



**White Paper:**

# **Over-the-Counter Naloxone: Benefits and Considerations**

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# What is *naloxone*?

Naloxone is an opioid antagonist which competes with opioids and displaces them at opioid receptor sites<sup>1</sup>. Naloxone has been widely used to reverse the effects of opioids in the setting of opioid overdose. It is available as both an intranasal formulation, as well as a parenteral formulation that can be used as an intravenous (IV), intramuscular (IM), or subcutaneous (SC) injection. Naloxone's onset of action is fast, providing reversal of opioid overdose in as little as 2-5 min<sup>1</sup>. Side effects of naloxone are mild and consistent with acute opioid withdrawal: nausea, vomiting, diarrhea, and flushing. Additionally, with the IV, IM, and SC injections, patients may experience redness and/or tenderness around the injection site<sup>1</sup>.

TABLE 1. NALOXONE DOSING<sup>1</sup>:

Brand Name	Route of Administration	Initial Dose	Additional Dose(s)
Generic	IV, IM, SC	0.4mg - 2mg	May repeat every 2-3 minutes
Evzio	Auto-injector (IM or SC)	2mg (1 prefilled auto-injector)	May repeat every 2-3 minutes until medical assistance becomes available
Zimhi	IM,SC	5mg (1 prefilled syringe)	May repeat every 2-3 minutes until medical assistance becomes available
Narcan Kloxxado, Generic	Intranasal	4mg or 8mg (contents of 1 nasal spray)	May repeat every 2-3 minutes until medical assistance becomes available

The most commonly known form of naloxone available for use at home is the Narcan intranasal spray. At the time of writing, it is the only naloxone formulation to have applied for OTC use; on March 29, 2023, this application received FDA approval.

## How does naloxone help in an opioid overdose?

A lay person can recognize a possible opioid overdose if a patient is unresponsive, has shallow or irregular breathing, and/or has pinpoint pupils<sup>2</sup>. Naloxone can be administered to any patient with a suspected opioid overdose; the causative agent does not need to be confirmed before administration. With its minor side effect profile, there is little harm in administering naloxone to an unconscious patient.

### Who should currently be prescribed take-home naloxone<sup>3,4</sup>?

- All patients who are prescribed medicines to treat opioid use disorder.
- Patients at an increased risk of opioid overdose:
  - With a history of overdose
  - With a history of substance use disorder
  - With sleep-disordered breathing
  - Taking higher dosages of opioids (e.g. ≥50 MME/day)
  - Taking benzodiazepines with opioids
  - At risk for returning to a high dose of opioid to which they have lost tolerance (i.e. patients undergoing tapering, or those recently released from prison)

### Who would benefit from OTC naloxone?

OTC naloxone would be an option for anyone who wants to have it on hand. This can those at risk of opioid overdose due to illicit drug use, someone who works with people at risk of opioid overdose, or simply someone who just wants to have it on hand in case of an emergency.

**TABLE 2. PRICING OF NALOXONE:**

Medication	Manufacturer	Route of Administration	Generics	Cost per package
<b>Naloxone HCl 2mg prefilled auto-injector, single use</b>	Multiple generic manufacturers	SC, IM	Yes (multiple)	Generic: \$16
<b>Narcan Nasal Spray (naloxone HCl) 4mg</b>	Emergent Biosolutions	Intranasal	Yes (3)	Brand: \$125 Generic: \$83
<b>Kloxxado nasal spray 8mg</b>	Hikma	Intranasal	No	\$125
<b>Zimhi (naloxone HCl) 5mg/0.5mL prefilled syringe, single use</b>	US WorldMeds	SC, IM	No	\$125

### **Perspectives on patient impact:**

With the recommendation coming from the FDA to allow the IM and intranasal formulations to become available to patients OTC, along with the FDA approval of Adapt Pharma's application for Narcan to become available as the first OTC naloxone product, patients will soon be able to purchase Narcan intranasal spray at their own discretion. We should see costs to come down on OTC and prescription forms of naloxone, along with expanding patient-access to this life-saving medication. While there is no way of knowing how prices will be impacted, they will likely follow a similar pattern to Plan B Emergency Contraceptive, whose price decreased with its approval as an OTC medication.

There are currently no guidelines in places from the Centers for Medicare and Medicaid Services (CMS) nor the federal government as to what health insurance companies may or may not be required to cover for OTC naloxone products. Payers will need to evaluate what clients will need to contribute and what will be covered under their plans.

Getting naloxone over the counter status removes a long-standing barrier-to-care, and helps to normalize the conversation around drug addiction as a disease that requires care. This is an important move in the right direction in our fight against the opioid epidemic.

### **References:**

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