		Type: Drug Guideline	Document reference: 2940	Manual Classification: Waikato DHB Drug Guidelines
Title: Morphine for NICU			Effective date: 30 March 2016	
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			Document expiry date: 30 March 2019	

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1. Purpose and scope

To facilitate the safe administration of injectable morphine within the Neonatal Intensive Care Unit (NICU).

Note: oral morphine is used to reduce withdrawal symptoms in babies whose mothers were taking opioids while pregnant, but this is not covered under this guideline – see Procedure 1589 “Drug dependent mothers and Finnegan score” for information for this indication.

2. Drug


Drug	Morphine, morphine sulphate
Drug action	<p>Morphine sulphate is a narcotic analgesic which stimulates opioid receptors in the central nervous system. Morphine produces respiratory depression by direct effect upon brain stem respiratory centres. No major effect upon cardiovascular system in analgesic doses. Resistance and capacitance vessels are dilated by the opioids. Gastrointestinal secretions and motility are decreased while tone is increased. Stimulates smooth muscle of biliary and urinary tracts.</p> <p>Morphine is well absorbed from gastrointestinal tract but has high first pass metabolism. Low binding (20%) to plasma protein. Hepatic metabolism to glucuronides and other metabolites. Excretion via the kidney with significant amounts of unchanged drug in the neonate. Accumulation can occur if renal impairment. The pharmacokinetics of morphine in the neonate is very variable.</p> <p>Rapid onset of action after parenteral administration. Peak effect after 20-60 minutes. Duration of analgesic effect variable (may persist up to 7 hours). Analgesic effects occur with plasma concentrations of 100-150 ng/mL. Respiratory depression may occur with plasma concentrations > 300ng/mL.³</p>
Indications	<ul style="list-style-type: none"> • Analgesia • Sedation
Presentation	<p>Morphine sulphate 10mg/ml ampoule</p> <ul style="list-style-type: none"> • Clear colourless to slightly yellow² • Solution does not contain any antioxidant or preservative • pH of these solutions ranges from 3.2 to 4.0²
Route	<ul style="list-style-type: none"> • IM, subcut or IV (as bolus) • IV or central venous access device (as continuous infusion) • Oral for Neonatal Abstinence Syndrome – see separate procedure
Dose	<p>Bolus Usual starting dose of 50 to 100 mcg/kg/dose IV, SC or IM (references range from 25-200mcg/kg/dose).^{1,3,4} Repeat as required, usually up to every 4 to 6 hours</p> <p>Continuous IV Infusion Loading dose of 100-150mcg/kg over 1 hour followed by 10-50mcg/kg/hr^{1,3,5,6} Usual range is 10-20mcg/kg/hr^{1,3,5}</p>
Contraindications	<ul style="list-style-type: none"> • Known hypersensitivity to opiates
Precautions	<ul style="list-style-type: none"> • Impaired respiratory function • Hypovolaemia and hypotension • Conditions associated with raised intracranial pressure, acute head injury, comatose patients • Hepatic and/or renal impairment

	Document reference: 2940	Effective date: 30 Mar 2016	Expiry date: 30 Mar 2019	Page: 2 of 3
	Title: Morphine for NICU		Type: Drug Guideline	Version: 01

	<ul style="list-style-type: none"> • Cardiac arrhythmias • Extreme prematurity • Neurological disorders • Obstructive bowel disorders, acute abdomen, delayed gastric emptying
Compatibilities & Incompatibilities	<ul style="list-style-type: none"> • Compatible with sodium chloride 0.45% and 0.9%, glucose 2.5%, 5% and 10%, 5% glucose/ sodium chloride combinations, potassium chloride 20mmol/L • Incompatible with many medications, especially if alkaline e.g. amphotericin B, cefepime, phenobarbitone and phenytoin¹
Adverse effects	<ul style="list-style-type: none"> • Respiratory depression (enhanced susceptibility in neonates) • Gastrointestinal disturbances (nausea, vomiting, constipation, ileus, delayed gastric emptying, cramps) • Transient hypertonia • Hypotension • Urinary retention, dry mouth • Physical dependence • Hypersensitivity, urticaria, pruritis

