Naloxone

Newborn use only

2025

Alert	Naloxone should not be administered to neonates born to known or suspected opiate dependent mothers, as naloxone can precipitate acute withdrawal syndrome and seizures.
Indication	Reversal of respiratory depression from therapeutic or toxic dose of opiates. **NOTE:** Naloxone is not recommended as part of initial resuscitative efforts in the delivery room for newborns with respiratory depression. Heart rate and oxygenation should be restored by supporting ventilation.
Action	Pure opioid antagonist. Little or no agonistic activity. It is thought to act as a competitive antagonist at mu, kappa, and sigma opioid receptors in the central nervous system.[14]
Drug Type	Semisynthetic opioid antagonist
Trade Name	DBL Naloxone Hydrochloride Injection; Naloxone Juno Solution for injection; Naloxone SXP Solution; Narcan Solution for injection;
Presentation	400 microgram/1 mL of naloxone hydrochloride ampoule
Dose	IV 10 microgram/kg, repeat after 2-3 minutes if no response. Larger doses up to 100 microgram/kg may be used on occasions if no response to regular doses. **DO NOT USE AT DELIVERY IN INFANTS BORN TO MOTHERS SUSPECTED OR KNOWN TO BE DEPENDENT ON OPIOIDS.** **CAUTION**: **Infants on prolonged opioid infusion may develop acute withdrawal following naloxone.**
Dose adjustment	Therapeutic hypothermia – No information. ECMO – No information. Hepatic impairment – No information. Renal impairment – No information.
Maximum dose	Larger doses up to 100 microgram/kg may be used on occasions if no response to regular doses.
Route	Intravenous (IV) - Preferred. IM - If IV not available. Subcutaneous
Preparation	400 microgram/1 mL. No preparation is required.
Administration	IV/IM/SC[14] Use undiluted. Intravenous (IV) bolus. Intramuscular (IM) in anterolateral aspect of thigh. Subcutaneous in anterolateral aspect of thigh.
Monitoring	Continuous cardiorespiratory monitoring – Duration is dependent on the treating condition. (Refer to pharmacokinetics section). Resuscitation facilities must be readily available.
Contraindications	Hypersensitivity to naloxone or to any of the excipients. Newborn infants at birth whose mothers are known or suspected to be dependent on opioids.
Precautions	
Drug Interactions	When naloxone is used post-operatively to reverse the central depressive effects of opioid agonists, the dose of naloxone must be carefully titrated to achieve the desired effect without interfering with control of post-operative pain or causing other adverse effects.[14]
Adverse Reactions	Acute withdrawal syndrome (tachycardia, tachypnoea, hypertension, tremors, vomiting and seizures) in neonates born to known or suspected opiate dependent mothers. Cardiac arrest – there is a case report of a preterm neonate who developed cardiac arrest.[13]
Overdose	Treatment of overdosage is symptomatic and supportive. AUSTRALIA Contact the Poisons Information Centre on 13 11 26 for information on the management of overdose. NEW ZEALAND Contact the National Poisons Centre on 0800 764 766 for information on the management of overdose.
Compatibility	Fluids:[17] Glucose 5%, sodium chloride 0.9%.

