential Level II HCPCS Codes for Billing OLINVYK

<table>
<thead>
<tr>
<th>HCPCS Code</th>
<th>Description</th>
<th>Use</th>
</tr>
</thead>
<tbody>
<tr>
<td>J3490*</td>
<td>Unclassified Drug</td>
<td>Most payers and sites of service</td>
</tr>
<tr>
<td>C9399</td>
<td>Unclassified Drugs or Biologics</td>
<td>Outpatient Claims billed under Medicare using the Hospital Outpatient Prospective Claims System</td>
</tr>
</tbody>
</table>

*Alternative temporary billing code J9999 can be used in place of J3490.

Please see Full Prescribing Information at OLINVYK.com, and Important Safety Information, including Boxed Warning, on pages 15-17.
Providers should consult with their local payers to identify the most appropriate administration coding procedures and required documentation. The following codes are for physician-administered intravenous push of OLINVYK.

<table>
<thead>
<tr>
<th>CPT Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>96374</td>
<td>Therapeutic, prophylactic, or diagnostic injection (specify substance or drug); intravenous push, single or initial substance/drug</td>
</tr>
<tr>
<td>96376</td>
<td>Each subsequent IV push of same drug at intervals &gt;30 minutes</td>
</tr>
</tbody>
</table>

Please see Full Prescribing Information at OLINVYK.com, and Important Safety Information, including Boxed Warning, on pages 15-17.
POTENTIAL INTERNATIONAL CLASSIFICATION OF DISEASES, 10TH REVISION, CLINICAL MODIFICATION (ICD-10-CM) CODES FOR USE WHEN BILLING AN OLINVYK CLAIM.

The International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) is a system used by physicians and other healthcare providers to classify and code all diagnoses, symptoms, and procedures recorded in conjunction with hospital care in the United States.

ICD-10-CM is composed of codes with 3, 4, 5, 6, or 7 characters. Codes with 3 characters are included in ICD-10-CM as the heading of a category of codes that may be further subdivided by the use of fourth, fifth, sixth, or seventh characters to provide greater specificity. A 3-character code is to be used only if it is not further subdivided. While diagnosis coding to the correct level of specificity is the goal for all claims, for 12 months after ICD-10 implementation, if a valid ICD-10 code from the right family is submitted, Medicare fee-for-service will process and not audit valid ICD-10 codes unless such codes fall in.
## POTENTIAL ICD-10-CM CODES FOR USE WHEN BILLING AN OLINVYK CLAIM USE MOST SPECIFIC SUB-CODING POSSIBLE

<table>
<thead>
<tr>
<th>ICD-10-CM Code</th>
<th>Code Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>D25.9</td>
<td>Leiomyoma of uterus, unspecified</td>
</tr>
<tr>
<td>M48.062</td>
<td>Spinal stenosis, lumbar region with neurogenic claudication</td>
</tr>
<tr>
<td>M19.90</td>
<td>Unspecified osteoarthritis, unspecified site</td>
</tr>
<tr>
<td>K40.0</td>
<td>Bilateral inguinal hernia, with obstruction, without gangrene</td>
</tr>
<tr>
<td>K80.80</td>
<td>Other cholelithiasis without obstruction</td>
</tr>
<tr>
<td>M16.31</td>
<td>Unilateral osteoarthritis resulting from hip dysplasia, right hip</td>
</tr>
</tbody>
</table>

Not an exclusive list. ICD-10-CM codes are a sample of diagnoses associated with surgical procedures in which OLINVYK may be used.

Please see Full Prescribing Information at OLINVYK.com, and Important Safety Information, including Boxed Warning, on pages 15-17.
PHYSICIAN OFFICE SAMPLE CLAIM FORM: CMS-1500

Item 19 - When billing a not-otherwise-classified HCPCS code like J3490, some payers may ask providers to specify OLINVYK (oliceridine) injection with dosage administered and NDC number.

NOTE:
Some payers require alternate product codes (i.e., Medicaid claims). Please consult with your relevant payers.

Item 21 - Indicate diagnosis/diagnoses using appropriate ICD-10-CM codes, such as M16.31 (Unilateral osteoarthritis resulting from hip dysplasia, right hip).

Item 24D - Indicate appropriate CPT and HCPCS codes and modifiers if required. Enter the CPT code 96374 for initial IV push (therapeutic, prophylactic, or diagnostic injection - intravenous push, single or initial substance/drug). If subsequent IV push is required, enter in new row CPT code 96376 on subsequent row.

