ONE DRUG · ONE PAGE

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ICU Drugs

A Bedside Handbook of 100 Critical Care Drugs

Class and mechanism · ICU dose · dilution and infusion · dose adjustment in renal, hepatic and other conditions · cautions · antidotes — with a summary table for every drug class

Sedatives · Analgesics · Paralytics · Reversal agents · Vasopressors · Inotropes · Antiarrhythmics · Antihypertensives · Diuretics & electrolytes · Antimicrobials · Steroids · Anticoagulants · Antidotes



By

Dr. Gireesh Kumar K.P.

For intensivists, emergency physicians, anaesthetists, residents, interns, ICU nurses and clinical pharmacists

AETCM ICU Drugs

One Drug · One Page — A Bedside Handbook of 100 Critical Care Drugs

Anaesthetic and sedative agents · Analgesics · Neuromuscular blockers · Reversal agents
Vasopressors and inotropes · Antiarrhythmics · Antihypertensives and vasodilators
Diuretics and electrolytes · Antimicrobials · Corticosteroids · Anticoagulants and other ICU agents



Dr. Gireesh Kumar K.P.

Academy for Emergency, Trauma & Critical care Medicine (AETCM)
First Edition · October 2026

Disclaimer. This book is a learning and quick-reference guide for medical students, nurses and registered practitioners. Drug doses, dilutions and adjustments follow international guidelines, product information and standard critical-care references current at the time of writing (October 2026), but dosing, formulations, concentrations and availability vary between institutions and products. Always check current product information, local ICU protocols and the patient's clinical condition, renal and hepatic function, weight, pregnancy status and interactions before prescribing, and seek specialist or pharmacist advice when in doubt. Drug names are given as generic (non-proprietary) names. The author and publisher accept no liability for any consequence arising from the use of this information.

Preface

Every night in every intensive care unit, a doctor or nurse stands at a bedside with a syringe pump in hand and asks the same questions: How much? In what dilution? Is it safe in this kidney, this liver, this potassium, this blood pressure? And if something goes wrong — what reverses it? The answers are scattered across product inserts, textbooks, guidelines and protocols. This book brings them together.

Each of the 100 drugs most often used in critical care has exactly one page, laid out in the same order every time: the drug and its class, how it works, the ICU dose for each common indication, how to dilute it and run the infusion, how to adjust the dose in renal failure, liver failure, shock, electrolyte imbalance and other special situations, the cautions and adverse effects that matter at the bedside, and the antidote or reversal strategy. A short ICU pearl closes every page. At the end of each drug class a full-page summary table lets you compare the whole group at a glance.

Doses are drawn from current international guidelines and critical-care references — the Surviving Sepsis Campaign, the PADIS guideline for pain, agitation and delirium, resuscitation guidelines, neurocritical-care and toxicology recommendations — together with product information, and are written for adult patients. Syringe-pump dilutions are given in the 50 ml format used in most Indian ICUs. Brand names have been deliberately omitted; only generic names are used.

A handbook cannot replace clinical judgement, local protocols or a pharmacist's advice. But a clear page, read quickly and correctly at 3 a.m., can prevent a ten-fold dilution error or a missed renal adjustment. I hope this book becomes that page for you.



Dr. Gireesh Kumar K.P.
Academy for Emergency, Trauma & Critical care Medicine (AETCM)
October 2026

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Contents

Front matter

Preface 3
How to use this book · Abbreviations 5

1. Anaesthetic and Sedative Agents

1. Propofol 7
2. Ketamine 8
3. Etomidate 9
4. Midazolam 10
5. Lorazepam 11
6. Diazepam 12
7. Remimazolam 13
8. Thiopental 14
9. Methohexital 15
10. Sevoflurane 16
11. Isoflurane 17
12. Desflurane 18
13. Nitrous Oxide 19
14. Dexmedetomidine 20
15. Clonidine 21

Class summary table 22

2. Analgesics — Opioids and Non-Opioids

16. Fentanyl 23
17. Morphine 24
18. Hydromorphone 25
19. Remifentanil 26
20. Sufentanil 27
21. Alfentanil 28
22. Methadone 29
23. Codeine 30
24. Tramadol 31
25. Nalbuphine 32
26. Ketorolac 33
27. Paracetamol (Acetaminophen) 34
28. Ibuprofen 35

Class summary table 36

3. Neuromuscular Blocking Agents

29. Succinylcholine (Suxamethonium) 37
30. Rocuronium 38
31. Vecuronium 39
32. Cisatracurium 40
33. Pancuronium 41
34. Atracurium 42

Class summary table 43

4. Reversal Agents

35. Naloxone 44
36. Flumazenil 45
37. Neostigmine 46
38. Sugammadex 47
39. Protamine Sulfate 48

Class summary table 49

5. Vasopressors and Inotropes

40. Norepinephrine (Noradrenaline) 50
41. Epinephrine (Adrenaline) 51
42. Vasopressin 52
43. Phenylephrine 53
44. Dopamine 54
45. Dobutamine 55
46. Milrinone 56
47. Levosimendan 57
48. Angiotensin II 58
49. Ephedrine 59

Class summary table 60

6. Antiarrhythmics and Cardiac Medications

50. Amiodarone 61
51. Adenosine 62
52. Lidocaine (Lignocaine) 63
53. Atropine 64
54. Esmolol 65
55. Metoprolol 66
56. Propranolol 67
57. Digoxin 68
58. Procainamide 69
59. Sotalol 70
60. Ibutilide 71
61. Verapamil 72
62. Diltiazem 73

Class summary table 74

7. Antihypertensives and Vasodilators

63. Nitroglycerin (Glyceryl Trinitrate) 75
64. Sodium Nitroprusside 76
65. Nicardipine 77
66. Clevidipine 78
67. Labetalol 79
68. Hydralazine 80
69. Enalaprilat 81

Class summary table 82

8. Diuretics and Fluid / Electrolyte Management

70. Furosemide 83
71. Torsemide (Torasemide) 84
72. Bumetanide 85
73. Mannitol 86
74. Hypertonic Saline (3% NaCl) 87
75. Spironolactone 88
76. Acetazolamide 89
77. Potassium Chloride (KCl) 90
78. Magnesium Sulfate 91
79. Calcium Gluconate / Calcium Chloride 92
80. Sodium Bicarbonate 93

Class summary table 94

9. Antimicrobials — Antibiotics, Antifungals and Antivirals

81. Meropenem 95
82. Vancomycin 96
83. Piperacillin–Tazobactam 97
84. Cefepime 98
85. Ceftriaxone 99
86. Ciprofloxacin 100
87. Amphotericin B 101
88. Fluconazole 102
89. Acyclovir (Aciclovir) 103

Class summary table 104

10. Corticosteroids and Anti-inflammatory Agents

90. Hydrocortisone 105
91. Methylprednisolone 106
92. Dexamethasone 107

Class summary table 108

11. Anticoagulants, Thrombolytics and Other ICU Agents

93. Heparin Sodium (Unfractionated Heparin) 109
94. Enoxaparin 110
95. Alteplase (tPA) 111
96. Insulin (Regular / Soluble) 112
97. Pantoprazole 113
98. Haloperidol 114
99. Quetiapine 115
100. Acetylcysteine (N-Acetylcysteine) 116

Class summary table 117

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How to use this book

One drug, one page. Every drug page follows the same blocks: **Drug and class** · **Mechanism of action** · **Dose in ICU** · **Drug dilution and infusion** · **Dose adjustment** (renal, hepatic and other conditions such as shock, electrolyte imbalance, obesity or age) · **Cautions and adverse effects** · **Antidote / reversal** · **ICU pearl**.

Class summary tables. After the last drug of each class, a full-page orange-headed table summarises dose, dilution, adjustment, key cautions and antidote for every drug in that class.

Doses. Adult doses for a typical 70 kg patient. Weight-based doses use actual body weight unless stated (use ideal or adjusted body weight for hydrophilic drugs in obesity). Titrate infusions to a defined target (RASS, CPOT, MAP, heart rate, aPTT, drug levels).

Dilutions. Syringe-pump dilutions are standardised to a 50 ml syringe where possible. Label every syringe with drug, total amount, volume, concentration, date and time. Ampoule strengths vary between manufacturers — check the ampoule before you draw up.

Renal adjustment is given by creatinine clearance (Cockcroft–Gault). In AKI, creatinine lags behind true GFR: give full loading doses and adjust maintenance doses as function changes. CRRT clearance varies with effluent dose.

Generic names only. Brand names are not used anywhere in this book.

Abbreviations

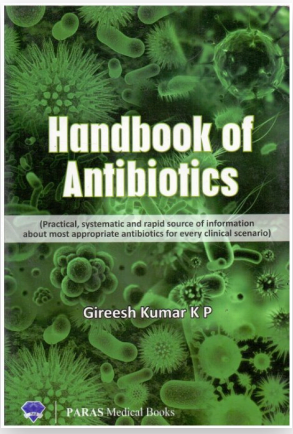
ACD	anaesthetic-conserving device	**MH**	malignant hyperthermia
AKI	acute kidney injury	**NCSE**	non-convulsive status epilepticus
aPTT	activated partial thromboplastin time	**NMBA**	neuromuscular blocking agent
AUC	area under the concentration–time curve	**NMS**	neuroleptic malignant syndrome
AWS	alcohol withdrawal syndrome	**NS**	0.9% sodium chloride
BD	twice daily	**ODS**	osmotic demyelination syndrome
BPS / CPOT	Behavioural Pain Scale / Critical-care Pain Observation Tool	**OP**	organophosphate
		PADIS	pain, agitation, delirium, immobility, sleep guideline
CrCl	creatinine clearance (ml/min)		
CRRT	continuous renal replacement therapy	**PRIS**	propofol infusion syndrome
D5 / D10	5% / 10% dextrose	**q6h**	every 6 hours
ECT	electroconvulsive therapy	**QTc**	corrected QT interval
ET	end-tidal	**RASS**	Richmond Agitation–Sedation Scale
HD	haemodialysis	**RSI**	rapid sequence intubation
HDIE / HIET	high-dose insulin euglycaemia therapy	**SE**	status epilepticus
HFrEF	heart failure with reduced ejection fraction	**SUP**	stress-ulcer prophylaxis
ICP	intracranial pressure	**TdP**	torsades de pointes
IM / IV / SC	intramuscular / intravenous / subcutaneous	**TG**	triglycerides
LAST	local anaesthetic systemic toxicity	**TOF / PTC**	train-of-four / post-tetanic count
MAC	minimum alveolar concentration	**VTE**	venous thromboembolism
MAP	mean arterial pressure	**WPW**	Wolff–Parkinson–White (pre-excitation)

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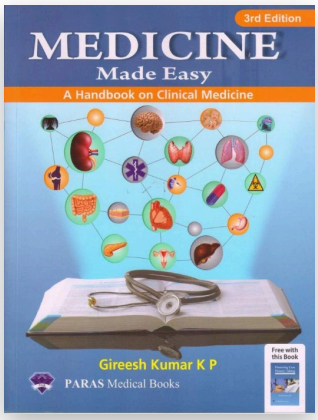
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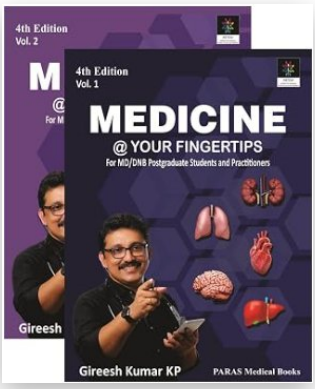
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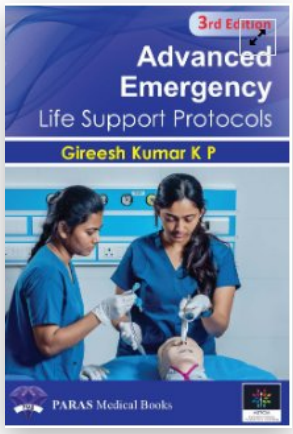
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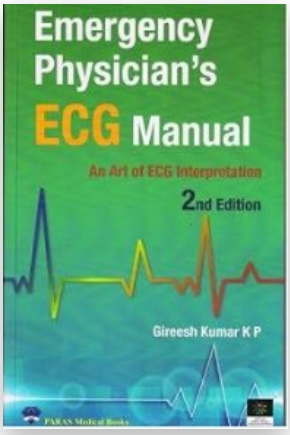
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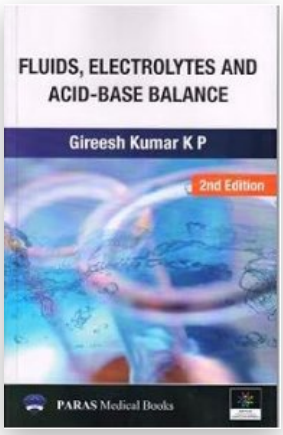
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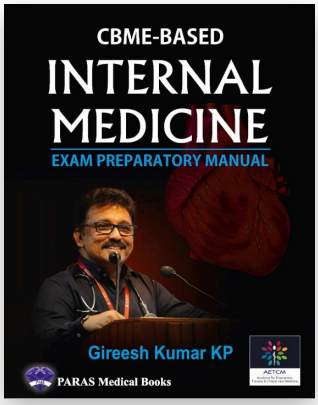
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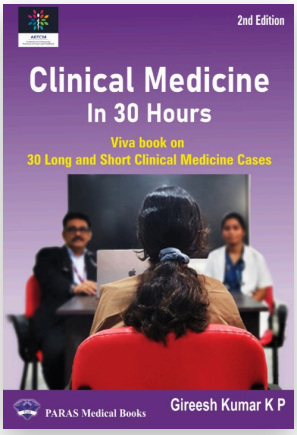
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Propofol

Intravenous general anaesthetic / sedative (alkylphenol, lipid emulsion)

1

Drug and class

Propofol — Intravenous general anaesthetic / sedative (alkylphenol, lipid emulsion).

Mechanism of action

Potentiates GABA-A receptor chloride conductance, causing dose-dependent sedation, hypnosis and amnesia; no analgesia. Rapid redistribution gives quick offset; reduces cerebral metabolic rate, cerebral blood flow and ICP.

Dose in ICU

- **Induction:** 1–2.5 mg/kg IV (0.5–1 mg/kg in elderly, shock or hypovolaemia), titrated in 10–20 mg increments
- **ICU sedation:** start 5 mcg/kg/min (0.3 mg/kg/h); titrate by 5–10 mcg/kg/min every 5–10 min; usual 5–50 mcg/kg/min (0.3–3 mg/kg/h)
- **Refractory status epilepticus:** 1–2 mg/kg bolus, then 20–200 mcg/kg/min (EEG-guided)
- Keep sedation light (RASS 0 to −2) unless deep sedation is specifically indicated

Drug dilution and infusion

- Use **undiluted** 1% (10 mg/ml) emulsion in a 50 ml syringe; a 2% (20 mg/ml) form reduces lipid volume
- Strict asepsis: discard syringe and tubing every 12 h (6 h once decanted from vial); supports bacterial growth
- Example: 70 kg at 25 mcg/kg/min = 105 mg/h = 10.5 ml/h of 1%

Dose adjustment — renal, hepatic and other conditions

Renal	No adjustment
Hepatic	No adjustment; titrate to effect
Other	Reduce dose in elderly, hypovolaemia and low cardiac output. Counts as nutrition: 1.1 kcal/ml lipid — adjust feeds; check triglycerides every 48 h (stop/reduce if >400 mg/dl)

Cautions and adverse effects

- Hypotension and bradycardia (vasodilation, myocardial depression) — worst after bolus in shock
- **Propofol infusion syndrome** (dose >4 mg/kg/h for >48 h): metabolic acidosis, rhabdomyolysis, hyperkalaemia, arrhythmia, Brugada-like ECG, AKI, raised lactate — stop at once
- Hypertriglyceridaemia and pancreatitis; green urine; pain on injection (use large vein)
- Respiratory depression and apnoea; no analgesic effect — pair with an opioid

Antidote / reversal

No specific antidote. Stop infusion, support haemodynamics; for PRIS — stop drug, switch sedative, treat acidosis/hyperkalaemia, consider renal replacement therapy or ECMO.

