

PRODUCT MONOGRAPH
INCLUDING PATIENT MEDICATION INFORMATION

Naloxone Hydrochloride Injection USP

Naloxone Hydrochloride

0.4 mg/mL solution for injection

USP

Opioid Antagonist

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NALOXONE HYDROCHLORIDE INJECTION USP

Naloxone Hydrochloride

PART I: HEALTH PROFESSIONAL INFORMATION

SUMMARY PRODUCT INFORMATION

Route of Administration	Dosage Form / Strength	All Nonmedicinal Ingredients
Subcutaneous, Intramuscular	solution for injection, 0.4 mg/mL	hydrochloric acid, sodium chloride, and water for injection

INDICATIONS AND CLINICAL USE

Naloxone Hydrochloride Injection USP (naloxone hydrochloride) is a pure opioid antagonist indicated for emergency use to reverse known or suspected opioid overdoses, as manifested by respiratory depression and/or severe central nervous system depression.

Naloxone Hydrochloride Injection USP can be administered by a bystander (non-healthcare professional) before emergency medical assistance becomes available but it is not intended to be a substitute for professional medical care. Emergency medical assistance (calling 911) should be requested immediately when an opioid overdose is suspected, before injecting naloxone.

CONTRAINDICATIONS

- Patients who are hypersensitive to this drug or to any ingredient in the formulation or component of the container. For a complete listing, see the DOSAGE FORMS, COMPOSITION AND PACKAGING section of the product monograph.

WARNINGS AND PRECAUTIONS

Serious Warnings and Precautions

- Emergency medical assistance (calling 911) should be requested immediately when an opioid overdose is suspected, before injecting naloxone (see WARNINGS AND PRECAUTIONS, Rebound Opioid Toxicity).

- Individuals with a satisfactory response to an initial dose of naloxone should be kept under continued surveillance (see WARNINGS AND PRECAUTIONS, Rebound Opioid Toxicity); repeated doses of naloxone should be administered as needed until the emergency medical services become available (see DOSAGE AND ADMINISTRATION).
- Caregivers administering naloxone should be prepared to assist the patient for potential adverse reactions such as aggressive reactions, convulsions and vomiting. Special attention is warranted if naloxone is administered to a neonate (see WARNINGS AND PRECAUTIONS, Acute Opioid Withdrawal Syndrome and Special Populations, Pediatrics).

General

In the absence of opioids, in opioid naïve people, naloxone shows essentially no pharmacologic activity. In opioid tolerant people, naloxone may trigger an acute opioid withdrawal syndrome (see WARNINGS AND PRECAUTIONS, Acute Opioid Withdrawal Syndrome).

Naloxone does not counteract overdoses due to: barbiturates, benzodiazepines, psychostimulants (e.g., cocaine, amphetamines, methylphenidate, etc.), alcohol, or any other non-opioid drug such as non-opioid tranquilizers, anesthetics or sedatives. However, mistakenly administering naloxone to a person that is unconscious because of a non-opioid overdose or for other reasons is unlikely to create more harm.

Rebound Opioid Toxicity

Rebound opioid toxicity is the re-emergence of an opioid overdose manifestation, including respiratory depression, following the temporary reversal of the opioid overdose with naloxone. The patient who has responded satisfactorily to naloxone should be kept under continued surveillance and repeated doses of naloxone should be administered as necessary until the emergency medical services take charge of the patient (see DOSAGE AND ADMINISTRATION). Repeated doses are often required as the duration of action of most opioids exceeds that of naloxone, and therefore, re-emergence of opioid overdose manifestation is likely.

