

The Role of NARCAN® Nasal Spray in Reversing Opioid Overdoses



 **NARCAN**® (naloxone HCl)
NASAL SPRAY 4mg

ADAPT
PHARMA

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ADAPT Pharma, Inc. Radnor, PA

The Overdose Epidemic

Presented for Educational Background Only. No claims are made for any effect of NARCAN on the opioid overdose epidemic described in the following slides.

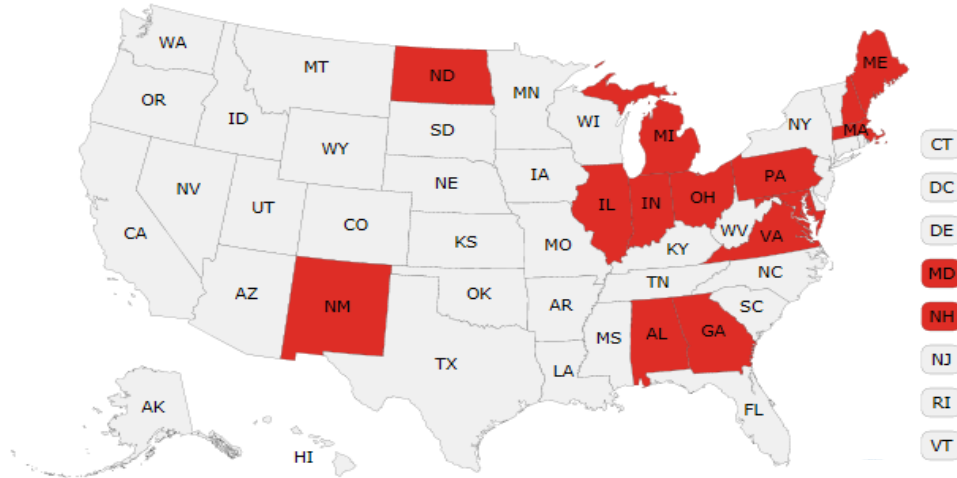
According to Nora D. Volkow, Director of the National Institute of Drug Abuse (NIDA), accidental opioid overdose is a ***“public health epidemic with devastating consequences.”***²

10,574¹

2014 overdose deaths
related to heroin

18,893¹

2014 overdose deaths
related to prescription
opioid pain relievers



Red States Showed Statistically Significant Drug Overdose Death Rate Increase From 2013 to 2014

¹ Center for Disease Control and Prevention, National Center for Health Statistics, National Vital Statistics System, Mortality File. (2015). Number and Age-Adjusted Rates of Drug-poisoning Deaths Involving Opioid Analgesics and Heroin: United States, 2000–2014. Atlanta, GA: Center for Disease Control and Prevention.
² National Institute on Drug Abuse, The Science on Drug Abuse and Addiction. (May 2015) What is the Federal Government Doing to Combat the Opioid Abuse Epidemic: Nora D Volkow. Available at
³ Center for Disease Control and Prevention, Morbidity and Mortality Weekly Report (MMWR). (January 2016). Increases in Drug and Opioid Overdose Deaths - United States, 2000 - 2014. Atlanta, GA: Center for Disease Control and Prevention.

Facts About Opioid Overdose

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- Overdoses claimed over 29,000 lives in 2014. That's an average of **one every 17 minutes**.¹
- **Overdoses now surpass car crashes** as the leading cause of accidental death in the US.²
- Most accidental opioid overdoses **occur in people's homes**.³
- Overdoses related to fentanyl are **occurring at an alarming rate throughout the U.S.** and represent a significant threat to public health and safety⁴
 - Often laced in heroin, fentanyl and fentanyl analogues produced in illicit clandestine labs are up to 100 times more powerful than morphine and 30-50 times more powerful than heroin.



¹Centers for Disease Control and Prevention, National Center for Health Statistics. Number and age-adjusted rates of drug-poisoning deaths involving opioid analgesics and heroin: United States, 2000–2014. http://www.cdc.gov/nchs/data/health_policy/AADR_drug_poisoning_involving_OA_Heroin_US_2000-2014.pdf. Data extracted July 6, 2016.

²Centers for Disease Control and Prevention, National Center for Injury Prevention and Control. Details of leading causes of death: unintentional injuries. Web-based Injury Statistics Query and Reporting System (WISQARS) [online]. 2013.

³Centers for Disease Control and Prevention, National Center for Health Statistics. Multiple cause of death: United States, 1999–2014. CDC WONDER [online]. Data extracted July 6, 2016. <http://www.cdc.gov/injury/wisqars/fatal.html>. 2013. Data extracted November 19, 2015.