ICU PEARL Rising lactate, CK or triglycerides in a patient on high-dose propofol is PRIS until proved otherwise.

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Ketamine

Intravenous dissociative anaesthetic / analgesic (phencyclidine derivative)

2

Drug and class

Ketamine — Intravenous dissociative anaesthetic / analgesic (phencyclidine derivative).

Mechanism of action

Non-competitive NMDA-receptor antagonist producing dissociative anaesthesia and potent analgesia; indirect sympathomimetic (catecholamine reuptake inhibition) preserving BP, airway reflexes and respiratory drive; bronchodilator.

Dose in ICU

- **Induction / RSI:** 1–2 mg/kg IV (0.5–1 mg/kg in shock); 4–6 mg/kg IM
- **Analgesia (sub-dissociative):** 0.1–0.3 mg/kg IV bolus; infusion 0.1–0.5 mg/kg/h
- **Sedation / analgosedation:** 0.5–2 mg/kg/h as an adjunct (opioid-sparing)
- **Status asthmaticus:** 1 mg/kg bolus, then 0.5–2 mg/kg/h
- **Agitation (excited delirium):** 4–5 mg/kg IM or 1–2 mg/kg IV

Drug dilution and infusion

- Available 10 mg/ml and 50 mg/ml
- Infusion: 500 mg (10 ml of 50 mg/ml) + 40 ml NS = **10 mg/ml** in 50 ml syringe
- Analgesic infusion: 100 mg in 50 ml NS = 2 mg/ml; compatible with NS and D5

Dose adjustment — renal, hepatic and other conditions

Renal	No adjustment
Hepatic	Reduce dose and avoid prolonged infusion in severe hepatic impairment (hepatically metabolised to norketamine)
Other	Use the lower range in catecholamine-depleted shock — direct myocardial depression may unmask hypotension

Cautions and adverse effects

- Hypertension, tachycardia, raised myocardial O_2 demand — caution in ACS, aortic dissection, severe uncontrolled hypertension
- Emergence reactions, hallucinations; avoid in active psychosis/schizophrenia
- Hypersalivation, laryngospasm (rare), raised intra-ocular pressure
- Prolonged/high-dose use: cholestatic liver injury, ulcerative cystitis
- Older concern about raised ICP is not significant when ventilation is controlled

Antidote / reversal

No antidote. Treat emergence agitation with midazolam 1–2 mg IV; glycopyrrolate for secretions.

ICU PEARL The induction agent of choice in haemodynamic instability and bronchospasm — but halve the dose in profound shock.

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Etomidate

3

Intravenous induction agent (carboxylated imidazole)

Drug and class

Etomidate — Intravenous induction agent (carboxylated imidazole).

Mechanism of action

Positive modulator of GABA-A receptors (β2/β3 subunits) causing rapid hypnosis with minimal effect on BP and myocardial contractility. Reversibly inhibits adrenal 11β-hydroxylase, suppressing cortisol synthesis for 6–24 h.

Dose in ICU

- **Induction / RSI:** 0.2–0.3 mg/kg IV over 30–60 s (usual adult 20 mg)
- Reduce to 0.15–0.2 mg/kg in elderly, severe shock or hepatic failure
- **Not for infusion or repeated doses** — sustained adrenal suppression

Drug dilution and infusion

- Use undiluted 2 mg/ml (10 ml ampoule = 20 mg) into a running IV line
- Lipid or propylene-glycol formulations exist; give into a large vein to reduce pain

Dose adjustment — renal, hepatic and other conditions

Renal	No adjustment
Hepatic	Reduce dose (protein binding and clearance reduced in cirrhosis)
Other	Elderly and low cardiac output — slower onset, use lower dose

Cautions and adverse effects

- Adrenal suppression after a single dose — debated harm in sepsis; consider hydrocortisone if refractory shock follows
- Myoclonus (up to 50–80%), may mimic seizures; pain on injection; nausea and vomiting
- No analgesia — does not blunt intubation pressor response
- Avoid in porphyria

Antidote / reversal

No antidote. If vasopressor-refractory shock develops after etomidate, give hydrocortisone 50 mg IV 6-hourly.

ICU PEARL Haemodynamically the most stable induction agent; use once, never as a sedative infusion.

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Midazolam

Short-acting water-soluble benzodiazepine sedative / anticonvulsant

Drug and class

Midazolam — Short-acting water-soluble benzodiazepine sedative / anticonvulsant.

Mechanism of action

Binds the benzodiazepine site of the GABA-A receptor, increasing chloride channel opening frequency → sedation, anxiolysis, anterograde amnesia and anticonvulsant effect. Metabolised by CYP3A4 to active α-hydroxymidazolam.

Dose in ICU

- **Procedural / bolus sedation:** 0.02–0.08 mg/kg IV (1–2 mg), repeat every 5–15 min
- **Infusion:** 0.02–0.1 mg/kg/h (usual 1–7 mg/h) — benzodiazepine-sparing strategies preferred (PADIS)
- **Status epilepticus:** 10 mg IM (>40 kg) or 0.2 mg/kg IV; refractory SE 0.2 mg/kg bolus then 0.05–2 mg/kg/h (EEG-guided)
- **Intubation adjunct:** 0.05–0.1 mg/kg

Drug dilution and infusion

- Ampoules 1 mg/ml and 5 mg/ml
- Infusion: 50 mg in 50 ml NS or D5 = **1 mg/ml** (high-dose SE: 100 mg in 50 ml = 2 mg/ml)
- Bolus: dilute to 1 mg/ml and give over 1–2 min

Dose adjustment — renal, hepatic and other conditions

Renal	Active glucuronide metabolite accumulates in AKI/CKD — reduce dose by 50%, prolonged sedation
Hepatic	Reduce dose by 50% in cirrhosis; prolonged half-life
Other	Obesity and long infusions → accumulation (context-sensitive half-life). CYP3A4 inhibitors (fluconazole, clarithromycin, diltiazem, ritonavir) raise levels

Cautions and adverse effects

- Respiratory depression and hypotension, especially with opioids or in hypovolaemia
- Delirium (independent risk factor), prolonged ventilation, ICU-acquired weakness
- Tolerance and withdrawal after >5–7 days — taper 10–20% per day
- Paradoxical agitation in elderly

Antidote / reversal

Flumazenil 0.2 mg IV, repeated 0.1–0.2 mg every minute to max 1 mg (avoid in chronic benzodiazepine use or seizure risk).

ICU PEARL Daily sedation interruption and a target RASS 0 to −2 prevent most midazolam accumulation problems.

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Lorazepam

Intermediate-acting benzodiazepine sedative / anticonvulsant

5

Drug and class

Lorazepam — Intermediate-acting benzodiazepine sedative / anticonvulsant.

Mechanism of action

GABA-A receptor positive modulator at the benzodiazepine site. Less lipophilic than diazepam, so longer duration of anticonvulsant effect (12–24 h); conjugated by glucuronidation without active metabolites.

Dose in ICU

- **Status epilepticus (first line):** 0.1 mg/kg IV at 2 mg/min (max 4 mg per dose), repeat once after 5–10 min
- **Sedation bolus:** 0.02–0.04 mg/kg IV (max 2 mg) every 2–6 h
- **Infusion (rarely used):** 0.01–0.1 mg/kg/h, max 10 mg/h
- **Alcohol withdrawal:** 1–4 mg IV every 10–30 min symptom-triggered (CIWA-Ar)

Drug dilution and infusion

- Ampoule 2 mg/ml (contains propylene glycol and benzyl alcohol); refrigerate
- For IV push dilute with an **equal volume** of NS or D5 and give ≤2 mg/min
- If infused, keep concentration ≤1 mg/ml in D5 and watch for precipitation

Dose adjustment — renal, hepatic and other conditions

Renal	Propylene glycol accumulates in AKI — avoid prolonged infusion
Hepatic	Glucuronidation relatively preserved — safer than midazolam/diazepam in mild–moderate disease; reduce in severe
Other	Elderly: lower doses. Check osmolal gap during infusion (>10–12 suggests propylene glycol toxicity)

Cautions and adverse effects

- Respiratory depression, hypotension, over-sedation, delirium
- **Propylene glycol toxicity** with high-dose infusion: high-anion-gap metabolic acidosis, raised osmolal gap, AKI, haemolysis
- Thrombophlebitis; tolerance and withdrawal after prolonged use

Antidote / reversal

Flumazenil 0.2 mg IV increments (max 1 mg); avoid in benzodiazepine-dependent or seizure patients.

ICU PEARL The preferred IV benzodiazepine for status epilepticus because of its long anticonvulsant duration.

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Diazepam

Long-acting benzodiazepine sedative / anticonvulsant / muscle relaxant

6

Drug and class

Diazepam — Long-acting benzodiazepine sedative / anticonvulsant / muscle relaxant.

Mechanism of action

GABA-A receptor positive modulator. Highly lipid-soluble: very rapid CNS entry then redistribution (short anticonvulsant effect), but long elimination half-life (20–100 h) with active metabolite desmethyldiazepam.

Dose in ICU

- **Status epilepticus:** 0.15–0.2 mg/kg IV (max 10 mg per dose) at ≤5 mg/min, repeat once; rectal 0.2–0.5 mg/kg
- **Alcohol withdrawal:** 10–20 mg IV every 5–10 min until calm (symptom-triggered); oral 10–20 mg 1–4 hourly
- **Tetanus / muscle spasm:** 5–10 mg IV 4–8 hourly
- **Anxiolysis / sedation:** 2–10 mg IV

Drug dilution and infusion

- Ampoule 5 mg/ml; give **undiluted** slowly into a large vein — dilution causes precipitation
- Not recommended for continuous infusion (adsorbs to PVC, accumulates)
- Emulsion formulations cause less phlebitis

Dose adjustment — renal, hepatic and other conditions

Renal	No major adjustment; caution with repeated doses
Hepatic	Markedly prolonged half-life — reduce dose 50% or prefer lorazepam
Other	Elderly: half-life up to 100 h — use smaller, less frequent doses

Cautions and adverse effects

- Respiratory depression, hypotension, prolonged sedation from accumulation
- Thrombophlebitis and pain on injection; propylene glycol vehicle
- Paradoxical agitation; dependence and withdrawal

Antidote / reversal

Flumazenil 0.2 mg IV increments to max 1 mg (caution: may precipitate seizures).

ICU PEARL Excellent for alcohol withdrawal because its long-acting metabolite gives a built-in taper.

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Remimazolam

Ultra-short-acting ester benzodiazepine sedative

7

Drug and class

Remimazolam — Ultra-short-acting ester benzodiazepine sedative.

Mechanism of action

GABA-A benzodiazepine-site agonist like midazolam, but contains an ester bond rapidly hydrolysed by tissue carboxylesterase-1 to an inactive metabolite — organ-independent, predictable offset (context-insensitive half-life ≈ 7–8 min).

Dose in ICU

- **Procedural sedation:** 5 mg IV over 1 min; top-up 2.5 mg at ≥2-min intervals (elderly/ASA III–IV: 2.5–5 mg)
- **General anaesthesia (where licensed):** induction 6–12 mg/kg/h until loss of consciousness, maintenance 1 mg/kg/h (0.1–2.5)
- **ICU sedation (off-label/research):** 0.05–0.4 mg/kg/h titrated to RASS

Drug dilution and infusion

- Lyophilised powder: 20 mg vial + 8.2 ml NS = **2.5 mg/ml**; 50 mg vial + 20 ml NS = 2.5 mg/ml for infusion
- Compatible with NS, D5 and Ringer's lactate; flush line before and after

Dose adjustment — renal, hepatic and other conditions

Renal	No adjustment
Hepatic	Severe hepatic impairment (Child-Pugh C): prolonged recovery — titrate carefully, lower doses
Other	Elderly and ASA III–IV: reduce dose

Cautions and adverse effects

- Hypotension (less than propofol), respiratory depression, hypoxia
- Contains dextran 40 — contraindicated in dextran hypersensitivity
- Potentiated by opioids; limited ICU outcome data

Antidote / reversal

Flumazenil 0.2 mg IV, titrated (fully reverses sedation).

ICU PEARL A benzodiazepine that behaves like remifentanil — useful when rapid offset and haemodynamic stability are both needed.

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Thiopental

Ultra-short-acting barbiturate anaesthetic / anticonvulsant

8

Drug and class

Thiopental — Ultra-short-acting barbiturate anaesthetic / anticonvulsant.

Mechanism of action

Binds a barbiturate site on GABA-A receptors prolonging chloride channel opening (direct agonist at high doses); inhibits AMPA glutamate receptors. Profoundly reduces cerebral metabolic rate ($CMRO_2$), cerebral blood flow and ICP.

Dose in ICU

- **Induction:** 3–5 mg/kg IV (1–2 mg/kg in shock/elderly)
- **Refractory status epilepticus:** 2–5 mg/kg bolus, then 1–5 mg/kg/h to EEG burst suppression
- **Refractory intracranial hypertension:** 3–5 mg/kg bolus, then 1–5 mg/kg/h titrated to burst suppression
- Wean slowly after 24–48 h of seizure control

Drug dilution and infusion

- Reconstitute 500 mg with 20 ml sterile water = **25 mg/ml (2.5%)**; pH 10.5
- Infusion: use 25 mg/ml via a **central line**; do not mix with acidic drugs (NMBAs, opioids precipitate)

Dose adjustment — renal, hepatic and other conditions

Renal	Increased free fraction (hypoalbuminaemia) — reduce dose
Hepatic	Reduce dose; markedly prolonged elimination
Other	Zero-order kinetics at high doses — recovery takes days after long infusions

Cautions and adverse effects

- Hypotension, myocardial depression — often needs vasopressors
- Immunosuppression, ileus, hypothermia, hypokalaemia during infusion with **rebound hyperkalaemia** on stopping
- Extravasation and intra-arterial injection cause tissue necrosis and gangrene
- Contraindicated in acute porphyria; laryngospasm, bronchospasm

Antidote / reversal

No antidote. Supportive care; for intra-arterial injection — leave cannula, inject heparin and vasodilator (papaverine/lidocaine), consider sympathetic block.

ICU PEARL Check potassium 6-hourly during and for 48 h after thiopental coma — the rebound can be lethal.

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Methohexital

Ultra-short-acting methylated barbiturate anaesthetic

9

Drug and class

Methohexital — Ultra-short-acting methylated barbiturate anaesthetic.

Mechanism of action

Barbiturate GABA-A modulator, 2–3 times as potent as thiopental with faster hepatic clearance and quicker recovery. Unlike other barbiturates, it lowers the seizure threshold and can activate epileptic foci.

Dose in ICU

- **Induction:** 1–1.5 mg/kg IV over 30 s
- **Electroconvulsive therapy:** 0.75–1 mg/kg IV (agent of choice)
- **Procedural sedation:** 0.5–1 mg/kg IV; maintenance 20–40 mg every 4–7 min
- Rectal (children): 25 mg/kg

Drug dilution and infusion

- Reconstitute 500 mg with 50 ml sterile water or NS = **10 mg/ml (1%)**; alkaline (pH 10–11)
- Do not use Ringer's lactate; incompatible with acidic solutions
- Not used as a continuous ICU infusion

Dose adjustment — renal, hepatic and other conditions

Renal	No adjustment
Hepatic	Reduce dose (hepatic clearance)
Other	Elderly/shock: use lower doses

Cautions and adverse effects

- Hypotension, respiratory depression, apnoea
- Excitatory effects: myoclonus, hiccups, cough; may provoke seizures — avoid in epilepsy unless intended
- Pain on injection; intra-arterial injection → necrosis
- Contraindicated in porphyria

Antidote / reversal

No antidote; supportive care.

ICU PEARL The barbiturate that provokes seizures — that is why psychiatrists love it for ECT.

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Sevoflurane

Inhalational volatile anaesthetic (fluorinated methyl isopropyl ether)

10

Drug and class

Sevoflurane — Inhalational volatile anaesthetic (fluorinated methyl isopropyl ether).

Mechanism of action

Enhances GABA-A and glycine receptor function, inhibits NMDA and two-pore K^+ channels → hypnosis and immobility. Low blood:gas solubility (0.65) gives rapid onset/offset; potent bronchodilator; non-pungent.

