Waikato District Health Board	Type: **Drug Guideline**	Document reference: **2940**	Manual Classification: **Waikato DHB Drug Guidelines**
Title: **Morphine for neonates**			Effective date: **17 November 2021**
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BRIEF ADMINISTRATION GUIDE

For detailed information refer to The **Australasian Neonatal Medicines Formulary** morphine guidelines **morphine 10mg/mL parenteral** and **morphine oral**

Critical Note: there are minor variations between the ANMF and Waikato DHB best practice within this drug guideline – see yellow shaded text

Indications:
- Analgesia, sedation
- Neonatal abstinence syndrome (NAS) secondary to opioids

Route: Intravenous (preferred parenteral route), Intramuscular, Subcutaneous, Oral

- Parenteral supplied as morphine sulphate 10 mg/mL ampoule
  - The pH of morphine is 3 to 5
- Oral supplied as morphine hydrochloride 1 mg/mL liquid

Dose:

Analgesia

- **IV injection** (or IM or subcut if IV route unavailable): Initially 50 microgram/kg/dose (range 25-100 microgram/kg/dose), adjusted according to response.
  Maximum of 200 microgram/kg/dose. Repeat dose every 4 to 6 hours if required.

- **Continuous IV Infusion:** Consider using a loading dose (dose as for IV injection), then initially 10 microgram/kg/hour, titrated carefully to effect.
  Usual dose range is 5 to 40 microgram/kg/hr

- **Oral**: Initially 50 – 200 micrograms/kg, adjusted according to response every 4 to 6 hours

Neonatal abstinence syndrome (oral)

a) Secondary to maternal opioid dependency
   Initially 40 microgram/kg every 4 hours. Increase as necessary to a maximum dose of 200 microgram/kg.
   Wean dose by 10% of original dose every 48-72 hours and discontinue when dose is 40 microgram/kg/day
   Note: may be given in conjunction with clonidine (1 microgram/kg every 4 hours)

b) Secondary to prolonged infant opioid infusion
   If weaning from IV morphine commence oral morphine at twice the daily IV dose
   If weaning from IV fentanyl commence oral morphine using a conversion ratio of 1:20
   (See Appendix 1 for an example calculation)
   Dose frequency usually every 4 to 6 hours
   Adjust dose to clinical condition

Adjust dose according to Finnegan score and clinical condition. As a guide; reduce dose by 10-25% every 2 to 4 days (titrated to Finnegan score and clinical condition).

Note:
- **IV to oral ratio** of morphine is 1:2 i.e. oral dose is twice that of IV
- Fentanyl IV to morphine IV ratio is unknown but likely in the range of 1:10 to 1:30 i.e. morphine dose is 10 to 30 times that of fentanyl. Convert conservatively then adjust as needed
- *For ease of conversion from IV to oral first convert medicines to equivalent 24 hour dosing*
- Clearance reduced with decreased age; very preterm infants may need smaller doses
- Reduce dose in renal impairment
- Tolerance likely to develop with prolonged use. Wean dose slowly after use greater than 2 weeks

Preparation and administration

Compatible fluids: glucose 5%, glucose 10%, sodium chloride 0.9%, sodium chloride 0.45%, glucose in sodium chloride combinations

Direct IV Injection

- Dilute 1 mL of morphine 10 mg/mL with 19 ml of compatible fluid to make 20 mL of a **500 microgram/mL** solution. If a weaker concentration is required, prepare as per the table below.
- Draw up the prescribed dose
- Administer as a slow IV injection over at least 5 minutes.

Note: If an IV morphine infusion is already running a bolus should be administered using this solution and with Guardrails settings (morphine BOLUS*)

Continuous IV Infusion

- Select the concentration of morphine required based on the weight of the infant and in the context of any fluid restrictions (refer to appendix 2 for assistance) and dilute the appropriate volume of morphine injection using compatible fluid in accordance with the table below:

Final Morphine Concentration	40 microgram/mL	200 microgram/mL
Volume of morphine (10 mg / 1 mL)	0.2 mL	1 mL
Volume of compatible fluid	49.8 mL	49 mL
Total volume	50 mL	50 mL

- Administer at the prescribed rate by continuous IV infusion using a syringe driver with Guardrails settings (morphine)

$$\text{Rate (mL/hr)} = \frac{\text{Dose (microgram/kg/hr) x Weight (kg)}}{\text{Concentration (microgram/mL)}}$$

Intramuscular or Subcutaneous Injection (if IV route unavailable and parenteral route desired, or for palliation)

- Dilute 1 mL of morphine 10 mg/mL with 9 ml of compatible fluid to make 10 mL of a 1 mg/mL solution
- Draw up prescribed dose and administer immediately

Oral

- Draw up prescribed dose in an oral syringe.
- Can be diluted with water or breast milk prior to administration if desired. Administration with food is preferable.

