

FREQUENTLY ASKED QUESTIONS ABOUT EMERGENCY TREATMENT FOR OPIOID OVERDOSE

What is NARCAN® (naloxone HCl) Nasal Spray?

NARCAN® Nasal Spray is a prescription medicine used for the treatment of an opioid emergency such as an overdose or a possible opioid overdose with signs of breathing problems and severe sleepiness or not being able to respond.

NARCAN® Nasal Spray is to be given right away and does not take the place of emergency medical care. Get emergency medical help right away after giving the first dose of NARCAN Nasal Spray, even if the person wakes up.

Naloxone, the active ingredient in NARCAN® Nasal Spray, competes with opioids to bind with the same receptors in the brain. Usually, it reverses the effects of opioid overdose in 2 to 3 minutes. Additional doses of NARCAN® Nasal Spray may be required until emergency medical assistance becomes available. Re-administer NARCAN® Nasal Spray, using a new nasal spray, every 2 to 3 minutes if the patient does not respond or responds and then relapses into respiratory depression.

NARCAN® Nasal Spray helps to reverse the life-threatening effects of opioid overdose. Since most accidental overdoses occur in a home setting,¹ it was developed for first responders, as well as family, friends, and caregivers.



When was NARCAN® Nasal Spray 4 mg approved by the FDA?

On November 18, 2015, after Fast Track Designation and Priority Review, the U.S. Food and Drug Administration (FDA) approved NARCAN® (naloxone HCl) Nasal Spray 4 mg for commercial use in the United States.

What is the strength and volume of NARCAN® Nasal Spray?

NARCAN® Nasal Spray 4 mg dosing is designed for effective intranasal delivery by delivering approximately the same amount of naloxone as a 2 mg dose of intramuscular (IM) injection of naloxone.² The 4 mg dose of NARCAN® Nasal Spray is concentrated in a 0.1 mL spray.

What is the most important information I should know about NARCAN® Nasal Spray?

NARCAN® Nasal Spray is used to temporarily reverse the effects of opioid medicines. The medicine in NARCAN® Nasal Spray has no effect in people who are not taking opioid medicines. Always carry NARCAN® Nasal Spray with you in case of an opioid emergency.

1. Use NARCAN® Nasal Spray right away if you or your caregiver think signs or symptoms of an opioid emergency are present, even if you are not sure, because an opioid emergency can cause severe injury or death. Signs and symptoms of an opioid emergency may include:
 - unusual sleepiness and you are not able to awaken the person with a loud voice or by rubbing firmly on the middle of their chest (sternum)
 - breathing problems including slow or shallow breathing in someone difficult to awaken or who looks like they are not breathing
 - the black circle in the center of the colored part of the eye (pupil) is very small, sometimes called "pinpoint pupils" in someone difficult to awaken
2. Family members, caregivers, or other people who may have to use NARCAN® Nasal Spray in an opioid emergency should know where NARCAN® Nasal Spray is stored and how to give NARCAN® Nasal Spray before an opioid emergency happens.

Please see Indications and Important Safety Information throughout this document

FREQUENTLY ASKED QUESTIONS ABOUT EMERGENCY TREATMENT FOR OPIOID OVERDOSE

3. **Get emergency medical help right away after giving the first dose of NARCAN® Nasal Spray.** Rescue breathing or CPR (cardiopulmonary resuscitation) may be given while waiting for emergency medical help.
4. The signs and symptoms of an opioid emergency can return after NARCAN® Nasal Spray is given. If this happens, give another dose after 2 to 3 minutes using a new NARCAN® Nasal Spray and watch the person closely until emergency help is received.

Does NARCAN® (naloxone HCl) Nasal Spray require assembly?

No. NARCAN® Nasal Spray is needle free and does not require assembly. It's designed for ease of use for non-medical personnel.

Does NARCAN® Nasal Spray need to be inhaled?

No. NARCAN® Nasal Spray was designed to be absorbed into the blood stream through the nasal mucosa (lining of the nose.) It does not need to be inhaled. Breathing is not required for administration.