Dose in ICU

- **MAC** ≈ 2.0% (adult, 40 y); lower in elderly and with opioids
- **Anaesthesia:** 1–2.5% end-tidal (0.5–1.3 MAC); inhalational induction up to 8%
- **ICU sedation** via anaesthetic-conserving device (ACD): 0.5–1.0% end-tidal (≈0.3–0.5 MAC); syringe pump 2–10 ml/h liquid
- **Rescue in refractory status asthmaticus / status epilepticus** under expert supervision

Drug dilution and infusion

- Delivered by calibrated vaporiser or ACD in the breathing circuit — not diluted
- Requires end-tidal agent monitoring and active scavenging

Dose adjustment — renal, hepatic and other conditions

Renal	Caution in pre-existing renal disease (fluoride and compound A); prefer isoflurane for long ICU sedation in AKI
Hepatic	No adjustment
Other	Lower MAC with age, hypothermia, pregnancy, opioids

Cautions and adverse effects

- **Malignant hyperthermia** trigger — contraindicated if susceptible
- Hypotension (vasodilation); QT prolongation; emergence delirium
- Prolonged use: nephrogenic diabetes insipidus — monitor urine output and sodium
- Compound A with dry CO_2 absorbent and low flows

Antidote / reversal

Malignant hyperthermia: stop agent, hyperventilate with 100% O_2, **dantrolene 2.5 mg/kg IV**, repeat to 10 mg/kg; active cooling.

ICU PEARL Inhaled sedation shortens wake-up time and spares opioids, but always watch serum sodium for nephrogenic DI.

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Isoflurane

Inhalational volatile anaesthetic (halogenated methyl ethyl ether)

11

Drug and class

Isoflurane — Inhalational volatile anaesthetic (halogenated methyl ethyl ether).

Mechanism of action

Volatile anaesthetic acting on GABA-A, glycine and NMDA receptors and K^+ channels. Blood:gas solubility 1.4; strong bronchodilator and cerebral/systemic vasodilator; minimal metabolism (0.2%).

Dose in ICU

- **MAC** ≈ 1.15% (adult)
- **Anaesthesia:** 0.8–1.5% end-tidal
- **ICU sedation** via ACD: 0.2–0.6% end-tidal (0.1–0.5 MAC); start 3–5 ml/h liquid, titrate
- **Refractory status asthmaticus / refractory status epilepticus:** 0.5–1.5% end-tidal titrated to effect/EEG

Drug dilution and infusion

- Delivered by vaporiser or ACD; not diluted
- End-tidal gas monitoring and scavenging mandatory

Dose adjustment — renal, hepatic and other conditions

Renal	No adjustment (minimal fluoride)
Hepatic	No adjustment; rare immune hepatitis
Other	Reduce MAC in elderly; dead space of ACD adds to tidal volume in small patients

Cautions and adverse effects

- Hypotension from vasodilation; tachycardia; possible coronary steal
- Malignant hyperthermia trigger
- Pungent — not for inhalational induction; increases cerebral blood flow and ICP at >1 MAC
- Hepatitis (rare)

Antidote / reversal

Malignant hyperthermia: dantrolene 2.5 mg/kg IV repeated as needed.

ICU PEARL The volatile of choice for long-term ICU sedation — least metabolised, cheap and a powerful bronchodilator.

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Desflurane

Inhalational volatile anaesthetic (fluorinated methyl ethyl ether)

12

Drug and class

Desflurane — Inhalational volatile anaesthetic (fluorinated methyl ethyl ether).

Mechanism of action

Volatile anaesthetic with the lowest blood:gas solubility (0.42) — fastest onset and recovery; acts on GABA-A, glycine and NMDA receptors. Very low metabolism (0.02%).

Dose in ICU

- **MAC** ≈ 6% (adult)
- **Anaesthesia maintenance:** 3–9% end-tidal (0.5–1.5 MAC)
- Not used for inhalational induction; not used with ICU sedation devices

Drug dilution and infusion

- Requires a heated, pressurised (Tec 6-type) vaporiser — boiling point 23 °C
- End-tidal monitoring and scavenging

Dose adjustment — renal, hepatic and other conditions

Renal	No adjustment
Hepatic	No adjustment
Other	MAC lower in elderly

Cautions and adverse effects

- Airway irritation: cough, laryngospasm, breath-holding — avoid in asthma and children for induction
- Sympathetic surge (tachycardia, hypertension) with rapid increase in concentration
- Malignant hyperthermia trigger; carbon monoxide with desiccated absorbent
- Very high greenhouse impact — avoid when alternatives exist

Antidote / reversal

Malignant hyperthermia: dantrolene 2.5 mg/kg IV.

ICU PEARL Fastest wake-up of all volatiles, but irritant and environmentally costly — an OT drug, not an ICU sedative.

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Nitrous Oxide

13

Inhalational analgesic / anaesthetic adjunct gas

Drug and class

Nitrous Oxide — Inhalational analgesic / anaesthetic adjunct gas.

Mechanism of action

NMDA-receptor antagonist with release of endogenous opioids and descending noradrenergic inhibition → analgesia and mild anxiolysis. Very insoluble (blood:gas 0.47); MAC 104%, so it cannot produce anaesthesia alone at atmospheric pressure.

Dose in ICU

- **Analgesia:** 50% N_2O / 50% O_2 premixed, self-administered by demand valve (labour, dressings, procedures)
- **Anaesthesia adjunct:** 50–70% in oxygen (reduces volatile requirement)
- Limit routine exposure to <6 h; give 100% O_2 for 3–5 min at the end

Drug dilution and infusion

- Supplied as gas cylinders (blue) or premixed 50:50 cylinders; delivered via flowmeter/demand valve
- Premixed cylinder: avoid use below −6 °C (gases separate)

Dose adjustment — renal, hepatic and other conditions

Renal	No adjustment
Hepatic	No adjustment
Other	Vitamin B12 deficiency — avoid; pregnancy first trimester — avoid

Cautions and adverse effects

- Expands closed gas spaces: contraindicated in pneumothorax, bowel obstruction, air embolism, pneumocephalus, middle-ear surgery, recent eye gas injection
- Diffusion hypoxia at discontinuation
- Inactivates vitamin B12 (methionine synthase): megaloblastic anaemia, subacute combined degeneration with prolonged/repeated use
- Raises pulmonary vascular resistance and ICP; nausea and vomiting

Antidote / reversal

No antidote. Stop and give 100% O_2; for neurotoxicity give hydroxocobalamin and methionine.

ICU PEARL Never give N_2O to a trauma patient until a pneumothorax has been excluded.

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Dexmedetomidine

Centrally acting selective α2-adrenoceptor agonist sedative

14

Drug and class

Dexmedetomidine — Centrally acting selective α2-adrenoceptor agonist sedative.

Mechanism of action

Highly selective α2-agonist (α2:α1 1600:1) acting on the locus coeruleus to produce 'cooperative', arousable sedation resembling natural sleep, with analgesic-sparing and sympatholytic effects and minimal respiratory depression.

Dose in ICU

- **Maintenance:** 0.2–0.7 mcg/kg/h, titrate every 30 min; up to 1.4–1.5 mcg/kg/h
- **Loading** 1 mcg/kg over 10 min — usually omitted in ICU (hypotension, bradycardia, transient hypertension)
- **Agitated delirium / non-intubated:** 0.2–0.7 mcg/kg/h; facilitates NIV tolerance and weaning
- Infusions >24 h are common in practice; taper over 24–48 h after prolonged use

Drug dilution and infusion

- Vial 100 mcg/ml (2 ml) — must be diluted
- 200 mcg (2 ml) + 48 ml NS = **4 mcg/ml** in 50 ml syringe (some use 8 mcg/ml)
- Example: 70 kg at 0.5 mcg/kg/h = 35 mcg/h = 8.75 ml/h of 4 mcg/ml

Dose adjustment — renal, hepatic and other conditions

Renal	No adjustment (metabolites inactive), though sedation may be more pronounced
Hepatic	Reduce dose (hepatic clearance falls 30–50%); start 0.2 mcg/kg/h
Other	Elderly, heart block, hypovolaemia and high-spinal patients: start low

Cautions and adverse effects

- Bradycardia, sinus arrest, heart block — avoid in 2nd/3rd degree block without pacing
- Hypotension (and hypertension with loading dose); dry mouth
- Rebound hypertension, tachycardia and agitation after abrupt stop of prolonged infusion
- Not suitable when deep sedation or paralysis is required

Antidote / reversal

No specific antidote (atipamezole is veterinary). Stop infusion; atropine/glycopyrrolate for bradycardia; fluids/vasopressor for hypotension.

ICU PEARL The only ICU sedative that lets the patient stay calm yet cooperative and breathing — ideal for weaning and NIV.

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Clonidine

Centrally acting α2-adrenoceptor agonist (sedative adjunct, antihypertensive)

Drug and class

Clonidine — Centrally acting α2-adrenoceptor agonist (sedative adjunct, antihypertensive).

Mechanism of action

Partial α2-agonist (α2:α1 200:1) reducing central sympathetic outflow → sedation, anxiolysis, analgesic potentiation and lowering of BP and HR; attenuates opioid and alcohol withdrawal.

Dose in ICU

- **IV sedation adjunct:** 0.5–2 mcg/kg/h infusion; bolus 75–150 mcg slow IV over 10 min
- **Enteral:** 50–150 mcg 6–8 hourly — used to wean dexmedetomidine or treat opioid/alcohol withdrawal
- **Hypertension (oral):** 0.1 mg 8–12 hourly, max 2.4 mg/day

Drug dilution and infusion

- Ampoule 150 mcg/ml
- Infusion: 750 mcg (5 ml) + 45 ml NS = **15 mcg/ml** in 50 ml syringe
- Bolus: dilute 150 mcg in 10 ml NS, give over 10 min

Dose adjustment — renal, hepatic and other conditions

Renal	≈50% renally excreted — reduce dose 25–50% in CrCl <30; not dialysed
Hepatic	No major adjustment
Other	Elderly and hypovolaemic: start low

Cautions and adverse effects

- Hypotension, bradycardia, heart block
- **Rebound hypertension** and agitation on abrupt withdrawal — taper over 2–4 days
- Dry mouth, ileus, sedation; long half-life (12–16 h) — slow titration

Antidote / reversal

No specific antidote; supportive care. Naloxone may partly reverse CNS/respiratory depression in overdose; atropine for bradycardia.

ICU PEARL Enteral clonidine is a cheap bridge to stop dexmedetomidine without rebound agitation.

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CHAPTER 1 · CLASS SUMMARY

Anaesthetic and Sedative Agents — At a Glance

Intravenous, inhalational and α2-agonist sedatives used for induction, sedation and refractory seizures

Drug	ICU dose	Dilution / infusion	Renal / hepatic / other	Key cautions	Antidote
Propofol	Induction 1–2.5 mg/kg; sedation 5–50 mcg/kg/min	Undiluted 10 mg/ml; change set every 12 h	None renal/hepatic; reduce in elderly/shock	Hypotension, PRIS, ↑TG, pancreatitis	None
Ketamine	RSI 1–2 mg/kg; analgesia 0.1–0.5 mg/kg/h; sedation 0.5–2 mg/kg/h	500 mg/50 ml = 10 mg/ml	Reduce in severe hepatic failure	↑BP/HR, emergence, secretions, cystitis	None (midazolam for emergence)
Etomidate	0.2–0.3 mg/kg IV single dose	Undiluted 2 mg/ml	Reduce in hepatic failure/elderly	Adrenal suppression, myoclonus	None (hydrocortisone if shock)
Midazolam	Bolus 1–2 mg; infusion 0.02–0.1 mg/kg/h; SE 0.2 mg/kg	50 mg/50 ml = 1 mg/ml	↓50% in renal & hepatic failure	Resp depression, delirium, accumulation	Flumazenil
Lorazepam	SE 0.1 mg/kg (max 4 mg) ×2; sedation 0.02–0.04 mg/kg	Dilute 1:1 for IV push; infusion ≤1 mg/ml D5	Avoid infusion in AKI; safer in mild liver disease	PG toxicity, resp depression	Flumazenil
Diazepam	SE 0.15–0.2 mg/kg (max 10 mg); AWS 10–20 mg q5–10 min	Undiluted, ≤5 mg/min; no infusion	↓ in hepatic failure/elderly	Accumulation, phlebitis	Flumazenil
Remimazolam	Procedural 5 mg then 2.5 mg; GA 1 mg/kg/h maintenance	Reconstitute to 2.5 mg/ml	None renal; caution Child C	Hypotension, dextran allergy	Flumazenil
Thiopental	Induction 3–5 mg/kg; coma 2–5 mg/kg then 1–5 mg/kg/h	25 mg/ml central line	↓ in renal & hepatic failure	Hypotension, K^+ swings, necrosis, porphyria	None
Methohexital	Induction 1–1.5 mg/kg; ECT 0.75–1 mg/kg	10 mg/ml (1%)	↓ in hepatic failure	Seizures, hypotension, porphyria	None
Sevoflurane	MAC 2%; ICU sedation 0.5–1% ET	Vaporiser / ACD	Caution renal disease	MH, hypotension, nephrogenic DI	Dantrolene (MH)
Isoflurane	MAC 1.15%; ICU sedation 0.2–0.6% ET	Vaporiser / ACD	None	Hypotension, MH, ↑ICP	Dantrolene (MH)
Desflurane	MAC 6%; maintenance 3–9%	Heated vaporiser	None	Airway irritation, ↑HR, MH	Dantrolene (MH)
Nitrous Oxide	Analgesia 50% in O_2; adjunct 50–70%	Gas — flowmeter / demand valve	Avoid in B12 deficiency	Expands air spaces, diffusion hypoxia	None (100% O_2)
Dexmedetomidine	0.2–0.7 (max 1.5) mcg/kg/h; avoid load	200 mcg/50 ml = 4 mcg/ml	↓ in hepatic failure	Bradycardia, hypotension, rebound	None (atropine)
Clonidine	IV 0.5–2 mcg/kg/h; enteral 50–150 mcg q6–8h	750 mcg/50 ml = 15 mcg/ml	↓25–50% if CrCl <30	Bradycardia, rebound HTN	None (supportive)

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Fentanyl

Synthetic phenylpiperidine opioid analgesic (pure μ-agonist)

16

Drug and class

Fentanyl — Synthetic phenylpiperidine opioid analgesic (pure μ-agonist).

Mechanism of action

Potent μ-opioid receptor agonist (≈100 × morphine), highly lipid-soluble with rapid onset (1–2 min) and short duration after a single dose. With infusion it accumulates in fat and its context-sensitive half-life lengthens. No histamine release.

Dose in ICU

- **Bolus analgesia:** 0.35–0.5 mcg/kg IV (25–100 mcg) every 30–60 min
- **Infusion:** 0.7–10 mcg/kg/h (usual 25–200 mcg/h), titrated to CPOT/BPS
- **Intubation / RSI adjunct:** 1–3 mcg/kg IV 3 min before induction
- **Procedures (dressings, lines):** 25–50 mcg IV boluses

Drug dilution and infusion

- Ampoule 50 mcg/ml
- Infusion: 500 mcg (10 ml) + 40 ml NS = **10 mcg/ml** in 50 ml syringe (high-dose: 1000 mcg in 50 ml = 20 mcg/ml)
- Example: 100 mcg/h = 10 ml/h of 10 mcg/ml

Dose adjustment — renal, hepatic and other conditions

Renal	No adjustment — opioid of choice in AKI/CKD (no active metabolites); mild accumulation in uraemia
Hepatic	Reduce dose; prolonged effect in cirrhosis (CYP3A4 metabolism)
Other	CYP3A4 inhibitors (azoles, macrolides, diltiazem, ritonavir) raise levels; obesity and long infusions → accumulation

Cautions and adverse effects

- Respiratory depression, sedation, hypotension (sympatholysis), bradycardia
- Chest-wall (truncal) rigidity with rapid large boluses — may need NMBA
- Ileus, constipation, urinary retention, nausea; tolerance and withdrawal after >5–7 days
- Serotonin syndrome with SSRIs, linezolid, methylene blue

Antidote / reversal

Naloxone 0.04–0.4 mg IV titrated (start 0.04 mg in ventilated or opioid-dependent patients); infusion may be needed after long fentanyl infusions.