Respiratory

Naloxone is not effective against respiratory depression due to non-opioid drugs (see WARNINGS AND PRECAUTIONS, General). A single dose of naloxone may not reverse respiratory depression (or reversal may be incomplete) if the opioid overdose is caused by certain partial agonist opioids such as buprenorphine and pentazocine or highly potent opioids such as fentanyl. Additional doses of naloxone administered at close intervals may be required in such cases (see DOSAGE AND ADMINISTRATION, Recommended Dose and Dosage Adjustment). Similarly, an opioid overdose caused by very large dose of any opioid may also require administration of multiple doses of naloxone at close intervals (see DOSAGE AND ADMINISTRATION, Recommended Dose and Dosage Adjustment). In addition to naloxone, other resuscitative measures such as maintenance of a free airway, artificial ventilation and cardiac massage could be executed by a bystander (non-health care professionals) if the bystander knows how to perform the manoeuvres. Moreover, vasopressor agents should be

employed (if available) whenever necessary if a healthcare professional is present.

Acute Opioid Withdrawal Syndrome

Naloxone Hydrochloride Injection USP should be administered with caution to persons who are known or suspected to be physically dependent on opioids. In such cases, an abrupt and complete reversal of opioid effects may precipitate an acute opioid withdrawal syndrome. The severity of such a syndrome will depend on the degree of physical dependence, the dose, affinity and potency of the opioid that induced the overdose, and the dose of naloxone administered.

The signs and symptoms of an acute opioid withdrawal syndrome include, but are not limited to: body aches, pain, fever/pyrexia, sweating/hyperhidrosis, runny nose, sneezing, piloerection, yawning, weakness, asthenia, shivering, chills, tremor/trembling, convulsions/seizures, nervousness, restlessness, irritability, aggressive behavior, diarrhea, nausea, vomiting, abdominal cramps, increased blood pressure and tachycardia. In the dependent neonate, signs also include excessive crying as well as hyperactive reflexes and the acute withdrawal may be life-threatening if not recognized and properly treated (see WARNINGS AND PRECAUTIONS, *Special Populations*, Pediatrics).

Caregivers administering naloxone to any patient should always be prepared for potential reactions associated with acute opioid withdrawal syndrome and to assist the patient to minimize harm when experiencing these reactions. For example, a patient should be positioned in lateral decubitus to prevent choking if vomiting occurs; sharp or dangerous objects should be moved away in case of seizures to protect the patient from injury, but the patient should not be restrained.

Cardiovascular - Postoperative

Several instances of hypotension, hypertension, ventricular tachycardia and fibrillation, and pulmonary edema have been reported. Rare cases of cardiac arrest have also been reported. These have occurred in postoperative patients with pre-existing cardiovascular disorders and/or other drugs may have contributed to the adverse events. A direct relationship to naloxone has not been established.

Neurologic

Convulsions or seizures after naloxone administration have been rarely reported and the relationship between naloxone and convulsion or seizure is unclear. If convulsions or seizures occur, sharp or dangerous objects should be moved away to protect the patient from injury but the patient should not be restrained.

Special Populations

Pregnant Women: There are, no adequate and well-controlled studies in pregnant women. Although reproduction studies performed in mice and rats at doses up to 1000 times the human dose revealed no evidence of impaired fertility or harm to the fetus due to naloxone, administration of naloxone to an opioid-dependent pregnant woman may induce an acute opioid withdrawal syndrome (see WARNINGS AND PRECAUTIONS, Acute Opioid Withdrawal Syndrome), which may precipitate preterm labor or fetal distress. Because of this risk and because animal reproduction studies are not always predictive of human response, naloxone should be used during pregnancy only if clearly needed.

Nursing Women: It is not known whether naloxone is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when naloxone is administered to a nursing woman.

Pediatrics: An accidental opioid exposure is possible in the pediatric population. Naloxone administration may cause an acute opioid withdrawal syndrome which may be life-threatening in neonates if not recognized and properly treated (see WARNINGS AND PRECAUTIONS, Acute Opioid Withdrawal Syndrome). Naloxone should be administered to a neonate only if clearly needed. As for any use of naloxone, emergency medical assistance (*i.e.*, 911) should be requested immediately, before injecting naloxone in a neonate.

