Remifentanil – Standard concentration 2026

Newborn use only

Key Points	Schedule 8 drug. Chest wall rigidity has been reported in infants if remifentanil is given as a rapid bolus in <60 seconds or at higher dose. Chest wall rigidity can be treated with naloxone and muscle relaxants. Loading/bolus dose may cause bradycardia and hypotension.
Indication	1. Premedication for non-emergency intubation 2. Short term infusion for analgesia/sedation in ventilated infants
Action	A potent μ (mu)-receptor agonist with rapid onset of action – peak analgesic action within 1 minute. Rapidly metabolised into inactive metabolites by non-specific plasma esterases with a half-life of 3-5 minutes.
Contraindications	Known hypersensitivity to fentanyl or remifentanil.
Precautions	Rapid injection (<60 seconds) of remifentanil is associated with chest wall rigidity. A bolus dose of 1 microgram/kg may cause hypotension.
Dose	**Premedication for intubation** **IV Bolus:** 1 microgram/kg/dose - **Administer over at least 1 minute.**[1] Administer atropine prior to remifentanil to prevent bradycardia. Dose may be repeated in 2-3 minutes if needed. **Short term analgesia/sedation in mechanically ventilated infants (ANMF expert group consensus)**[2,3] IV infusion: 0.1–0.3 microgram/kg/minute. Suggested starting dose: 0.1 microgram/kg/minute and then titrate using a validated pain score. Infusion duration is to be limited **to a maximum of 72 hours.** IV loading or intermittent bolus dose on maintenance infusion can be given at 0.1 microgram/kg/dose but watch for bradycardia and hypotension. **Note:** Data in neonates are limited on IV infusion on short and long-term safety. While it has very rapid onset of action (within 1 minute of administration) and ultra short duration (about 5 minutes) due to rapid clearance, 3 main concerns with prolonged maintenance infusion are (1) rapid development of tolerance, (2) hyperalgesia, and (3) severe withdrawal after stopping prolonged infusion.
Maximum dose	0.3 microgram/kg/minute.
Route	IV
Presentation	Remifentanil Powder [remifentanil hydrochloride] for infusion 1 mg, 2 mg, 5 mg. **Trade names:** Remifentanil Viatris, Remifentanil-AFT, Ultiva, Remifentanil Demogen
Preparation	NOTE: Use the smallest volume syringe available/suitable for drawing up the drug for the preparation. (e.g. for <1 mL draw up – use 1 mL syringe). For 10 mL syringe - Recommend using syringe that has markings at 0.2mL increments **Some brands of remifentanil may require protection from light. Refer to product information.** **IV bolus** **Reconstitution:** Add 1 mL of water for injection **for each** 1 mg of remifentanil to make a 1 mg/mL solution. **Further DILUTE:** **Step 1:** Draw up 0.5 mL (500 microgram) of the above solution and add to 19.5 mL glucose 5% or sodium chloride 0.9% to make a final volume of 20 mL with a concentration of 25 microgram/mL. **Step 2:** From the above solution, draw up 0.8 mL (20 microgram) and add to 19.2 mL glucose 5% or sodium chloride 0.9% to make a final volume of 20 mL with a concentration of 1 microgram/mL. **IV infusion** **Note: Refer to Appendix for table to assist with concentration selection.** The standard concentrations outlined in this monograph were developed taking into consideration a minimum patient weight of **0.4 kg** and a minimum infusion rate of **0.1 mL/hour**. For patients weighing less than 0.4kg, further dilution may be required.

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Prime the line as close to the entry point as possible to reduce the dead space – however, care should be taken not to deliver excess volume.

Weight suggestions for infusion concentrations below are a guide only. Clinicians may choose infusion concentration different to the suggested based on expected dose and the corresponding 24-hour fluid volumes

Remifentanil concentration	**20 microgram/mL**
0.1 microgram/kg/min is equal to	0.3 mL/kg/hour

20 mL Syringe

Reconstitution: Add 1 mL of water for injection **for each** 1 mg of remifentanil to make a 1 mg/mL solution.

Further DILUTE:

Add the reconstituted solution to the compatible fluid* to make a diluted solution as per table below:

Remifentanil concentration	**20 microgram/mL**
Volume of remifentanil (1000 microgram/mL)	0.4 mL (400 microgram)
Volume of compatible fluid*	19.6 mL
Total volume	20 mL

* Compatible fluid: glucose 5% or sodium chloride 0.9%

50 mL Syringe

Reconstitution: Add 1 mL of water for injection **for each** 1 mg of remifentanil to make a 1 mg/mL solution.