ICU PEARL Treat pain first — 'analgosedation' with fentanyl often removes the need for any hypnotic.

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Morphine

Natural phenanthrene opioid analgesic (pure μ-agonist)

Drug and class

Morphine — Natural phenanthrene opioid analgesic (pure μ-agonist).

Mechanism of action

μ-opioid receptor agonist in brain, spinal cord and periphery. Hydrophilic, slower onset (5–10 min, peak 15–30 min). Metabolised to morphine-6-glucuronide (active, analgesic) and morphine-3-glucuronide (neuro-excitatory), both renally excreted. Releases histamine.

Dose in ICU

- **Bolus:** 2–4 mg IV every 1–2 h (0.05–0.1 mg/kg)
- **Infusion:** 2–30 mg/h (usual 1–5 mg/h), titrated to pain score
- **Acute pulmonary oedema / ACS:** 2–4 mg IV slow — use sparingly (no outcome benefit)
- **Palliative dyspnoea:** 1–2 mg IV/SC as needed

Drug dilution and infusion

- Ampoules 10 mg/ml (and 15 mg/ml)
- Infusion: 50 mg (5 ml) + 45 ml NS = **1 mg/ml** in 50 ml syringe
- Bolus: dilute 10 mg to 10 ml (1 mg/ml) and give over 4–5 min

Dose adjustment — renal, hepatic and other conditions

Renal	**Avoid** if CrCl <30 or on dialysis — M6G/M3G accumulate (prolonged sedation, myoclonus, seizures); CrCl 30–50: reduce dose 25–50% and lengthen interval
Hepatic	Reduce dose and frequency; may precipitate encephalopathy
Other	Elderly, hypovolaemia: lower doses; histamine release — caution in asthma and shock

Cautions and adverse effects

- Respiratory depression, sedation, delirium
- Hypotension (venodilation, histamine), bronchospasm, pruritus, flushing
- Ileus, nausea, vomiting, urinary retention, sphincter of Oddi spasm
- Tolerance, dependence, withdrawal after prolonged use

Antidote / reversal

Naloxone 0.04–0.4 mg IV titrated, repeat every 2–3 min; in renal failure the effect may outlast naloxone — consider infusion.

ICU PEARL Morphine in a patient with AKI is a slow-release sedative — switch to fentanyl.

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Hydromorphone

Semi-synthetic hydrogenated ketone opioid analgesic (μ-agonist)

18

Drug and class

Hydromorphone — Semi-synthetic hydrogenated ketone opioid analgesic (μ-agonist).

Mechanism of action

Potent μ-opioid agonist, 5–7 times as potent as morphine IV, with similar onset (5 min) and duration (2–4 h). Metabolised by glucuronidation to hydromorphone-3-glucuronide (neuro-excitatory, renally cleared); less histamine release than morphine.

Dose in ICU

- **Bolus:** 0.2–0.6 mg IV every 1–2 h (opioid-naïve: start 0.2 mg)
- **Infusion:** 0.5–3 mg/h, titrated to pain score
- **PCA:** 0.1–0.2 mg demand, lockout 6–10 min
- Equianalgesic: 1.5 mg IV hydromorphone ≈ 10 mg IV morphine

Drug dilution and infusion

- Ampoules 1, 2, 10 mg/ml — check strength carefully (high-potency product errors)
- Infusion: 10 mg in 50 ml NS = **0.2 mg/ml**
- Bolus: dilute to 0.2–1 mg/ml, give over 2–3 min

Dose adjustment — renal, hepatic and other conditions

Renal	Reduce dose 25–50% (CrCl <30); H3G accumulates → myoclonus, agitation, seizures
Hepatic	Reduce starting dose by 50% in moderate impairment
Other	Elderly: start 0.1–0.2 mg

Cautions and adverse effects

- Respiratory depression, sedation, hypotension
- Neuro-excitation (myoclonus, hyperalgesia) with high doses or renal failure
- Constipation, nausea, pruritus, urinary retention
- Dose-conversion errors from morphine — check potency

Antidote / reversal

Naloxone 0.04–0.4 mg IV titrated.

ICU PEARL A useful alternative to morphine in haemodynamically fragile patients, but it is NOT safe in renal failure either.

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Remifentanil

Ultra-short-acting synthetic opioid analgesic (anilidopiperidine μ-agonist)

Drug and class

Remifentanil — Ultra-short-acting synthetic opioid analgesic (anilidopiperidine μ-agonist).

Mechanism of action

Potent μ-agonist with an ester linkage hydrolysed by non-specific blood and tissue esterases. Context-sensitive half-life 3–4 min regardless of infusion duration; offset is organ-independent and predictable.

Dose in ICU

- **ICU analgosedation:** 0.5–15 mcg/kg/h (≈0.01–0.25 mcg/kg/min); start 0.1 mcg/kg/min, titrate by 0.025 every 5 min
- Optional loading 1.5 mcg/kg only in controlled settings
- **Anaesthesia:** 0.05–0.5 mcg/kg/min
- Before stopping, give a longer-acting analgesic (morphine/fentanyl/paracetamol) — analgesia ends within minutes

Drug dilution and infusion

- Lyophilised powder 1 mg, 2 mg, 5 mg — reconstitute with NS or D5
- Infusion: 1 mg in 50 ml NS = **20 mcg/ml** (2 mg in 40 ml = 50 mcg/ml for higher doses)
- Use a dedicated line or close-to-patient port; do not give boluses through a line containing remifentanil

Dose adjustment — renal, hepatic and other conditions

Renal	No adjustment
Hepatic	No adjustment
Other	Dose by ideal body weight in obesity; elderly — halve starting dose

Cautions and adverse effects

- Bradycardia, hypotension, muscle rigidity with rapid bolus
- Opioid-induced hyperalgesia and acute tolerance after stopping
- Profound respiratory depression — only in monitored/ventilated patients
- Contains glycine — not for epidural or intrathecal use

Antidote / reversal

Naloxone 0.04–0.4 mg IV titrated; usually unnecessary — stop infusion, effects end within 5–10 min.

ICU PEARL Ideal for neuro-patients needing frequent wake-up assessments; plan transitional analgesia before you switch it off.

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Sufentanil

Potent synthetic phenylpiperidine opioid analgesic (μ-agonist)

Drug and class

Sufentanil — Potent synthetic phenylpiperidine opioid analgesic (μ-agonist).

Mechanism of action

Highly selective μ-agonist, 5–10 times as potent as fentanyl, very lipophilic with rapid onset and a context-sensitive half-life shorter than fentanyl for infusions <8 h; marked sedative effect; CYP3A4 metabolism.

Dose in ICU

- **ICU infusion:** 0.2–1 mcg/kg/h (usual 0.25–0.5 mcg/kg/h)
- **Bolus:** 0.1–0.3 mcg/kg IV (5–20 mcg)
- **Intubation adjunct:** 0.1–0.3 mcg/kg
- Sublingual tablets 30 mcg used for procedural analgesia where available

Drug dilution and infusion

- Ampoule 50 mcg/ml
- Infusion: 250 mcg (5 ml) + 45 ml NS = **5 mcg/ml** in 50 ml syringe
- Example: 70 kg at 0.3 mcg/kg/h = 21 mcg/h = 4.2 ml/h

Dose adjustment — renal, hepatic and other conditions

Renal	No major adjustment; slight accumulation with long infusions
Hepatic	Reduce dose (hepatic CYP3A4 clearance)
Other	Obesity: dose by lean weight; elderly reduce 50%; CYP3A4 inhibitors raise levels

Cautions and adverse effects

- Respiratory depression, bradycardia, hypotension
- Chest-wall rigidity with rapid boluses
- Ileus, nausea; tolerance and withdrawal
- Ten-fold dose errors when confused with fentanyl concentrations

Antidote / reversal

Naloxone 0.04–0.4 mg IV titrated.

ICU PEARL Dose in tenths of fentanyl's: 1 mcg sufentanil ≈ 7–10 mcg fentanyl.

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Alfentanil

Short-acting synthetic anilidopiperidine opioid analgesic (μ-agonist)

Drug and class

Alfentanil — Short-acting synthetic anilidopiperidine opioid analgesic (μ-agonist).

Mechanism of action

μ-agonist ≈ 1/4–1/10 the potency of fentanyl, with low pKa giving very rapid onset (1 min) and short duration. Small volume of distribution; hepatic CYP3A4 metabolism to inactive metabolites — a good choice in renal failure.

Dose in ICU

- **Bolus:** 5–10 mcg/kg IV (250–500 mcg) for procedures
- **ICU infusion:** 0.5–1 mcg/kg/min (≈2 mg/h in 70 kg); range 0.5–10 mg/h titrated
- **Intubation adjunct:** 10–20 mcg/kg

Drug dilution and infusion

- Ampoules 500 mcg/ml (and ICU concentrate 5 mg/ml)
- Infusion: 10 mg (20 ml of 500 mcg/ml) + 30 ml NS = **200 mcg/ml** in 50 ml syringe
- Concentrate 5 mg/ml must be diluted before use

Dose adjustment — renal, hepatic and other conditions

Renal	No adjustment — no active metabolites
Hepatic	Reduce dose; clearance markedly reduced in cirrhosis
Other	**Strong CYP3A4 interactions** (erythromycin, fluconazole, diltiazem) — prolonged effect

Cautions and adverse effects

- Respiratory depression, bradycardia, hypotension
- Muscle rigidity with rapid bolus
- Variable clearance (CYP3A4 genetics) — unpredictable recovery after long infusions
- Nausea, ileus

Antidote / reversal

Naloxone 0.04–0.4 mg IV titrated.

ICU PEARL The 'renal-friendly' opioid in many European ICUs — watch interacting CYP3A4 drugs.

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Methadone

Synthetic long-acting opioid (μ-agonist, NMDA antagonist)

22

Drug and class

Methadone — Synthetic long-acting opioid (μ-agonist, NMDA antagonist).

Mechanism of action

μ-opioid agonist with additional NMDA antagonism and serotonin/noradrenaline reuptake inhibition. Long and highly variable half-life (15–60 h); high oral bioavailability (80%). Used to wean long-term opioid infusions and prevent iatrogenic withdrawal.

Dose in ICU

- **ICU opioid weaning:** 2.5–10 mg enterally 8–12 hourly (e.g., start 5 mg 8-hourly when fentanyl >7 days), then reduce fentanyl infusion by 20–50% daily
- **IV:** 2.5–10 mg every 8–12 h (IV ≈ 2 × oral potency)
- **Opioid use disorder:** continue home dose after verification; split if QT risk
- Reassess dose on days 3–5 when steady state is reached

Drug dilution and infusion

- Oral solution 1 mg/ml or tablets 5/10 mg via nasogastric tube
- IV 10 mg/ml: give undiluted slowly or diluted in 50 ml NS over 15 min

Dose adjustment — renal, hepatic and other conditions

Renal	CrCl <10: give 50–75% of dose; not dialysed
Hepatic	Caution in severe disease — reduce dose, slower titration
Other	QTc >500 ms or other QT drugs: avoid; CYP3A4/2B6 inducers (rifampicin, phenytoin) lower levels; inhibitors raise levels

Cautions and adverse effects

- **QT prolongation and torsades de pointes** — baseline and follow-up ECG
- Delayed respiratory depression (accumulates over 3–5 days)
- Hypoglycaemia (high dose), constipation, sedation
- Many drug interactions

Antidote / reversal

Naloxone — repeated doses or infusion needed because of the long half-life.

ICU PEARL Methadone's analgesia lasts 6–8 h but its respiratory depression can last days — titrate slowly.

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Codeine

Opioid analgesic / antitussive (weak μ-agonist prodrug)

Drug and class

Codeine — Opioid analgesic / antitussive (weak μ-agonist prodrug).

Mechanism of action

Weak μ-agonist that is a prodrug: ≈10% is converted by CYP2D6 to morphine, which provides most of the analgesia. Poor metabolisers get no effect; ultra-rapid metabolisers may develop morphine toxicity.

Dose in ICU

- **Analgesia:** 30–60 mg orally/NG every 4–6 h, max 240 mg/day
- **Antitussive:** 15–30 mg every 6–8 h
- **Diarrhoea (high stoma output):** 30–60 mg 6–8 hourly
- Not given IV (histamine release, hypotension)

Drug dilution and infusion

- Oral tablets 15/30/60 mg or syrup; crush or use syrup via NG tube
- Often combined with paracetamol — count total paracetamol dose

Dose adjustment — renal, hepatic and other conditions

Renal	**Avoid** in severe renal impairment (morphine metabolites accumulate); reduce if CrCl 10–50
Hepatic	Avoid in severe hepatic impairment — unpredictable conversion
Other	CYP2D6 inhibitors (fluoxetine, paroxetine, quinidine) abolish effect; avoid in children <12 y, breastfeeding, CYP2D6 ultra-rapid metabolisers

Cautions and adverse effects

- Constipation, nausea, sedation, respiratory depression
- Unpredictable effect from CYP2D6 polymorphism — fatal toxicity in ultra-rapid metabolisers
- Histamine release, hypotension if given IV

Antidote / reversal

Naloxone 0.4 mg IV, repeat as required.

ICU PEARL A poor ICU analgesic — use it for cough or stoma output, not for pain.

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Tramadol

Atypical centrally acting opioid analgesic (weak μ-agonist, SNRI)

Drug and class

Tramadol — Atypical centrally acting opioid analgesic (weak μ-agonist, SNRI).

Mechanism of action

Weak μ-agonist (mostly via its CYP2D6 metabolite O-desmethyltramadol) plus serotonin and noradrenaline reuptake inhibition, enhancing descending pain inhibition. Little respiratory depression at therapeutic doses.

Dose in ICU

- **IV/oral:** 50–100 mg every 4–6 h, max 400 mg/day (300 mg/day if >75 years)
- **Postoperative loading:** 100 mg, then 50 mg every 10–20 min to 250 mg in first hour (rarely needed)
- Use as part of multimodal analgesia with paracetamol

Drug dilution and infusion

- Ampoule 50 mg/ml (2 ml)
- Dilute 100 mg in **100 ml NS** and infuse over 20–30 min (reduces nausea), or give slowly over 2–3 min

Dose adjustment — renal, hepatic and other conditions

Renal	CrCl <30: every 12 h, max 200 mg/day; avoid extended-release; partially dialysed
Hepatic	Cirrhosis: 50 mg every 12 h
Other	Elderly >75 y: max 300 mg/day; avoid in epilepsy, raised ICP, MAOI/SSRI therapy

Cautions and adverse effects

- **Seizures** (dose-related; risk with renal failure, epilepsy, bupropion)
- **Serotonin syndrome** with SSRIs, SNRIs, linezolid, ondansetron in combination
- Nausea and vomiting (common), dizziness, sweating
- Hypoglycaemia and hyponatraemia (SIADH)

Antidote / reversal

Naloxone reverses opioid effects but may increase seizure risk; benzodiazepines for seizures; cyproheptadine for serotonin toxicity.

ICU PEARL Count the serotonergic drugs on the chart before you prescribe tramadol.

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Nalbuphine

Mixed agonist–antagonist opioid (κ-agonist, μ-antagonist)

Drug and class

Nalbuphine — Mixed agonist–antagonist opioid (κ-agonist, μ-antagonist).

Mechanism of action

κ-receptor agonist providing analgesia and sedation, with μ-receptor antagonism. Ceiling effect on respiratory depression (≈30 mg); can reverse μ-opioid respiratory depression and pruritus while preserving some analgesia.

