Kloxxado® is a safety net for people in recovery

Relapse shouldn't be the end

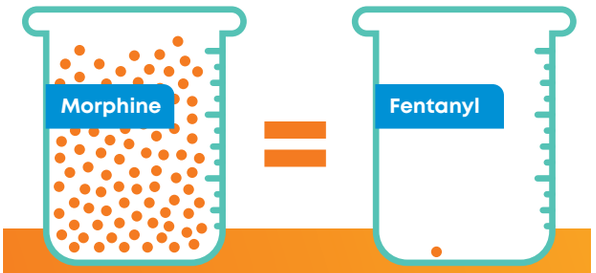
- Long term use of opioids can cause people to develop a tolerance, which would lead them to need a higher/or more frequent dose of the drug to get the desired effects.[1]
- Illicitly manufactured fentanyl could be mixed into street drugs without the person knowing.[2,3]
- Naloxone is an essential part of treatment[4]

40-60%
relapse

Rates for substance use disorder relapses are comparable to those for other chronic diseases.[5]

Fentanyl overdoses may require a higher dose of naloxone for reversing its effects due to its higher potency.[2]

*The recent rise in deaths from synthetic opioids are typically attributed to illicitly manufactured fentanyl, not pharmaceutical fentanyl.[3]



Fentanyl is 50–100x stronger than morphine.[6]

KLOXXADO® (naloxone HCl) Nasal Spray 8 mg Important Safety Information

INDICATION

KLOXXADO® is an opioid antagonist indicated for the emergency treatment of known or suspected opioid overdose, as manifested by respiratory and/or central nervous system depression, for adult and pediatric patients. KLOXXADO® is intended for immediate administration as emergency therapy in settings where opioids may be present. KLOXXADO® is not a substitute for emergency medical care.

CONTRAINDICATIONS

• Hypersensitivity to naloxone hydrochloride or to any of the other ingredients in KLOXXADO®.

WARNINGS AND PRECAUTIONS

• **Risk of Recurrent Respiratory and Central Nervous System Depression**
Seek emergency assistance immediately after administration of the first does of KLOXXADO® and keep the patient under continued surveillance. The duration of action of most opioids may exceed that of KLOXXADO®, resulting in a return of respiratory and/or central nervous system depression after an initial improvement in symptoms. Administer additional doses as necessary if the patient is not adequately responding or responds and then relapses back into respiratory depression.

See full ISI on back and enclosed Full Prescribing Information.

Kloxxado® (naloxone HCl) nasal spray 8 mg

KLOXXADO® (naloxone HCl) Nasal Spray 8 mg Important Safety Information, continued

WARNINGS AND PRECAUTIONS, continued

- **Risk of Limited Efficacy With Partial Agonists or Mixed Agonist/Agonists**
  Reversal of respiratory depression by partial agonists or mixed agonist/antagonists, such as buprenorphine and pentazocine, may be incomplete. Larger or repeat doses of naloxone hydrochloride may be required.
- **Precipitation of Severe Opioid Withdrawal**
  Use in patients who are opioid-dependent may precipitate opioid withdrawal characterized by body aches, diarrhea, tachycardia, fever, runny nose, sneezing, piloerection, sweating, yawning, nausea or vomiting, nervousness, restlessness or irritability, shivering or trembling, abdominal cramps, weakness and increased blood pressure. In neonates, opioid withdrawal may be life-threatening if not recognized and properly treated and may include convulsion, excessive crying and hyperactive reflexes. Monitor the patient for the development of the signs and symptoms of opioid withdrawal. For more information about management of opioid withdrawal, see the full Prescribing Information.

  Abrupt reversal of opioid effects in persons who were physically dependent on opioids has precipitated an acute withdrawal syndrome. In some patients, there was aggressive behavior upon abrupt reversal of an opioid overdose.

  Abrupt postoperative reversal of opioid depression after using naloxone hydrochloride may result in nausea, vomiting, sweating, tremulousness, tachycardia, hypotension, hypertension, seizures, ventricular tachycardia and fibrillation, pulmonary edema and cardiac arrest. Death, coma and encephalopathy have been reported as sequelae of these events. These events have primarily occurred in patients who had pre-existing cardiovascular disorders or received other drugs that may have similar adverse cardiovascular effects. Monitor these patients closely in an appropriate healthcare setting.

ADVERSE REACTIONS

In two pharmacokinetic studies, a total of 47 healthy adult volunteers were exposed to a single dose of KLOXXADO®, one spray in one nostril.

- Adverse reactions were reported in two subjects for each of the following: abdominal pain, asthenia, dizziness, headache, nasal discomfort, and presyncope.
- Signs of nasal inflammation and nasal congestion were observed
- Serious adverse reactions reported: none

The following most frequently reported events (in decreasing frequency) have been identified primarily during post-approval use of naloxone hydrochloride: withdrawal syndrome, vomiting, nonresponsiveness to stimuli, drug ineffective, agitation, somnolence, and loss of consciousness.

USE IN SPECIFIC POPULATIONS

- **Pregnancy**
  Naloxone may precipitate opioid withdrawal in the pregnant woman and fetus. Careful monitoring is needed until the fetus and mother are stabilized.
- **Infants**
  In situations where the primary concern is for infants at risk for opioid overdose, consider the availability of alternate naloxone-containing products.

For more information, please see the full Prescribing Information and Patient Information at https://kloxxado.com/.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit https://www.fda.gov/medwatch or call 1-800-FDA-1088.

Distributed by: Hikma Specialty USA Inc.
Columbus, OH 43228

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