Further DILUTE:

Add the reconstituted solution to the compatible fluid* to make a diluted solution as per table below:

Remifentanil concentration	**20 microgram/mL**
Volume of remifentanil (1000 microgram/mL)	1 mL (1000 microgram)
Volume of compatible fluid*	49 mL
Total volume	50 mL

* Compatible fluid: glucose 5% or sodium chloride 0.9%

Compatibility

Fluids: Glucose 5%, glucose 5% in sodium chloride 0.9%, sodium chloride 0.9%, sodium chloride 0.45%, water for injection. Not tested with glucose 10%.
Amino acids at Y site: No information.
Lipid emulsion at Y site: No information.
Y-site:[4] Aciclovir sodium, adrenaline (epinephrine) hydrochloride, alfentanil hydrochloride, amikacin sulfate, amiNOPHYLLine, amiODARONe hydrochloride, ampicillin sodium, aziTHROMYCIN, aztreonam, buprenorphine hydrochloride, calcium gluconate, cefaZOLin sodium, cefEPIME hydrochloride, cefOTAXIME, cefotetan disodium, cefoxitin, cefTAZIDIME, cefTRIAXONE sodium, cefuroxime, ciPROFLOXAcin, clindamycin phosphate, dexAMETHASOne sodium phosphate, digoxin, dobutamine hydrochloride, dopamine hydrochloride, fentanyl, flucONAZOLe, ganciclovir sodium, gentamicin sulfate, heparin sodium, hydrocortisone sodium succinate, imipenem-cilastatin sodium, insulin regular, isoprenaline hydrochloride, lidocaine (lignocaine) hydrochloride, magnesium sulfate, mannitol, methylprednisolone sodium succinate, metoclopramide hydrochloride, metronidazole, midazolam hydrochloride, milrinone lactate, morphine sulfate, netilmicin sulfate, nitroglycerin, noradrenaline (norepinephrine) bitartrate, octreotide acetate, ondansetron hydrochloride, pancuronium bromide, phenylephrine hydrochloride, piperacillin sodium-tazobactam sodium, potassium acetate, potassium chloride, potassium phosphates, ranitidine hydrochloride, rocuronium bromide, sodium acetate, sodium

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	bicarbonate, sufentanil citrate, sulfamethoxazole-trimethoprim, theophylline, thiopental sodium, ticarcillin disodium-clavulanate potassium, tobramycin sulfate, vancomycin hydrochloride, vasopressin, vecuronium bromide, zidovudine. **Variable compatibility at Y-site:** Propofol, amphotericin, DIAzepam, furosemide.
Incompatibility	
Administration	**IV BOLUS: Administer over at least 1 minute.** Flush with 1 mL of sodium chloride 0.9% over at least 1 minute. Onset of action is immediate. Half-life is approximately 3–10 minutes. **CONTINUOUS IV INFUSION**: Via syringe driver. Note: It is advisable to use a dedicated IV line where possible. Upon ceasing the continuous infusion, flush the line with 1 mL of sodium chloride 0.9% over 1 hour.
Monitoring	Full cardiorespiratory monitoring. Monitor for urinary retention.
Drug Interactions	Remifentanil enhances the action of other sedatives and hypnotics. Cardiovascular effects may be enhanced by beta blockers and calcium channel blockers.
Adverse Reactions	Respiratory depression, chest wall rigidity (can be treated with naloxone and muscle relaxants), bradycardia and asystole (may respond to atropine), hypotension, postoperative hypertension.
Overdose	Respiratory depression can be treated with naloxone. Bradycardia and asystole can be treated with atropine. AUSTRALIA Contact the Poisons Information Centre on **13 11 26** for further information on the management of overdose NEW ZEALAND Contact the National Poisons Centre on **0800 764 766** for further information on the management of overdose
Stability	Reconstituted product should be used promptly and any unused material discarded according to local Schedule 8 drug policy.
Storage	Store below 25°C. Some brands may require protection from light. Refer to product information.
Excipients	AFT, Viatris and Demogen brands contain glycine, hydrochloric acid
Special Comments	Treat chest wall rigidity with supportive measures, neuromuscular blocking agents or naloxone. Chest wall rigidity can last a few minutes. Duration of action 5-10 minutes.
Evidence	**Overview** Remifentanil is a synthetic opioid similar to fentanyl and acts primarily as μ (mu)-opioid receptor agonist. Analgesic strength is 100–200 times that of morphine. Other differences: Remifentanil has a very rapid onset of action (within 1 minute) in comparison to fentanyl 3–4 min or morphine 20 min after administration. It also has ultra-short duration of action for about 5 minutes with no accumulation with repeated administration. It's ultra short action is because of the metabolism by non-specific plasma and tissue esterases independent of liver and kidney function. However, remifentanil is not without risks. Reported side effects include respiratory depression, apnoea, bradycardia, and chest wall rigidity similar to other opioids.[5] Chest wall rigidity is particularly more common with rapid bolus given in less than 1 minute.[6] **Efficacy and safety:** **<u>Premedication for intubation</u>** ***Remifentanil:*** In RCTs (LOE II): Badiee et al in 40 preterm infants undergoing the InSurE procedure compared remifentanil 2 microgram/kg over 2 minutes and atropine versus placebo and atropine. Infants who received remifentanil felt less pain but there was no difference in duration of endotracheal intubation procedure, number of attempts and oxygen desaturation between groups. Chest wall rigidity occurred in 4/20 (20%) infants and laryngospasm in 6 infants.[7] Avino et al in preterm infants ≥28 weeks gestation undergoing elective intubation compared remifentanil 1 microgram/kg over 60 seconds and atropine (n=36) versus morphine 100 microgram/kg, midazolam 50 microgram/kg and atropine (n=35). Remifentanil was at least as effective as the morphine-midazolam regimen with a similar incidence of >2 intubation attempts and no difference in intubation conditions, time or adverse events. No significant between-group difference was reported for hypotension, bradycardia, or adverse events.[1]

