

# NALOXONE (Kloxxado, Narcan Nasal Spray, RiVive, Zimhi) Fact Sheet [G]

## Bottom Line:

Naloxone is an opioid antagonist that is used to rapidly reverse opioid overdose. It's important to recommend having this life-saving treatment on hand to all your patients with opioid use disorder. We recommend the generic, and now over-the-counter, nasal formulations.

## FDA Indications:

**Emergency treatment of known or suspected opioid overdose.**

## Dosage Forms:

- **Intranasal (Narcan Nasal Spray, RiVive, [G]):** 3 mg/0.1 mL, 4 mg/0.1 mL.
- **Intranasal (Kloxxado):** 8 mg/0.1 mL.
- **Injectable prefilled syringe (Zimhi):** 5 mg/0.5 mL.
- **Auto-injector (G):** 10 mg.

## Dosage Guidance:

Intranasal: Bystander to spray single dose (3, 4, or 8 mg) in one nostril; may repeat into other nostril with additional doses every two to three minutes if no or minimal response until patient responsive or emergency response arrives. The drug is absorbed automatically into the nasal mucosa, which is why it is effective in patients who are unconscious and cannot sniff it.

**Monitoring:** No routine monitoring recommended unless clinical picture warrants. Any person revived from an opioid overdose with naloxone should be evaluated in an emergency room.

**Cost:** Intranasal (generic): \$; Kloxxado, Zimhi: \$\$\$

## Side Effects:

Most common: Symptoms of opioid withdrawal, including body aches, sweating, runny nose, sneezing, piloerection, yawning, weakness, shivering or trembling, nervousness, restlessness or irritability, diarrhea, nausea or vomiting, abdominal cramps, increased blood pressure, and tachycardia.

## Mechanism, Pharmacokinetics, and Drug Interactions:

- Opioid antagonist.
- Metabolized primarily by conjugation (non-P450) in the liver;  $t_{1/2}$ : 1.36 hours.

## Clinical Pearls:

- Because treatment of overdose with this opioid antagonist must be performed by someone other than the patient, instruct recipients to inform those around them that they have naloxone rescue and ensure that those people have been instructed in recognizing overdose symptoms and administering the medication.
- Evzio auto-injector offered a novel device with voice instructions but was very expensive; it has been discontinued by the manufacturer and is no longer available. Zimhi is a new injectable (SC/IM) prefilled syringe for layperson use but comes in a much higher 5 mg dose and delivers nearly five-fold higher peak serum concentrations, which could result in very severe precipitated withdrawal symptoms.
- Like Zimhi, Kloxxado is a higher-dose formulation that was developed to combat the presumed need for repeated doses of naloxone after overdose with higher-potency opioids such as fentanyl. Whether multiple doses are required has been controversial, and use of this high-dose antagonist could result in severe precipitated withdrawal. Kloxxado is likely overkill for most patients—stick to the 4 mg intranasal formulation, which has a proven track record and is less expensive.
- Most opioids have a longer duration of action than naloxone, so it's likely that overdose symptoms (CNS depression and respiratory depression) will return after initial improvement. Therefore, patients should continue to be monitored and should receive medical attention after emergency dose(s) provided.
- Intranasal forms of naloxone rescue administration, if broadly distributed to those at risk, could make overdose rescue a more acceptable and widespread practice. Recently, it's become available over the counter.
- Check out the Prescribe to Prevent website ([www.prescribetoprevent.org](http://www.prescribetoprevent.org)) for prescriber resources such as webinars, toolkits, patient education materials, and medical-legal resources.

## Fun Fact:

The new ultra-high-dose (10 mg) auto-injector formulation is specifically indicated for use by military personnel and chemical incident responders for potential exposure to "ultra-potent weaponized opioids."