ADVERSE REACTIONS

Abrupt reversal of opioid depression may result in nausea, vomiting, sweating, tachycardia, increased blood pressure and tremulousness.

Hypotension, hypertension, ventricular tachycardia and fibrillation, cardiac arrest and pulmonary edema have been associated with the use of naloxone postoperatively (see WARNINGS AND PRECAUTIONS, Cardiovascular - Postoperative).

Seizures have been reported to occur infrequently after the administration of naloxone; however, a causal relationship has not been established.

DRUG INTERACTIONS

Drug-Drug Interactions

Interactions with other drug products have not been established.

Drug-Food Interactions

Interactions with food have not been established.

Drug-Herb Interactions

Interactions with herbal products have not been established.

Drug-Laboratory Interactions

Interactions with laboratory tests have not been established.

DOSAGE AND ADMINISTRATION

Dosing Considerations

Emergency medical assistance (calling 911) should be requested immediately when an opioid overdose is suspected, before injecting naloxone (see WARNINGS AND PRECAUTIONS, Rebound Opioid Toxicity).

Naloxone Hydrochloride Injection USP may be administered intramuscularly, or subcutaneously. The intramuscular route of administration is recommended for bystanders (non-healthcare professionals).

Since the duration of action of most opioids exceeds that of naloxone, the patient should be kept under continued surveillance and repeated doses of naloxone should be administered, as necessary (see WARNINGS AND PRECAUTIONS, Respiratory; Rebound Opioid Toxicity).

Recommended Dose and Dosage Adjustment

Naloxone should be administered to neonates only if clearly needed (see WARNINGS AND PRECAUTIONS, Special Populations, Pediatrics).

Known or Suspected Opioid Overdosage

Children 0 to 1 year old

Initial Dose

An initial dose of 0.4 mg of Naloxone Hydrochloride Injection USP (intramuscular, or subcutaneous) should be administered.

Repeat Doses

If the desired degree of improvement in respiratory functions is not obtained, doses of 0.4 mg should be repeated at 2 to 3 minute intervals until the desired degree of reversal is reached. Additional supportive and/or resuscitative measures may be helpful while awaiting emergency medical assistance (see WARNINGS AND PRECAUTIONS, Respiratory).

Children over 1 year old and adults

Initial Dose

An initial dose of 0.4 mg to 2 mg of Naloxone Hydrochloride Injection USP (intramuscular, or subcutaneous) should be administered.

A caregiver should be aware that the risk of acute opioid withdrawal syndrome will be higher in the patient receiving higher doses of naloxone. In such cases, the caregiver should be prepared for potential reactions associated with acute opioid withdrawal syndrome and to assist the patient to minimize harm when experiencing these reactions (see WARNINGS AND PRECAUTIONS, Acute Opioid Withdrawal Syndrome).

Repeat Doses

If the desired degree of improvement in respiratory functions is not obtained, doses of 0.4 mg should be repeated at 2 to 3 minute intervals until the desired degree of reversal is reached. Additional supportive and/or resuscitative measures may be helpful while awaiting emergency

medical assistance (see WARNINGS AND PRECAUTIONS, Respiratory).

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration whenever solution and container permit. Do not use the drug product if the solution is discoloured or contains a precipitate.

ACTION AND CLINICAL PHARMACOLOGY

Mechanism of Action

While the mechanism of action of naloxone hydrochloride is not fully understood, the preponderance of evidence suggests that naloxone antagonizes the opioid effects by competing for the same receptor sites.

Pharmacodynamics

Naloxone hydrochloride prevents or reverses the effects of opioids, including respiratory depression, sedation, and hypotension. Also, it can reverse the psychosomimetic and dysphoric effects of agonist-antagonists such as pentazocine. Naloxone hydrochloride is an essentially pure opioid antagonist, *i.e.*, it does not possess the agonistic or morphine-like properties characteristic of other opioid antagonists; naloxone does not produce respiratory depression, psychosomimetic effects or pupillary constriction.