3. Administration

Competency for administration	This procedure is carried out by, or under, the direct supervision of a registered nurse / registered midwife who holds generic IV certification and Neonatal specific certifications NCV/NAC, as well as Guardrails competency.
Preparation & Administration	<p>Bolus Dilute dose to 1ml with sterile water. Recommended concentration is 5mg/ml or weaker^{5,7} If intravenous administration give by slow push over 4-5 minutes.⁵</p> <p>Continuous IV Infusion Dilute as per 'NICU Drugs' computer software available on all desktops in the NICU. If this resource is not available, dilute as per the default dilution below: Dilute 0.5mg/kg morphine up to 20mL with compatible fluid and mix well. This results in infusion rate: 0.1mL/hr = 2.5micrograms/kg/hour Recommended concentration for continuous infusion is 1mg/ml or weaker (commonly 0.1mg/mL)^{1,5,7}</p>
Observations and management	<ul style="list-style-type: none"> • Assess IV site closely for signs of extravasation • Assess for signs of adverse reactions • Continuous cardiorespiratory and blood pressure monitoring¹ • Monitor oxygen saturations • Monitor respiratory status closely¹ • Monitor urinary and bladder functions¹ • Observe for abdominal distension or loss of bowel sounds¹
Storage	<ul style="list-style-type: none"> • Store in controlled drug cupboard at room temperature below 25°C • Protect from light. Solutions that change to a yellow colour are still suitable for use² • Dilutions are stable for up to 24 hours at room temperature
Special considerations	<ul style="list-style-type: none"> • Tolerance likely to develop with prolonged use • Wean slowly after prolonged use, greater than 2 weeks

	Document reference: 2940	Effective date: 30 Mar 2016	Expiry date: 30 Mar 2019	Page: 3 of 3
	Title: Morphine for NICU		Type: Drug Guideline	Version: 01

Rescue medication	Naloxone should be readily available to reverse adverse effects
	For management of morphine overdose and/or toxicity: <ul style="list-style-type: none"> • Discontinue morphine • Supportive therapy (i.e. ventilation) • Naloxone - 0.1mg/kg/dose IV or IM

4. Guardrails Information⁸

Guardrails Drug Name	Morphine CC			
Pump	0.4-1kg	1-2kg	2-3kg	3-5kg
Weight range				
Concentration (microgram/ml)				
Default	20	50	100	150
Minimum	6.6	16.6	33.3	50
Maximum	50	100	150	250
Administration Rate (microgram/kg/hr)				
Soft minimum	2.5	2.5	2.5	2.5
Default	5	5	5	5
Soft maximum	30	30	30	30
Hard maximum	50	50	50	50
Bolus: 50-100mcg/kg administered at a rate of 0.83mL/minute				

5. Associated Documents

- Waikato DHB Procedure Drug dependent mothers and Finnegan score. Document reference number 1589. <https://intranet.sharepoint.waikato.health.govt.nz/site/pol/published/Infants%20born%20to%20drug%20Dependent%20Mothers%20-%20Management%20of.pdf>

6. References

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- 3 Auckland NICU Drug Protocols – Morphine, October 2004. Available from: <http://www.adhb.govt.nz/newborn/DrugProtocols/Default.htm> Last accessed 7th December 2015.
- 4 The New Zealand Formulary Editorial Team. New Zealand Formulary for Children. Morphine. New Zealand Formulary, NZ. Last accessed 23rd November 2015. Available from http://nzfchildren.org.nz/nzf_2515
- 5 Phelps SJ, Hak EB, Crill CM, editors. Teddy Bear Book: Pediatric Injectable Drugs. 10th Edition. Morphine. Bethesda, MD: American Society of Health-System Pharmacists; 2013.
- 6 The New Zealand Medicines and Medical Devices Safety Authority (Medsafe): Morphine, Data sheet, Hospira. Last accessed 23rd November 2015. Available from <http://www.medsafe.govt.nz/profs/datasheet/d/dblMorphinesulphbpinj.pdf>
- 7 The Royal Children's Hospital Melbourne: Paediatric Injectable Guidelines 4th Edition, Morphine. Published July 2011, Melbourne Australia.
- 8 Guardrails Data Sheets, Waikato Hospital, Hamilton, NZ, May2015.

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