

Our communities need more naloxone

- Overdose deaths reached 93,000 in the past year, a nearly 30% increase over the year of the pandemic,¹ largely driven by illicitly manufactured synthetic opioids.²
- Real-world use suggests that more naloxone may be required to reverse an overdose on synthetic opioids³
- 78% of overdose reversal attempts with Narcan® (naloxone HCl) nasal spray 4mg⁴ involved 2 or more doses in 2020-2021,⁴ and the frequency of naloxone multi-dosing has been increasing.⁵

Kloxxado™ (naloxone HCl) Nasal Spray 8 mg provides more medicine for your community at a familiar price

- Naloxone is a safe medication. It is indicated for emergency treatment of known or suspected opioid overdose, as manifested by respiratory and/or central nervous system depression, for adult and pediatric patients.⁶
- Naloxone side effects may be uncomfortable, but they are not life-threatening. Unlike naloxone, the overdose may be life-threatening.^{8,9}
- Package: 2 nasal spray devices per box, 8 mg per spray.⁶
- Public Access Price: \$75/kit— talk to your account director to see if you are eligible for any special promotions.
- Warnings and Precautions: risk of recurrent respiratory & CNS depression, risk of limited efficacy with partial agonists or mixed agonist/antagonists, precipitation of severe opioid withdrawal, and risk of CV effects.⁶



Hikma is a longstanding US provider of high-quality, affordable medicines

- Hikma offers >220 medicines in the US, most made in the US, with ~1900 US employees and 3 large manufacturing/R&D sites.¹⁰
- Hikma is a strong public health partner, providing critical medicines involved in the treatment of COVID-19 patients (including dexamethasone), as well as substance use disorder (including buprenorphine).¹⁰

For any additional questions, please reach out to your account director, or email communityhealth@hikma.com.

References:

1. <https://www.cnn.com/2021/07/17/health/us-drug-overdose-deaths-pandemic/index.html>, accessed July 19, 2021
2. <https://www.cdc.gov/drugoverdose/pubs/featured-topics/save-lives-now.html>, Accessed June 21, 2021
3. <https://emergency.cdc.gov/han/han00384.asp>, last updated October 26, 2015, Accessed June 21, 2021
4. Abdelal R, Banerjee AR, Carlberg-Racich S, Darwaza N, Ito D, Shoaff J, Epstein J. Real world study of multiple naloxone administration for opioid overdose reversal among bystanders [abstract F6]. In: Journal of Managed Care & Specialty Pharmacy Meeting Supplement 2021;27(10-a Suppl):S54.
5. Geiger et. al. 2019, "Who receives naloxone from emergency medical services? Characteristics of calls and recent trends," Substance Abuse, DOI: 10.1080/08897077.2019.1640832
6. Kloxxado™ (Naloxone HCl) Nasal Spray [prescribing information]. Berkeley Heights, NJ: Hikma Pharmaceuticals USA, Inc.; 2021
7. Narcan® (Naloxone HCl) Nasal Spray [prescribing information]. Plymouth Meeting, PA: Adapt Pharma, Inc.; 2020
8. <https://www.drugabuse.gov/drug-topics/opioids/opioid-overdose-reversal-naloxone-narcan-evzio>, Accessed June 21, 2021
9. <https://www.fda.gov/consumers/consumer-updates/having-naloxone-hand-can-save-life-during-opioid-overdose>, Accessed June 21, 2021
10. Hikma Internal Information

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

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 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/Antagonists**

Reversal of respiratory depression by partial agonists or mixed agonist/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.

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, which you can find on our website at www.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., Berkeley Heights, NJ 07922

hikma.