What is the “improvised nasal naloxone” kit?

The improvised nasal naloxone kit consists of injectable 2 mg/2 mL vials combined with a mucosal atomizer device.³

Is the “improvised nasal naloxone” kit approved by the FDA?

No. The use of naloxone hydrochloride injection combined with a mucosal atomizer device for an improvised nasal naloxone kit is not FDA approved.

What is the strength and volume of “improvised nasal naloxone”?

The pharmacokinetic properties of the improvised nasal naloxone kit is not published. In particular, the impact of the formulation and large volume sprayed (2 mL) on bioavailability is not known and thus the exposure cannot be estimated.³

Does the “improvised nasal naloxone” kit require assembly?

Yes. Assembly of the improvised nasal naloxone kit is required.⁴

Why is volume and concentration important?

As the nasal cavity is a viable route for drug administration of a nasal formulation, the anatomy/physiology of each individual patient can vary. Optimal delivery volumes for intranasal (IN) drug administration are <0.2 mL/nostril. Administration of a higher naloxone concentration administered in small volumes will result in higher bioavailability (or drug absorption) and facilitate administration.⁵

A formulation at a lower naloxone concentration (less active drug in a higher volume) may lead to poor absorption and suboptimal drug delivery due to the increased volume administered in the nasal cavity.

What are FDA requirements when seeking approval for a community use naloxone?

The FDA has taken the opportunity to work with companies that were partnering with the National Institute on Drug Abuse (NIDA) to establish a pharmacokinetic standard for new formulations of naloxone. The FDA leveraged what is known about the safety and efficacy of existing approved naloxone products and pharmacokinetics as a path forward for the approval of these products.⁶

FREQUENTLY ASKED QUESTIONS ABOUT EMERGENCY TREATMENT FOR OPIOID OVERDOSE

What products have met the FDA requirements regarding usability by nonmedical individuals?

As of June 1, 2017, there are 2 products currently approved by the FDA for community use:

- EVZIO® (naloxone auto injector)
- NARCAN® (naloxone HCl) Nasal Spray

What is the difference between community use and hospital use naloxone?

Naloxone use in a healthcare setting requires administration by a trained healthcare professional and is labeled for intravenous (IV), intramuscular (IM), or subcutaneous (SC) use, supplied in a vial.

Naloxone use in a community setting refers to specific products that are approved by the FDA with instructions for use. It is expected that laypersons can use these products without any specialized training, supplied as a device in nasal spray or auto-injector format.

Is NARCAN® (naloxone HCl) Nasal Spray indicated for all opioids, including fentanyl and carfentanil?

NARCAN® Nasal Spray 4 mg is an opioid antagonist indicated for the emergency treatment of known or suspected opioid overdose.

NARCAN® Nasal Spray has been used to treat individuals in whom any opioids are present, including fentanyl and illicit variations of fentanyl. Multiple doses of NARCAN® Nasal Spray may be necessary.

Although no clinical trials have specifically addressed the efficacy of NARCAN® Nasal Spray in patients with overdoses of derivatives of fentanyl, retrospective data showed that high-dose naloxone was effective against new, highly-potent opioid substances.⁷

Who should not use NARCAN® Nasal Spray?

Do not use NARCAN® Nasal Spray if you are allergic to naloxone hydrochloride or any of the ingredients in NARCAN® Nasal Spray.

What should I tell my healthcare provider before using NARCAN® Nasal Spray?

Before using NARCAN® Nasal Spray, tell your healthcare provider about all of your medical conditions, including if you:

- have heart problems
- are pregnant or plan to become pregnant. Use of NARCAN® Nasal Spray may cause withdrawal symptoms in your unborn baby. Your unborn baby should be examined by a healthcare provider right away after you use NARCAN® Nasal Spray.
- are breastfeeding or plan to breastfeed. It is not known if NARCAN® Nasal Spray passes into your breast milk.