NOTE:
Individual payers will require documentation to adjudicate any claim billed with an unlisted CPT code. Please consult with your relevant payer. Additional information on the procedure may be placed in Item 19.

Item 24E - Refer to the diagnosis for this service (see box 21). Enter only one diagnosis pointer per line.

Item 24G - Enter number of milligrams of active ingredient utilized in one row, followed by number of milligrams wasted in subsequent row.

Please see Full Prescribing Information at OLINVYK.com, and Important Safety Information, including Boxed Warning, on pages 15-17.
**SAMPLE CMS-1500 CLAIM FORM (PHYSICIAN OFFICE BILLING)**

This form is for informational use only. Trevena is not responsible for the information submitted on this form.

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**HEALTH INSURANCE CLAIM FORM**

**APPROVED BY NATIONAL UNIFORM CLAIM COMMITTEE (NUCC) 02/12**

<table>
<thead>
<tr>
<th>Field</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. M.D., D.O., or D.C.</td>
<td>Medicare, Medicaid, TRICARE, CHAMPVA, Other Health Plan, FED/Civilian, Other</td>
</tr>
<tr>
<td>2. PATIENT’S NAME (Last Name, First Name, Middle Initial)</td>
<td>Smith, Joe B</td>
</tr>
<tr>
<td>3. PATIENT’S ADDRESS (No., Street)</td>
<td>123 State St</td>
</tr>
<tr>
<td>4. PATIENT’S RELATIONSHIP TO INSURED</td>
<td>Same</td>
</tr>
<tr>
<td>5. PATIENT’S SOCIAL SECURITY NUMBER</td>
<td>12345-6789</td>
</tr>
<tr>
<td>6. PATIENT’S DATE OF BIRTH</td>
<td>12/31/1950</td>
</tr>
<tr>
<td>7. INSURED’S NAME (Last Name, First Name, Middle Initial)</td>
<td>Smith, Joe B</td>
</tr>
<tr>
<td>8. INSURED’S ADDRESS (No., Street)</td>
<td>Same</td>
</tr>
</tbody>
</table>

**ADDITIONAL CLAIM INFORMATION (FIELD 19)**

Enter drug name, dosage, and NDC.

**DIAGNOSIS CODE (FIELD 21)**

M16.31

**PRODUCT CODE (FIELD 24D)**

Olinvyk (oliceridine), 1 mg, 71308-011-10

**PROCEDURE CODE(S) (FIELD 24D)**

J3490

**SERVICE UNITS (FIELD 24G)**

For rows with procedure-specific CPT codes, enter ‘1’. For rows with product HCPCS code, enter number of units billed (where units are smallest billable units – 1 mg).

**PROCEDURE CODE(S) (FIELD 24D)**

Note: 96374 to be used for initial IV push, and 96376 to be used for additional IV push (entered in subsequent row).

**Note:** Contact payer for specific coding requirements for billing wastage. For Medicare claims and some Commercial claims (not including those for J3490, J3590, or J9999), it may be necessary to enter one product row for utilized product amount and separate product row for wasted amount. Row corresponding to wasted amount would have ‘JW’ entered into modifier field. Not necessary if amount of wasted active ingredient < smallest billable unit (1 mg).

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Please see Full Prescribing Information at OLINVYK.com, and Important Safety Information, including Boxed Warning, on pages 15-17.
2020 HOPD SAMPLE CLAIM FORM: UB-04/CMS 1450

Locator Box 42 - List revenue codes in ascending order.
• For Medicare, revenue code 0636 (drugs that require detailed coding)
• For non-Medicare payers, revenue code 0250 (general pharmacy)
• Injection services may be reported with revenue code 0510 (clinic, general service)

Locator Box 43 - NDC code.

Locator Box 44 - Indicate appropriate CPT and HCPCS codes and modifiers if required. Enter the CPT code 96374 for initial IV push (therapeutic, prophylactic, or diagnostic injection - intravenous push, single or initial substance/drug). If subsequent IV push is required, enter in new row CPT code 96376 on subsequent row. In addition, in separate row, Medicare claims require HCPCS C9399, Private payers may require C9399 or J3490.

NOTE: Individual payers will require documentation to adjudicate any claim billed with an unlisted CPT code. Please consult with your local payer.

Locator Box 46 - Enter number of milligrams of active ingredient utilized in one row, followed by number of milligrams wasted in subsequent row.

Locator Box 47 - Indicate total charges.

Locator Box 67 - Indicate diagnosis/diagnoses using appropriate ICD-10-CM codes, such as M16.31 (Unilateral osteoarthritis resulting from hip dysplasia, right hip).

