CAFFEINE CITRATE

Indication	• Treatment of apnoea of prematurity[1-3] • Prevention of apnoea of prematurity[3] (birthweight less than 1250 g or gestational age less than 32 weeks) • Facilitate extubation from mechanical ventilation[3]

ORAL

Presentation	• Oral solution: 20 mg in 1 mL • QH-Central Pharmacy product: 20 mg in 1 mL
Dosage[1,2] (loading)	• 20–80 mg/kg ONCE
Dosage[1,2] (maintenance)	• Commence 24 hours after loading dose • 5–20 mg/kg daily o Start at 10–20 mg/kg daily
Preparation	• Draw up prescribed dose into oral/enteral syringe
Administration	• Oral/OGT/NGT with feeds to reduce gastric irritation[4]

INTRAVENOUS

Presentation	• Vial: 40 mg in 2 mL
Dosage[1,2] (loading)	• 20–80 mg/kg ONCE
Dosage[1,2] (maintenance)	• Commence 24 hours after loading dose • 5–20 mg/kg daily o Start at 10–20 mg/kg daily
Dilution	• If dose is **greater than or equal to 10 mg** (0.5 mL) o Nil dilution required, may be administered undiluted
	• If dose is **less than 10 mg** (0.5 mL) o Draw up 40 mg (2 mL) and make up to 8 mL total volume with water for injection o *Concentration now equal to 5 mg/mL* • Draw up the prescribed dose plus sufficient volume to prime the line
Administration	• Prime the infusion line and reduce total syringe volume to the prescribed dose • IV infusion via syringe driver pump o If dose is greater than 20 mg/kg, administer over 30 minutes[1,2] o If dose is less than or equal to 15 mg/kg, administer over 10 minutes[1,2] • On completion, disconnect syringe and infusion line • Flush access port at same rate as infusion

Contraindication Caution	• Contraindication o Concurrent administration of other xanthine preparations[5] • Caution o If gastrointestinal bleeding, seizure disorders, liver or renal impairment[2] o If heart rate greater than 180 bpm, withhold until SMO review and consider other causes
Special considerations	• Prescribe as caffeine citrate (not caffeine base)[1,4] o 2 mg caffeine citrate=1 mg caffeine base • Preparation for administration o Small dose volumes can be difficult to administer accurately to VLBW infants, therefore diluted preparation is the preferred option in this cohort • Approximate time to reach steady state blood levels is 5–6 days (i.e. apnoea may occur until steady state is reached, despite loading dose) • UAC route: consult with neonatologist/paediatrician prior to use and refer to Queensland Clinical Guideline: *Neonatal medicines*[6]
Monitoring	• Drug levels not routinely required[1,3,4] • Cardio-respiratory monitoring (continue 5–7 days after cessation)[4] • Number and severity of apnoeic episodes, assess for irritability/agitation

Compatibility	• Fluids o 5% glucose[7], 10% glucose[7], 0.9% sodium chloride[7] • Y-site o Fentanyl[7], heparin sodium[7]
Incompatibility	• PN and fat emulsion: co-infusion with caffeine not recommended (evidence limited) o If unavoidable, seek pharmacist advice first, filter infusion and flush before and after • Drugs o Aciclovir[7], glyceryl trinitrate[7]
Interactions	• Theophylline, aminophylline: do not administer concomitantly[7] • Phenytoin: may decrease caffeine plasma levels[5] • Fluconazole, verapamil, ciprofloxacin: may increase caffeine plasma levels[5]
Stability	• Oral solution o Store below 25 °C o Discard 4 weeks after opening or as per local policy • Vial o Store below 30 °C[7,8] o Expect clear and colourless solution[7] • Infusion solution o Stable for 24 hours below 25 °C[7]
Side effects	• Blood pathology: hyperglycaemia[1], hypoglycaemia[1] • Circulatory: tachycardia[1], arrhythmias[1] • Gastrointestinal: vomiting[7], reduced weight gain[1], NEC (association has been reported)[2] • Nervous: agitation[1] • Signs of toxicity: gastric irritation[1] (e.g. feed intolerance/vomiting), agitation/irritability[2], tachycardia[2], tachypnoea[7], hyperglycaemia[7], tremors[7], seizures[7], diuresis[2] o Serious toxicity is associated with serum levels greater than 50 micrograms/mL[1,2]
Actions	• CNS and cardiac muscle stimulant, bronchial smooth muscle relaxant and diuretic[2] • Increases the respiratory rate (breaths/minute) in premature infants and reduces the number of short and prolonged attacks of apnoea[8] • In ventilator dependent preterm infants reduces pulmonary resistance and increases lung compliance with a concomitant reduction in the requirement for inspired oxygen[8]
Abbreviations	bpm: beats per minute, CNS: central nervous system, IV: intravenous, NEC: necrotising enterocolitis, NGT: nasogastric tube, OGT: orogastric tube, PN: parenteral nutrition, SMO: senior medical officer, UAC: umbilical arterial catheter, VLBW: very low birth weight
Keywords	apnoea of prematurity, caffeine citrate, extubation, methylxanthines, neonatal medicine, neonatal monograph

The Queensland Clinical Guideline *Neonatal medicines*[6] is integral to and should be read in conjunction with this monograph. Refer to the disclaimer. Destroy all printed copies of this monograph after use.

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Document history

ID number	Effective	Review	Summary of updates
NMedQ19.006-V1-R24	June 2019	June 2024	Endorsed by Queensland Neonatal Services Advisory Group (QNSAG)
NMedQ19.006-V2-R24	06/02/2023	June 2024	• Added to preparation instructions: prescribed dose greater than 0.5 mL (10 mg) may be given undiluted • Added to special considerations: small dose volumes can be difficult to administer accurately to VLBW infants therefore diluted preparation is the preferred option in this cohort • Added to signs of toxicity: tremors and tachypnoea • Deleted UAC icon: wording amended about administration via UAC • Added QR code Minor referencing updates
NMedQ25.006-V3-R30	23/05/2025	23/05/2030	Full review: Endorsed by QNSAG • Amended: start maintenance dose FROM 10 mg/kg TO 10–20 mg/kg • No change to loading dose or frequency • Updated: monitoring, compatibility, incompatibility, interactions, side effects, actions

QR code