Monitoring

- Continuous cardiorespiratory monitoring
- Document blood pressure, heart rate, respiratory rate and oxygen saturation hourly during treatment
- Observe for urinary retention, abdominal distension or loss of bowel sounds
- Monitor the level of sedation using the Neonatal Pain and Sedation Score (NPASS), where indicated
- When being used for NAS Finnegan scoring should be performed every 3-4 hours

Storage and Stability

- Store in a Controlled Drug Safe
- Discard any unused portion of the injection solution from the ampoule
- Diluted solutions should be used within 24 hours

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 plus Guardrails competency (if administering IV) as well as Neonatal specific competency NCV/NAC (if administering via CVAD).

Guardrails

Morphine is Guardrail profiled on the CC pump for NICU as **two entries; ensure you select the correct entry**. Following are the guardrail limits:

Guardrails Drug Name	Morphine	Morphine BOLUS*
Concentration (mcg/ml)		
Minimum	40	40
Maximum	1000	1000
Dose rate (mcg/kg/hr)		
Default	10	600
Soft minimum	5	150
Soft maximum	40	1200
Hard max	60	2400

Associated documents

- Waikato DHB NICU guideline. Management of Newborns delivered to Drug Dependent Mothers. Reference number 1589
- Waikato DHB. Naloxone for neonates Drug Guideline. Reference number 2941

References

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- Weaning of Opioids and Benzodiazepines. . Auckland DHB guideline. August 2017. https://www.starship.org.nz/guidelines/weaning-of-opioids-and-benzodiazepines/

Note: **Printed copies are only valid on the day of printing – they are not controlled and may not be the current version in use. Please refer to the online version.**

Appendix 1

Dose conversion example (morphine IV to oral morphine):
Baby is receiving morphine 20 microgram/kg/hr

- ⇨ 20 microgram/kg/hr x 24hr = 480 microgram/kg/day
- ⇨ Using a conversion factor of 2:
  morphine (IV) 480 microgram/kg/day x 2 = morphine (oral) 960 microgram/kg/day

- ⇨ If adminstering oral morphine every 4 hours i.e. 6 times per day:
  morphine (oral) 960 microgram/kg/day ÷ 6 = 160 microgram/kg/dose

- ⇨ Prescription is for morphine oral 160 microgram/kg q4h

Dose conversion example (fentanyl IV to oral morphine):
Baby is receiving fentanyl 4 microgram/kg/hr

- ⇨ 4 microgram/kg/hr x 24hr = 96 microgram/kg/day
- ⇨ Using a conversion factor of 10 for IV fentanyl to IV morphine (Note: conversion is approx 1:10 to 1:30 but start with conservative dosing i.e. use 1:10):
  fentanyl (IV) 96 microgram/kg/day x 10 = morphine (IV) 960 microgram/kg/day

- ⇨ Using a conversion factor of 2 for IV morphine to oral morphine:
  morphine (IV) 960 microgram/kg/day x 2 = morphine (oral) 1920 microgram/kg/day

- ⇨ If adminstering oral morphine every 4 hours i.e. 6 times per day:
  morphine 1920 microgram/kg/day ÷ 6 = 320 microgram/kg/dose

- ⇨ Prescription is for morphine oral 320 microgram/kg q4h

Appendix 2

Infusion tables to assist concentration selection

Table 1: Infusion rates when using morphine concentration **40 microgram/mL**
(most useful for neonates ≤ 2 kg)

Rate (mL/hr)	0.1	0.2	0.3	0.4	0.5	0.6	0.7	0.8	0.9	1
Weight (kg)	**Approximate micrograms/kg/hour**									
0.5	8	16	24	32	40	48	56	64	72	80
1	4	8	12	16	20	24	28	32	36	40
1.5	3	5	8	11	13	16	19	21	24	27
2	2	4	6	8	10	12	14	16	18	20
2.5	2	3	5	6	8	10	11	13	14	16
3	1	3	4	5	7	8	9	11	12	13
3.5	1	2	3	5	6	7	8	9	10	11

Table 2: Infusion rates when using morphine concentration **200 microgram/mL**
(likely useful for neonates >2 kg)

Rate (mL/hr)	0.1	0.2	0.3	0.4	0.5	0.6	0.7	0.8	0.9	1
Weight (kg)	**Approximate micrograms/kg/hour**									
1	20	40	60	80	100	120	140	160	180	200
1.5	13	27	40	53	67	80	93	107	120	133
2	10	20	30	40	50	60	70	80	90	100
2.5	8	16	24	32	40	48	56	64	72	80
3	7	13	20	27	33	40	47	53	60	67
3.5	6	11	17	23	29	34	40	46	51	57
4	5	10	15	20	25	30	35	40	45	50
4.5	4	9	13	18	22	27	31	36	40	44
5	4	8	12	16	20	24	28	32	36	40