

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use NARCAN® NASAL SPRAY safely and effectively. See full prescribing information for NARCAN® NASAL SPRAY.

NARCAN® (naloxone hydrochloride) nasal spray
Initial U.S. Approval: 1971

-----INDICATIONS AND USAGE-----

NARCAN 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. (1)

NARCAN Nasal Spray is intended for immediate administration as emergency therapy in settings where opioids may be present. (1)

NARCAN Nasal Spray is not a substitute for emergency medical care. (1)

-----DOSAGE AND ADMINISTRATION-----

- NARCAN Nasal Spray is for intranasal use only. (2.1)
- Seek emergency medical care immediately after use. (2.1)
- Administration of a single spray of NARCAN Nasal Spray intranasally into one nostril. (2.2)
- Administer additional doses of NARCAN Nasal Spray, using a new nasal spray with each dose, if the patient does not respond or responds and then relapses into respiratory depression, additional doses of NARCAN Nasal Spray may be given every 2 to 3 minutes until emergency medical assistance arrives. (2.2)
- Additional supportive and/or resuscitative measures may be helpful while awaiting emergency medical assistance. (2.2)

-----DOSAGE FORMS AND STRENGTHS-----

Nasal spray: 2 mg and 4 mg of naloxone hydrochloride in 0.1 mL. (3)

-----CONTRAINDICATIONS-----

Hypersensitivity to naloxone hydrochloride. (4)

-----WARNINGS AND PRECAUTIONS-----

- **Risk of Recurrent Respiratory and CNS Depression:** Due to the duration of action of naloxone relative to the opioid, keep 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. (5.1)

- **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. (5.2)
- **Precipitation of Severe Opioid Withdrawal:** Use in patients who are opioid dependent may precipitate opioid withdrawal. In neonates, opioid withdrawal may be life-threatening if not recognized and properly treated. Monitor for the development of opioid withdrawal. (5.3)
- **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. (5.3)

-----ADVERSE REACTIONS-----

The following adverse reactions were observed in a NARCAN Nasal Spray clinical study: increased blood pressure, constipation, toothache, muscle spasms, musculoskeletal pain, headache, nasal dryness, nasal edema, nasal congestion, nasal inflammation, rhinalgia, and xeroderma. (6)

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.

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

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FULL PRESCRIBING INFORMATION: CONTENTS*

- 1 INDICATIONS AND USAGE**
- 2 DOSAGE AND ADMINISTRATION**
 - 2.1 Important Administration Instructions
 - 2.2 Dosing in Adults and Pediatric Patients
 - 2.3 Dosing Modifications due to Partial Agonists or Mixed Agonist/Antagonists
- 3 DOSAGE FORMS AND STRENGTHS**
- 4 CONTRAINDICATIONS**
- 5 WARNINGS AND PRECAUTIONS**
 - 5.1 Risk of Recurrent Respiratory and Central Nervous System Depression
 - 5.2 Risk of Limited Efficacy with Partial Agonists or Mixed Agonist/Antagonists
 - 5.3 Precipitation of Severe Opioid Withdrawal
- 6 ADVERSE REACTIONS**
- 8 USE IN SPECIFIC POPULATIONS**
 - 8.1 Pregnancy
 - 8.2 Lactation
 - 8.4 Pediatric use
 - 8.5 Geriatric Use

- 11 DESCRIPTION**
- 12 CLINICAL PHARMACOLOGY**
 - 12.1 Mechanism of Action
 - 12.2 Pharmacodynamics
 - 12.3 Pharmacokinetics
- 13 NONCLINICAL TOXICOLOGY**
 - 13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility
- 16 HOW SUPPLIED/STORAGE AND HANDLING**
 - 16.1 How Supplied
 - 16.2 Storage and Handling
- 17 PATIENT COUNSELING INFORMATION**

*Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

NARCAN Nasal Spray is 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.

Limitations of Use:

Restrict prescription of NARCAN Nasal Spray 2 mg to 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.

2 DOSAGE AND ADMINISTRATION

2.1 Important Administration Instructions

NARCAN Nasal Spray is for intranasal use only.

No additional device assembly is required.

Because treatment of suspected opioid overdose must be performed by someone other than the patient, instruct the prescription recipient to inform those around them about the presence of NARCAN Nasal Spray and the *Instructions for Use*.

Instruct the patient or caregiver to read the *Instructions for Use* at the time they receive a prescription for NARCAN Nasal Spray. Emphasize the following instructions to the patient or caregiver:

- Administer NARCAN Nasal Spray as quickly as possible because prolonged respiratory depression may result in damage to the central nervous system or death. Since the duration of action of most opioids exceeds that of naloxone hydrochloride and the suspected opioid overdose may occur outside of supervised medical settings, seek immediate emergency medical assistance, keep the patient under continued surveillance until emergency personnel arrive, and administer repeated doses of NARCAN Nasal Spray, as necessary. Always seek emergency medical assistance in the event of a suspected, potentially life-threatening opioid emergency after administration of the first dose of NARCAN Nasal Spray.
- Additional doses of NARCAN Nasal Spray may be required until emergency medical assistance becomes available.
- Do not attempt to reuse NARCAN Nasal Spray. Each NARCAN Nasal Spray contains a single dose of naloxone and cannot be reused.
- 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.