In the absence of opioids, in opioid naïve people, naloxone shows essentially no pharmacologic activity. In opioid tolerant people, naloxone may trigger an acute opioid withdrawal syndrome (see WARNINGS AND PRECAUTIONS, Acute Opioid Withdrawal Syndrome). Naloxone has not been shown to produce tolerance or to cause physical or psychological dependence.

Pharmacokinetics

Following parenteral administration naloxone hydrochloride is rapidly distributed in the body. It is metabolized in the liver, primarily by glucuronide conjugation, and excreted in urine.

STORAGE AND STABILITY

Naloxone Hydrochloride Injection USP should be stored between 20 and 25°C. Protect from freezing and from light.

DOSAGE FORMS, COMPOSITION AND PACKAGING

Naloxone Hydrochloride Injection USP 0.4 mg/mL:

Each mL of sterile aqueous injectable solution contains: 0.4 mg naloxone hydrochloride, 9 mg sodium chloride, hydrochloric acid to adjust pH, water for injection. The solution is clear and colourless, essentially free from visible particles. Naloxone Hydrochloride Injection USP is single-use and preservative-free.

Naloxone Hydrochloride Injection USP is available as:

- 1 mL single-use prefilled syringes (0.4 mg/mL) with a stacked needle (22G ½”) inserted into a needle safety device packaged in opaque blisters, available in a box of 10 units (discard unused portion after intervention).

The stopper is not made with natural rubber latex.

PART II: SCIENTIFIC INFORMATION

PHARMACEUTICAL INFORMATION

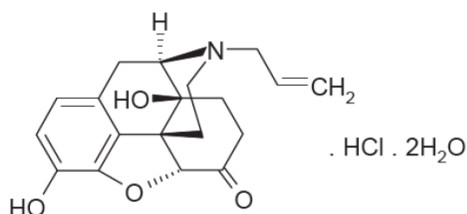
Drug Substance

Proper name: Naloxone hydrochloride

Chemical name: 17-Allyl-4,5 α -epoxy-3,14-dihydroxymorphinan-6-one hydrochloride, dihydrate

Molecular formula and molecular mass: $C_{19}H_{21}NO_4 \cdot HCl \cdot 2 H_2O$ and 399.87 g/mol

Structural formula:



Physicochemical properties:

Naloxone hydrochloride (as Naloxone Hydrochloride Dihydrate), an opioid antagonist, is an synthetic congener of oxymorphone. In structure it differs from oxymorphone in that the methyl group on the nitrogen atom is replaced by an allyl group.

Naloxone hydrochloride (as Naloxone Hydrochloride Dihydrate) occurs as a white to slightly off-white powder, and is soluble in water, in dilute acids, and in strong alkali; slightly soluble in alcohol; practically insoluble in ether and in chloroform. It melts at about 200-205°C. The pH of aqueous solutions is acidic.

DETAILED PHARMACOLOGY

Single subcutaneous doses of naloxone as high as 24 mg/70 kg (0.343 mg/kg) and multiple doses of 90 mg daily, for two weeks, administered to normal volunteers produced no behavioural or physiological changes, yet its antagonistic activity to subsequent morphine challenge persisted.

Naloxone hydrochloride at doses of 0.7 to 10 mg administered intravenously to heroin addicts abolished the effects of 10 to 20 mg of heroin whether administered before or after the heroin. The effects of the heroin began to recur three hours after naloxone administration, indicating naloxone

has a shorter duration of action than heroin.

Naloxone was able to reverse the respiratory depression induced by various anesthetics: morphine, fentanyl, cyclazocine, pentazocine, meperidine, alphaprodine, oxymorphone, nalorphine and levallorphan in patients, whether administered IV, IM or SC at 0.4 to 2 mg/mL. Naloxone caused no respiratory depression, psychotomimetic effects, clinically significant circulatory effects, nor analgesia when administered alone. Subjects did not develop tolerance to naloxone. Temporary nausea and vomiting were reported in two studies, but as other anesthetics/analgesics were being administered concurrently, these effects could not be causally related to naloxone.