	Fluids (Y-site):[17] Lactated Ringer's solution. **Y-site:**[17] Amikacin, amiodarone, anidulafungin, azithromycin, caffeine citrate, calcium chloride, calcium gluconate, cefotaxime, ceftazidime, ceftriaxone, clindamycin, defibrotide, desmopressin, dexamethasone, dexmedetomidine, digoxin, dobutamine, dopamine, epinephrine (adrenaline), epoetin alfa, ertapenem, erythromycin lactobionate, esmolol, etoposide, etoposide phosphate, famotidine, fentanyl citrate, fluconazole, fludarabine, fluorouracil, folic acid, furosemide, ganciclovir, gentamicin, glucagon, glycopyrrolate, heparin sodium, hydrocortisone, imipenem/cilastatin, insulin human regular, linezolid, meropenem, methylprednisolone, metronidazole, midazolam, morphine sulfate, norepinephrine bitartrate, octreotide acetate, penicillin G (benzylpencillin), phenobarbital, piperacillin/tazobactam, potassium chloride, promethazine, propofol, pyridoxine, ranitidine, rocuronium, sodium acetate, sodium bicarbonate, sodium nitroprusside, succinylcholine (suxamethonium), ticarcillin, ticarcillin/clavulanate, tobramycin, vancomycin, vasopressin, vecuronium bromide, verapamil, voriconazole, zoledronic acid.
Incompatibility	Do not mix with preparations containing sulfite, metabisulfite or any alkaline solution. **Fluids:** No information. **TPN:** No information. **Y-site:** Amphotericin, calcium folinate, diazepam, diazoxide, magnesium pantoprazole, phenytoin, sulfamethoxazole/trimethoprim, thiopental.
Stability	Infusion solution: Use within 24 hours.
Storage	Store below 25°C. Protect from light.
Excipients	Hydrochloric acid, sodium chloride, water for injections.
Special Comments	Always establish and maintain adequate respiration before administration of naloxone. Majority of infants born following intrapartum opioid administration do not require naloxone.
Evidence	**Efficacy** **2010 American Heart Association –** Neonatal resuscitation: Naloxone is not recommended as part of initial resuscitative efforts in the delivery room for newborns with respiratory depression. Heart rate and oxygenation should be restored by supporting ventilation.[1] **Opioid-exposed newborn infants with respiratory maladaptation to birth:** Systematic review[2] reported 9 trials (316 infants) that compared the effects of naloxone versus placebo. The dose of naloxone used ranged from 0.01 to 0.07 mg/kg with the exception of one study in which a total dose of 0.2 mg IMI was given. None of these trials specifically recruited infants with cardiorespiratory or neurological depression. The main outcomes reported were measures of respiratory function in the first six hours of life. There is some evidence that naloxone increases alveolar ventilation. The trials did not assess the effect on admission to a neonatal unit and failure to establish breastfeeding. The existing evidence from randomised controlled trials is insufficient to determine whether naloxone confers any important benefits to newborn infants with cardiorespiratory or neurological depression that may be due to intrauterine exposure to opioid. (LOE I GOR D) **Reversal of opioid effect to facilitate extubation:** A case series reported the outcomes of 31 infants with a mean birth weight of 1178 grams and mean gestational age 28.4 weeks who were intubated after IV atropine 0.02 mg/kg, fentanyl 3 micrograms/kg and succinylcholine 2 mg/kg for surfactant administration. Infants with an adequate respiratory drive were immediately extubated while those with apnoea or hypopnea received naloxone 0.1 mg/kg/dose, repeated if needed. Twelve of thirteen (92%) infants in the naloxone group were extubated within 30 minutes of surfactant administration while 12/18 (67%) in the non-naloxone group were extubated within the same time frame. No adverse reactions were noted.[3] Conclusion: Naloxone may be effective in reversing the respiratory depression from opioid administration and facilitate extubation in preterm infants intubated for the InSurE procedure. Clinical trials are required to confirm this finding and its safety. (LOE IV GOR D). **Reduction of side effects of opioids:** There are no trials in newborns specifically for this indication. There are case reports of response to naloxone in newborn infants with morphine-induced muscle rigidity and hypoxaemia during mechanical ventilation.[4,5] In an RCT, low dose naloxone infusion 0.25 microgram/kg/hour did not decrease fentanyl requirements in critically ill, mechanically ventilated children aged 1 day to 18 years.[6] In 23 children aged 5 months to 18 years in intensive care receiving opioid therapy, enteral naloxone for treating constipation increased stool output but induced

