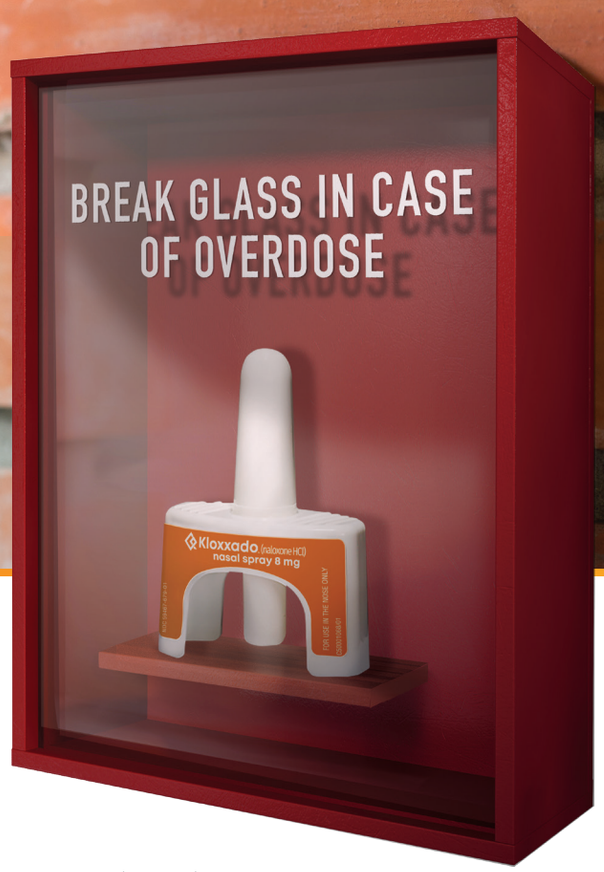
Kloxxado™ (naloxone HCl) nasal spray



Twice as ready to save a life

34% of opioid overdose reversals involved ≥2 doses of naloxone, according to a 2016 study of Narcan® Nasal Spray distributed to community groups across the country.[14]

KLOXXADO has twice as much naloxone per dose (8 mg) as NARCAN® Nasal Spray to counteract the risks of potent opioids.

The following adverse reactions were reported with KLOXXADO in two adult subjects each: abdominal pain, asthenia, dizziness, headache, nasal discomfort, and presyncope.[1]

Who should carry KLOXXADO:

- Anyone taking high strength or otherwise chronic opioids (e.g. ≥ 50MME)
- Anyone taking opioids of any dose with a benzodiazepine
- Anyone with certain respiratory conditions taking opioids (e.g. COPD or sleep apnea)
- Anyone taking opioids of any dose with non-opioid substance use disorder or other mental health disorder
- Anyone with a history of overdose or substance use disorder, including PWUD and patients in recovery
- People likely to observe an overdose, particularly family, friends, or caregivers

$0 could reverse an opioid overdose[21]

KLOXXADO is the first naloxone nasal spray to offer a copay card.

Pay as little as $0 (up to $40 savings for eligible patients)[21]

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.

See full ISI on pages 2 and 3.

KLOXXADO (naloxone hydrochloride) Nasal Spray important safety information

WARNINGS AND PRECAUTIONS

- **Risk of Recurrent Respiratory and Central Nervous System Depression**
  Seek emergency assistance immediately after administration of the first dose 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.

- **Risk of Limited Efficacy With Partial Agonists or Mixed Agonist/Agonists**
  Reversal of respiratory depression by partial agonists or mixed/antagonists 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.

References

1 KLOXXADO® (Naloxone HCl) Nasal Spray [prescribing information]. Columbus, OH: Hikma Specialty USA, Inc.; 2021.

2 Avetian et. al. 2018, “Use of naloxone nasal spray 4mg in the community setting: a survey of use by community organizations”, Current Medical Research and Opinion

3 HHS: Non-fatal opioid overdose and associated health outcomes: final summary report. Sept. 4, 2019

4 Naloxone. National Institutes of Health. Accessed March 26, 2021. https://www.drugabuse.gov/publications/drugfacts/naloxone

FULL PRESCRIBING INFORMATION LOCATED IN POCKET

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.