When naloxone is administered intravenously the onset of action is generally apparent within two minutes; the onset of action is only slightly less rapid when it is administered subcutaneously or intramuscularly. The duration of action is dependent upon the dose and route of administration. Intramuscular administration produces a more prolonged effect than intravenous administration. The requirement for repeat doses will also be dependent upon the amount, type, and route of administration of the opioid being antagonized.

Following parenteral administration naloxone is rapidly distributed in the body. It is metabolized in the liver, primarily by glucuronide conjugation, and excreted in urine. In one study the mean serum half-life in adults was 4.7 minutes for the distribution phase and 64 minutes for the elimination phase. In a neonatal study the mean plasma half-life was observed to be 3.1 ± 0.5 hours.

In a nine-week study of nine males (22 to 47 years of age) who were addicted to opioids, naloxone was administered in single daily oral doses in increments of 50 mg (3 subjects), 100 mg (4 subjects) and 300 mg (2 subjects). Up to 3000 mg of naloxone hydrochloride daily was administered (1 subject). No significant toxic symptoms occurred over nine weeks of naloxone administration. Sporadic abnormal laboratory findings including elevated white blood cell counts occurred, but are common in cases of opioid addiction. One patient receiving 1500 mg of naloxone daily reported psychic depression, apathy and decreased appetite, which were relieved when the dosage was decreased.

TOXICOLOGY

Acute Toxicity

The maximum nontoxic subcutaneous dose in rats was 50 mg/kg.

In acute SC toxicity studies in newborn rats, the LD₅₀ is 260 mg/kg. Naloxone was only twice as toxic in newborn as in six week old rats. At toxic doses naloxone produced excitation, hyperactivity, salivation, tremors, and tonic-clonic convulsions. Respiration was slightly stimulated in rabbits as shown by the minute-volume measurements.

Subacute Toxicity

Subacute SC toxicity experiments in rats and monkeys and a subacute IV toxicity experiment in dogs demonstrated very little cumulative toxicity and no organic pathological changes.

Reproduction and Teratology

Reproduction studies in mice and rats using naloxone hydrochloride dosages up to 1000 times the usual human dosage have not revealed evidence of impaired fertility or harm to the fetus.

Mutagenicity and Carcinogenicity

Mutagenicity and carcinogenicity studies have not been conducted using naloxone.

REFERENCES

1. Jasinski DR, Martin WR, Haertzes CA. The human pharmacology and abuse potential of N-allylnoroxymorphone (Naloxone). *J Pharm. Exp Ther* 1967;157(2):420.
2. Smits SE, Takemori AE. Quantitative studies on the antagonism by naloxone of some narcotic and narcotic antagonist analgesics. *Br J Pharm* 1970;39:627.
3. Longnecker DE, Grazis PA, Eggers GWN. Naloxone for antagonism of morphine-induced respiratory depression. *Anesth Analg* 1973;52:447.
4. Foldes FF, Davidson GM, Duncalf D, Kuwabara S, Siker ES. The respiratory, circulatory and analgesic effects of naloxone-narcotic mixtures in anaesthetized subjects. *Can Anæsth Soc J* 1965;12(6):608.
5. Anderson R, Dobloug I, Refstad S. Postanæsthetic use of naloxone hydrochloride after moderate doses of fentanyl. *Acta Anæsthesiol Scand* 1976;20:255.
6. Tigerstedt I. Naloxone as narcotic antagonist after balanced anaesthesia. *Acta Anæsthesiol Scand* 1977;21:481.
7. Jasinski DR, Martin WR, Sapira JD. Antagonism of the subjective behavioural pupillary and respiratory depressant effects of cyclazocine by naloxone. *Clin Pharm Ther* 1967;9(2):215.
8. Kallos T, Smith TC. Naloxone reversal of pentazocine-induced respiratory depression. *JAMA* 1968;204:932.
9. Foldes FF, Duncalf D, Kuwabara S. The respiratory, circulatory, and narcotic antagonistic effects of nalorphine, levallorphan and naloxone in anaesthetized subjects. *Can Anæsth Soc J* 1969;16(2):151.
10. Fink M, Zaks A, Sharoff R, Mora A, Bruner A, Levit S, Freedman AM. Naloxone in heroin dependence. *Clin Pharm Ther* 1968;9(5):568.
11. Fujimoto JM. Isolation of naloxone-3-glucuronide from human urine. *Proc Soc Exp Biol Med* 1970;133:317.
12. Ngai SH, Berkowitz BA, Yang JC, Hempstead J, Spector S. Pharmacokinetics of naloxone in rats and in man—basis for its potency and short duration of action. *Anesthesiology* 1976;44:398.
13. Moreland TA, Brice JEH, Walker CHM. Naloxone pharmacokinetics in the newborn. *Br J Clin Pharmacol* 1980;9:609.

