BRIEF ADMINISTRATION GUIDE

(For more detailed guideline information please see the following pages)

Indications:
- Opioid induced respiratory and CNS depression[1-5]
- Opioid overdose[1,2,5]

Route:
- Intravenous (preferred)[1,2,6]
- Intramuscular or subcutaneous (recommended only if intravenous access is not available as onset of action may be delayed and absorption can be erratic and unpredictable in children)[1,2,6]

Dose:

100 microgram/kg/dose (0.25 ml/kg/dose)[1,2,4,5]

Dose may be repeated at 2 to 3 minute intervals if required according to response[3,5,6]

Note:
- The duration of naloxone antagonism may be less than the clearance of the opiate being antagonised, thus repeat doses may be required[4,5]
- If no response is seen after 2 to 3 doses, respiratory and central nervous system depression is unlikely to be secondary to opioids[1]

Supplied as: Naloxone hydrochloride 400 microgram/ml ampoule[1]

Preparation and administration:

Direct IV Injection
- Administer prescribed dose undiluted by intravenous injection over 30 seconds[6-8]
- Naloxone can be diluted to aid administration by adding 400 microgram (1 ml) naloxone to 9 ml of sodium chloride 0.9% to produce a 40 microgram/ml solution[6-8]

Intramuscular Injection
- Administer prescribed dose undiluted by intramuscular injection[6,8]

Subcutaneous Injection
- Administer prescribed dose undiluted by subcutaneous injection[6,8]

Monitoring:

- Monitor heart rate, blood pressure, respiratory rate, pulse oximetry and level of consciousness closely for at least 6 hours after naloxone is used[6,8]
- Assess for signs of anaphylaxis or adverse reactions, including acute withdrawal which may present with seizures, excessive crying and hyperactive reflexes[2]
- Monitor for injection site reactions[9]

1. Purpose and scope

To facilitate the safe and effective use of naloxone in neonates.

2. Drug

Drug	Naloxone, naloxone hydrochloride
Drug action	Naloxone is a pure opioid antagonist that competes and displaces opioids at opioid receptor sites. It prevents or reverses the effects of opioids, including respiratory depression, sedation and hypotension. Naloxone does not possess agonist properties and therefore does not produce respiratory depression, psychomimetic effects or pupillary constriction. In the absence of opioids it exhibits essentially no pharmacological activity[3,5,6]. Following parenteral administration, naloxone is rapidly distributed in the body. When administered intravenously its onset of action is rapid (within 2 minutes); the onset of action is slightly less rapid when administered subcutaneously or intramuscularly (up to 5 minutes). The duration of action is variable depending on the dose and route of administration. Intramuscular administration has more prolonged effects than intravenous administration due to a depot effect[3,5,6].
Indications	• Opioid induced respiratory and CNS depression[1-5] • Opioid overdose[1,2,5]
Presentation	• Naloxone hydrochloride 400 microgram/ml ampoule[1] • Clear colourless solution. Excipients include sodium chloride, water for injection[3,8].
Route	• Intravenous (preferred)[1,2,6] • Intramuscular or subcutaneous (recommended only if intravenous access is not available as onset of action may be delayed and absorption can be erratic and unpredictable in children)[1,2,6]
Dose	100 microgram/kg/dose (0.25 ml/kg/dose)[1,2,4,5] Dose may be repeated at 2 to 3 minute intervals if required according to response[3,5,6]. <u>Note:</u> • The duration of naloxone antagonism may be less than the clearance of the opiate being antagonised, thus repeat doses may be required[5,6]. • If no response is seen after 2 to 3 doses, respiratory and central nervous system depression is unlikely to be secondary to opioids[1].
Contraindications	• Hypersensitivity to naloxone or any component of the preparation[3,6,10] • Infants of mothers who are known or suspected to be physically dependant on opioids (may precipitate acute abstinence syndrome)[1,10,11]
Precautions	• Naloxone is an adjuvant therapy to resuscitation efforts for opioid induced respiratory and CNS depression. Before naloxone is administered, restore heart rate and colour by supporting ventilation[2-4] • A recurrence of respiratory and/or CNS depression may occur following an initial improvement in symptoms[2,6] • Naloxone has no effect on non-opioid induced respiratory or CNS depression[2,5,10] • Cardiovascular disease or use of medications known to cause