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Choong et al in 30 term and preterm infants undergoing elective intubation compared remifentanil 3 microgram/kg over 60 seconds and atropine versus fentanyl 2 microgram/kg over 60 seconds, succinylcholine 2 mg/kg and atropine 20 microgram/kg and reported no significant difference in time to intubation but better intubation conditions with fentanyl and succinylcholine. Muscle rigidity was a concern at doses of 3 µg/kg in this trial.[8]

Remifentanil combination: In RCTs (LOE II): Norman et al in 34 preterm infants undergoing elective intubation compared rapid sequence induction (RSI) with glycopyrrolate, thiopental 2–3 mg/kg, remifentanil 1microgram/kg (duration of administration not reported) and suxamethonium and versus atropine + morphine 0.3 mg/kg. RSI had superior intubation conditions, shorter duration of intubation and was associated with reduced duration of aEEG/EEG depression.[9,10] Pereira e Silva et al in 20 preterm infants undergoing elective intubation compared remifentanil 1 microgram/kg and midazolam 200 microgram/kg over 60 seconds versus morphine 150 microgram/kg and midazolam 200 microgram/kg. Intubation conditions in the remifentanil group were significantly better than in the morphine group.[11]

Procedural analgesia in spontaneously breathing infants

Insertion of PICC: In RCTs: Lago et al in 54 preterm spontaneously breathing undergoing PICC insertion compared remifentanil 0.03 microgram/kg/min versus placebo and sucrose and non-nutritive sucking. Remifentanil reduced NIPP and PIPP scores and cardiovascular and movement response to PICC insertion but did not make the PICC easier or quicker.[12] Shin et al, in their RCT, evaluated 2 remifentanil dosages in mechanically ventilated preterm infants during peripherally inserted central catheter insertion. They compared remifentanil 0.1 microgram/kg/min versus 0.25 microgram/kg/min. There was no difference in the Premature Infant Pain Profile; there were three episodes of apnoea (42.9%) and one of bradycardia (14.3%) in the high-dose group.[13]

INSURE (Intubation, surfactant and extubation) procedure: Welzing et al evaluated intubating conditions, extubation times and outcome in 21 preterm infants of 29-32 weeks gestation receiving remifentanil as induction agent for the INSURE procedure. Premedication for the INSURE procedure included atropine 10 µg/kg followed by remifentanil 2 µg/kg infused over 60 sec. Remifentanil provided excellent or good intubating conditions in all patients. We observed no serious side effects after remifentanil infusion, in particular, no thorax rigidity, clinically significant bradycardia or arterial hypotension.[14]

Minimally invasive surfactant therapy (MIST): MIST is more commonly practised in the Australian setting than INSURE and there is no evidence to suggest remifentanil is safe or efficacious as procedural analgesia for MIST.