14. Zaks A, Jones T, Fink M, Freedman AM. Naloxone treatment of opiate dependence. JAMA 1971;215(13):2108.
15. AHFS Drug Information 90. American Pharmacist Society 1990;1111.
16. Blumberg H, Wernick T, Dayton HB, Hansen RE, Rapaport DN. Toxicologic studies on the narcotic antagonist naloxone. Tox Appl Pharm 1966;8:335.
17. S.O.S Naloxone Hydrochloride Injection Product Monograph, Sandoz Canada, Submission Control #203781, Date of Revision April 26, 2017.

PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

NALOXONE HYDROCHLORIDE INJECTION USP **Naloxone Hydrochloride Injection** **1 mL prefilled syringes, (0.4 mg/mL)** **Preservative-free**

Read this carefully before administering **Naloxone Hydrochloride Injection USP** and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **Naloxone Hydrochloride Injection USP**.

Serious Warnings and Precautions

- Before injecting Naloxone Hydrochloride Injection USP, call for emergency medical assistance (by calling 911) immediately when an opioid overdose is suspected (see WARNINGS AND PRECAUTIONS, Rebound Opioid Toxicity in the Product Monograph);
- Individuals with a satisfactory response to an initial dose of naloxone should be kept under continued surveillance (see WARNINGS AND PRECAUTIONS, Rebound Opioid Toxicity in the Product Monograph). Repeated doses of Naloxone Hydrochloride Injection USP should be administered as needed until the emergency medical services become available (see DOSAGE AND ADMINISTRATION in the Product Monograph).
- Caregivers administering naloxone should be prepared to assist the patient for potential adverse reactions such as aggressive reactions, convulsions and vomiting. Special attention is warranted if Naloxone Hydrochloride Injection USP is administered to a newborn less than four weeks old (see WARNINGS AND PRECAUTIONS, Acute Opioid Withdrawal Syndrome and *Special Populations*, Pediatrics in the Product Monograph).

What is Naloxone Hydrochloride Injection USP used for?

Naloxone Hydrochloride Injection USP is used to treat someone who has or may have overdosed on opioids (a type of medication used to treat pain). It can be used by anyone (non-healthcare professional) to reverse the effects of the overdose until medical help arrives. Signs of an opioid overdose include:

- trouble breathing
- extreme drowsiness
- pale and clammy skin
- slow or no heartbeat
- passing out
- unable to be woken up

How does Naloxone Hydrochloride Injection USP work?

Opioid drugs work by acting on specific receptors found in the brain and in the nervous system. When these drugs attach to those receptors, they reduce the amount of pain you feel. Naloxone Hydrochloride Injection USP works by blocking these specific receptors. When these receptors are blocked, the opioid drugs can no longer work on them. This helps reduce the effects of the opioid drugs.

What are the ingredients in Naloxone Hydrochloride Injection USP?

Medicinal ingredient: naloxone hydrochloride

Non-medicinal ingredients: hydrochloric acid (to adjust pH), 9 mg sodium chloride, and water for injection.