⁴DEA Issues Nationwide Alert on Fentanyl as Threat to Health and Public Safety. <https://www.dea.gov/divisions/hq/2015/hq031815.shtml>. Data extracted July 18, 2016

New Formulations of Naloxone

Naloxone will not solve the underlying problems of the opioid epidemic...

“We cannot stand by while Americans are dying. While naloxone will not solve the underlying problems of the opioid epidemic, we are speeding to review new formulations that will ultimately save lives that might otherwise be lost to drug addiction and overdose.” said Stephen Ostroff, M.D., acting commissioner, Food and Drug Administration.¹

¹FDA moves quickly to approve easy-to-use nasal spray to treat opioid overdose Naloxone in nasal spray form provides important new alternative for family members, first responders. <http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm473505.htm>. Data extracted July 12, 2016.

NARCAN® (naloxone HCl) Nasal Spray

First and Only FDA-Approved Nasal Form of Naloxone

- Indicated for the emergency treatment of known or suspected opioid overdose, as manifested by respiratory and/or central nervous system depression
- Blocks or reverses the effects of opioid medications and substances, such as heroin or fentanyl
- NARCAN® Nasal Spray is the first and only FDA-approved nasal form of naloxone
- It is now available as a ready-to-use, needle-free, 4mg concentrated dose in a single spray
- NARCAN® is not a substitute for emergency medical care



INDICATIONS

NARCAN® (naloxone hydrochloride) Nasal Spray is an opioid antagonist indicated for the emergency treatment of known or suspected opioid overdose, as manifested by respiratory and/or central nervous system depression. NARCAN® Nasal Spray is intended for immediate administration as emergency therapy in settings where opioids may be present.

NARCAN® Nasal Spray is not a substitute for emergency medical care.

IMPORTANT SAFETY INFORMATION

NARCAN® Nasal Spray is contraindicated in patients known to be hypersensitive to naloxone hydrochloride.

Precipitation of Severe Opioid Withdrawal: Use in patients who are opioid dependent may precipitate opioid withdrawal characterized by body aches, diarrhea, increased heart rate (tachycardia), fever, runny nose, sneezing, goose bumps (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 be characterized by convulsions, excessive crying, and hyperactive reflexes. Monitor for the development of opioid withdrawal.

Please see Indications and Important Safety Information on slides 6 & 7

NARCAN® Nasal Spray Indication & Important Safety Information

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IMPORTANT SAFETY INFORMATION

NARCAN® Nasal Spray is contraindicated in patients known to be hypersensitive to naloxone hydrochloride.

Seek emergency medical assistance immediately after initial use, keeping the patient under continued surveillance.

Risk of Recurrent Respiratory and CNS Depression: Due to the duration of action of naloxone relative to the opioid, keep the patient under continued surveillance and administer repeat doses of naloxone using a new nasal spray with each dose, as necessary, while awaiting emergency medical assistance.

Risk of Limited Efficacy with Partial Agonists or Mixed Agonists/Antagonists: Reversal of respiratory depression caused by partial agonists or mixed agonists/antagonists, such as buprenorphine and pentazocine, may be incomplete. Larger or repeat doses may be required.

NARCAN® Nasal Spray Indication & Important Safety Information

IMPORTANT SAFETY INFORMATION (continued)

Precipitation of Severe Opioid Withdrawal: Use in patients who are opioid dependent may precipitate opioid withdrawal characterized by body aches, diarrhea, increased heart rate (tachycardia), fever, runny nose, sneezing, goose bumps (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 be characterized by convulsions, excessive crying, and hyperactive reflexes. Monitor for the development of opioid withdrawal.

Risk of Cardiovascular (CV) Effects: Abrupt postoperative reversal of opioid depression may result in adverse CV effects. These events have primarily occurred in patients who had pre-existing CV disorders or received other drugs that may have similar adverse CV effects. Monitor these patients closely in an appropriate healthcare setting after use of naloxone hydrochloride.

The following adverse reactions were observed in a NARCAN Nasal Spray clinical study: increased blood pressure, musculoskeletal pain, headache, nasal dryness, nasal edema, nasal congestion, and nasal inflammation.

See Instructions for Use and full prescribing information in the use of this product available from the presenter at this event.

To report SUSPECTED ADVERSE REACTIONS, contact Adapt Pharma, Inc. at 1-844-4NARCAN (1-844-462-7226) or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

NARCAN[®] (naloxone HCl) Nasal Spray

No Specialized Training Required. Use in Accordance with the Instructions for Use

1 Identify Opioid Overdose and Check for Response

Ask person if he or she is okay and shout name.
Shake shoulders and firmly rub the middle of their chest.