Dose in ICU

- **Analgesia:** 10–20 mg IV/IM/SC every 3–6 h (0.1–0.3 mg/kg); max single dose 20 mg, max 160 mg/day
- **Opioid-induced pruritus:** 2.5–5 mg IV
- **Partial reversal of opioid respiratory depression:** 2.5–5 mg IV titrated

Drug dilution and infusion

- Ampoule 10 mg/ml
- Give undiluted slowly over 3–5 min, or dilute in 10 ml NS

Dose adjustment — renal, hepatic and other conditions

Renal	Reduce dose (use lower dose / longer interval)
Hepatic	Reduce dose — hepatic metabolism
Other	Avoid in opioid-dependent patients

Cautions and adverse effects

- Precipitates **withdrawal** in opioid-dependent patients and antagonises concurrent μ-agonists
- Sedation, dizziness, sweating, dysphoria
- Respiratory depression (ceiling effect, but still additive with sedatives)

Antidote / reversal

Naloxone (higher doses may be needed).

ICU PEARL Nalbuphine treats opioid itch without losing all your analgesia — but never give it to a patient on a fentanyl infusion for pain.

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Ketorolac

Parenteral non-steroidal anti-inflammatory drug (pyrrolo-pyrrole NSAID)

Drug and class

Ketorolac — Parenteral non-steroidal anti-inflammatory drug (pyrrolo-pyrrole NSAID).

Mechanism of action

Non-selective reversible COX-1 and COX-2 inhibitor, reducing prostaglandin synthesis — analgesia comparable to moderate opioid doses, with anti-inflammatory and antipyretic effects; inhibits platelet aggregation.

Dose in ICU

- **IV/IM:** 30 mg every 6 h (max 120 mg/day)
- **Age >65 y, weight <50 kg or renal impairment:** 15 mg every 6 h (max 60 mg/day)
- **Maximum duration 5 days** (IV + oral combined)

Drug dilution and infusion

- Ampoule 30 mg/ml
- IV bolus over ≥15 s undiluted, or dilute in 50 ml NS over 15–30 min

Dose adjustment — renal, hepatic and other conditions

Renal	**Avoid** in AKI, CrCl <30, hypovolaemia; reduce dose in mild impairment
Hepatic	Avoid in severe hepatic impairment/cirrhosis with ascites (AKI, bleeding)
Other	Avoid with active bleeding, coagulopathy, thrombocytopenia, peptic ulcer, after CABG, in pregnancy (third trimester)

Cautions and adverse effects

- Acute kidney injury, hyperkalaemia, fluid retention
- Gastrointestinal bleeding and ulceration; surgical-site bleeding
- Bronchospasm in aspirin-sensitive asthma
- Cardiovascular thrombotic events

Antidote / reversal

No antidote. Stop drug; PPI for GI protection; supportive care; dialysis rarely needed.

ICU PEARL Excellent opioid-sparing analgesic — but in the ICU, only for the patient with normal kidneys, normal volume and no bleeding risk.

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Paracetamol (Acetaminophen)

Antipyretic / analgesic (para-aminophenol derivative)

Drug and class

Paracetamol (Acetaminophen) — Antipyretic / analgesic (para-aminophenol derivative).

Mechanism of action

Central COX inhibition (peroxidase site) and activation of descending serotonergic pathways and the cannabinoid system; minimal peripheral anti-inflammatory or antiplatelet effect.

Dose in ICU

- **IV/oral:** 1 g every 6 h (max 4 g/day) if weight ≥50 kg
- **Weight <50 kg:** 15 mg/kg every 6 h (max 60 mg/kg/day)
- **Risk factors** (malnutrition, chronic alcohol, dehydration, hepatic impairment): max 3 g/day (some use 2 g/day)
- Minimum 4 h between doses; 6 h if CrCl ≤30

Drug dilution and infusion

- Ready-to-use 10 mg/ml (100 ml = 1 g); infuse over 15 min
- For 15 mg/kg doses, withdraw the excess volume before infusing; do not dilute below 1 mg/ml

Dose adjustment — renal, hepatic and other conditions

Renal	CrCl ≤30: minimum interval 6 h; HD: give after dialysis
Hepatic	Max 2–3 g/day; avoid in acute liver failure
Other	Low body weight, malnutrition, chronic alcohol use, glutathione depletion: reduce to ≤3 g/day

Cautions and adverse effects

- Hepatotoxicity in overdose or with risk factors
- **IV paracetamol-induced hypotension** — common in septic and critically ill patients (vasodilation)
- Masking of fever; rash, thrombocytopenia (rare)
- Duplicate prescribing with combination products

Antidote / reversal

Acetylcysteine (see drug 100) — start if level above treatment line or if >150 mg/kg ingested/unknown time.

ICU PEARL The foundation of multimodal ICU analgesia — but watch the BP after IV doses in septic shock.

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Ibuprofen

28

Non-selective NSAID (propionic acid derivative) — IV and oral

Drug and class

Ibuprofen — Non-selective NSAID (propionic acid derivative) — IV and oral.

Mechanism of action

Reversible inhibition of COX-1 and COX-2, reducing prostaglandin synthesis — analgesic, antipyretic and anti-inflammatory; reversible antiplatelet effect.

Dose in ICU

- **IV:** 400–800 mg every 6 h over 30 min (max 3200 mg/day)
- **Fever:** 400 mg IV every 4–6 h
- **Oral/NG:** 400 mg every 6–8 h (max 2400 mg/day for analgesia)
- Ensure adequate hydration before IV doses

Drug dilution and infusion

- IV concentrate 800 mg/8 ml — dilute to ≤4 mg/ml (e.g., 800 mg in 200 ml NS/D5), infuse over 30 min
- Ready-to-use bags (e.g., 400 mg/100 ml) where available

Dose adjustment — renal, hepatic and other conditions

Renal	Avoid in AKI, CrCl <30, hypovolaemia; use lowest dose for shortest time
Hepatic	Avoid in severe hepatic impairment
Other	Avoid with bleeding, peptic ulcer, heart failure, after CABG, third-trimester pregnancy, aspirin-sensitive asthma

Cautions and adverse effects

- AKI, hyperkalaemia, sodium and fluid retention
- GI bleeding, ulceration, platelet dysfunction
- Cardiovascular events; worsening heart failure
- Bronchospasm in NSAID-sensitive asthma

Antidote / reversal

No antidote; supportive care, PPI.

ICU PEARL IV ibuprofen is an effective antipyretic, but in the ICU the kidney pays for every NSAID dose.

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CHAPTER 2 · CLASS SUMMARY

Analgesics — Opioids and Non-Opioids — At a Glance

Analgesia-first sedation: opioids, opioid-sparing and multimodal agents

Drug	ICU dose	Dilution / infusion	Renal / hepatic / other	Key cautions	Antidote
Fentanyl	Bolus 25–100 mcg; infusion 25–200 mcg/h (0.7–10 mcg/kg/h)	500 mcg/50 ml = 10 mcg/ml	Opioid of choice in renal failure; ↓ in liver failure	Resp depression, rigidity, ileus	Naloxone
Morphine	Bolus 2–4 mg q1–2h; infusion 2–30 mg/h	50 mg/50 ml = 1 mg/ml	Avoid CrCl <30; ↓ in liver failure	Histamine, hypotension, metabolites	Naloxone
Hydromorphone	Bolus 0.2–0.6 mg q1–2h; infusion 0.5–3 mg/h	10 mg/50 ml = 0.2 mg/ml	↓25–50% renal; ↓50% hepatic	Neuro-excitation, potency errors	Naloxone
Remifentanil	0.5–15 mcg/kg/h (0.01–0.25 mcg/kg/min)	1 mg/50 ml = 20 mcg/ml	No adjustment; dose by IBW	Bradycardia, hyperalgesia on stop	Naloxone
Sufentanil	Infusion 0.2–1 mcg/kg/h; bolus 0.1–0.3 mcg/kg	250 mcg/50 ml = 5 mcg/ml	↓ in hepatic failure	Rigidity, resp depression, potency errors	Naloxone
Alfentanil	Bolus 5–10 mcg/kg; infusion 0.5–1 mcg/kg/min	10 mg/50 ml = 200 mcg/ml	None renal; ↓ hepatic	CYP3A4 interactions, rigidity	Naloxone
Methadone	Weaning 2.5–10 mg enteral q8–12h; IV 2.5–10 mg	Oral 1 mg/ml; IV diluted 50 ml	↓ if CrCl <10; caution hepatic	QT/TdP, delayed resp depression	Naloxone (infusion)
Codeine	30–60 mg oral q4–6h (max 240 mg/day)	Oral/NG only	Avoid severe renal/hepatic failure	CYP2D6 variability, constipation	Naloxone
Tramadol	50–100 mg q4–6h; max 400 mg/day	100 mg in 100 ml NS over 20–30 min	CrCl <30: q12h max 200 mg; cirrhosis 50 mg q12h	Seizures, serotonin syndrome	Naloxone (partial)
Nalbuphine	10–20 mg q3–6h (max 160 mg/day); pruritus 2.5–5 mg	Undiluted 10 mg/ml slow IV	↓ in renal & hepatic failure	Withdrawal, antagonises μ-agonists	Naloxone
Ketorolac	30 mg q6h (15 mg if elderly/renal); ≤5 days	Undiluted or in 50 ml NS	Avoid AKI/CrCl <30, cirrhosis	AKI, GI bleed, platelets	None
Paracetamol (Acetaminophen)	1 g q6h (max 4 g/day); 15 mg/kg if <50 kg	Ready 10 mg/ml over 15 min	CrCl ≤30: q6h min; hepatic max 2–3 g	Hepatotoxicity, IV hypotension	Acetylcysteine
Ibuprofen	IV 400–800 mg q6h (max 3.2 g/day)	≤4 mg/ml over 30 min	Avoid AKI, severe liver disease	AKI, GI bleed, HF	None

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Succinylcholine (Suxamethonium)

Depolarising neuromuscular blocking agent (dicholine ester)

29

Drug and class

Succinylcholine (Suxamethonium) — Depolarising neuromuscular blocking agent (dicholine ester).

Mechanism of action

Two linked acetylcholine molecules that bind nicotinic receptors at the motor end-plate, causing sustained depolarisation (fasciculations) then flaccid paralysis (phase I block). Onset 45–60 s, duration 5–10 min; hydrolysed by plasma (pseudo-)cholinesterase.

Dose in ICU

- **RSI:** 1–1.5 mg/kg IV (actual body weight); myasthenia gravis is resistant — 1.5–2 mg/kg (rocuronium + sugammadex often preferred)
- **IM (no IV access):** 3–4 mg/kg (max 150 mg)
- **Laryngospasm:** 0.1–0.5 mg/kg IV
- Avoid repeated doses (bradycardia, phase II block)

Drug dilution and infusion

- Ampoule 50 mg/ml (2 ml = 100 mg); draw up undiluted (some dilute to 10 mg/ml)
- Store at 2–8 °C (stable ~14 days at room temperature)
- Not used as an infusion in ICU

Dose adjustment — renal, hepatic and other conditions

Renal	No dose change, but **avoid if K^+ >5.5 mmol/L** — raises K^+ by 0.5–1 mmol/L
Hepatic	Severe liver disease lowers cholinesterase — modestly prolonged block
Other	Plasma cholinesterase deficiency (genetic, pregnancy, organophosphate poisoning) → prolonged apnoea

Cautions and adverse effects

- **Life-threatening hyperkalaemia** with up-regulated receptors: burns >24–48 h, crush injury, spinal cord injury/stroke >72 h, prolonged immobilisation, myopathies, Guillain–Barré, critical illness >3–5 days
- Malignant hyperthermia trigger; masseter spasm
- Bradycardia and asystole (especially repeat doses, children); raised intra-ocular, intragastric and ICP; myalgia
- Anaphylaxis (most common NMBA cause)

Antidote / reversal

No reversal agent — support ventilation until spontaneous recovery. Hyperkalaemia: calcium, insulin–dextrose; malignant hyperthermia: dantrolene 2.5 mg/kg.

ICU PEARL Before every succinylcholine dose ask: what is the potassium, and how long has this patient been in bed?

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Rocuronium

Intermediate-acting aminosteroid non-depolarising NMBA

30

Drug and class

Rocuronium — Intermediate-acting aminosteroid non-depolarising NMBA.

Mechanism of action

Competitive antagonist of acetylcholine at nicotinic end-plate receptors. At 1.2 mg/kg gives intubating conditions in 60 s (comparable to succinylcholine); duration 30–60 min (up to 90 min at RSI dose). Eliminated mainly in bile.

Dose in ICU

- **RSI:** 1.2 mg/kg IV (actual or adjusted body weight in obesity)
- **Routine intubation:** 0.6 mg/kg
- **Maintenance bolus:** 0.1–0.2 mg/kg
- **Infusion:** 8–12 mcg/kg/min (0.5–0.7 mg/kg/h), titrated to TOF 1–2 of 4

Drug dilution and infusion

- Vial 10 mg/ml (5 ml = 50 mg)
- Infusion: use **undiluted 10 mg/ml** (500 mg/50 ml) in syringe pump
- Example: 70 kg at 10 mcg/kg/min = 42 mg/h = 4.2 ml/h
- Store at 2–8 °C (≈60 days at room temperature)

Dose adjustment — renal, hepatic and other conditions

Renal	Modestly prolonged duration — titrate to TOF
Hepatic	Prolonged duration (biliary excretion) — reduce maintenance dose
Other	Prolonged by hypothermia, acidosis, hypokalaemia, hypermagnesaemia, aminoglycosides, volatile agents; elderly

Cautions and adverse effects

- Awareness — always ensure adequate sedation/analgesia before and during paralysis
- Prolonged weakness / critical illness myopathy with long infusions and steroids
- Anaphylaxis; pain on injection in awake patients
- Eye care, DVT prophylaxis and pressure-area care during paralysis

Antidote / reversal

Sugammadex 2 mg/kg (TOF 2), 4 mg/kg (deep block), **16 mg/kg** for immediate reversal after 1.2 mg/kg; or neostigmine 0.05 mg/kg + glycopyrrolate when TOF ≥2.

ICU PEARL Rocuronium plus sugammadex on the shelf has replaced succinylcholine for most RSIs.

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Vecuronium

Intermediate-acting aminosteroid non-depolarising NMBA

Drug and class

Vecuronium — Intermediate-acting aminosteroid non-depolarising NMBA.

Mechanism of action

Competitive nicotinic receptor antagonist at the neuromuscular junction; onset 2–3 min, duration 25–40 min. Hepatic deacetylation to 3-desacetylvecuronium (≈50–80% potency), cleared renally; no histamine release, cardiovascularly stable.

Dose in ICU

- **Intubation:** 0.08–0.1 mg/kg IV
- **Maintenance bolus:** 0.01–0.015 mg/kg
- **Infusion:** 0.8–1.2 mcg/kg/min (0.05–0.07 mg/kg/h) titrated to TOF 1–2

Drug dilution and infusion

- Lyophilised powder 10 mg — reconstitute with 10 ml water = **1 mg/ml**
- Infusion: 50 mg in 50 ml = 1 mg/ml
- Reconstituted solution: use within 24 h

Dose adjustment — renal, hepatic and other conditions

Renal	Active metabolite accumulates → prolonged paralysis; reduce infusion, monitor TOF
Hepatic	Prolonged duration; reduce dose
Other	Prolonged with hypothermia, acidosis, magnesium, aminoglycosides; obesity — dose by IBW

Cautions and adverse effects

- Prolonged weakness after long infusions, especially with corticosteroids (critical illness myopathy)
- Awareness without sedation
- Anaphylaxis (rare)

Antidote / reversal

Sugammadex 2–4 mg/kg (16 mg/kg for immediate reversal); neostigmine 0.05 mg/kg with glycopyrrolate when TOF ≥2.

ICU PEARL In renal failure, vecuronium paralysis can last days — choose cisatracurium.

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Cisatracurium

Intermediate-acting benzylisoquinolinium non-depolarising NMBA

Drug and class

Cisatracurium — Intermediate-acting benzylisoquinolinium non-depolarising NMBA.

Mechanism of action

Competitive nicotinic antagonist; a stereoisomer of atracurium ≈4 times as potent. Eliminated by **Hofmann degradation** (pH and temperature dependent) independent of liver and kidney; little histamine release.

