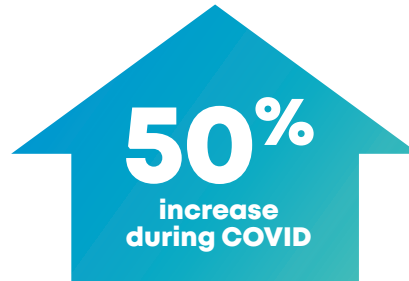


Our Communities Need Access to All Forms of Naloxone

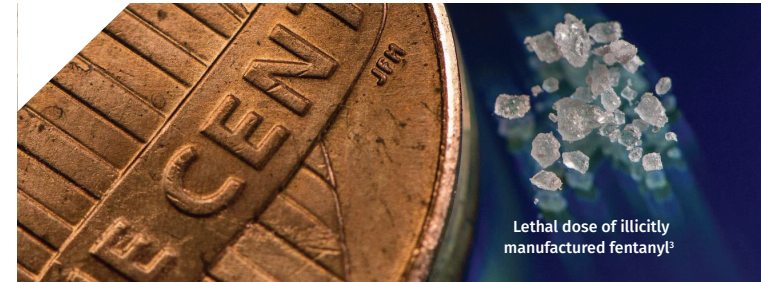
Enable the provision and use of KLOXXADO® (naloxone HCl) Nasal Spray 8 mg



100,000+ people died of drug overdose in 2021, largely attributed to illicitly manufactured fentanyl.^{1,2}

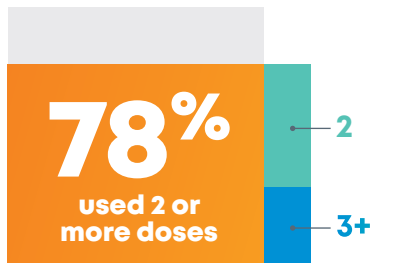


During COVID, annual **overdose deaths surged 50%**.¹



Illicit fentanyl is 50x stronger than heroin.⁴

Within 4 minutes of no oxygen, permanent brain damage can occur, causing death.⁵



78% of opioid overdose reversals involved 2 or more doses of naloxone, while 30% involved 3+ doses, according to the 2021 MORE study, a survey of people who administered NARCAN® (naloxone HCl) Nasal Spray 4 mg.⁶



77% of respondents in the 2021 MORE study would prefer a naloxone dose of 8 mg over 4 mg in the nasal spray.⁶

KLOXXADO® 8 mg contains **twice as much** naloxone per dose as Narcan® 4 mg.^{7,8}

- Only KLOXXADO® contains 8 mg per spray upfront in a single dose.⁷
- KLOXXADO® is made in the USA.
- Community Health pricing is available.



About Hikma Pharmaceuticals

- 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.⁹
- 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).⁹

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/Agonists

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.

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

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Narcan® Is a registered trademark of Emergent Operations Ireland Limited.

1. Ahmad FB, Rossen LM, Sutton P. Provisional drug overdose death counts. National Center for Health Statistics. 2021. Accessed August 4, 2022. 2. Prescription Behavior Surveillance System (PBSS): Issue Brief. National Center for Injury Prevention and Control/Centers for Disease Control and Prevention. Accessed August 4, 2022. 3. Facts about Fentanyl. United States Drug Enforcement Administration. <https://www.dea.gov/resources/facts-about-fentanyl>. Accessed August 4, 2022. 4. Stop Overdose, 2022, "The Facts About Fentanyl," CDC, <https://www.cdc.gov/stopoverdose/fentanyl>, Accessed 2022 0819. 5. Zibbell J, et al. Non-fatal opioid overdose and associated health outcomes: final summary report. US Department of Health and Human Services. <https://aspe.hhs.gov/basic-report/non-fatal-opioid-overdose-and-associated-health-outcomes-final-summary-report>. Accessed August 4, 2022. 6. Abdelal, R., Raja Banerjee, A., Carlberg-Racich, S. et al. Real-world study of multiple naloxone administration for opioid overdose reversal among bystanders. *Harm Reduct J* 19, 49 (2022). 7. KLOXXADO® (Naloxone HCl) Nasal Spray [prescribing information]. Columbus, OH: Hikma Specialty USA Inc.; 2021. 8. NARCAN® (Naloxone HCl) Nasal Spray [prescribing information]. Plymouth Meeting, PA: Adapt Pharma, Inc.; 2020. 9. Hikma Internal Information.