

Background

Drug overdoses are occurring at an alarming rate in the United States. Many overdoses have been linked to opioid analgesics, which may have been obtained from community pharmacies. One potential solution is to offer take-home naloxone.

Patient Selection

Naloxone should be considered for all patients exposed to opioids regardless of the source. The risk of a potentially fatal opioid overdose is a hazard of the drug and the drug combinations that are used. This applies to those who take opioids for pain and who misuse them.

Additional overdose risk factors include the following:

- Concurrent use of benzodiazepines or alcohol^{1,2}
- History of opioid addiction or other substance use disorder³
- Comorbid mental illness³
- Obtaining prescriptions from multiple pharmacies and prescribers⁴
- Daily opioid doses exceeding 100 mg of morphine equivalents³⁻⁶
- Receiving a methadone prescription⁷
- Recent emergency medical care for opioid poisoning/intoxication/overdose⁸
- Recent release from incarceration/prison/jail⁹
- Recent discharge from opioid detoxification or abstinence-based program¹⁰
- Comorbid renal dysfunction, hepatic disease, or respiratory diagnoses (smoking/COPD/emphysema /asthma/sleep apnea/other)

Naloxone is a bystander-administered medication, and the request for naloxone may come from caregivers or friends.

How It Is Supplied

Naloxone for take-home use can be supplied as an intramuscular (IM) injection or as an intranasal (IN) spray. Both formulations are effective. The intranasal formulation can be dispensed as a commercially available

product or a kit that requires assembly. In many cases, the commercially produced naloxone nasal spray may be preferred by patients and caregivers due to cost and ease of assembly/administration. There is also an IM auto-injector. Pharmacists should note that dosing and administration instructions vary among the formulations.

Intranasal Spray

IN nasal spray: commercially available as a twin pack with directions for administration included



Figure 1. IN nasal spray

IN kits should contain: 2 naloxone 2 mg/2 ml prefilled syringes, 2 atomizers, step-by-step instructions for responding to an opioid overdose, and directions for naloxone administration.



Figure 2. Intranasal kit Used with permission. San Francisco Department of Public Health. Naloxone for opioid safety: a provider's guide to prescribing naloxone to patients who use opioids. January 2015.

Intramuscular Injection

IM kits should contain: 2 naloxone 0.4 mg/ml vials, 2 IM syringes, step-by-step instructions for responding to an opioid overdose, and directions for naloxone administration.



Figure 3. Intramuscular kit Used with permission. San Francisco Department of Public Health. *Naloxone for opioid safety: a provider's guide to prescribing naloxone to patients who use opioids.* January 2015.

IM auto-injector: commercially available as a twin pack with directions for administration included.



Figure 4. IM auto-injector

Prescribing and Dispensing**Intranasal**

Naloxone 4 mg/0.1 ml nasal spray, 2 pack single spray devices

NDC No. 69457-353-02

Naloxone 2mg/0.1 ml nasal spray, 4 pack single spray devices

NDC No. 69547-212-04

SIG: Spray entire contents of device into 1 nostril upon signs of opioid overdose. Call 911. May repeat $\times 1$.

Intranasal

Naloxone 2 mg/2 ml prefilled syringe, 2 syringes

NDC No. 76329-3369-01

SIG: One spray into each nostril upon signs of opioid overdose. Call 911. May repeat $\times 1$.

Atomizer No. 2

SIG: Use as directed for naloxone administration

Intramuscular

Naloxone 0.4 mg/ml single dose vial, 2 vials

NDC No. 00409-1215-01

SIG: Inject 1 ml IM upon signs of opioid overdose. Call 911. May repeat $\times 1$.

Syringe 3 ml 25G $\times 1$ inch No. 2

SIG: Use as directed for naloxone administration

Intramuscular Auto-injector

Naloxone 2 mg/0.4 ml,

NDC 60842-051-01

No. 1 twin pack

SIG: Use one auto-injector upon signs of opioid overdose. Call 911. May repeat $\times 1$.

Acquisition and Reimbursement

The single-dose vial, prefilled syringe, IM syringes, commercial nasal spray, and auto-injector are available from pharmacy wholesale distributors. The atomizers for IN kit are available from medical supply vendors, and in some cases, can be purchased directly from the pharmacy wholesaler, or obtained from point persons within the pharmacy corporation.

Table. Nasal Atomizer Vendor Contacts

Vendor	Item No.	Contact
American Medical	MAD 300	888-988-5350
Teleflex	MAD 300	919-544-8000

Medicaid, Medicare, and many private insurance companies will pay for naloxone. However, at present, health plans do not have a viable way to pay for the atomizer, which lacks any unique identifier, such as a NDC number.

To cover the cost of the atomizer, some pharmacies are charging patients directly. In other cases, the atomizers are included with the drug at no additional charge. Some pharmacies have been successful billing for the atomizer under durable medical equipment (DME). New Mexico provides a reimbursement code for the entire kit, including the pharmacist's time.