	withdrawal symptoms.[7] Conclusion: There is no role for naloxone for reducing the side effects of opioids in newborn infants. (GOR B – evidence for harm) **Post-operative apnoeas in preterm infants:** The combined effect of anaesthetics and prematurity, each of which itself results in raised endorphin activity, may result in apnoeas in preterm infants in the perioperative period. Naloxone at a dose of 5–10 microgram/kg has been used to reverse respiratory effects of anaesthetics and narcotics in the post-operative period.[8-11] **Safety:** There are few data regarding adverse effects of naloxone in newborn infants. There is concern regarding precipitating opioid withdrawal in patients with prolonged opioid exposure.[1] Naloxone should not be administered to babies whose mothers are known or suspected to be addicted to opioids. In such cases, an abrupt and complete reversal of opioid effects may precipitate an acute withdrawal syndrome.[12] There is a case report of a preterm neonate who developed cardiac arrest following treatment with naloxone (dose 100 mcg/kg) for a ten-fold morphine overdose.[13] **Pharmacokinetics** Naloxone has an onset of action within 1 to 2 minutes following intravenous administration and within 2 to 5 minutes following subcutaneous or intramuscular administration. The duration of action depends on the dose and route of administration and is more prolonged following intramuscular administration than after intravenous administration. The duration of action is reported to be up to several hours but the practical duration is probably 1 hour or less.[14] The mean plasma half-life of naloxone has been reported to be about 60 minutes in adults with a range of from about 30 to 80 minutes, and about 3 hours in neonates.[14] In newborns, after intravenous administration of 35 (n = 6) and 70 (n = 6) micrograms of naloxone, peak levels of 4 to 15 ng/mL and 9 to 20 ng/mL respectively were reached in 5 to 40 min and the mean plasma half-life after both doses was 3.1 ± 0.5 hours. Peak levels of 7 to 35 ng/ml were reached 0.5 to 2 hour after intramuscular administration of 200 microgram (n = 17). The fall in concentration after this was consistently biphasic with the levels declining rapidly between one and four hours and then slowly from four hours onwards. Plasma concentrations at 24–36 hours after IM administration were as high as they were 4 hours after IV administration of 35 microgram which may account for the prolonged duration of action when this route is used.[15] In 26 infants born to mothers who received pethidine, naloxone was not observed to have any agonist activity, but the recommended IV dose (0.01 mg/kg) had only a slight and delayed antagonist action as measured by respiratory function tests. A more rapid and improved antagonism was noted after this dose was doubled (0.02 mg/kg). The plasma elimination-phase half-life of naloxone after intravenous cord injection was about 3 hours.[16]
References	1. Kattwinkel J, Perlman JM, Aziz K, Colby C, Fairchild K, Gallagher J, Hazinski MF, Halamek LP, Kumar P, Little G, McGowan JE. Neonatal resuscitation: 2010 American Heart Association guidelines for cardiopulmonary resuscitation and emergency cardiovascular care. Pediatrics. 2010 Nov 1;126(5):e1400-13. 2. Moe-Byrne T, Brown JV, McGuire W. Naloxone for opiate-exposed newborn infants. Cochrane Database Syst Rev. 2018 Oct 12;10(10):CD003483. 3. Elmekkawi A, Abdelgadir D, Van Dyk J, Choudhury J, Dunn M. Use of naloxone to minimize extubation failure after premedication for INSURE procedure in preterm neonates. Journal of Neonatal-Perinatal Medicine. 2016; 9:363-706. 4. Van Der Lee R, Ceelie I, Tibboel D, De Wildt SN. Muscle rigidity and respiratory compromise in a term neonate during morphine infusion; serious adverse event determined by using the naranjo algorithm. Clinical Pharmacology and Therapeutics. 2009;1):S69-S70. 5. Barr PA. Hypoxaemia during mechanical ventilation for severe hyaline membrane disease following sedation with morphine sulphate. Australian Paediatric Journal. 1981;17:296-7. 6. Darnell CM, Thompson J, Stromberg D, Roy L, Sheeran P. Effect of low-dose naloxone infusion on fentanyl requirements in critically ill children. Pediatrics. 2008;121:e1363-71. 7. Tofil NM, Benner KW, Faro SJ, Winkler MK. The use of enteral naloxone to treat opioid-induced constipation in a pediatric intensive care unit. Pediatr Crit Care Med. 2006;7:252-4. 8. Fischer CG, Cook DR. The respiratory and narcotic antagonistic effects of naloxone in infants. Anesthesia & Analgesia. 1974 Nov 1;53(6):849-52. 9. Gerhardt T, Bancalari E, Cohen H, Rocha LF. Use of naloxone to reverse narcotic respiratory depression in the newborn infant. The Journal of pediatrics. 1977 Jun 1;90(6):1009-12.

10. Beilin B, Vatashsky E, Aronson HB, Weinstock M. Naloxone reversal of postoperative apnea in a premature infant. Anesthesiology: The Journal of the American Society of Anesthesiologists. 1985 Sep 1;63(3):317-8.
11. Suwa K, Takahashi K, Iizuka Y, Lefor AK. High-Dose Remifentanil Anesthesia With Minimal Sedation in Neonates: A Single-Center Retrospective Study. Cureus. 2024 Aug 26;16(8):e67801.
12. Gibbs J, Newson T, Williams J, Davidson DC. Naloxone hazard in infant of opioid abuser. The Lancet. 1989 Jul 15;334(8655):159-60.
13. Deshpande G, Gill A. Cardiac arrest following naloxone in an extremely preterm neonate. European journal of pediatrics. 2009 Jan 1;168(1):115.
14. DBL Naloxone hydrochloride injection. Product info. Accessed online on 3rd April 2025.
15. Moreland TA, Brice JE, Walker CH, Parija AC. Naloxone pharmacokinetics in the newborn. Br J Clin Pharmacol. 1980;9:609-12.
16. Bonta BW, Gagliardi JV, Williams V, Warshaw JB. Naloxone reversal of mild neurobehavioral depression in normal newborn infants after routine obstetric analgesia. Journal of Pediatrics. 1979;94:102-5.
17. MerativeTM Micromedex® Complete IV Compatibility (electronic version). Merative, Ann Arbor, Michigan, USA. Available at: https://www.micromedexsolutions.com/ (cited: Apr/03/2025).

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