

Alert	High alert medication: High risk of causing significant patient harm when used in error. Schedule 8 (S8) medicine. Must be stored and handled according to local S8 drug policy.									
Indication	Analgesia. Sedation.									
Action	Binds to specific G protein-coupled opioid receptors that are located in brain and spinal cord regions involved in the transmission and modulation of pain.									
Drug Type	Opioid analgesic agent.									
Trade Name	Aspen Fentanyl; DBL Fentanyl; Fentanyl GH; Fentanyl Solution (AstraZeneca); Sublimaze									
Presentation	500 microgram/10 mL ampoule; 100 microgram/2 mL ampoule									
Dosage/Interval	<p>Bolus/loading dose 0.5–4 microgram/kg/dose over 3–5 minutes every 2–4 hours</p> <p>Continuous IV Infusion 0.5–5 microgram/kg/hour. General starting dose: 1 microgram/kg/hour. Titrate using a validated pain score.</p> <p>Pre-medication for intubation 2–4 microgram/kg bolus. Wait at least 3 minutes for onset of action after giving the dose.</p>									
Route	IV									
Maximum Daily Dose										
Preparation/Dilution	<p>SINGLE STRENGTH continuous IV infusion</p> <table border="1"> <thead> <tr> <th>Infusion strength</th> <th>Prescribed amount</th> </tr> </thead> <tbody> <tr> <td>1 mL/hour = 5 microgram/kg/hour</td> <td>250 microgram/kg fentanyl and make up to 50 mL</td> </tr> </tbody> </table> <p>Using 500 microgram/10 mL injection draw up 5 mL/kg (250 microgram/kg fentanyl) and make up to 50 mL with sodium chloride 0.9% or glucose 5% or glucose 10% with a concentration of 1 mL/hour = 5 microgram/kg/hour.</p> <p>DOUBLE STRENGTH continuous IV infusion</p> <table border="1"> <thead> <tr> <th>Infusion strength</th> <th>Prescribed amount</th> </tr> </thead> <tbody> <tr> <td>1 mL/hour = 10 microgram/kg/hour</td> <td>500 microgram/kg fentanyl and make up to 50 mL</td> </tr> </tbody> </table> <p>Using 500 microgram/10 mL injection draw up 10 mL/kg (500 microgram/kg fentanyl) and make up to 50 mL with sodium chloride 0.9% or glucose 5% or glucose 10% with a concentration of 1 mL/hour = 10 microgram/kg/hour.</p> <p>IV BOLUS/LOADING DOSE</p> <p>Neonates < 1 kg Using 100 microgram/2 mL injection draw up 1 mL (50 microgram fentanyl) and add 24 mL sodium chloride 0.9% to make a final volume of 25 mL with a concentration of 2 microgram/mL.</p> <p>Neonates ≥ 1 kg Using 100 microgram/2 mL injection draw up 1 mL (50 microgram fentanyl) and add 9 mL sodium chloride 0.9% to make a final volume of 10 mL with a concentration of 5 microgram/mL.</p> <p>PRE-MEDICATION FOR INTUBATION As above for IV bolus.</p>		Infusion strength	Prescribed amount	1 mL/hour = 5 microgram/kg/hour	250 microgram/kg fentanyl and make up to 50 mL	Infusion strength	Prescribed amount	1 mL/hour = 10 microgram/kg/hour	500 microgram/kg fentanyl and make up to 50 mL
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Administration	IV slow push over 3–5 minutes IV infusion via syringe pump
Monitoring	Care should be taken in using fentanyl in neonates with hepatic or renal dysfunction. Full cardiorespiratory monitoring is required. Monitor for urinary retention.
Contraindications	Known hypersensitivity to fentanyl.
Precautions	Tolerance can occur with use >5–7 days. Withdrawal has been reported in patients who have received continuous infusions for >5days. Chest wall rigidity can occur at higher doses. May cause respiratory depression. May cause urinary retention. May decrease intestinal motility.
Drug Interactions	Ketoconazole and erythromycin are potent inhibitors of fentanyl metabolism. When given in combination with amiodarone can cause profound bradycardia, sinus arrest and hypotension.
Adverse Reactions	Nausea and/or vomiting Muscle/chest wall rigidity (usually naloxone responsive). Naloxone 0.01–0.04 mg/kg reversed muscle rigidity immediately allowing resuscitation in a case series of 8 patients. At high doses can cause neuro-excitation and rarely seizure like activity/myoclonic movements. Respiratory depression. Bradycardia (usually atropine responsive). Urinary retention.
Compatibility	Fluids: Sodium chloride 0.9%, glucose 5%, glucose 10% (not tested) Y-site: Abciximab, adrenaline hydrochloride, amiodarone, anidulafungin, atracurium, atropine, bivalirudin, caffeine citrate, caspofungin, cisatracurium, dexamethasone, doripenem, esmolol, haloperidol lactate, heparin sodium, hydrocortisone sodium succinate, hyoscine hydrobromide ⁸ , ketorolac, labetalol, levomepromazine, linezolid,, metoclopramide, midazolam, milrinone, palonosetron, pancuronium, potassium chloride, remifentanyl, vecuronium
Incompatibility	Fluids: No information. Y-site: Azithromycin, thiopentone.
Stability	Protect from light.
Storage	Ampoule: Store below 25°C. Protect from light. Discard remainder after use (in line with S8 drug legislation). Store in Dangerous Drug (DD) safe and record use in DD register.
Special Comments	In comparison to morphine, fentanyl has a quicker onset of action (3 minutes), shorter duration (90 minutes) of action and less haemodynamic instability. Fentanyl is 50–100 times more potent than morphine. It blocks endocrine stress responses. It causes less histamine release than morphine. It decreases pain-induced increases in pulmonary vascular resistance.
Evidence summary	Efficacy Opioids are to be used selectively based on clinical judgment and evaluation of pain indicators, although there are limitations to pain measurement in newborns ¹ (LOE 1 GOR B). A short course of low dose fentanyl by infusion reduces behavioural sedation scores, O ₂ desaturations and neuroendocrine stress responses in preterm ventilated infants ² (LOE II, GOR B). Continuous infusion of fentanyl in the post-operative period achieves acceptable pain control but there may be increased need for ventilator support ³ (LOE II, GOR C). In very preterm infants on mechanical ventilation, continuous fentanyl infusion plus boluses of fentanyl reduces acute pain and increases side effects but does not reduce prolonged pain compared with boluses of fentanyl alone ⁴ (LOE II GOR B).