Naloxone Storage Information

- Store naloxone in an easily accessible place in the original package at room temperature. Avoid light exposure.
- The shelf life of naloxone is generally 12 to 18 months. If stored properly, naloxone should be effective until at least the expiration date on the packaging.
- Do not insert naloxone into the prefilled syringe until ready to use. Once inserted, it expires within 2 weeks.
- Monitor the expiration date on naloxone and replace before it expires. When there are no other alternatives, expired naloxone can be administered but may not be as effective.

Supporting Laws and Regulations

State laws to support naloxone access fall under three categories:

- **Good Samaritan:** protects individuals who call for help at the scene of an overdose from being arrested for drug possession.
- **Liability protection/third party administration:** protects the prescriber, pharmacist, and the bystander who may be administering the naloxone. It also allows bystanders to be prescribed naloxone for use on opioid overdose victims.
- **Collaborative practice agreement/Standing Order:** allows pharmacists to dispense naloxone to at-risk individuals without a traditional hand-written/faxed prescription. It may be done with individual physicians or on a statewide basis.

The Network for Public Health Law has an updated [summary of state laws](#) supporting access to naloxone.¹¹

Examples of Successful State and Local Models

New Mexico: In 2001, New Mexico enacted legislation to protect third parties who administer naloxone to an overdose victim. This was followed by a Good Samaritan statute in 2007 and pharmacist prescribing in 2014. To obtain prescribing authority, pharmacists need to complete a 2-hour certification course every 2 years. The State Medicaid program pays for naloxone, the atomizer, and the consultation time via a specific NDC number for the entire naloxone kit.

California: San Francisco's Department of Public Health expanded naloxone access by making the atomizer and education brochures available in primary care clinics. Naloxone was co-prescribed with opioid analgesics and picked up at community pharmacies. Patients were trained both at the primary care clinic and the community pharmacy. Pharmacist training and outreach was done by the Public Health Department. Pharmacists also make naloxone available to methadone and buprenorphine maintenance patients at a specialty mental health pharmacy run by the Department of Public Health under a collaborative practice agreement.

Rhode Island: All Walgreens and CVS Pharmacies in Rhode Island make IM and IN naloxone available without a prescription under a collaborative practice agreement. The pharmacy chains have secured atomizer access through their supply systems, and the collaborative drug therapy agreement is signed by one physician for the state. The University of Rhode Island offers [continuing education training](#).¹²

Collaborative Practice Agreements

- [New Mexico](#)¹³
- [Washington State](#)¹⁴
- [San Francisco Department of Public Health](#)¹⁵
- [Providers' Clinical Support System for Opioid Therapies](#) (PCSS-O): Description of collaborative practice with focus on Rhode Island¹⁶

Frequently Asked Questions

What are signs of opioid overdose?

- Skin is pale and/or clammy to the touch.
- Body is limp.
- Fingernails or lips have a blue or purple cast.
- Patient is vomiting or making gurgling noises.
- Patient is unarousable.
- Breathing is very slow or stopped.

What is rescue breathing?

Rescue breathing involves essentially breathing for someone else. By providing rescue breathing during an opioid overdose, the rescuer can potentially prevent the patient from developing organ damage. See the patient information sheets for details on how to administer rescue breaths.

How quickly does naloxone work?

Naloxone works within 2 to 5 minutes, depending on how naloxone has been administered.

How long should a bystander remain with the overdose victim after naloxone has been administered?

Bystanders should remain with the overdose victim until help arrives. Naloxone only has a 30 to 90-minute duration of action. Patients who have overdosed on a long-acting opioid may initially respond and then succumb to overdose symptoms again. It is important to remain with the patient to continue to provide support and additional doses of naloxone (if required) until help arrives.

Is naloxone effective in treating other types of overdoses?

No, naloxone is only effective in reversing an opioid overdose. At times, it may be difficult to distinguish opioid overdose symptoms from other overdoses or illnesses. Therefore, it is important to immediately seek medical help and administer naloxone, if it is possible someone has had an opioid overdose.

What happens if you administer expired naloxone?

Naloxone's full efficacy cannot be guaranteed beyond the expiration date. However, in urgent situations without alternatives, it will not hurt the patient to administer expired naloxone and may provide some benefit.

Can the intranasal naloxone be assembled in advance?

The shelf life of the assembled prefilled syringe is only 2 weeks; therefore, it is recommended that the atomizer is attached to the syringe but the naloxone is not inserted until ready to administer.

Can naloxone be administered to pregnant women?

Yes, in an opioid overdose, naloxone can and should be administered to a pregnant woman. However, there is risk for opioid withdrawal.

When should I recommend Naloxone NS 2mg?

The answer to this question is unclear. As of 2018, this product was approved but is not available to purchase. It is intended for use in "opioid-dependent patients expected to be at risk for severe opioid withdrawal in situations where there is a low risk for accidental or intentional opioid exposure by household contacts". The 4 mg/0.1 ml Narcan NS is routinely used at this time.

Is Evzio available in 0.4mg/0.4ml or 2 mg/4ml strength?

Initially, Evzio was approved in the 0.4mg/0.4ml strength. In 2017, the manufacturer discontinued this product and replaced it with 2mg/0.4ml. Patients may have the lower strength product, which is still in date. They do not need to replace the product until it expires.