Locator Box 80 - When billing a not OTHERWISE-classified HCPCS code like J3490, some payers may ask providers to specify OLINVYK (oliceridine) injection with dosage administered and NDC code.

Please see Full Prescribing Information at OLINVYK.com, and Important Safety Information, including Boxed Warning, on pages 15-17.
Please see Full Prescribing Information at OLINVYK.com, and Important Safety Information, including Boxed Warning, on pages 15-17.
1. **NDC National Drug Code**: The Drug Listing Act of 1972 requires registered drug establishments to provide the Food and Drug Administration (FDA) with a current list of all drugs manufactured, prepared, propagated, compounded, or processed by it for commercial distribution. (See Section 510 of the Federal Food, Drug, and Cosmetic Act (Act) (21 U.S.C. § 360)). Drug products are identified and reported using a unique, three-segment number, called the National Drug Code (NDC), which serves as a universal product identifier for drugs. FDA publishes the listed NDC numbers and the information submitted as part of the listing information in the NDC Directory which is updated daily. The information submitted as part of the listing process, the NDC number, and the NDC Directory are used in the implementation and enforcement of the Act.

2. **HCPCS Level II Coding Process & Criteria**: The Centers for Medicare and Medicaid (CMS) published on August 17, 2000 (45 CFR 162.10002) to implement the HIPAA requirement for standardized coding systems established the HCPCS level II codes as the standardized coding system for describing and identifying health care equipment and supplies in health care transactions that are not identified by the HCPCS level I, CPT codes. The HCPCS level II coding system was selected as the standardized coding system because of its wide acceptance among both public and private insurers. Public and private insurers were required to be in compliance with the August 2000 regulation by October 1, 2002. The HCPCS Level II Coding Process/Criteria document describes HCPCS level II coding procedures and coding criteria.


4. **CPT®, Current Procedural Terminology**: The American Medical Association developed and maintains the official Current Procedural Terminology (CPT®) code set. According to the AMA website ([https://www.ama-assn.org/practice-management/cpt/cpt-overview-and-code-approval](https://www.ama-assn.org/practice-management/cpt/cpt-overview-and-code-approval)), the CPT is the most widely accepted medical nomenclature used to report medical procedures and services under public and private health insurance programs. CPT is maintained by the CPT Editorial Panel, which meets three times a year to discuss issues associated with new and emerging technologies as well as difficulties encountered with procedures and services and their relation to CPT codes.

5. **CMS 1500 Form**: The Form CMS-1500 is the standard paper claim form to bill Medicare Fee-For-Service (FFS) Contractors when a paper claim is allowed. In addition to billing Medicare, Form CMS-1500 may be suitable for billing various government and some private insurers. [https://www.cms.gov/outreach-and-education/medicare-learning-network-mln/mlnproducts/downloads/837p-cms-1500.pdf](https://www.cms.gov/outreach-and-education/medicare-learning-network-mln/mlnproducts/downloads/837p-cms-1500.pdf)

6. **UB-04 (CMS-1450) Form**: The Form CMS-1450, also known as the UB-04, is the standard claim form to bill Medicare Administrative Contractors (MACs) when a paper claim is allowed. In addition to billing Medicare, the 837l and Form CMS-1450 may be suitable for billing various government and some private insurers. [https://www.cms.gov/Outreach-and-Education/Medicare-Learning-Network-MLN/MLNProducts/Downloads/837l-FormCMS-1450-ICN006926.pdf](https://www.cms.gov/Outreach-and-Education/Medicare-Learning-Network-MLN/MLNProducts/Downloads/837l-FormCMS-1450-ICN006926.pdf)

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Please see Full Prescribing Information at OLINVYK.com, and Important Safety Information, including Boxed Warning, on pages 15-17.
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 a new chemical entity and is indicated in adults for the management of acute pain severe enough to require an intravenous opioid analgesic and for whom alternative treatments are inadequate.

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.

Please see Full Prescribing Information at OLINVYK.com, and Important Safety Information, including Boxed Warning, on pages 15-17.
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 olliceridine (e.g., anaphylaxis)

WARNINGS AND PRECAUTIONS

- OLINVYK contains olliceridine, 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, anxiolitics, 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.

Please see Full Prescribing Information at OLINVYK.com, and Important Safety Information, including Boxed Warning, on pages 15-17.
IMPORTANT SAFETY INFORMATION (continued)

• 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 CO₂ retention, such as those with evidence of increased intracranial pressure or brain tumors, as a reduction in 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.

• 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 negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088.

Please see Full Prescribing Information, including Boxed Warning.