Naloxone Hydrochloride Injection USP comes in the following dosage forms:

Solution for injection: 0.4 mg/ mL

Do not use Naloxone Hydrochloride Injection USP only if:

- you are sure that the patient is allergic to naloxone hydrochloride or to any of the ingredients in Naloxone Hydrochloride Injection USP.

Other warnings you should know about:

Non-opioid overdoses: Naloxone Hydrochloride Injection USP does not reduce the effects of an overdose caused by other drugs such as:

- barbiturates
- benzodiazepines
- psychostimulants (for example cocaine, amphetamines or methylphenidate)
- alcohol
- anesthetics
- sedatives

Giving Naloxone Hydrochloride Injection USP to a person because of a non-opioid overdose is unlikely to cause more harm.

Reoccurrence Opioid Symptoms: It may be possible that the symptoms of an opioid overdose reoccur even after a dose of Naloxone Hydrochloride Injection USP has been given. You should:

- monitor the patient
- give repeated doses of Naloxone Hydrochloride Injection USP to the patient if needed
- wait for emergency medical help to arrive

Opioid Dependant Patients: Naloxone Hydrochloride Injection USP should be given with caution to patients who may be or are known to be physically dependant on opioids. Giving this drug to these patients may cause them to go into opioid withdrawal and cause opioid withdrawal syndrome.

Caregivers who give of Naloxone Hydrochloride Injection USP to any patient should always be prepared for symptoms of opioid withdrawal syndrome and should try to help minimize any potential harm to the patient when they experience these reactions.

Some of the signs of opioid syndrome include:

- pain
- fever
- sweating
- runny nose
- sneezing
- yawning
- weakness
- shivering/chills
- tremor/trembling
- convulsions/seizures. Sharp and dangerous objects should be moved away to prevent injury
- vomiting. The patient should be placed on his or her side to prevent choking if they vomit
- increased blood pressure

Patients who have had surgery: Naloxone Hydrochloride Injection USP should be given with caution to patients who have had a recent surgery. The following have occurred:

- high and low blood pressure
- increased heart rate
- rapid irregular heartbeat
- a build-up of fluid in the lungs
- in rare cases cardiac arrest

Pregnant Women: Naloxone Hydrochloride Injection USP should only be used in pregnant women when clearly needed.

Pediatrics: An accidental exposure to an opioid drug is possible. Naloxone Hydrochloride Injection USP should be given only if clearly needed.

The following may interact with Naloxone Hydrochloride Injection USP:

There are no known drug interactions with Naloxone Hydrochloride Injection USP.

How to administer Naloxone Hydrochloride Injection USP:

- Do not use the drug product if the solution is discoloured or contains a precipitate.
- Call for emergency medical help (911) **before** you give the injection.
- If you are a bystander, a family member or a friend (non–medical healthcare professional): give the injection into the muscle (intramuscularly).
- If you are a health care professional: the injection can be given:
 - underneath the skin (subcutaneously) or
 - into the muscle (intramuscularly).

Usual Dose:

- Initial Dose: Inject 1 mL
- Repeat Doses: Inject 1 mL after 2 to 3 minutes if the person does not respond by breathing normally or waking up.

Four steps overdose response

Step 1: Check for signs of opioid overdose

- Breathing difficulties: Look for signs of breathing by placing your cheek near the nose and mouth of the person to feel their breath. Take only about 10 seconds to check this (**Figure 1**).



Figure 1

Other signs of overdose include:

- Excessive drowsiness
- Pale and clammy skin
- Slow or no heartbeat
- Passing out (loss of consciousness) or unable to be woken up

Step 2: Call 911

Step 3: Give Naloxone Injection

- Take the blister packaging and remove the syringe of Naloxone Hydrochloride Injection USP. Using your fingers, remove the cap. **(Figure 2)**.

