Medicine Guideline

Naloxone for treatment of opioid induced over-sedation and respiratory depression

Areas where Protocol/Guideline applicable	SESLHD
Authorised Prescribers:	SESLHD Medical Officers and person authorised by SESLHD Standing Order
Important Safety Considerations	Repeated doses or infusion of naloxone may be required, especially with longer acting opioids, slow-release formulations, and those with active metabolites, to maintain effect as the half-life of naloxone is less than 1 hour (shorter than all opioids). If the patient does not respond to repeated doses of naloxone, other causes of sedation and respiratory depression must be considered. Excretion of some opioids and/or their active metabolites may be delayed in renal impairment, and they will accumulate; extended naloxone treatment may be required. Ensure opioid patches are removed, opioid infusions are ceased, and patient-controlled analgesia (PCA) buttons are removed prior to administration of naloxone. DO NOT administer any further opioids. Maintain intravenous access. If naloxone is administered on the ward, seek expert advice (e.g., toxicology, critical care) regarding the patient's ongoing management.
Indication for use	Reversal of opioid related side effects including respiratory depression and over sedation, without reversal of analgesia
Clinical condition	**Opioid induced – the patient MUST have received an opiate dose** • Respiratory Depression - respiratory rate ≤ five (5) breathes per minute • Over Sedation – not responsive or difficult to rouse, sedation score three (3)
Proposed Place in Therapy	In accordance with Clinical Emergency Response System (CERS)
Adjunctive Therapy	Administer oxygen at 10 L/min via a Hudson Mask
Contra-indications	Hypersensitivity to naloxone
Precautions	In patients with opioid dependence, rapid reversal of opioid effects may lead to an acute withdrawal syndrome (i.e., pain, agitation, and aggression) and an abrupt return of severe pain that is then very difficult to control. Palliative Care: naloxone is not indicated for opioid induced drowsiness and/or delirium that is not life threatening or for patients on opioids who are dying.

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Adverse Effects	**Post-operatively:** hypotension, hypertension, ventricular tachycardia and fibrillation, dyspnoea, pulmonary oedema and cardiac arrest. **Opioid depression:** abrupt reversal may result in nausea, vomiting, sweating, increased blood pressure, hyperventilation, tremulousness, seizures, ventricular tachycardia and fibrillation, pulmonary oedema and cardiac arrest. **Opioid dependence:** patients may occasionally have more severe effects (e.g., seizure, pulmonary oedema, ventrilcular arrhythmias). Violent behaviour, nervousness, restlessness, excitement and irritability may also occur.
Important Drug Interactions	**Opioids** Naloxone is a competitive antagonist at opioid receptors, reversing effects of opioids; rapid reversal may precipitate acute withdrawal syndrome in opioid dependence.
Intermittent Naloxone	
Dosage	**Intravenous administration** 100 – 200 micrograms, repeated every 2 to 3 minutes to a maximum 400 micrograms, if required. Smaller doses may be appropriate in elderly or frail patients, patients with renal or hepatic impairment or palliative care patients (e.g., 40 microgram increments). *Where intravenous access is not available, administer 400 micrograms subcutaneously or intramuscularly.*
Duration of therapy	Until the effects of respiratory depression are reversed (e.g., respiratory rate > 10 breaths/minute with no cyanosis). Repeated doses of naloxone should be administered as clinically appropriate e.g., re-emergence of respiratory depression and/or over sedation. If no response after 400 micrograms has been administered, seek expert advice (e.g., toxicology, critical care). Reconsidered diagnosis of opioid toxicity. Patients who experience prolonged respiratory compromise may be considered for a continuous naloxone infusion. In buprenorphine overdose, larger doses of up to 10 mg may be required.
Prescribing Instructions	For patients receiving an opioid prescribed on a NSW Health Pain Chart, naloxone MUST be prescribed on the Pain Chart. For all other patients, naloxone is to be prescribed in the PRN section of eMEDs or eRIC.
Administration Instructions	Administer undiluted as a bolus injection. For smaller doses, dilute 400 microg to 10 mL sodium chloride 0.9% (concentration 40 microg/mL)

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Continuous Naloxone Infusion	
Dosage	Naloxone 2 mg in 500 mL sodium chloride 0.9% or glucose 5% (concentration 4 microg/mL). Usual hourly rate of infusion is half to two-thirds of the total effective bolus dose. The infusion rate to be titrated according to patient's level of consciousness (GCS > 12), respiratory rate (RR>10/min) and oxygen saturation (>95%).
Duration of therapy	Until symptoms of over-sedation and/or respiratory depression have resolved.
Prescribing Instructions	Continuous naloxone infusions MUST be prescribed in eFluids or eRIC.
Administration Instructions	Dilute 2 mg (five ampoules of 400 microg) to 500 mL of compatible fluid.

Monitoring requirements	Patients requiring continuous naloxone infusion MUST be transferred to a high acuity area for monitoring.
	
	Remain with the patient and call for assistance. Call 2222 and activate a Code Blue. Observe closely for the patient's response. The patient should open their eyes and talk within 1 – 2 minutes following administration of naloxone.
	
	Monitor for symptoms of persistent opioid toxicity. Every 1 to 2 minutes monitor respiratory rate, sedation levels and oxygen saturation until the patient is more alert and respiratory rate is > 10 breathes per minute.
	Continue monitoring:
	• Every 5 minutes for the first hour,
	• Every 15 minutes for the next hours, then,
	  ○ Hourly for 6 houts after an immediate release opioid
	  ○ Hourly for 12 hours after a slow release opioid
	  ○ Hourly for 24 hours after methadone
	
	Monitor for symptoms of rapid reversal of opioid effects – nausea, vomiting, sweating, tachycardia, tremor, and tachypnoea.
	
	Monitor for symptoms of opioid withdrawal – severe pain, agitation, dilated pupils, rapid RR, increased pulse, and blood pressure.
	
	Patients receiving a continuous naloxone infusion require continuous cardiac monitoring for adverse cardiovascular effects – acute pulmonary oedema, hypotension, hypertension ventricular tachycardia and fibrillation.
	
	Refer to Management of Deteriorating Patient – Clinical Emergency Response System (CERS)

Management of Complications	If naloxone does not produce the desired effect, other differential diagnoses must be considered (e.g., hypoglycaemia). Opioid administration can be resumed following review by a medical officer (usually at a reduced dose) when the patient is easily roused and the respiratory rate > 10 breaths/min.

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Basis of Protocol/Guideline:	1. Agency for Clinical innovation. Pain Management Network. Quick steps through Opioid Management. 2023. 2. MIMs Online. DBL Naloxone Hydrochloride Injection. 01 May 2023 3. Australian Injectable Drugs Handbook. Naloxone. 8th Edition. 2023 4. Clarke SFJ, Dargan PI, and Jones AL. Naloxone in opioid poisoning: walking the tightrope. Emergency Medicine Journal 2005; 22:612-616. 5. ANZCOR Guidelines. Guideline 9.5.2 – First Aid Management of Opioid Overdose. 2023. 6. Australian Medicines Handbook. Naloxone. 2023 7. eTG. Toxicology and Toxinology. Opioid Poisoning: general management. Treatment for opioid poisoning. 2020.
	• POWH CLIN044 Naloxone Administration for Opioid Induced Respiratory Depression • RHW NALOXONE – Treatment of opioid induced over-sedation, respiratory depression, pruritis and nausea • POWH CLIN055 NALOXONE Critical Care Services Intravenous Drug Protocol
Groups consulted in development of this guideline	Pain Management, Palliative Care, Nursing, Pharmacy

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