

## **NARCAN**

**Naloxone Hydrochloride Injection 0.4 mg/mL**

## **NARCAN NEONATAL**

**Naloxone Hydrochloride Injection 0.02mg/mL**

### **Presentation**

In structure it differs from oxymorphone in that the methyl group on the nitrogen atom is replaced by an allyl group.

Naloxone Hydrochloride= (-)-17-Allyl-4, 5-epoxy-3, 14-dihydroxymorphinan-, 6-one hydrochloride.

Naloxone hydrochloride 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. Narcan injection is available as a sterile solution for intravenous, intramuscular and subcutaneous administration in two concentrations. 0.02mg and 0.4mg of naloxone hydrochloride per mL. Each mL of either strength contains 8.6mg of sodium chloride: and 2.0mg of methylhydroxybenzoate and propylhydroxybenzoate as preservatives in a ratio of 9 to 1. PH is adjusted to 3.5 + 0.5 with hydrochloric acid.

### **Use**

#### ***Actions***

Narcan (naloxone hydrochloride), a narcotic antagonist, is a synthetic congener of oxymorphone. Narcan (naloxone hydrochloride) prevents or reverses the effects of opioids including respiratory depression, sedation and hypotension. Also, it can reverse the psychotomimetic and dysphoric effects of agonist-antagonists such as pentazocine. Narcan (naloxone hydrochloride) is an essentially pure narcotic antagonist, i.e. it does not possess the "agonistic" or morphine-like properties characteristic of other narcotic antagonists; Narcan does not produce respiratory depression, psychotomimetic effects of pupillary constriction. In the absence of narcotics or agonistic effects of other narcotic antagonists it exhibits essentially no pharmacologic activity.

Narcan has not been shown to produce tolerance nor to cause physical or psychological dependence. In the presence of physical dependence on narcotics Narcan will produce withdrawal symptoms.

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

#### ***Pharmaokinetics***

When Narcan 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 of Narcan. Intramuscular administration produces a more prolonged effect than intravenous administration. The requirement for repeat doses of Narcan, however, will also be dependent upon the amount, type and route of administration of the narcotic being antagonised.

Following parenteral administration Narcan is rapidly distributed in the body. It is metabolised in the liver, primarily by glucuronide conjugation and excreted in the urine. In one study the serum half-life in adults ranged from 30 to 81 minutes (mean  $64 \pm 12$  minutes). In a neonatal study the mean plasma half-life was observed to be  $3.1 \pm 0.5$  hours.

### ***Indications***

Narcan is indicated for the complete or partial reversal of narcotic depression, including respiratory depression, induced by opioids including natural and synthetic narcotics, propoxyphene, methadone and the narcotic antagonist analgesics: nalbuphine, pentazocine and butorphanol. Narcan is also indicated for the diagnosis of suspected acute opioid overdose.

### **Dosage and Administration**

Narcan (naloxone hydrochloride) may be administered intravenously, intramuscularly, or subcutaneously. The most rapid onset of action is achieved by intravenous administration and it is recommended in emergency situations. Since the duration of action of some narcotics may exceed that of Narcan the patient should be kept under continued surveillance and repeated doses of Narcan should be administered, as necessary.

The 10mL presentation should be used for one patient only, within 6 hours of administration of the initial dose.

**Intravenous infusion:** Narcan may be diluted for intravenous infusion in normal saline or 5% dextrose solutions. The addition of 2mg of Narcan in 500mL of either solution provides a concentration of 0.004mg/mL. Mixtures should be used within 24 hours. After 24 hours, the remaining unused solution must be discarded. The rate of administration should be titrated in accordance with the patient's response.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration whenever solution and container permit. Narcan should not be mixed with preparations containing bisulphite, metabisulphite, long-chain or high molecular weight anions, or any solution having an alkaline pH. No drug or chemical agent should be added to Narcan unless its effect on the chemical and physical stability of the solution has first been established.

### ***Usage in Adults***

Narcotic Overdose - Known or Suspected. An initial dose of 0.4mg to 2mg of Narcan may be administered intravenously. If the desired degree of counteraction and

improvement in respiratory functions is not obtained it may be repeated at 2 to 3 minute intervals. If no response is observed after 10mg of Narcan have been administered, the diagnosis of narcotic induced or partial narcotic induced toxicity should be questioned. Intramuscular or subcutaneous administration may be necessary if the intravenous route is not available.

Postoperative Narcotic Depression. For the partial reversal of narcotic depression following the use of narcotics during surgery, smaller doses of Narcan are usually sufficient. The dose of Narcan should be titrated according to the patient and response. For the initial reversal of respiratory depression, Narcan should be injected in increments of 0.1 to 0.2mg intravenously at two to three minute intervals to the desired degree of reversal i.e. adequate ventilation and alertness without significant pain or discomfort. Larger than necessary dosage of Narcan may result in significant reversal of analgesia and increase in blood pressure. Similarly, too rapid reversal may induce nausea, vomiting, sweating or circulatory stress.