Dose in ICU

- **Intubation:** 0.15–0.2 mg/kg IV (onset 3–5 min)
- **Infusion:** 1–3 mcg/kg/min (range 0.5–10) titrated to TOF 1–2
- **Early severe ARDS** (P/F <150, 48 h): 15 mg bolus, then 37.5 mg/h fixed dose (ACURASYS regimen) — selective use

Drug dilution and infusion

- Vials 2 mg/ml (and 5 mg/ml)
- Infusion: **undiluted 2 mg/ml** (100 mg/50 ml); or 150 mg in 50 ml = 3 mg/ml
- Store at 2–8 °C; stable 21 days at room temperature

Dose adjustment — renal, hepatic and other conditions

Renal	No adjustment (organ-independent elimination)
Hepatic	No adjustment
Other	Hypothermia and acidosis slow Hofmann degradation; tachyphylaxis with prolonged use

Cautions and adverse effects

- Awareness without adequate sedation
- ICU-acquired weakness with prolonged use; laudanosine (minimal) — seizure risk theoretical
- Bradycardia; anaphylaxis (rare)

Antidote / reversal

Neostigmine 0.05 mg/kg + glycopyrrolate 0.01 mg/kg when TOF ≥2. **Sugammadex does not work.**

ICU PEARL The paralytic of choice in combined renal and hepatic failure — but sugammadex cannot reverse it.

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Pancuronium

Long-acting aminosteroid non-depolarising NMBA

33

Drug and class

Pancuronium — Long-acting aminosteroid non-depolarising NMBA.

Mechanism of action

Competitive nicotinic antagonist with long duration (60–100 min). Vagolytic (muscarinic M2 block) and sympathomimetic — causes tachycardia and hypertension. ≈80% renally excreted; active 3-hydroxy metabolite.

Dose in ICU

- **Intubation:** 0.06–0.1 mg/kg IV
- **Maintenance:** 0.01–0.02 mg/kg every 60–100 min
- Intermittent boluses preferred to infusion (infusion 1 mcg/kg/min rarely used)

Drug dilution and infusion

- Ampoule 2 mg/ml; give undiluted
- Store at 2–8 °C

Dose adjustment — renal, hepatic and other conditions

Renal	**Avoid** in renal failure (markedly prolonged)
Hepatic	Prolonged duration; larger initial dose may be needed (increased Vd), smaller maintenance
Other	Elderly: prolonged action; hypothermia and acidosis potentiate

Cautions and adverse effects

- Tachycardia, hypertension, increased myocardial O_2 demand — avoid in ischaemic heart disease
- Prolonged residual paralysis and post-operative pulmonary complications
- Critical illness myopathy with steroids

Antidote / reversal

Neostigmine 0.05 mg/kg + glycopyrrolate when TOF ≥2. Sugammadex binds pancuronium with lower affinity — higher doses (4 mg/kg) may be needed.

ICU PEARL A cheap long-acting paralytic, but its tachycardia and renal clearance make it a poor ICU choice.

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Atracurium

Intermediate-acting benzylisoquinolinium non-depolarising NMBA

34

Drug and class

Atracurium — Intermediate-acting benzylisoquinolinium non-depolarising NMBA.

Mechanism of action

Competitive nicotinic antagonist eliminated by Hofmann degradation and ester hydrolysis (organ-independent). Releases histamine at higher doses; metabolite laudanosine is renally/hepatically cleared and epileptogenic at high levels.

Dose in ICU

- **Intubation:** 0.4–0.5 mg/kg IV (onset 2–3 min, duration 20–35 min)
- **Maintenance bolus:** 0.1–0.2 mg/kg
- **Infusion:** 5–10 mcg/kg/min (0.3–0.6 mg/kg/h) titrated to TOF

Drug dilution and infusion

- Ampoule 10 mg/ml
- Infusion: **undiluted 10 mg/ml** (250 mg in 25 ml, or 500 mg in 50 ml); or dilute to 5 mg/ml with NS
- Store at 2–8 °C; inject bolus slowly over 60 s to reduce histamine release

Dose adjustment — renal, hepatic and other conditions

Renal	No dose change; laudanosine accumulates with long infusions
Hepatic	No dose change; laudanosine accumulation
Other	Hypothermia and acidosis prolong action; incompatible with alkaline drugs (thiopental)

Cautions and adverse effects

- Histamine release: hypotension, flushing, bronchospasm
- Laudanosine-related seizures with prolonged high-dose infusion in organ failure
- Awareness; ICU-acquired weakness

Antidote / reversal

Neostigmine 0.05 mg/kg + glycopyrrolate when TOF ≥2; sugammadex ineffective.

ICU PEARL Organ-independent like cisatracurium, but more histamine — inject slowly.

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CHAPTER 3 · CLASS SUMMARY

Neuromuscular Blocking Agents — At a Glance

Depolarising and non-depolarising paralytics for intubation, ventilation and ARDS

Drug	ICU dose	Dilution / infusion	Renal / hepatic / other	Key cautions	Antidote
Succinylcholine (Suxamethonium)	RSI 1–1.5 mg/kg IV; IM 3–4 mg/kg	Undiluted 50 mg/ml; fridge	Avoid if K^+ >5.5; ↑ in cholinesterase deficiency	Hyperkalaemia, MH, bradycardia	None (supportive; dantrolene for MH)
Rocuronium	RSI 1.2 mg/kg; infusion 8–12 mcg/kg/min	Undiluted 10 mg/ml; fridge	↑ duration in hepatic failure	Awareness, myopathy, anaphylaxis	Sugammadex; neostigmine
Vecuronium	0.08–0.1 mg/kg; infusion 0.8–1.2 mcg/kg/min	Reconstitute 1 mg/ml	↓ in renal & hepatic failure	Prolonged weakness, steroids	Sugammadex; neostigmine
Cisatracurium	0.15–0.2 mg/kg; infusion 1–3 mcg/kg/min; ARDS 37.5 mg/h	Undiluted 2 mg/ml; fridge	No adjustment	Awareness, weakness	Neostigmine (not sugammadex)
Pancuronium	0.06–0.1 mg/kg; maintenance 0.01–0.02 mg/kg	Undiluted 2 mg/ml	Avoid in renal failure	Tachycardia, residual block	Neostigmine; sugammadex (partial)
Atracurium	0.4–0.5 mg/kg; infusion 5–10 mcg/kg/min	Undiluted 10 mg/ml; fridge	No dose change	Histamine release, laudanosine	Neostigmine

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Naloxone

Pure competitive opioid receptor antagonist

35

Drug and class

Naloxone — Pure competitive opioid receptor antagonist.

Mechanism of action

Competitive antagonist at μ, κ and δ opioid receptors with highest affinity for μ; reverses respiratory depression, sedation and hypotension within 1–2 min IV. Duration 45–90 min — shorter than most opioids.

Dose in ICU

- **Opioid toxicity (spontaneously breathing, apnoeic):** 0.4–2 mg IV/IM, repeat every 2–3 min to max 10 mg
- **Opioid-dependent or post-operative/ICU patient:** titrate 0.04–0.1 mg IV every 2 min to adequate breathing (not full arousal)
- **Infusion:** two-thirds of the effective reversal dose per hour, titrated
- **Intranasal:** 4 mg (or 2 mg); IM 0.4–0.8 mg

Drug dilution and infusion

- Ampoule 0.4 mg/ml
- Titration bolus: dilute 0.4 mg in 10 ml NS = **40 mcg/ml**
- Infusion: 2 mg in 50 ml NS = 40 mcg/ml (or 4 mg in 100 ml)

Dose adjustment — renal, hepatic and other conditions

Renal	No adjustment
Hepatic	No adjustment (prolonged half-life)
Other	Long-acting opioids (methadone, sustained release) — infusion and ≥6–12 h observation

Cautions and adverse effects

- Acute opioid withdrawal: agitation, vomiting, aspiration, hypertension, tachycardia
- Non-cardiogenic pulmonary oedema, arrhythmias, cardiac arrest (rare, high dose)
- Re-narcotisation as naloxone wears off
- Reverses analgesia — severe pain after surgery

Antidote / reversal

—

ICU PEARL The goal is breathing, not waking: titrate small doses in opioid-dependent patients.

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Flumazenil

Competitive benzodiazepine receptor antagonist (imidazobenzodiazepine)

Drug and class

Flumazenil — Competitive benzodiazepine receptor antagonist (imidazobenzodiazepine).

Mechanism of action

Competitively blocks the benzodiazepine binding site of the GABA-A receptor, reversing sedation and respiratory depression from benzodiazepines and Z-drugs. Onset 1–2 min, duration 30–60 min (shorter than most benzodiazepines).

Dose in ICU

- **Reversal of procedural sedation:** 0.2 mg IV over 15 s; repeat 0.1–0.2 mg every 60 s to max 1 mg (max 3 mg/h)
- **Infusion (resedation):** 0.1–0.4 mg/h titrated
- **Diagnostic test** for prolonged sedation in ICU: 0.5 mg IV

Drug dilution and infusion

- Ampoule 0.1 mg/ml (5 ml = 0.5 mg); give undiluted
- Infusion: 1 mg in 50 ml NS/D5 = 20 mcg/ml

Dose adjustment — renal, hepatic and other conditions

Renal	No adjustment
Hepatic	Reduce repeat doses (clearance reduced) — titrate slowly
Other	Elderly — start 0.1 mg

Cautions and adverse effects

- **Seizures** — contraindicated in chronic benzodiazepine use, epilepsy on benzodiazepines, raised ICP, and mixed overdose with TCAs or other pro-convulsants
- Acute withdrawal, agitation, arrhythmias
- Resedation after 30–60 min — observe ≥2 h

Antidote / reversal

—

ICU PEARL Use flumazenil to reverse procedural sedation — never as a routine 'coma cocktail' in unknown overdoses.

Free download and more resources: www.aetcm.com

Neostigmine

Reversible acetylcholinesterase inhibitor (quaternary carbamate)

37

Drug and class

Neostigmine — Reversible acetylcholinesterase inhibitor (quaternary carbamate).

Mechanism of action

Inhibits acetylcholinesterase, increasing acetylcholine at nicotinic end-plates (reverses non-depolarising block) and at muscarinic sites (bradycardia, secretions, gut motility). Ceiling effect — cannot reverse deep block.

Dose in ICU

- **NMBA reversal:** 0.04–0.07 mg/kg IV (max 5 mg) when TOF count ≥2–4, **with** glycopyrrolate 0.2 mg per 1 mg neostigmine (or atropine 0.02 mg/kg)
- **Acute colonic pseudo-obstruction (Ogilvie):** 2–2.5 mg IV over 3–5 min with ECG monitoring and atropine at the bedside
- **Myasthenia gravis:** 0.5–2.5 mg IV/IM every 3–4 h (1 mg IV ≈ 30 mg oral pyridostigmine)
- **Paralytic ileus (off-label):** 0.4–0.8 mg/h infusion

Drug dilution and infusion

- Ampoule 0.5 mg/ml (and 2.5 mg/ml)
- Give undiluted slowly with glycopyrrolate in the same syringe, or dilute 2.5 mg in 50 ml NS over 30–60 min

Dose adjustment — renal, hepatic and other conditions

Renal	Half-life prolonged (50% renal) — reduce repeat doses
Hepatic	No adjustment
Other	Avoid in mechanical bowel/urinary obstruction, peritonitis; caution in asthma, bradycardia, recent MI

Cautions and adverse effects

- Bradycardia, asystole, heart block (give anticholinergic)
- Bronchospasm, bronchorrhoea, salivation, vomiting, colic
- Cholinergic crisis (weakness worsens) with overdose in myasthenia
- Paradoxical weakness if given after full spontaneous recovery

Antidote / reversal

Atropine 0.5–1 mg IV (repeat) or glycopyrrolate for muscarinic effects.

ICU PEARL Always quantify the block with TOF before neostigmine — it cannot reverse a deep block.

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Sugammadex

Selective relaxant binding agent (modified γ-cyclodextrin)

38

Drug and class

Sugammadex — Selective relaxant binding agent (modified γ-cyclodextrin).

Mechanism of action

Encapsulates free aminosteroid NMBA molecules (rocuronium > vecuronium >> pancuronium) in plasma in a 1:1 complex, creating a concentration gradient that pulls drug away from the neuromuscular junction. No anticholinesterase effects; does not reverse benzylisoquinoliniums or succinylcholine.

Dose in ICU

- **Moderate block (TOF count ≥2):** 2 mg/kg IV
- **Deep block (PTC 1–2):** 4 mg/kg IV
- **Immediate reversal** (3 min after rocuronium 1.2 mg/kg — 'cannot intubate, cannot oxygenate'): **16 mg/kg** IV
- Dose on actual body weight

Drug dilution and infusion

- Vial 100 mg/ml (2 ml = 200 mg; 5 ml = 500 mg)
- Give undiluted as a rapid IV bolus over 10 s

Dose adjustment — renal, hepatic and other conditions

Renal	CrCl <30: not recommended (complex not cleared) — high-flux dialysis removes it
Hepatic	No adjustment
Other	Repeat NMBA within 24 h: use benzylisoquinolinium or high-dose rocuronium (1.2 mg/kg)

Cautions and adverse effects

- Anaphylaxis and hypersensitivity (rare)
- Marked bradycardia and asystole within minutes of dosing
- Reduces efficacy of hormonal contraceptives — use additional method for 7 days
- Transient prolongation of aPTT/PT

Antidote / reversal

Treat anaphylaxis (adrenaline); atropine for bradycardia.

ICU PEARL Rocuronium RSI plus 16 mg/kg sugammadex ready is the safety net when the airway fails.

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Protamine Sulfate

Heparin antagonist (basic, arginine-rich protein from salmon sperm)

39

Drug and class

Protamine Sulfate — Heparin antagonist (basic, arginine-rich protein from salmon sperm).

Mechanism of action

Strongly basic protein that binds strongly acidic heparin forming an inactive stable salt complex; neutralises unfractionated heparin completely and low-molecular-weight heparin anti-IIa activity but only ≈60% of anti-Xa activity. In excess it is itself a weak anticoagulant.

Dose in ICU

- **UFH bolus reversal:** 1 mg per 100 units of heparin given in the previous 2–3 h (0–30 min: 1 mg/100 U; 30–60 min: 0.5–0.75 mg; >2 h: 0.25–0.375 mg)
- **UFH infusion:** reverse the heparin given in the last 2–3 h (e.g., 1250 U/h → ≈30 mg)
- **Enoxaparin** within 8 h: 1 mg per 1 mg enoxaparin; 8–12 h: 0.5 mg per 1 mg; second dose 0.5 mg per 1 mg if bleeding continues
- **Maximum 50 mg per dose**; recheck aPTT/ACT 5–15 min after

Drug dilution and infusion

- Ampoule 10 mg/ml
- Give **slowly ≤5 mg/min** (50 mg over 10 min); may dilute in 50–100 ml NS

Dose adjustment — renal, hepatic and other conditions

Renal	No adjustment
Hepatic	No adjustment
Other	Higher reaction risk: fish allergy, prior protamine or NPH/protamine insulin, vasectomy

Cautions and adverse effects

- Hypotension and bradycardia with rapid injection
- Anaphylaxis/anaphylactoid reactions; catastrophic pulmonary hypertension and RV failure
- Overdose causes anticoagulation and platelet dysfunction
- Heparin rebound after cardiac surgery

Antidote / reversal

Treat reactions: stop infusion, adrenaline, fluids, inhaled pulmonary vasodilators for pulmonary hypertensive crisis.

ICU PEARL Calculate, don't guess: excess protamine is itself an anticoagulant.