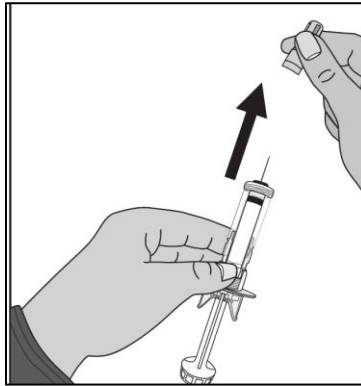


Figure 2

- Use the syringe to inject into either:
 - o The fleshy part of the outer arm (just below the shoulder)
 - o Front of the upper thighs
 - o Upper part of the buttocks **(Figure 3)**

You can inject through light clothing unless the person is wearing thick clothing (such as a jacket or sweater), you do not need to remove their clothes.

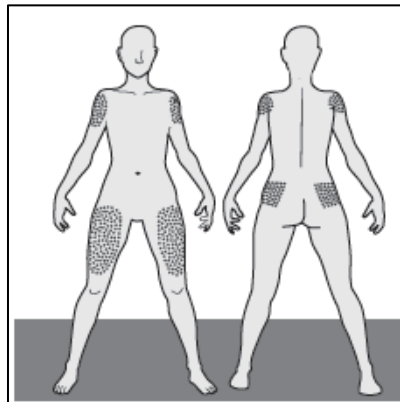


Figure 3

- Hold the syringe at a 90 degree angle to the body, about 10 cm away from the skin.
- Insert the needle into the muscle with a single, quick motion.
- Push down the plunger of the syringe with a slow, steady motion. **(Figure 4)**.

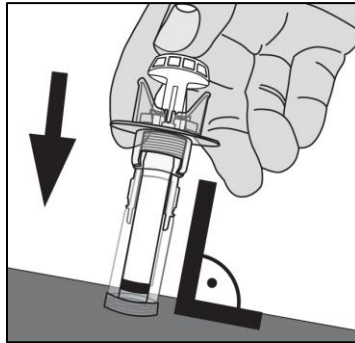


Figure 4

- Release the piston (the needle will be retracted) and carefully put the syringe out of the way, so that you can safely throw it away later.
- Give the used syringe to the paramedics or bring them to the nearest pharmacy for safe discarding. **Do not** reuse them.

Step 4: Evaluate and support.

- Put the person in "the recovery position" by placing them on their side, making sure that they are not able to roll over. You can do this by moving one leg so that the knee is bent at a right angle (90 degrees), and also moving one arm so that it is a right angle to the body. Then make sure that their airway is open by gentle tilting the head back and lifting the chin. Make sure that the airway is clear of anything blocking it. **(Figure 5).**

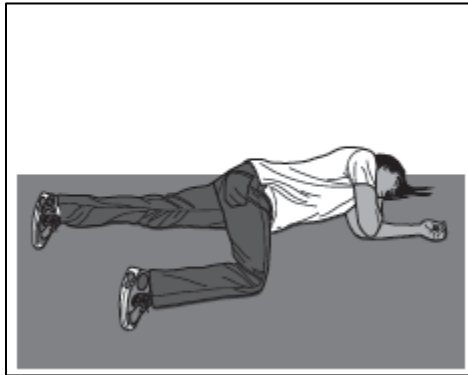


Figure 5

- Wait with the person until the ambulance arrives. Keep checking to make sure that they are still breathing.
- Repeat **Step 3** after 2 to 3 minutes if the person does not respond by breathing normally or waking up.

What are possible side effects from using Naloxone Hydrochloride Injection USP?

- nausea
- vomiting
- sweating
- rapid heart beat
- increased blood pressure
- feeling shaky

A few people have had a seizure after an injection of Naloxone Hydrochloride Injection USP. However, it is not known if this was caused after receiving the injection.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (<https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting.html>) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:

Store between 20°C-25°C. Protect from freezing and from light. Keep out of reach and sight of children.

If you want more information about Naloxone Hydrochloride Injection USP:

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website: (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html>), the manufacturer's website www.sterinova.com or by calling 1 844-329-2939.

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