Check for signs of opioid overdose:

- Will not wake up or respond to your voice or touch
 - Breathing is very slow, irregular, or has stopped
 - Center part of their eye is very small, sometimes called "pinpoint pupils"
- Lay the person on their back to receive a dose of NARCAN Nasal Spray.



2 Give NARCAN Nasal Spray

Remove NARCAN Nasal Spray from the box.
Peel back the tab with the circle to open the NARCAN Nasal Spray.



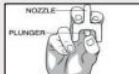
Hold the NARCAN nasal spray with your thumb on the bottom of the plunger and your first and middle fingers on either side of the nozzle.

Gently insert the tip of the nozzle into either nostril.

- Tilt the person's head back and provide support under the neck with your hand. Gently insert the tip of the nozzle into **one** nostril, until your fingers on either side of the nozzle are against the bottom of the person's nose.

Press the plunger firmly to give the dose of NARCAN Nasal Spray.

- Remove the NARCAN Nasal Spray from the nostril after giving the dose.



3 Call for emergency medical help, Evaluate, and Support

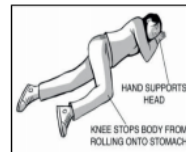
Get emergency medical help right away.

Move the person on their side (recovery position) after giving NARCAN Nasal Spray.

Watch the person closely.

If the person does not respond by waking up, to voice or touch, or breathing normally another dose may be given. NARCAN Nasal Spray may be dosed every 2 to 3 minutes, if available.

Repeat Step 2 using a new NARCAN Nasal Spray to give another dose in the other nostril. If additional NARCAN Nasal Sprays are available, repeat step 2 every 2 to 3 minutes until the person responds or emergency medical help is received.



IMPORTANT SAFETY INFORMATION

Seek emergency medical assistance immediately after initial use, keeping the patient under continued surveillance.

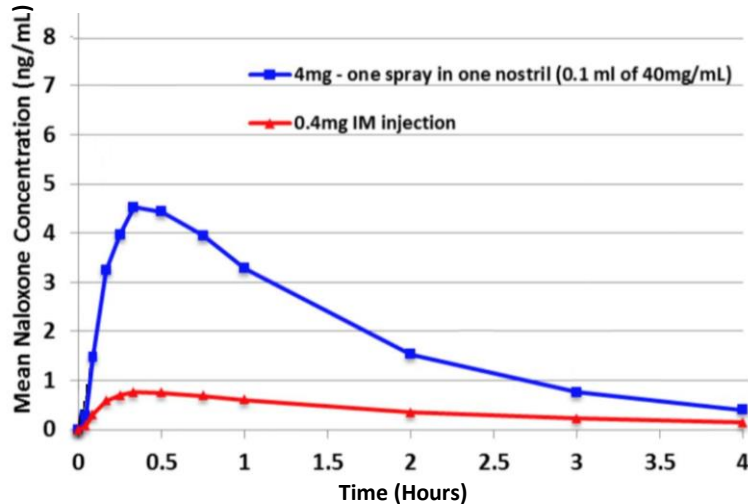
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Please see Indications and Important Safety Information on slides 6 & 7

NARCAN[®](naloxone HCl) Nasal Spray

Single concentrated dose delivers key Pharmacokinetic Parameters



- In this pharmacokinetic study of 30 healthy adult volunteers exposed to one spray of NARCAN Nasal Spray in one nostril or two sprays of NARCAN Nasal Spray, one in each nostril, the most common adverse reactions were: increased blood pressure, musculoskeletal pain, headache, nasal dryness, nasal edema, nasal congestion, and nasal inflammation.
- Intranasal (IN) administration of highly concentrated low volume formulation results in key pharmacokinetic parameters that either equal or exceed those observed with the approved 0.4 mg Intramuscular (IM) injection
- Earliest time sampled (2.5 minutes), plasma naloxone concentrations after IN administration of 2-4 mg were higher than following the 0.4 mg IM dose

NARCAN[®] (naloxone HCl) Nasal Spray

Commercial Pricing and US Communities™



Public Interest Price - \$37.50/device, \$75/carton (includes two 4 mg intranasal doses)

Adapt Pharma, in partnership with the National Association of Counties, National Governors Association, National League of Cities and United States Conference of Mayors, now offers NARCAN[®] Nasal Spray at a discounted Public Interest Price through the U.S. Communities Purchasing Alliance and Premier, Inc.