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CHAPTER 4 · CLASS SUMMARY

Reversal Agents — At a Glance

Antagonists of opioids, benzodiazepines, neuromuscular blockers and heparin

Drug	ICU dose	Dilution / infusion	Renal / hepatic / other	Key cautions	Antidote
Naloxone	0.04–0.4 mg titrated; 0.4–2 mg in overdose (max 10 mg)	0.4 mg/10 ml = 40 mcg/ml	No adjustment	Withdrawal, pulmonary oedema, re-narcotisation	—
Flumazenil	0.2 mg then 0.1–0.2 mg/min (max 1 mg); infusion 0.1–0.4 mg/h	Undiluted 0.1 mg/ml	↓ repeat doses in hepatic failure	Seizures, resedation	—
Neostigmine	0.04–0.07 mg/kg (max 5 mg) + glycopyrrolate; Ogilvie 2–2.5 mg	Undiluted with glycopyrrolate	Prolonged in renal failure	Bradycardia, bronchospasm	Atropine
Sugammadex	2 mg/kg (TOF ≥2); 4 mg/kg (deep); 16 mg/kg immediate	Undiluted 100 mg/ml bolus	Not if CrCl <30	Anaphylaxis, bradycardia, contraceptives	Supportive
Protamine Sulfate	1 mg/100 U UFH (last 2–3 h); 1 mg per mg enoxaparin; max 50 mg	10 mg/ml ≤5 mg/min	No adjustment	Hypotension, anaphylaxis, pulm HTN	Supportive

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Norepinephrine (Noradrenaline)

Catecholamine vasopressor — first-line agent in septic and most vasodilatory shock

Drug and class

Norepinephrine (Noradrenaline) — Catecholamine vasopressor — first-line agent in septic and most vasodilatory shock.

Mechanism of action

Potent α1-agonist (arterial and venous vasoconstriction, increased venous return) with modest β1 activity (maintains contractility and cardiac output). Raises MAP with little change in heart rate.

Dose in ICU

- **Infusion:** start 0.05–0.1 mcg/kg/min, titrate every 5–10 min to MAP ≥65 mmHg; usual 0.05–0.5 mcg/kg/min
- **>0.25–0.5 mcg/kg/min:** add vasopressin; consider hydrocortisone; refractory doses >1 mcg/kg/min
- Fixed-dose equivalent: 2–20 mcg/min
- Start early (do not wait for full fluid resuscitation); peripheral infusion acceptable short-term until central access

Drug dilution and infusion

- Ampoules commonly 2 mg/2 ml (check whether labelled as base or bitartrate salt: 2 mg salt ≈ 1 mg base)
- Standard: **4 mg in 50 ml** NS or D5 = **80 mcg/ml**; high-strength 8 mg in 50 ml = 160 mcg/ml; peripheral 4 mg in 250 ml = 16 mcg/ml
- Example: 70 kg at 0.1 mcg/kg/min = 7 mcg/min = 5.25 ml/h of 80 mcg/ml
- Dedicated lumen; never flush the line; double-pump changeover

Dose adjustment — renal, hepatic and other conditions

Renal	No adjustment
Hepatic	No adjustment
Other	Correct hypovolaemia, acidosis (pH <7.1 blunts response) and hypocalcaemia; MAOIs and TCAs potentiate effect

Cautions and adverse effects

- Digital, mesenteric, renal and skin ischaemia at high doses
- Tachyarrhythmias; reflex bradycardia; increased myocardial O_2 demand
- **Extravasation** → tissue necrosis (peripheral lines: check site hourly)
- Hyperglycaemia, lactate rise

Antidote / reversal

Extravasation: stop infusion, aspirate, infiltrate **phentolamine** 5–10 mg in 10 ml NS subcutaneously (or topical nitroglycerin / terbutaline infiltration).

ICU PEARL Calculate in mcg/kg/min, document the dilution in base units, and never bolus the line.

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Epinephrine (Adrenaline)

Endogenous catecholamine — inotrope / vasopressor; drug of choice in anaphylaxis and cardiac arrest

Drug and class

Epinephrine (Adrenaline) — Endogenous catecholamine — inotrope / vasopressor; drug of choice in anaphylaxis and cardiac arrest.

Mechanism of action

Dose-dependent β1/β2 effects at low doses (inotropy, chronotropy, vasodilation, bronchodilation) and α1 vasoconstriction at higher doses. Stabilises mast cells in anaphylaxis.

Dose in ICU

- **Cardiac arrest:** 1 mg IV/IO every 3–5 min (10 ml of 0.1 mg/ml)
- **Anaphylaxis:** 0.5 mg IM (0.5 ml of 1 mg/ml) anterolateral thigh, repeat every 5 min; refractory — infusion 0.05–0.1 mcg/kg/min
- **Shock (second agent / cardiogenic):** 0.05–0.5 mcg/kg/min (range 0.01–1)
- **Push-dose (peri-arrest):** 10–20 mcg IV boluses of 10 mcg/ml
- **Croup / post-extubation stridor:** nebulised 1 mg/ml, 1–5 ml

Drug dilution and infusion

- Ampoules 1 mg/ml (1:1000) and prefilled 0.1 mg/ml (1:10,000)
- Infusion: **4 mg in 50 ml** NS/D5 = **80 mcg/ml** (or 2 mg in 50 ml = 40 mcg/ml)
- Push-dose: 1 ml of 0.1 mg/ml + 9 ml NS = 10 mcg/ml

Dose adjustment — renal, hepatic and other conditions

Renal	No adjustment
Hepatic	No adjustment
Other	Beta-blocked patients may need glucagon; acidosis blunts response; use lower doses in cocaine toxicity

Cautions and adverse effects

- Tachycardia, arrhythmias, myocardial ischaemia
- **Lactic acidosis** (β2-driven aerobic glycolysis) and hyperglycaemia — do not misinterpret as hypoperfusion
- Splanchnic ischaemia; hypertension; hypokalaemia
- IV boluses of 1 mg/ml in a patient with a pulse can be fatal — check the concentration

Antidote / reversal

Extravasation: phentolamine 5–10 mg in 10 ml NS SC. Toxicity: short-acting β-blocker (esmolol) and vasodilator.

ICU PEARL IM 0.5 mg in the thigh is the first treatment for anaphylaxis — not hydrocortisone, not antihistamine.

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Vasopressin

Non-catecholamine vasopressor (antidiuretic hormone analogue)

42

Drug and class

Vasopressin — Non-catecholamine vasopressor (antidiuretic hormone analogue).

Mechanism of action

Acts on V1a receptors on vascular smooth muscle (vasoconstriction independent of adrenergic receptors), V2 receptors in collecting ducts (water reabsorption) and V1b (ACTH release). Corrects relative vasopressin deficiency of septic shock; less affected by acidosis.

Dose in ICU

- **Septic shock:** fixed 0.03 U/min (range 0.01–0.04) added when norepinephrine ≥0.25–0.5 mcg/kg/min — not titrated like catecholamines
- **Vasoplegia after cardiac surgery:** 0.01–0.06 U/min
- **Variceal bleeding (terlipressin preferred):** 0.2–0.4 U/min with nitroglycerin
- Wean last: reduce by 0.01 U/min every 30–60 min after norepinephrine <0.1

Drug dilution and infusion

- Ampoule 20 U/ml
- Infusion: **20 U in 50 ml** NS/D5 = **0.4 U/ml**; 0.03 U/min = 1.8 U/h = 4.5 ml/h
- Alternative: 40 U in 100 ml = 0.4 U/ml

Dose adjustment — renal, hepatic and other conditions

Renal	No adjustment
Hepatic	No adjustment
Other	Low cardiac output states — may reduce CO further; use cautiously in cardiogenic shock

Cautions and adverse effects

- Digital, mesenteric and coronary ischaemia; skin necrosis
- Reduced cardiac output, bradycardia
- Hyponatraemia (V2), thrombocytopenia
- Rebound hypotension if stopped abruptly

Antidote / reversal

No antidote; stop or reduce infusion; treat ischaemia; phentolamine for extravasation.

ICU PEARL Vasopressin is a 'catecholamine-sparing' add-on: fixed dose, early, not as a sole agent.

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Phenylephrine

Pure α1-adrenoceptor agonist vasopressor (synthetic non-catecholamine)

Drug and class

Phenylephrine — Pure α1-adrenoceptor agonist vasopressor (synthetic non-catecholamine).

Mechanism of action

Selective α1-agonist causing arterial and venous vasoconstriction, raising systemic vascular resistance and BP; no β effect — causes reflex bradycardia and may reduce cardiac output.

Dose in ICU

- **Bolus:** 50–200 mcg IV (usual 100 mcg) every 2–5 min for anaesthesia-induced or spinal hypotension
- **Infusion:** 0.5–6 mcg/kg/min (usual 10–200 mcg/min), titrated to MAP
- **Preferred** when tachyarrhythmia limits other agents, in HOCM, severe aortic stenosis (to maintain afterload)

Drug dilution and infusion

- Ampoule 10 mg/ml
- Bolus: 10 mg in 100 ml NS = **100 mcg/ml** (draw 10 ml syringe)
- Infusion: 10 mg in 50 ml = **200 mcg/ml** (20 mg in 50 ml = 400 mcg/ml for high doses)

Dose adjustment — renal, hepatic and other conditions

Renal	No adjustment
Hepatic	No adjustment
Other	Avoid as sole agent in cardiogenic shock or low cardiac output; MAOIs potentiate

Cautions and adverse effects

- Reflex bradycardia, reduced cardiac output and splanchnic perfusion
- Peripheral and organ ischaemia at high doses
- Extravasation necrosis; hypertension

Antidote / reversal

Extravasation: phentolamine 5–10 mg SC infiltration. Bradycardia: atropine/glycopyrrolate.

ICU PEARL The vasopressor for the tachycardic, vasodilated patient — and the wrong one when the heart is failing.

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Dopamine

Endogenous catecholamine — dose-dependent inotrope / vasopressor

44

Drug and class

Dopamine — Endogenous catecholamine — dose-dependent inotrope / vasopressor.

Mechanism of action

Dose-dependent receptor activity: 1–5 mcg/kg/min dopaminergic (D1 renal/mesenteric vasodilation), 5–10 β1 (inotropy, chronotropy), >10 α1 (vasoconstriction). Releases endogenous noradrenaline; suppresses prolactin and pituitary hormones.

Dose in ICU

- **Infusion:** 2–20 mcg/kg/min; start 5 mcg/kg/min, titrate by 2–5 every 10 min
- **Second-line** to norepinephrine in shock (more arrhythmias — SOAP II); consider in bradycardia with hypotension unresponsive to atropine (5–20 mcg/kg/min)
- **'Renal-dose' dopamine has no benefit** and should not be used

Drug dilution and infusion

- Ampoule 40 mg/ml (5 ml = 200 mg)
- Infusion: **200 mg in 50 ml** NS/D5 = **4 mg/ml** (4000 mcg/ml)
- Example: 70 kg at 5 mcg/kg/min = 350 mcg/min = 5.25 ml/h
- Central line preferred; inactivated by alkaline solutions (bicarbonate)

Dose adjustment — renal, hepatic and other conditions

Renal	No adjustment
Hepatic	No adjustment
Other	MAOI therapy: reduce dose to one-tenth; phaeochromocytoma — avoid

Cautions and adverse effects

- **Tachyarrhythmias** (atrial fibrillation, VT) — more than norepinephrine
- Myocardial ischaemia, digital ischaemia at high doses
- Immunosuppression and endocrine suppression (prolactin, GH, TSH)
- Extravasation necrosis

Antidote / reversal

Extravasation: phentolamine 5–10 mg in 10 ml NS SC infiltration.

ICU PEARL Dopamine does not protect the kidney — and it causes more arrhythmias than norepinephrine.

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Dobutamine

Synthetic catecholamine inotrope (β1-agonist)

Drug and class

Dobutamine — Synthetic catecholamine inotrope (β1-agonist).

Mechanism of action

Predominant β1-agonist (increases contractility and heart rate) with mild β2 (vasodilation) and α1 effects — net increase in cardiac output with modest fall in SVR; BP may fall.

Dose in ICU

- **Infusion:** start 2.5–5 mcg/kg/min, titrate by 2.5 every 10–30 min; usual 2.5–20 mcg/kg/min (max 40)
- **Cardiogenic shock / low cardiac output** with adequate BP (combine with norepinephrine if hypotensive)
- **Septic myocardial dysfunction** with persistent hypoperfusion despite adequate MAP and volume

Drug dilution and infusion

- Ampoule 12.5 mg/ml (20 ml = 250 mg)
- Infusion: **250 mg in 50 ml** NS/D5 = **5 mg/ml** (5000 mcg/ml)
- Example: 70 kg at 5 mcg/kg/min = 350 mcg/min = 4.2 ml/h
- Peripheral infusion possible (low extravasation risk); incompatible with bicarbonate

Dose adjustment — renal, hepatic and other conditions

Renal	No adjustment
Hepatic	No adjustment
Other	Beta-blocked patients: reduced response — consider milrinone/levosimendan

Cautions and adverse effects

- Tachycardia and arrhythmias, myocardial ischaemia
- Hypotension (β2 vasodilation), especially in hypovolaemia
- Avoid in HOCM with LVOT obstruction and severe aortic stenosis
- Tolerance after 72 h; eosinophilic myocarditis (rare)

Antidote / reversal

No antidote; reduce or stop (half-life 2 min); esmolol for tachyarrhythmia.

ICU PEARL Dobutamine raises flow, not pressure — fix the MAP first, then add dobutamine for the low output.

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Milrinone

Phosphodiesterase-3 inhibitor inodilator (bipyridine)

Drug and class

Milrinone — Phosphodiesterase-3 inhibitor inodilator (bipyridine).

Mechanism of action

Inhibits PDE-3 in myocardium and vascular smooth muscle, increasing cAMP independently of β-receptors → increased contractility, lusitropy and marked systemic and pulmonary vasodilation. Long half-life (2–3 h, longer in renal failure).

Dose in ICU

- **Infusion:** 0.125–0.75 mcg/kg/min (start 0.25–0.375)
- **Loading dose** 50 mcg/kg over 10 min — usually omitted (hypotension)
- **Indications:** low-output heart failure, β-blocked patients, right-ventricular failure with pulmonary hypertension, post-cardiac surgery

Drug dilution and infusion

- Ampoule 1 mg/ml (10 ml = 10 mg)
- Infusion: **10 mg in 50 ml** NS/D5 = **200 mcg/ml** (20 mg in 100 ml)
- Example: 70 kg at 0.375 mcg/kg/min = 26 mcg/min = 7.9 ml/h
- **Incompatible with furosemide** (precipitates) — separate line

Dose adjustment — renal, hepatic and other conditions

Renal	**Reduce**: CrCl 50 → 0.43; 40 → 0.38; 30 → 0.33; 20 → 0.28; 10 → 0.23; 5 → 0.2 mcg/kg/min (max)
Hepatic	No adjustment
Other	Hypovolaemia: correct first (severe hypotension); combine with norepinephrine if MAP low

Cautions and adverse effects

- Hypotension (vasodilation) — often needs vasopressor support
- Atrial and ventricular arrhythmias
- Thrombocytopenia; hypokalaemia
- Prolonged effect in AKI — accumulation

Antidote / reversal

No antidote; stop infusion and support BP with norepinephrine/vasopressin.

ICU PEARL The inotrope of choice for the β-blocked heart and the failing right ventricle — dose by creatinine clearance.

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Levosimendan

47

Calcium sensitiser inodilator (pyridazinone-dinitrile)

Drug and class

Levosimendan — Calcium sensitiser inodilator (pyridazinone-dinitrile).

Mechanism of action

Binds cardiac troponin C in a calcium-dependent manner, increasing contractility without raising intracellular calcium or O_2 demand; opens ATP-sensitive K^+ channels → systemic, coronary and pulmonary vasodilation. Active metabolite OR-1896 prolongs effects for 7–9 days.

Dose in ICU

- **Infusion:** 0.05–0.2 mcg/kg/min for 24 h (start 0.1; reduce to 0.05 if hypotension, increase to 0.2 if tolerated)
- **Loading dose** 6–12 mcg/kg over 10 min — omit if SBP <100 mmHg (commonly omitted)
- **Indications:** acute decompensated heart failure with low output, β-blocked patients, cardiogenic shock (with vasopressor), weaning from cardiac surgery

Drug dilution and infusion

- Vial 2.5 mg/ml (5 ml = 12.5 mg)
- Infusion: **12.5 mg in 500 ml D5** = **25 mcg/ml** (or 12.5 mg in 250 ml = 50 mcg/ml)
- Example: 70 kg at 0.1 mcg/kg/min = 7 mcg/min = 16.8 ml/h of 25 mcg/ml

Dose adjustment — renal, hepatic and other conditions

Renal	Not recommended if CrCl <30 (metabolite accumulates)
Hepatic	Avoid in severe hepatic impairment
Other	Correct hypovolaemia and hypokalaemia before starting; avoid if SBP <85 mmHg or severe LVOT obstruction

Cautions and adverse effects

- Hypotension (often needs norepinephrine)
- Atrial fibrillation, ventricular arrhythmias, tachycardia
- Hypokalaemia, headache
- Effects persist for a week after a single 24-h infusion

Antidote / reversal

No antidote; support BP with norepinephrine; treat arrhythmias.

