		Type: <b>Drug Guideline</b>	Document reference: <b>2911</b>	Manual Classification: <b>Waikato DHB Drug Guidelines</b>
Title: <b>Doxapram for neonates</b>			Effective date: <b>18 January 2019</b>	
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## BRIEF ADMINISTRATION GUIDE

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

- Indications:** Apnoea of prematurity unresponsive to caffeine (or aminophylline)<sup>1-5</sup>
- Route:** Intravenous<sup>2-7</sup> or Oral<sup>4,7</sup>
- Dose:** Continuous IV Infusion<sup>2,3,6</sup>
- Initially 0.5 mg/kg/hr, then increase in increments of 0.5 mg/kg/hr as needed to control apnoea up to a maximum rate of 2.5 mg/kg/hr (in practice usual maximum 1.5 mg/kg/hr)
  - Continue treatment until stable or for a maximum of 48 hours, then titrate to the lowest rate at which apnoea is controlled
- Oral<sup>4,7</sup>  
6 mg/kg every 6 hours
- Supplied as:** Doxapram 100 mg/5 ml (20 mg/ml) vial<sup>8,9</sup>

### Preparation and administration:

#### Continuous Intravenous Infusion<sup>2,3,9,10</sup>


- Select the concentration of doxapram required based on the weight of the infant and in the context of any fluid restrictions. The recommended concentration is 1 - 2 mg/ml, however higher concentrations have been used in fluid restricted infants via a central line only<sup>11</sup>
- Dilute 1 ml of doxapram (20 mg/ml) with 19 ml of compatible fluid to make 20 ml of a 1 mg/ml solution
- Visually inspect solution for precipitation and discolouration; do not use if present
- Administer at the prescribed rate by continuous infusion preferably via a central line to prevent the possibility of extravasation
- Prepare a fresh infusion solution at least every 24 hours
- Discard unused portion of the vial immediately after use

#### Oral<sup>4,7</sup>

- Draw up prescribed dose from the vial and dilute to 1 ml with glucose 5%
- Administer orally

### Monitoring:

- Document vital signs hourly and as required<sup>6</sup>
- Monitor blood pressure, heart rate and deep tendon reflexes prior to administration, every 4 hours during the infusion and as required<sup>8,9</sup>
- Monitor capillary or arterial blood gases periodically during treatment<sup>6,8,9</sup>
- Observe IV site for signs of extravasation
- Monitor for hypersensitivity reactions and severe adverse reactions<sup>9</sup>


	Document reference: <b>2911</b>	Effective date: <b>18 Jan 2019</b>	Expiry date: <b>18 Jan 2022</b>	Page: <b>2 of 4</b>
	Title: <b>Doxapram for neonates</b>		Type: <b>Drug Guideline</b>	Version: <b>02</b>

## 1. Purpose and scope

To facilitate the safe and effective use of doxapram in the Neonatal Intensive Care Unit (NICU).

## 2. Drug


<b>Drug</b>	<b>Doxapram</b>
<b>Drug action</b>	Doxapram is a respiratory stimulant with a fast onset and short duration of action. It acts directly by stimulating the central respiratory centres in the medulla, or indirectly by stimulation of peripheral carotid chemoreceptors. The resultant effect is an increase in resting minute ventilation, tidal volume and respiratory rate. A release in catecholamines has been noted following the use of doxapram, leading to a pressor effect, attributed to an increase in cardiac output rather than peripheral vasoconstriction <sup>2,5,6,8</sup> .
<b>Indications</b>	Apnoea of prematurity unresponsive to caffeine (or aminophylline) <sup>1-5</sup>
<b>Description</b>	Doxapram 100 mg/5 ml (20 mg/ml) vial <sup>8,9</sup> Clear colourless solution. Excipients include benzyl alcohol, water for injection <sup>9</sup>
<b>Route</b>	Intravenous <sup>2-7</sup> or Oral <sup>4,7</sup>
<b>Dose</b>	<b>Continuous IV Infusion<sup>2,3,6</sup></b> <ul style="list-style-type: none"> <li>Initially 0.5 mg/kg/hr, then increase in increments of 0.5 mg/kg/hr as needed to control apnoea up to a maximum rate of 2.5 mg/kg/hr (in practice usual maximum 1.5 mg/kg/hr)</li> <li>Continue treatment until stable or for a maximum of 48 hours, then titrate to the lowest rate at which apnoea is controlled</li> </ul> <b>Oral<sup>4,7</sup></b> <ul style="list-style-type: none"> <li>6 mg/kg every 6 hours</li> </ul>
<b>Contraindications</b>	<ul style="list-style-type: none"> <li>Hypersensitivity to doxapram or any component of the preparation<sup>1,2</sup></li> <li>Convulsive disorders<sup>2,3,8</sup></li> <li>Recent intraventricular haemorrhage or cerebral oedema<sup>2,3,8</sup></li> <li>Physical obstruction of the respiratory tract, or conditions resulting in restriction of chest wall, muscles of respiration or alveolar expansion<sup>3,8</sup></li> <li>Significant cardiovascular disorders, severe hypertension<sup>2,8</sup></li> </ul>
<b>Precautions</b>	<ul style="list-style-type: none"> <li>Use with caution in significantly impaired renal or hepatic function<sup>2,3,6</sup></li> <li>Avoid use in conjunction with mechanical ventilation<sup>2,3</sup></li> <li>Doxapram injection contains benzyl alcohol which is associated with gasping syndrome, a potentially fatal toxicity<sup>2,3</sup>.</li> <li>Hyperthyroidism<sup>2,3,8</sup></li> <li>Phaeochromocytoma<sup>2,8</sup></li> </ul>
<b>Incompatibilities</b>	<ul style="list-style-type: none"> <li>Compatible with glucose 5%, glucose 10% and sodium chloride 0.9%<sup>3,5,9</sup></li> <li>Incompatible with alkaline solutions such as aminophylline, furosemide and sodium bicarbonate<sup>3,6,8</sup></li> <li>There is no compatibility information available for parenteral nutrition, therefore use of a separate line is recommended where possible<sup>6,7</sup></li> </ul>