Analgesia/sedation in mechanically ventilated infants

Welzing et al in 23 term infants less than 60 days old on mechanical ventilation compared remifentanil 0.15 microgram/kg/min adjusted in steps of 0.05 microgram/kg/min versus fentanyl 0.05 microgram/kg/min and midazolam 0.8 microgram/kg/min adjusted in steps of 0.02 microgram/kg/min. Remifentanil infusion was increased by 24% and fentanyl by 47%. Median extubation time shorter with remifentanil (80.0 versus 782.5 min, p=0.005).[3] Pereira e Silva et al in 20 preterm infants managed with mechanical ventilation and surfactant compared remifentanil 1 microgram/kg and midazolam 200 microgram/kg for intubation then remifentanil 0.5 microgram/kg/min infusion versus morphine 150 microgram/kg and midazolam 200 microgram/kg for intubation then morphine 10 microgram/kg/hour infusion. The remifentanil group had a shorter time to awaken (1173 ± 608 versus 62 ± 56.7 mins) and extubation (1320 ± 650 versus 106.3 ± 82.8 mins).[2]

During laser for ROP: In RCTs: But et al in 91 preterm infants undergoing laser for ROP compared anaesthesia induced with midazolam 0.1 mg/kg and remifentanil 2 microgram/kg maintained with midazolam 0.1–0.2 mg/kg/hour and remifentanil 0.125–0.2 microgram/kg/min versus anaesthesia induced with 45% O_2 + 55% N_2O + 3–5% sevoflurane and fentanyl 1 microgram/kg maintained with 45% O_2 + 55% N_2O + 1–3% sevoflurane. There was no difference in complications or extubation time and mean arterial pressure values higher in remifentanil group only at 60 minutes.[15] Two case series reported analgesia/sedation with remifentanil alone or in combination in preterm infants undergoing laser for ROP. Demirel et al in 64 infants assessed remifentanil infusion 0.2 microgram/kg/min titrated up to 0.6 microgram/kg/min.

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	Remifentanil was infused at a mean rate 0.4 ± 0.1 microgram/kg/min. No major adverse effects were observed except two patients with reversible bradycardia and hypotension. Premature infant pain profile scores revealed no pain. Extubation time was 189 ± 110 minutes.[16] Costamagna et al in 46 infants assessed propofol 3 to 4 microgram/kg bolus for intubation, then infusion of remifentanil 0.2 to 4 microgram/kg/min and propofol 2 to 20 mg/kg/hour. All the patients maintained haemodynamic stability. 21/36 patients in spontaneous ventilation before surgery were extubated within 24 hours (58.3%), 14/36 were extubated after 24 hours (38.8%) and one patient could not be extubated.[17] **During surgery:** In RCTs: Davis et al in 60 infants undergoing pyloromyotomy compared remifentanil begun at 0.4 microgram/kg/min versus halothane expired concentration targeted 0.4% for maintenance anaesthesia. There was no difference in haemodynamic values, extubation times, discharge times, pain medications and adverse events between groups. There were no abnormal postoperative pneumograms in the remifentanil group versus three in the halothane group.[18] **Pharmacokinetics** Neonates and infants younger than 2 months of age had an enhanced clearance compared with older children indicating a high non-specific esterase activity already in very preterm infants.[19] The half-life in infants under 2 months was 5.4 ± 1.8 minutes.[20,21]
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Appendix

Infusion table to assist concentration selection

Table 1: Infusion rates when using remifentanil concentration **20 microgram/mL**

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/minute**									
0.5	0.07	0.13	0.2	0.27	0.33	0.4	0.47	0.53	0.6	0.67
1	0.03	0.07	0.1	0.13	0.17	0.2	0.23	0.27	0.3	0.33
1.5	0.02	0.04	0.07	0.09	0.11	0.13	0.16	0.18	0.2	0.22
2	0.02	0.03	0.05	0.07	0.08	0.1	0.12	0.13	0.15	0.17
2.5	0.01	0.03	0.04	0.05	0.07	0.08	0.09	0.11	0.12	0.13
3	0.01	0.02	0.03	0.04	0.06	0.07	0.08	0.09	0.1	0.11
3.5	0.01	0.02	0.03	0.04	0.05	0.06	0.07	0.08	0.09	0.1
4	0.01	0.02	0.03	0.03	0.04	0.05	0.06	0.07	0.08	0.08
4.5	0.01	0.01	0.02	0.03	0.04	0.04	0.05	0.06	0.07	0.07
5	0.01	0.01	0.02	0.03	0.03	0.04	0.05	0.05	0.06	0.07

$$\text{Rate (mL/hr)} = \frac{\text{Dose (microgram/kg/min) x Weight (kg) x 60}}{\text{Concentration (microgram/mL)}}$$

$$\text{Dose (microgram/kg/min)} = \frac{\text{Rate (mL/hr) x Concentration (microgram/mL)}}{\text{Weight (kg) x 60}}$$

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