Does naloxone reverse overdoses due to fentanyl and fentanyl analogues?

Yes, naloxone is effective in reversing overdoses by high potency opioids such as fentanyl and carfentanyl, however more than two doses of naloxone may be necessary. In geographic areas where high potency opioids have entered the drug supply chain, the provision of additional doses of take-home naloxone may be required.

For More Information

- www.prescribetoprevent.org
- [Overdose rescue/naloxone long-format training. August 23, 2012¹⁷](#)
- [SAMHSA Opioid Overdose Prevention Toolkit¹⁷](#)

Intranasal Naloxone Patient Information Sheet

Common brand names: Narcan

Uses: Naloxone is used to treat an opioid overdose. Naloxone can stop the effects of opioids for a short time.

Tell family/friends where naloxone is stored and how to use it in case of an opioid emergency.

Signs of an opioid overdose

Slowed breathing or stopped breathing, blue or gray lips and fingernails, pale and/or moist skin, unable to wake up or respond.

How to Use IN Naloxone

If you think someone may have overdosed on an opioid:

Step 1. Call 911.

Step 2. Give naloxone.

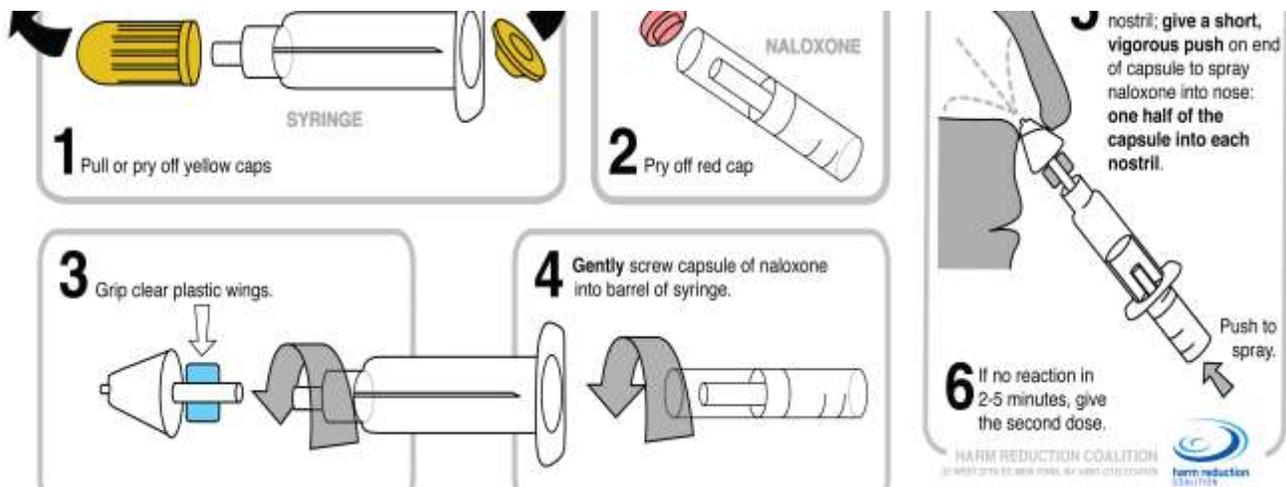


Image by Harm Reduction Coalition. <http://harmreduction.org/issues/overdose-prevention/tools-best-practices/od-kit-materials/>. Updated October 2014.

Step 3. Give a second dose of naloxone in 2 to 3 minutes if there is no response to the first dose.

Step 4. Follow the 911 dispatcher's instructions or perform rescue breathing if comfortable doing so.

Rescue Breathing

The key steps of rescue breathing include the following:

Step 1. Make sure nothing is in the person's mouth.

Step 2. Tilt the head back, lift chin, and pinch nose shut.

Step 3. Give one slow breath every 5 seconds; chest should rise.

Side effects

Anxiety, sweating, nausea/vomiting, or shaking. This is not a complete list of possible side effects. If you notice other effects not listed, contact your doctor or pharmacist.

Intramuscular Naloxone Patient Information Sheet

Uses: Naloxone is used to treat an opioid overdose. Naloxone can stop the effects of opioids for a short time.

Tell family/friends where naloxone is stored and how to use it in case of an opioid emergency.

Signs of an opioid overdose

Slowed breathing or stopped breathing, blue or gray lips and fingernails, pale and/or moist skin, unable to wake up or respond.

How to Use IM Naloxone

If you think someone may have overdosed on an opioid:

Step 1. Call 911.

Step 2. Give naloxone.



1 Remove cap from naloxone vial and uncover the needle



2 Insert needle through rubber plug with vial upside down
Pull back on plunger and take up 1 mL



3 Inject 1 mL of naloxone at a 90 degree angle into a large muscle (upper arm/thigh, outer buttocks)

Images in Public Domain. San Francisco Department of Public Health. Naloxone for opioid safety: a provider's guide to prescribing naloxone to patients who use opioids. January 2015.

Step 3. Give a second dose of naloxone in 2 to 3 minutes if there is no response to the first dose.

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Rescue Breathing

The key steps to rescue breathing include the following:

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