	<p>Safety Respiratory depression occurs when anaesthetic doses (greater than 5 microg/kg/min) are used and may also occur unexpectedly because of redistribution. Chest wall rigidity has occurred in 4% of neonates who received doses of 2.2 to 6.5 microg/kg, occasionally associated with laryngospasm⁵ (LOE IV GOR D). This was reversible with administration of naloxone. When controlling for other variables, the cumulative fentanyl dose did not correlate with neurodevelopmental outcomes in very low birth weight infants⁶ (LOE III GOR C). Tolerance may develop to analgesic doses⁷. Significant withdrawal symptoms have been reported in patients treated with continuous infusion for 5 days and longer (LOE IV GOR D).</p> <p>Pharmacokinetics Fentanyl is metabolised in the liver (CYP3A4) and excreted in the urine. There is wide variability in apparent volume of distribution and serum half-life can be up to 15 hours. There is significant correlation between postnatal age and total body clearance⁸.</p>
References	<ol style="list-style-type: none"> Bellu R, de Waal K, Zanini R. Opioids for neonates receiving mechanical ventilation: a systematic review and meta-analysis. <i>Arch Dis Child Fetal Neonatal Ed.</i> Jul;95(4):F241–251. Lago P, Benini F, Agosto C, Zacchello F. Randomised controlled trial of low dose fentanyl infusion in preterm infants with hyaline membrane disease. <i>Arch Dis Child Fetal Neonatal Ed.</i> Nov 1998;79(3):F194–197. Vaughn PR, Townsend SF, Thilo EH, McKenzie S, Moreland S, Denver KK. Comparison of continuous infusion of fentanyl to bolus dosing in neonates after surgery. <i>Journal of pediatric surgery.</i> Dec 1996;31(12):1616–1623. Ancora G, Lago P, Garetti E, et al. Efficacy and safety of continuous infusion of fentanyl for pain control in preterm newborns on mechanical ventilation. <i>The Journal of pediatrics.</i> Sep 2013;163(3):645–651 e641. Fahnenstich H, Steffan J, Kau N, Bartmann P. Fentanyl-induced chest wall rigidity and laryngospasm in preterm and term infants. <i>Critical care medicine.</i> Mar 2000;28(3):836–839. Lammers EM, Johnson PN, Ernst KD, et al. Association of fentanyl with neurodevelopmental outcomes in very-low-birth-weight infants. <i>The Annals of pharmacotherapy.</i> Mar 2014;48(3):335–342. Arnold JH, Truog RD, Scavone JM, Fenton T. Changes in the pharmacodynamic response to fentanyl in neonates during continuous infusion. <i>The Journal of pediatrics.</i> Oct 1991;119(4):639–643. Santeiro ML, Christie J, Stromquist C, Torres BA, Markowsky SJ. Pharmacokinetics of continuous infusion fentanyl in newborns. <i>J Perinatol.</i> Mar-Apr 1997;17(2):135–139. Fahnenstich H, Steffan J, Kau N, Bartmann P. Fentanyl-induced chest wall rigidity and laryngospasm in preterm and term infants. <i>Critical care medicine.</i> Mar 2000;28(3):836–839. Australian Injectable Drugs Handbook, 6th Edition, Society of Hospital Pharmacists of Australia 2014. Neofax accessed on www.neofax.micromedex.solutions.com on 28/10/15.

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