- The following adverse reactions were reported in two subjects each: 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.

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 Pharmaceuticals USA Inc., Berkeley Heights, NJ 07922

Kloxxado™ (naloxone HCl) nasal spray

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

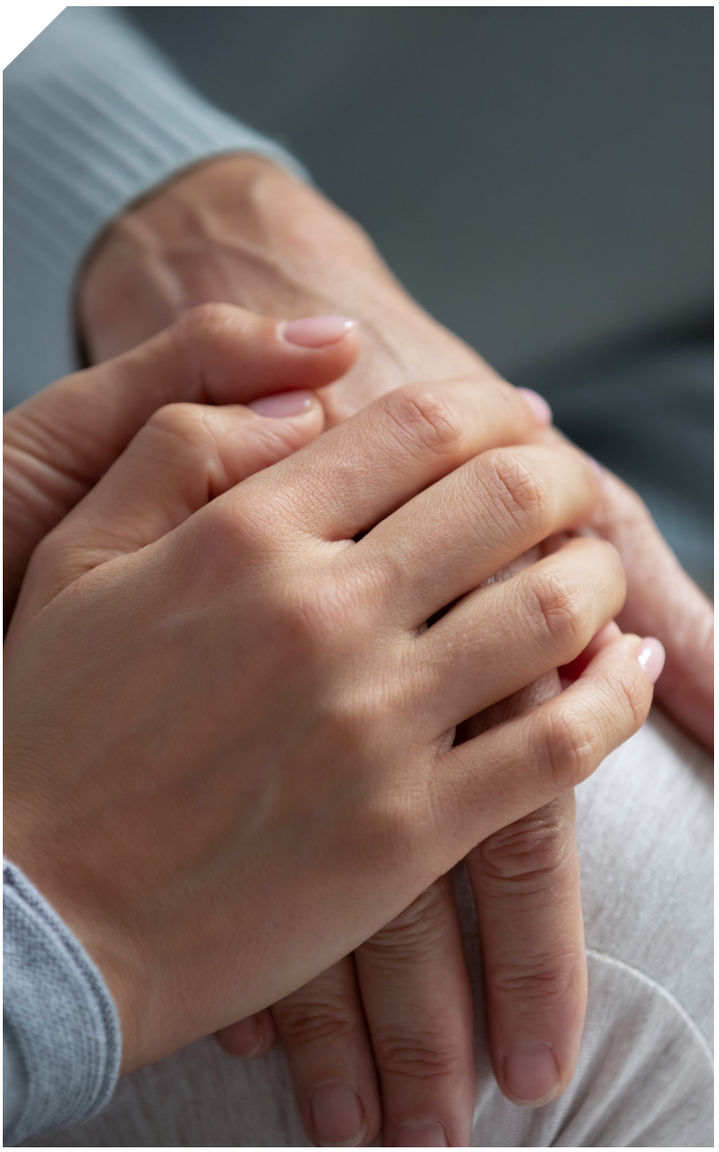
For US Health Care Professionals only.

HK-1112-v1

Kloxxado™ (naloxone HCl) nasal spray

Add KLOXXADO with opioids over 50 MME

Opioid dosing at or above 50 MME/day doubles the risk of overdose relative to <20 MME/day.



HHS guidelines recommend naloxone with any "high dose" / ≥50 MME* per day opioid prescription.

50 MME/day for select opioids[4]	
Codeine	333 mg/day
Hydrocodone	50 mg/day
Hydromorphone	12.5 mg/day
Methadone	12 mg/day
Morphine	50 mg/day
Oxycodone	33 mg/day
Oxymorphone	16.7 mg/day

*MME = "milligram morphine equivalent"
Used to enable a standardized comparison of opioid dose across products, often used as a gauge of the abuse or overdose potential of the amount of opioid that is being given at a particular time

IMPORTANT: There is no completely safe opioid dose, and this guide does not substitute for clinical judgment. Use caution when prescribing opioids at any dosage, and prescribe the lowest effective dose.

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.

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