

Alert	Caution with dosing: Caffeine citrate 2 mg = caffeine base 1 mg																								
Indication	<ol style="list-style-type: none"> 1. Treatment of apnoea of prematurity. 2. Weaning from mechanical ventilation. 3. Prevention of post-operative apnoea. 																								
Action	<p>Competitive inhibition of the actions of adenosine at cell surface receptors.</p> <p>Enhancement of respiratory effort and regularisation of breathing patterns through stimulation of central inspiratory drive and increased sensitivity of chemoreceptors to carbon dioxide.</p> <p>Increase in respiratory centre output, smooth muscle relaxation and cardiac output.</p> <p>Improvement in the contractility of the diaphragm and hence increasing the force of contraction and decreasing muscular fatigue.</p>																								
Drug Type	Central nervous system stimulant, respiratory stimulant.																								
Trade Name	Cafnea (caffeine citrate), Caffeine base (Auspman)																								
Presentation	<p>Caffeine citrate IV 40 mg/2 mL vial</p> <p>Caffeine citrate oral 25 mg/5 mL solution</p> <p>Caffeine base IV 50 mg/5 mL ampoule</p> <p>Caffeine base oral 10 mg/mL solution</p>																								
Dosage/Interval	<p><u>Caffeine citrate</u></p> <table border="1"> <thead> <tr> <th></th> <th>Loading dose</th> <th>Maintenance dose 24 hours after loading dose</th> <th>Post-Op apnoea (single dose)</th> </tr> </thead> <tbody> <tr> <td>IV</td> <td>20 mg/kg</td> <td>10 mg/kg (range 5–20mg/kg) daily</td> <td>10 mg/kg</td> </tr> <tr> <td>Oral</td> <td>20 mg/kg</td> <td>10 mg/kg (range 5–20mg/kg) daily</td> <td>10 mg/kg</td> </tr> </tbody> </table> <p>Maintenance dose may be increased or decreased as per the clinical need.</p> <p><u>Caffeine base</u></p> <table border="1"> <thead> <tr> <th></th> <th>Loading dose</th> <th>Maintenance dose 24 hours after loading dose</th> <th>Post-Op apnoea (single dose)</th> </tr> </thead> <tbody> <tr> <td>IV</td> <td>10 mg/kg</td> <td>5 mg/kg (range 2.5–10 mg/kg) daily</td> <td>5 mg/kg</td> </tr> <tr> <td>Oral</td> <td>10 mg/kg</td> <td>5 mg/kg (range 2.5–10 mg/kg) daily</td> <td>5 mg/kg</td> </tr> </tbody> </table> <p>Maintenance dose may be increased or decreased as per the clinical need.</p>		Loading dose	Maintenance dose 24 hours after loading dose	Post-Op apnoea (single dose)	IV	20 mg/kg	10 mg/kg (range 5–20mg/kg) daily	10 mg/kg	Oral	20 mg/kg	10 mg/kg (range 5–20mg/kg) daily	10 mg/kg		Loading dose	Maintenance dose 24 hours after loading dose	Post-Op apnoea (single dose)	IV	10 mg/kg	5 mg/kg (range 2.5–10 mg/kg) daily	5 mg/kg	Oral	10 mg/kg	5 mg/kg (range 2.5–10 mg/kg) daily	5 mg/kg
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Route	<p>IV</p> <p>Oral</p>																								
Maximum Daily Dose	<p>Loading dose: As high as 80 mg/kg of caffeine citrate has been reported; some centres repeat a load of 20 mg/kg as caffeine citrate to a maximum cumulative dose load of 80 mg/kg in refractory patients.</p> <p>Maintenance dose: Some centres increase the dose in 5 mg/kg daily increments of caffeine citrate to a maximum of 20 mg/kg/day in refractory patients based on clinical response ± serum caffeine concentrations.</p>																								
Preparation/Dilution	<p><u>IV INFUSION</u></p> <p><u>Caffeine citrate</u></p> <p>Draw up 1 mL (20 mg) of caffeine citrate and add 4 mL sodium chloride 0.9% or glucose 5% to make a final volume of 5 mL with a concentration of 4 mg/mL.</p> <p><u>Caffeine base</u></p> <p>Draw up 2 mL caffeine base (20 mg) and add 8 mL sodium chloride 0.9% or glucose 5% to make a final volume of 10 mL with a concentration of 2 mg/mL.</p>																								
Administration	<p>IV: Infuse loading dose over at least 30 minutes and maintenance over 10 minutes.</p> <p>ORAL: Solution may be administered without regard to feeds, however consider giving with feeds to reduce gastric irritation.</p>																								