Repeat doses of Narcan may be required at one to two hour intervals depending upon the amount, type (i.e. short or long acting) and time interval since last administration of narcotic. Supplemental intramuscular doses have been shown to produce a longer lasting effect.

### ***Usage in Children***

Narcotic Overdose - Known or Suspected. The usual initial dose in children is 0.01mg/kg body weight given I.V. If this dose does not result in the desired degree of clinical improvement a subsequent dose of 0.1mg/kg body weight may be administered. If an I.V. route of administration is not available, Narcan may be administered I.M. or S.C. in divided doses if necessary. Narcan can be diluted with sterile. Water for Injection.

Postoperative Narcotic Depression. Follow the recommendations and cautions under Adult Postoperative Depression. For the initial reversal of respiratory depression Narcan should be injected in increments of 0.005mg to 0.01mg intravenously at two to three minute intervals to the desired degree of reversal.

### ***Usage in Neonates***

Narcotic-induced Depression. The usual initial dose is 0.01mg/kg body weight administered I.V., I.M. or S.C. This dose may be repeated in accordance with adult administration guidelines for postoperative narcotic depression.

## **Contraindications**

Narcan is contraindicated in patients known to be hypersensitive to it.

## **Warnings and Precautions**

Narcan should be administered cautiously to persons including newborns or mothers who are known or suspected to be physically dependent on opioids. In such cases an

abrupt and complete reversal of narcotic effects may precipitate an acute abstinence syndrome.

The patient who has satisfactorily responded to Narcan should be kept under continued surveillance and repeated doses of Narcan should be administered, as necessary, since the duration of action of some narcotics may exceed that of Narcan.

Narcan is not effective against respiratory depression due to non-opioid drugs. In addition to Narcan, other resuscitative measures such as maintenance of a free airway, artificial ventilation, cardiac massage, and vasopressor agents should be available and employed when necessary to counteract acute narcotic poisoning.

Several instances of hypotension, hypertension, ventricular tachycardia and fibrillation, and pulmonary oedema have been reported. These have occurred in postoperative patients most of whom had pre-existing cardiovascular disorders or received other drugs which may have similar adverse cardiovascular effects. Although a direct cause and effect relationship has not been established, Narcan should be used with caution in patients with pre-existing cardiac disease or patients who have received potentially cardiotoxic drugs.

### ***Carcinogenesis, Mutagenesis, Impairment of Fertility***

Carcinogenicity and mutagenicity studies have not been performed with Narcan. Reproductive studies in mice and rats demonstrated no impairment of fertility.

### ***Use in Pregnancy***

Reproduction studies performed in mice and rats at doses up to 1,000 times the human dose, revealed no evidence of impaired fertility or harm to the foetus due to Narcan. There are, however, no adequate and well controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, Narcan should, therefore, be administered to pregnant patients only when, in the judgement of the physician, the potential benefits outweigh the possible hazards.

### ***Use in Lactation***

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

### **Adverse Effects**

Abrupt reversal of narcotic depression may result in nausea, vomiting, sweating, tachycardia, increased blood pressure, and tremulousness. In postoperative patients, larger than necessary dosage of Narcan may result in significant reversal of analgesia, and in excitement. Hypotension, ventricular tachycardia and fibrillation, and pulmonary oedema have been associated with the use of Narcan postoperatively (see Warnings and Precautions & Usage in Adults Postoperative Narcotic

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

## **Interactions**

Nil

## **Overdosage**

There is no clinical experience with Narcan overdosage in humans. In the mouse and rat the intravenous LD<sub>50</sub> is 150 ± 5mg/kg and 109 ± 4mg/kg respectively. In acute subcutaneous toxicity studies in newborn rats the LD<sub>50</sub> (95% CL) is 260 (228-296) mg/kg. Subcutaneous injection of 100mg/kg/day in rats for 3 weeks produced only transient salivation and partial ptosis following injection, no toxic effects were seen at 10mg/kg/day for 3 weeks.

## **Pharmaceutical Precautions**

Nil

## **Medicine Classification**

Prescription Medicine

## **Package Quantities**

0.4mg/mL of Narcan (naloxone hydrochloride) for intravenous, intramuscular and subcutaneous administration. Available in 1mL ampoules; boxes of 10 and 10mL vials,

0.02mg/mL of Narcan (naloxone hydrochloride) Neonatal Injection for intravenous, intramuscular and subcutaneous administration. Available in 2mL ampoules; boxes of 10

## **Further Information**

Nil

## **Name and Address**

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