Direct purchasers, such as EMS, law enforcement and community-based naloxone distribution programs, can order NARCAN[®] Nasal Spray at the Public Interest Price.

Wholesale Acquisition Cost - \$62.50/device, \$125/carton (includes two 4 mg intranasal doses)

NARCAN[®] (naloxone HCl) Nasal Spray

Free NARCAN[®] Nasal Spray High School Program



Adapt Pharma offers access to a free carton of NARCAN[®] (naloxone hydrochloride) Nasal Spray to all high schools in the United States through the state departments of education. This program was announced at the **Clinton Health Matters Initiative**, an initiative of the Clinton Foundation.

In addition, Adapt Pharma has provided a grant to the **National Association of School Nurses (NASN)** to support their educational efforts concerning opioid overdose education materials.



"Opioid addiction is the most pressing health threat in Pennsylvania today and the availability of naloxone is a critical component in our broad effort to address it... This generous donation will ensure that all public schools across the Commonwealth have access to naloxone. As a result many more lives will be saved and those young people, with their futures ahead of them, will be able to receive the treatment they need." – Department of Health Secretary Dr. Karen Murphy

For more information: <http://www.NARCANnasalspray.com/how-to-get-nns/partnerships/>

NARCAN[®] (naloxone HCl) Nasal Spray

Experience Program



In July 2016, Adapt Pharma provided a one-time donation of 5,000 cartons (10,000 doses) of NARCAN[®] Nasal Spray to each of the following organizations to assist them in their fight against the opioid overdose epidemic:

- Police Assisted Addiction and Recovery Initiative (P.A.A.R.I.)
- Harm Reduction Coalition (HRC)
- Clinton Health Matters Initiative
- Select police forces across the country from communities identified as hit hardest by opioid-related overdoses

NARCAN[®] (naloxone HCl) Nasal Spray

A Warm Welcome for the New Naloxone

- Availability is rapidly expanding (Law Enforcement, Retail, Caregiver)
- Ready to use and nasal dosage form facilitating expansion
- Public interest pricing
- Insurers and Retail Chains are implementing programs to broaden access
- Prescribing to at risk patients

NARCAN[®] (naloxone HCl) Nasal Spray

Opportunities to Make a Difference

- Standing Orders and Protocols need to be updated to include 4mg
- “Narcan” name has great recognition but confused with other products
- Distribution Models for Public Markets need to be developed
- Public Awareness needs to be built, de-stigmatized



THANK YOU!

* Please see Indications and Important Safety Information on slides 14 & 15



Appendix

Adapt Pharma

2014

Founded in Dublin, Ireland

Adapt Pharma Limited is a privately-held pharmaceutical company committed to positively impacting the lives of patients



2015

Based in Radnor, PA, Adapt Pharma Inc. was set up in April 2015

In-licensed global rights to late stage overdose reversal therapy, Naloxone Nasal Spray

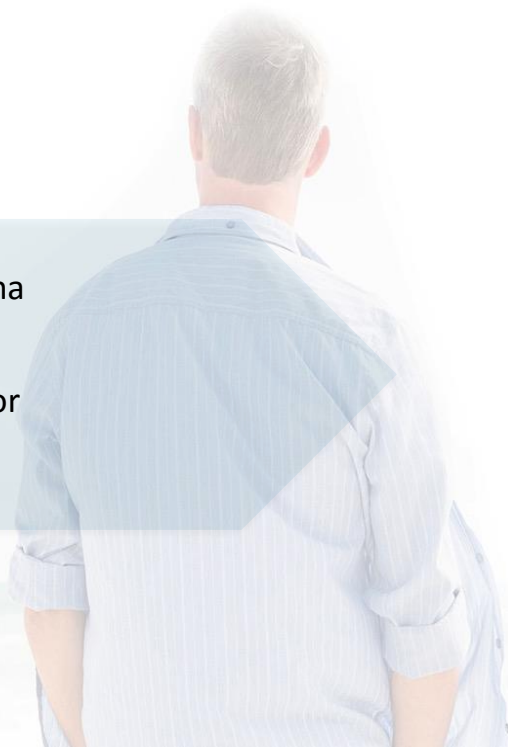


* Please see Indications and Important Safety Information on slides 21 & 22

Adapt Pharma

Our Mission

With **115 Years** of collective experience in the U.S. specialty pharma industry, our mission is to provide *simple, reliable, and accessible therapeutic options*, ensuring that patients, and those who care for them, have *access to the right treatment at the right time.*



Path to NARCAN® Nasal Spray



4mg Naloxone Nasal Spray

Previously developed by
Lightlake Therapeutics Inc., UK