	cardiovascular effects[3,6,10]
Incompatibilities	• Compatible with sodium chloride 0.9%, glucose 5%[2,7,10] • Do not mix with drugs with alkaline pH or with preparations containing bisulfite or metabisulfite[3,8,10]
Adverse effects	• Nausea, vomiting, diarrhoea, sweating[1,3,6] • Hypotension, hypertension, ventricular tachycardia and fibrillation, cardiac arrest[1,3,6,10] • Pulmonary oedema, dyspnoea, hyperventilation, hypoxia[1,3,6,10] • Excessive crying, headache, dizziness, irritability[1,6] • Hyperactive reflexes, tremor, paraesthesia[1,6,10] • Rare: seizures[1-3,6,10]

3. Administration

Competency for administration	This procedure is carried out by, or under, the direct supervision of a registered nurse/registered midwife who holds current Waikato DHB Generic Medicine Management and IV certification as well as Neonatal specific competency NCV/NAC.
Preparation & Administration	**Direct IV Injection** • Administer prescribed dose undiluted by intravenous injection over 30 seconds[6-8] • Naloxone can be diluted to aid administration by adding 400 microgram (1 ml) naloxone to 9 ml of sodium chloride 0.9% to produce a 40 micogram/ml solution[6-8] **Intramuscular Injection** • Administer prescribed dose undiluted by intramuscular injection[6,8] **Subcutaneous Injection** • Administer prescribed dose undiluted by subcutaneous injection[6,8]
Observations and management	• Monitor heart rate, blood pressure, respiratory rate, pulse oximetry and level of consciousness closely for at least 6 hours after naloxone is used[4,8]. • Assess for signs of anaphylaxis or adverse reactions, including acute withdrawal which may present with seizures, excessive crying and hyperactive reflexes[2] • Monitor for injection site reactions[9]
Special considerations (audit, funding, storage)	• Naloxone has a pH of 3.5[3,8] • Prepare immediately before use[8] • Visually inspect for particular matter or discolouration and do not use if present[8] • Ampoule should be stored at room temperature (below 25 °C) and protected from light[3,7] • Discard any unused contents remaining[7]
Rescue medication	Discontinue immediately and seek urgent medical assistance if anaphylaxis or severe adverse reactions occur. Administer adrenaline and maintain airway as appropriate.

4. Definitions

CNS	Central nervous system

5. References

1. New Zealand Formulary for Children (NZFC). 2018. Naloxone hydrochloride. Accessed 27th June 2018. Available from: https://www.nzfchildren.org.nz/nzf_7017
2. Truven Health Analytics Inc. Pediatrics and Neofax®. 2018. Naloxone monograph. Accessed 27th June 2018. Available from: http://www.micromedexsolutions.com.
3. Pfizer NZ Ltd. Naloxone hydrochloride Data Sheet. 12 April 2017. Available from: http://www.medsafe.govt.nz/profs/datasheet/d/dblnaloxonehydrochlorideinj.pdf
4. Canterbury DHB Neonatal Services. Naloxone Drug Information Sheet. March 2016. Available from: http://www.cdhb.health.nz/Hospitals-Services/Health-Professionals/Neonatal-Clinical-Resources/Neonatal-Drug-Information-Sheets.
5. Auckland DHB Newborn Services. Naloxone Hydrochloride Drug Protocol. November 1996. Available from: http://www.adhb.govt.nz/newborn/DrugProtocols
6. American Pharmacists Association. Pediatric & Neonatal Dosage Handbook. 20th edition. 2013.
7. The Royal Children's Hospital Melbourne. Paediatric Injectable Guidelines. Accessed 27th June 2018. Available from: https://pig.rch.org.au.
8. New Zealand Hospital Pharmacists Assoc. Inc. Notes on Injectable Drugs 7th ed, 2015.
9. Gray A, Wright J, Goodey V, Bruce L. Injectable Drugs Guide. Pharmaceutical Press; 2011.
10. Phelps SJ, Hagemann TM, Lee KR, Thompson AJ. The Teddy Bear Book: Pediatric Injectable Drugs. 10th edition. American Society of Health-System Pharmacists; 2013.
11. Ainsworth SB. Neonatal Formulary: Drug Use in Pregnancy and the First Year of Life 7th ed. John Wiley & Sons Incorporated; 2014.