- Administer NARCAN Nasal Spray in alternate nostrils with each dose.
- Administer NARCAN Nasal Spray according to the printed instructions on the device label and the *Instructions for Use*.
- Place the patient in the supine position. Prior to administration, be sure the device nozzle is inserted in either nostril of the patient, and provide support to the back of the neck to allow the head to tilt back. **Do not prime or test the device prior to administration.**
- To administer the dose press firmly on the device plunger.
- Remove the device nozzle from the nostril after use.
- Turn patient on their side as shown in the *Instructions for Use* and call for emergency medical assistance immediately after administration of the first dose of NARCAN Nasal Spray.

2.2 Dosing in Adults and Pediatric Patients

Initial Dosing

The recommended initial dose of NARCAN Nasal Spray in adults and pediatric patients is one spray delivered by intranasal administration into one nostril.

Repeat Dosing

Seek emergency medical assistance as soon as possible after administering the first dose of NARCAN Nasal Spray.

The requirement for repeat doses of NARCAN Nasal Spray depends upon the amount, type, and route of administration of the opioid being antagonized.

Administer NARCAN Nasal Spray in alternate nostrils with each dose.

If the patient responds to NARCAN Nasal Spray and relapses back into respiratory depression before emergency assistance arrives, administer an additional dose of NARCAN Nasal Spray using a new NARCAN Nasal Spray and continue surveillance of the patient.

If the desired response is not obtained after 2 or 3 minutes, administer an additional dose of NARCAN Nasal Spray using a new NARCAN Nasal Spray. If there is still no response and additional doses are available, administer additional doses of NARCAN Nasal Spray every 2 to 3 minutes using a new NARCAN Nasal Spray with each dose until emergency medical assistance arrives.

Additional supportive and/or resuscitative measures may be helpful while awaiting emergency medical assistance.

2.3 Dosing Modifications due to Partial Agonists or Mixed Agonist/Antagonists

Reversal of respiratory depression by partial agonists or mixed agonist/antagonists, such as buprenorphine and pentazocine, may be incomplete and require higher doses of naloxone

hydrochloride or repeated administration of NARCAN Nasal Spray using a new nasal spray [*see Warnings and Precautions (5.2)*].

3 DOSAGE FORMS AND STRENGTHS

NARCAN Nasal Spray is supplied as a single-dose intranasal spray containing 2 mg or 4 mg of naloxone hydrochloride in 0.1 mL.

4 CONTRAINDICATIONS

NARCAN Nasal Spray is contraindicated in patients known to be hypersensitive to naloxone hydrochloride or to any of the other ingredients.

5 WARNINGS AND PRECAUTIONS

5.1 Risk of Recurrent Respiratory and Central Nervous System Depression

The duration of action of most opioids may exceed that of NARCAN Nasal Spray resulting in a return of respiratory and/or central nervous system depression after an initial improvement in symptoms. Therefore, it is necessary to seek emergency medical assistance immediately after administration of the first dose of NARCAN Nasal Spray and to keep the patient under continued surveillance. Administer additional doses of NARCAN Nasal Spray if the patient is not adequately responding or responds and then relapses back into respiratory depression, as necessary [*see Dosage and Administration (2.2)*]. Additional supportive and/or resuscitative measures may be helpful while awaiting emergency medical assistance.

5.2 Risk of Limited Efficacy with Partial Agonists or Mixed Agonist/Antagonists

Reversal of respiratory depression by partial agonists or mixed agonist/antagonists such as buprenorphine and pentazocine, may be incomplete. Larger or repeat doses of naloxone hydrochloride may be required to antagonize buprenorphine because the latter has a long duration of action due to its slow rate of binding and subsequent slow dissociation from the opioid receptor [*see Dosage and Administration (2.3)*]. Buprenorphine antagonism is characterized by a gradual onset of the reversal effects and a decreased duration of action of the normally prolonged respiratory depression.

5.3 Precipitation of Severe Opioid Withdrawal

The use of NARCAN Nasal Spray in patients who are opioid-dependent may precipitate opioid withdrawal characterized by the following signs and symptoms: body aches, diarrhea, tachycardia, fever, runny nose, sneezing, 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 include the following signs and symptoms: convulsions, excessive crying, and hyperactive reflexes. Monitor the patient for the development of the signs and symptoms of opioid withdrawal.

There are limited data to inform if the 2 mg dose of NARCAN Nasal Spray will avoid precipitation of severe opioid withdrawal in the setting of opioid dependence. However, the 2

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