Tell your healthcare provider about the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

FREQUENTLY ASKED QUESTIONS ABOUT EMERGENCY TREATMENT FOR OPIOID OVERDOSE

What is the Wholesale Acquisition Cost for community use emergency rescue agents?

As of June 1, 2017, the Wholesale Acquisition Cost (WAC) for FDA approved community use products are:

- EVZIO® (naloxone auto injector): **\$4,100.00** (per package of 2 devices)
- NARCAN® (naloxone HCl) Nasal Spray: **\$125.00** (per package of 2 devices)

* Note: Wholesale Acquisition Cost (WAC) comparisons do not imply comparable efficacy or safety.

Does NARCAN® (naloxone HCl) Nasal Spray offer a discount to public customers (e.g. law enforcement, community-based organizations)?

NARCAN® Nasal Spray is available to all qualified group purchasers for \$37.50 per 4 mg dose (\$75 per carton of 2 doses). This pricing is available for all Qualified Group Purchasers, such as first responders (EMS, Fire Department, Police), community organizations and Departments of Health, regardless of size. This pricing represents a 40% discount off the Wholesale Acquisition Cost (WAC).

What are the possible side effects of NARCAN® Nasal Spray?

NARCAN® Nasal Spray may cause serious side effects, including:

Sudden opioid withdrawal symptoms. In someone who has been using opioids regularly, opioid withdrawal symptoms can happen suddenly after receiving NARCAN® Nasal Spray and may include: body aches, diarrhea, increased heart rate, fever, runny nose, sneezing, goose bumps, sweating, yawning, nausea or vomiting, nervousness, restlessness or irritability, shivering or trembling, stomach cramping, weakness, increased blood pressure.

In infants under 4 weeks old who have been receiving opioids regularly, sudden opioid withdrawal may be life-threatening if not treated the right way. Signs and symptoms include: seizures, crying more than usual, and increased reflexes.

These are not all of the possible side effects of NARCAN® Nasal Spray. Call your doctor for medical advice about side effects. You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088.

Please see accompanying full Prescribing Information, including the Patient Information and Instructions for Use.

References: 1. Centers for Disease Control and Prevention. Injury prevention and control: opioid overdose. <http://www.cdc.gov/drugoverdose/data/index.html>. Accessed September 14, 2016. 2. Adapt Pharma. NARCAN (naloxone hydrochloride) nasal spray [prescribing information]. Updated February 2017. Available at: <https://www.narcan.com/pdf/NARCAN-Prescribing-Information.pdf>. Accessed May 10, 2017. 3. Joint Meeting of the Anesthetic and Analgesic Drug Products Advisory Committee and the Drug Safety and Risk Management Advisory Committee. Adapt Pharma, Inc. Radnor, PA; October 5, 2016. 4. Eliza Wheeler et al. Guide to Developing and Managing Overdose Prevention and Take-Home Naloxone Projects. HARM Reduction Coalition. Oakland, CA. Fall 2012. 5. Grassin-Delyle S, Buenestado A, Naline E, et al. Intranasal drug delivery: an efficient and non-invasive route for systemic administration: focus on opioids. *PharmThera*. 2012;134(3):366–379. 6. Jennifer Nadel, MD et al. Clinical and Regulatory Perspectives on Naloxone Products Intended for Use in the Community: Joint Meeting of the Anesthetic and Analgesic Drug Products Advisory Committee and the Drug Safety and Risk Management Advisory Committee. Food and Drug Administration. October 5, 2016. 7. Helander A, Bäckberg M, Signell P, Beck O. Intoxications involving acrylfentanyl and other novel designer fentanyls - results from the Swedish STRIDA project. *Clin Toxicol (Phila)*. 2017 Mar 28:1-11

© 2017 Adapt Pharma, Inc. NARCAN® is a registered trademark of ADAPT Pharma Operations Limited. All other trademarks are property of their respective owners. NAR-US-222 Adapt Pharma, Inc., Radnor, PA

Please see Indications and Important Safety Information throughout this document