	Document reference: <b>2911</b>	Effective date: <b>18 Jan 2019</b>	Expiry date: <b>18 Jan 2022</b>	Page: <b>3 of 4</b>
	Title: <b>Doxapram for neonates</b>		Type: <b>Drug Guideline</b>	Version: <b>02</b>

<b>Adverse effects</b>	<ul style="list-style-type: none"> <li>• Hypertension (dose related)<sup>2,4,5</sup></li> <li>• QT prolongation, heart block, arrhythmias<sup>2,4,5,8</sup></li> <li>• Seizures in those with additional risk factors such as history of seizures, perinatal asphyxia, intracerebral hemorrhage or recent aminophylline, theophylline, or caffeine exposure<sup>2,4,5</sup></li> <li>• Irritability, jitteriness, erratic limb movements, excessive crying, sleep disturbances, early teeth eruption<sup>2,5,8</sup></li> <li>• Abdominal distention, vomiting, NEC, diarrhoea, bloody stools<sup>2,5,8</sup></li> <li>• Respiratory distress<sup>5,8</sup></li> <li>• Hyperglycaemia, glycosuria<sup>2,5</sup></li> <li>• Extravasation may cause thrombophlebitis or local skin irritation<sup>2,5</sup></li> <li>• Haemolysis may result from rapid infusion<sup>2,5,9</sup></li> <li>• Doxapram injection contains benzyl alcohol which is associated with gasping syndrome, a potentially fatal toxicity<sup>2,3</sup></li> <li>• High dose oral treatment may cause delayed gastric emptying<sup>4</sup></li> </ul>
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### 3. Administration

<b>Competency for administration</b>	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
<b>Preparation &amp; Administration</b>	<p><b>Continuous Intravenous Infusion<sup>2,3,9,10</sup></b></p> <ul style="list-style-type: none"> <li>• Select the concentration of doxapram required based on the weight of the infant and in the context of any fluid restrictions. The recommended concentration is 1 - 2 mg/ml, however higher concentrations have been used in fluid restricted infants via a central line only<sup>11</sup></li> <li>• Dilute 1 ml of doxapram (20 mg/ml) with 19 ml of compatible fluid to make 20 ml of a 1 mg/ml solution</li> <li>• Visually inspect solution for precipitation and discolouration; do not use if present</li> <li>• Administer at the prescribed rate by continuous infusion preferably via a central line to prevent the possibility of extravasation</li> <li>• Prepare a fresh infusion solution at least every 24 hours</li> <li>• Discard unused portion of the vial immediately after use</li> </ul> <p><b>Oral<sup>4,7</sup></b></p> <ul style="list-style-type: none"> <li>• Draw up prescribed dose from the vial and dilute to 1 ml with glucose 5%</li> <li>• Administer orally</li> </ul>
<b>Observations and management</b>	<ul style="list-style-type: none"> <li>• Document vital signs hourly and as required<sup>6</sup></li> <li>• Monitor blood pressure, heart rate and deep tendon reflexes prior to administration, every 4 hours during the infusion and as required<sup>8,9</sup></li> <li>• Monitor capillary or arterial blood gases periodically during treatment<sup>6,8,9</sup></li> <li>• Observe IV site for signs of extravasation</li> <li>• Monitor for hypersensitivity reactions and severe adverse reactions<sup>9</sup></li> </ul>
<b>Special considerations (audit, funding, storage)</b>	<ul style="list-style-type: none"> <li>• Doxapram injection is an unregistered medicine available under section 29 of the Medicines Act. Names of the patient and prescriber must be sent to Pharmacy when ordering</li> <li>• The pH of doxapram is 3.5 – 5<sup>9</sup></li> </ul>

	Document reference: <b>2911</b>	Effective date: <b>18 Jan 2019</b>	Expiry date: <b>18 Jan 2022</b>	Page: <b>4 of 4</b>
	Title: <b>Doxapram for neonates</b>	Type: <b>Drug Guideline</b>	Version: <b>02</b>	Authorising initials:

	<ul style="list-style-type: none"> <li>Store vials at room temperature (between 20°C and 25°C). Do not refrigerate<sup>8,9</sup></li> <li>Prepare diluted solution immediately before use (no stability information)<sup>9</sup></li> </ul>
<b>Rescue medication</b>	Discontinue immediately and seek urgent medical assistance if anaphylaxis or severe adverse reactions including sudden hypotension or dyspnoea occur. Administer oxygen and anticonvulsants if required for management of seizures <sup>8,9</sup> .

#### 4. Guardrails Information

Doxapram is Guardrail profiled on the CC pump for NICU. Following are the guardrail limits<sup>12</sup>:

Guardrails Drug Name Pump	Doxapram CC				
		0.4 – 1 kg	1 – 2 kg	2 – 3 kg	3 – 5 kg
<b>Concentration (mg/ml)</b>					
Minimum		1	1	1	1
Maximum		5	8	8	8
<b>Dose rate (mg/kg/hr)</b>					
Default		0.5	0.5	0.5	0.5
Soft minimum		0.5	0.5	0.5	0.5
Soft maximum		1.5	1.5	1.5	1.5
Hard max		2.55	2.55	2.55	2.55

#### 5. References

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