Monitoring	<p>Heart rate, number and severity of apnoea episodes and assess for agitation. Consider withholding dose if HR > 180 bpm. Cardiorespiratory monitoring should continue for at least 5-7 days after the cessation of caffeine treatment for apnoea. Therapeutic drug monitoring is usually not necessary. Trough concentrations may be taken one hour before the next dose is due but should only be done if using high doses or toxicity is suspected. Monitoring of serum drug concentration should be determined on approximately day 5 of therapy. Therapeutic trough serum concentration: 8–20 microg/mL (41–102 micromol/L) Potentially toxic: > 20–40 microg/mL (102–205 micromol/L) Toxic: > 40–50 microg/mL (205–257 micromol/L)</p>
Contraindications	Contraindicated in infants with hypersensitivity to methylxanthines or citrate.
Precautions	Use with caution in infants with impaired renal or hepatic function, seizure disorders, cardiovascular disease or congenital heart disease.
Drug Interactions	<p>Fluconazole and verapamil may decrease caffeine elimination. Phenytoin may increase caffeine elimination. Caffeine antagonises the effects of benzodiazepines. Other methylxanthines (theophylline, aminophylline) should not be used concomitantly.</p>
Adverse Reactions	<p>Arrhythmia (ventricular), flushing, tachycardia, vasodilatation, functional cardiac symptoms. Increased left ventricular output & increased stroke volume, hypotension. Agitation, irritability, restlessness, sleep disturbances, seizures (with toxic doses). May relax the lower oesophageal sphincter & increase gastric acid secretion leading to increased episodes of gastro-oesophageal reflux, gastritis, vomiting. Urticaria, alterations in serum glucose, diuresis, tachypnoea.</p>
Compatibility	<p>Fluids: Glucose 5%, Glucose 10%, Glucose 50% and sodium chloride 0.9%. Y-site: Dopamine, fentanyl, heparin, amino acid solutions and fat emulsions.</p>
Incompatibility	<p>Fluids: No information. Y-site: Aciclovir, frusemide, glyceryl trinitrate and ibuprofen lysine.</p>
Stability	<p>Caffeine citrate: Discard unused portion. Caffeine base: IV – discard unused portion. Oral solution – store at room temperature.</p>
Storage	Store below 30 °C
Special Comments	<p>Half-life in neonates: 72–96 hours (range 40–230 hours decreasing with advancing corrected gestational age). Time to peak serum concentration: Within 30 minutes to 2 hours in oral administration.</p>
Evidence summary	<p>Caffeine therapy for apnoea of prematurity reduces the rate of bronchopulmonary dysplasia in infants with very low birth weight ¹ (Level II, Grade A).</p> <p>Caffeine is the preferred treatment for apnoea in preterm infants as compared to theophylline (due to its higher therapeutic ratio, more reliable enteral absorption, longer half-life and less incidence of side effects) as it appears to have similar short-term effects on apnoea/bradycardia ³ (Level I, Grade A).</p> <p>Caffeine therapy for apnoea of prematurity improves the rate of survival without neurodevelopmental disability at 18 to 21 months in infants with very low birth weight ² (Level II, Grade B).</p> <p>Dosing: Loading 20 mg/kg caffeine citrate, maintenance 5 to 10 mg/kg caffeine citrate daily. ^{1,2} Loading 80 mg/kg caffeine citrate, maintenance 20 mg/kg caffeine citrate daily started in the peri-extubation period is more effective than 5 mg/kg daily maintenance dose at facilitating extubation, decreasing the duration of mechanical ventilation and reducing apnoea after extubation ⁸ (Level II).</p>

References	<ol style="list-style-type: none"> 1. Schmidt B, Roberts RS, Davis P, et al. Caffeine Therapy for Apnea of Prematurity. N Engl J Med, 2006, 354(20):2112–21. 2. Schmidt B, Roberts RS, Davis P, et al. Long-Term Effects of Caffeine Therapy for Apnea of Prematurity. N Engl J Med, 2007, 357(19):1893–902 3. Henderson-Smart DJ, Steer PA. Caffeine versus theophylline for apnea in preterm infants. Cochrane Database Syst Rev 2010;(1):CD000273 4. Caffeine: Paediatric drug information 2014, Version 60.0, Up-To-Date, viewed 08 July 2014, www.uptodate.com. 5. Young TE, Mangum B [2008]. Neofax 21st Edition: A manual of drugs used in neonatal care. Acorn Publishing, Inc. Raleigh, NC 27619. 6. Hey E. (Ed) [2003]. Neonatal Formulary 4th Edition. BMJ Publishing Group, London. 7. Product Information, Cafnea Injection and Cafnea Oral Solution, Phebra, Version 09, 2013. 8. Steer P, Flenady V, Shearman A, et al. High Dose Caffeine Citrate for Extubation of Preterm Infants: A Randomised Controlled Trial. Arch Dis Child Fetal Neonatal Ed, 2004, 89(6):F499–503. 9. Australian Injectable Drugs Handbook, 6th Edition, Society of Hospital Pharmacists of Australia 2014. 10. Caffeine citrate injection and liquid (Cafnea) MIMS online accessed 27th July 2015. 11. Neofax accessed on www.neofax.micromedex.solutions.com on 29th July 2015.
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