ICU PEARL One 24-hour infusion gives a week of inotropy — plan for it, and keep potassium above 4.

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Angiotensin II

48

Synthetic human angiotensin II vasopressor (for refractory vasodilatory shock)

Drug and class

Angiotensin II — Synthetic human angiotensin II vasopressor (for refractory vasodilatory shock).

Mechanism of action

Binds angiotensin AT1 receptors causing arteriolar vasoconstriction, aldosterone and vasopressin release; increases MAP via a third pathway independent of catecholamine and vasopressin receptors. Particularly useful in high-renin shock and ACE-inhibitor associated vasoplegia.

Dose in ICU

- **Start 20 ng/kg/min**; titrate by up to 15 ng/kg/min every 5 min to MAP ≥65
- Maximum 80 ng/kg/min in the first 3 h; maintenance ≤40 ng/kg/min
- Reduce other vasopressors as MAP improves; wean by 15 ng/kg/min every 5–15 min
- Availability limited in India

Drug dilution and infusion

- Vial 2.5 mg/ml
- Infusion: **2.5 mg in 500 ml NS** = **5000 ng/ml** (or 2.5 mg in 250 ml = 10,000 ng/ml for fluid restriction)
- Example: 70 kg at 20 ng/kg/min = 1400 ng/min = 16.8 ml/h of 5000 ng/ml
- Central line

Dose adjustment — renal, hepatic and other conditions

Renal	No adjustment
Hepatic	No adjustment
Other	Use with VTE prophylaxis; caution in active thrombosis, mesenteric ischaemia

Cautions and adverse effects

- **Arterial and venous thrombosis** — pharmacological VTE prophylaxis required
- Tachycardia, peripheral and digital ischaemia
- Fungal infection, delirium (reported in trials)
- Sensitive patients (ACE-inhibitor exposed) respond to very low doses

Antidote / reversal

No antidote; reduce infusion (half-life <1 min).

ICU PEARL Think of angiotensin II when shock is refractory despite norepinephrine and vasopressin — especially in the patient on an ACE inhibitor.

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Ephedrine

Mixed-acting sympathomimetic (direct and indirect α/β agonist)

Drug and class

Ephedrine — Mixed-acting sympathomimetic (direct and indirect α/β agonist).

Mechanism of action

Direct α- and β-agonist and indirect release of stored noradrenaline from nerve terminals → increased heart rate, contractility and vascular tone. Longer acting (10–60 min) than adrenaline; tachyphylaxis with repeated doses as stores deplete.

Dose in ICU

- **Bolus:** 5–10 mg IV every 3–5 min (max ≈50 mg cumulative)
- **IM/SC:** 25–50 mg
- **Indications:** hypotension after induction or spinal anaesthesia, especially with bradycardia

Drug dilution and infusion

- Ampoule 30 mg/ml (or 50 mg/ml)
- Dilute 30 mg (1 ml) to 10 ml NS = **3 mg/ml** (50 mg to 10 ml = 5 mg/ml)
- Not used as an infusion

Dose adjustment — renal, hepatic and other conditions

Renal	Partly renally excreted unchanged — repeated doses accumulate; titrate
Hepatic	No adjustment
Other	Ineffective after catecholamine depletion (prolonged shock, reserpine); MAOI therapy — hypertensive crisis

Cautions and adverse effects

- Tachycardia, hypertension, arrhythmias
- **Tachyphylaxis** after repeated doses
- Interaction with MAOIs, linezolid and TCAs (hypertensive crisis)
- CNS stimulation, urinary retention

Antidote / reversal

No antidote; supportive care; vasodilator or β-blocker for severe hypertension.

ICU PEARL A bridging bolus drug for transient hypotension — if you need repeated doses, start an infusion of a real vasopressor.

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CHAPTER 5 · CLASS SUMMARY

Vasopressors and Inotropes — At a Glance

Catecholamines, non-catecholamine vasopressors, inodilators and calcium sensitisers for shock

Drug	ICU dose	Dilution / infusion	Renal / hepatic / other	Key cautions	Antidote
Norepinephrine (Noradrenaline)	0.05–0.5 mcg/kg/min to MAP ≥65; >1 refractory	4 mg/50 ml = 80 mcg/ml	No adjustment	Ischaemia, arrhythmia, extravasation	Phentolamine (extravasation)
Epinephrine (Adrenaline)	Arrest 1 mg q3–5 min; anaphylaxis 0.5 mg IM; infusion 0.05–0.5 mcg/kg/min	4 mg/50 ml = 80 mcg/ml	No adjustment	Lactate ↑, arrhythmia, ischaemia	Phentolamine (extravasation)
Vasopressin	Fixed 0.03 U/min (0.01–0.04) in septic shock	20 U/50 ml = 0.4 U/ml	No adjustment	Ischaemia, ↓CO, hyponatraemia	None
Phenylephrine	Bolus 50–200 mcg; infusion 0.5–6 mcg/kg/min	Bolus 100 mcg/ml; infusion 200 mcg/ml	No adjustment	Reflex bradycardia, ↓CO	Phentolamine (extravasation)
Dopamine	2–20 mcg/kg/min (2nd line); no 'renal dose'	200 mg/50 ml = 4 mg/ml	No adjustment; ↓ with MAOI	Arrhythmias, ischaemia	Phentolamine (extravasation)
Dobutamine	2.5–20 mcg/kg/min	250 mg/50 ml = 5 mg/ml	No adjustment	Tachycardia, hypotension, ischaemia	None
Milrinone	0.125–0.75 mcg/kg/min; load usually omitted	10 mg/50 ml = 200 mcg/ml	Renal dose reduction (max 0.2–0.43)	Hypotension, arrhythmia	None
Levosimendan	0.05–0.2 mcg/kg/min ×24 h; load optional	12.5 mg/500 ml D5 = 25 mcg/ml	Avoid CrCl <30, severe liver failure	Hypotension, AF, hypokalaemia	None
Angiotensin II	20 ng/kg/min, max 80 (first 3 h), maintenance ≤40	2.5 mg/500 ml = 5000 ng/ml	No adjustment	Thrombosis, ischaemia	None
Ephedrine	5–10 mg IV boluses (max ~50 mg); IM 25–50 mg	30 mg in 10 ml = 3 mg/ml	Accumulates in renal failure	Tachyphylaxis, MAOI interaction	None

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Amiodarone

Class III antiarrhythmic (with class I, II and IV actions) — benzofuran derivative

Drug and class

Amiodarone — Class III antiarrhythmic (with class I, II and IV actions) — benzofuran derivative.

Mechanism of action

Blocks K^+ channels (prolongs action potential and refractory period), plus Na^+ channel, β-adrenergic and Ca^{2+} channel blockade; non-competitive α/β antagonism causes vasodilation. Very large volume of distribution, half-life weeks.

Dose in ICU

- **VF / pulseless VT (after 3rd shock):** 300 mg IV/IO bolus; further 150 mg after 5th shock
- **Stable VT / AF with haemodynamic compromise:** 150–300 mg (5 mg/kg) IV over 10–60 min, then 900 mg over 24 h (1 mg/min ×6 h, then 0.5 mg/min ×18 h)
- **AF rate/rhythm in critically ill:** 5–7 mg/kg over 30–60 min, then 1.2–1.8 g/24 h; total loading ≈10 g including oral
- **Oral:** 200 mg 8-hourly ×1 week, 12-hourly ×1 week, then 100–200 mg daily

Drug dilution and infusion

- Ampoule 50 mg/ml (3 ml = 150 mg)
- **Dilute in D5 only** (unstable in NS): loading 300 mg in 50–250 ml D5; maintenance 900 mg in 500 ml D5 (1.8 mg/ml) or 600 mg in 50 ml D5 by central line
- Concentrations >2 mg/ml must go via central line (phlebitis); arrest bolus may be given undiluted or in 20 ml D5

Dose adjustment — renal, hepatic and other conditions

Renal	No adjustment; not dialysed
Hepatic	Use with caution; stop if transaminases >3 × normal (acute IV hepatitis)
Other	Correct K^+ and Mg^{2+} first; halve digoxin dose; reduce warfarin 30–50%; interacts with statins, ciclosporin, tacrolimus

Cautions and adverse effects

- Hypotension and bradycardia during IV loading (polysorbate vehicle); heart block
- QT prolongation (TdP uncommon); thrombophlebitis
- Long-term: thyroid dysfunction (hypo/hyper), pulmonary fibrosis, hepatotoxicity, corneal deposits, photosensitivity, neuropathy
- Acute pulmonary toxicity/ARDS (rare) with high FiO_2

Antidote / reversal

No antidote. Bradycardia: atropine, pacing; hypotension: fluids, vasopressors.

ICU PEARL Amiodarone goes in dextrose, through a central line when concentrated — and halve the digoxin.

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Adenosine

Endogenous purine nucleoside antiarrhythmic (unclassified)

Drug and class

Adenosine — Endogenous purine nucleoside antiarrhythmic (unclassified).

Mechanism of action

Stimulates A1 receptors in the AV node, activating K^+ channels and hyperpolarising nodal tissue → transient AV block that terminates AV-nodal re-entrant tachycardias and unmasks atrial flutter/atrial tachycardia. Half-life <10 s (taken up by red cells and endothelium).

Dose in ICU

- **Regular narrow-complex SVT:** 6 mg rapid IV push followed by 20 ml NS flush; if no response after 1–2 min, 12 mg; may repeat 12 mg once
- **Central line:** start 3 mg
- **Heart transplant, dipyridamole or carbamazepine therapy:** start 1–3 mg (exaggerated effect)
- Also diagnostic in regular broad-complex tachycardia (only if regular and monomorphic)

Drug dilution and infusion

- Vial 3 mg/ml (2 ml = 6 mg); give undiluted
- Use antecubital/large vein, three-way tap and immediate 20 ml flush; raise the arm
- Record a rhythm strip during injection

Dose adjustment — renal, hepatic and other conditions

Renal	No adjustment
Hepatic	No adjustment
Other	Theophylline/caffeine antagonise (higher doses needed); dipyridamole and carbamazepine potentiate

Cautions and adverse effects

- Transient asystole/bradycardia, flushing, chest discomfort, dyspnoea, sense of doom (warn patient)
- Bronchospasm — avoid in severe asthma (use verapamil)
- **Contraindicated in pre-excited AF** (WPW with irregular broad tachycardia) — may precipitate VF
- Second/third-degree AV block, sick sinus without pacemaker

Antidote / reversal

Aminophylline/theophylline 50–100 mg IV for persistent bradycardia or bronchospasm (rarely needed).

ICU PEARL An irregular broad-complex tachycardia is never treated with adenosine.

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Lidocaine (Lignocaine)

Class Ib antiarrhythmic / amide local anaesthetic

52

Drug and class

Lidocaine (Lignocaine) — Class Ib antiarrhythmic / amide local anaesthetic.

Mechanism of action

Blocks fast Na^+ channels preferentially in depolarised, ischaemic ventricular tissue, shortening action potential duration; little effect on atrial tissue. Also used for analgesia and to blunt airway reflexes.

Dose in ICU

- **VF / pulseless VT (alternative to amiodarone):** 1–1.5 mg/kg IV; repeat 0.5–0.75 mg/kg every 5–10 min to max 3 mg/kg
- **Stable VT / post-arrest maintenance:** 1–4 mg/min infusion (20–50 mcg/kg/min)
- **Analgesic infusion (opioid-sparing):** 1–1.5 mg/kg bolus, then 1–2 mg/kg/h (ideal body weight)
- **Airway (intubation, raised ICP):** 1.5 mg/kg IV 3 min before

Drug dilution and infusion

- Preservative-free 2% (20 mg/ml) for IV; never use preparations with adrenaline IV
- Infusion: 1 g in 250 ml D5/NS = **4 mg/ml** (or 2 g in 500 ml); syringe 1 g in 50 ml = 20 mg/ml

Dose adjustment — renal, hepatic and other conditions

Renal	No adjustment (metabolites may accumulate with long infusions)
Hepatic	Reduce infusion rate by 50% (also in heart failure, shock, elderly) — high hepatic extraction
Other	Check levels (1.5–5 mcg/ml) if infusion >24 h; β-blockers and cimetidine raise levels

Cautions and adverse effects

- **Local anaesthetic systemic toxicity**: perioral numbness, tinnitus, confusion, seizures, then arrhythmias and cardiovascular collapse
- Bradycardia, AV block, hypotension
- Methaemoglobinaemia (rare)

Antidote / reversal

Local anaesthetic toxicity: **20% lipid emulsion** 1.5 ml/kg IV over 1 min, then 0.25 ml/kg/min (repeat bolus ×2, max 12 ml/kg); benzodiazepines for seizures.

ICU PEARL In shock and liver failure the same dose doubles the level — halve the infusion.

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Atropine

Antimuscarinic (anticholinergic) — tertiary amine belladonna alkaloid

Drug and class

Atropine — Antimuscarinic (anticholinergic) — tertiary amine belladonna alkaloid.

Mechanism of action

Competitive antagonist at muscarinic acetylcholine receptors: blocks vagal effects on the SA and AV nodes (increases heart rate and AV conduction), dries secretions, relaxes smooth muscle; reverses muscarinic features of cholinergic poisoning. No effect on nicotinic (muscle) features.

Dose in ICU

- **Symptomatic bradycardia:** 1 mg IV every 3–5 min to max 3 mg (ERC 0.5 mg repeats)
- **Organophosphate / carbamate poisoning:** 1.8–3 mg IV, **double the dose every 5 min** until atropinised (clear chest, HR >80, SBP >80, dry axillae); then infusion 10–20% of the total loading dose per hour
- **With neostigmine:** 0.015–0.02 mg/kg
- **Antisialagogue:** 0.3–0.6 mg IV/IM

Drug dilution and infusion

- Ampoules 0.6 mg/ml (and 1 mg/ml); give undiluted IV push
- OP infusion: e.g., 30 mg in 50 ml NS = 0.6 mg/ml (concentration by dose required)
- Doses <0.5 mg may cause paradoxical bradycardia

Dose adjustment — renal, hepatic and other conditions

Renal	No adjustment
Hepatic	No adjustment
Other	Ineffective in heart transplant (denervated) and infranodal block (Mobitz II, complete block with wide QRS) — pace/use adrenaline

Cautions and adverse effects

- Tachycardia, myocardial ischaemia
- **Anticholinergic toxicity**: agitated delirium, hyperthermia, ileus, urinary retention, mydriasis, dry hot skin
- Angle-closure glaucoma

Antidote / reversal

Anticholinergic toxicity: stop/reduce infusion (in OP poisoning), cool; **physostigmine** 0.5–2 mg slow IV (non-OP cases).

ICU PEARL In organophosphate poisoning titrate to a dry chest, not to pupil size or heart rate alone.

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Esmolol

Ultra-short-acting cardioselective β1-blocker (class II)

Drug and class

Esmolol — Ultra-short-acting cardioselective β1-blocker (class II).

Mechanism of action

Selective β1-adrenoceptor antagonist hydrolysed by red-cell esterases (half-life 9 min) — rapidly titratable rate control and BP reduction; effect gone 10–20 min after stopping.

Dose in ICU

- **Loading:** 500 mcg/kg over 1 min (optional)
- **Infusion:** 50 mcg/kg/min; increase by 50 mcg/kg/min every 4–5 min (re-bolus optional) to max 200–300 mcg/kg/min
- **Aortic dissection:** target HR <60 and SBP <120 — start before vasodilator
- **SVT / AF rate control, peri-operative hypertension, thyrotoxicosis**

Drug dilution and infusion

- Vials 10 mg/ml (10 ml) and premixed 10 mg/ml bags (2.5 g/250 ml); concentrate 250 mg/ml must be diluted
- Infusion: **2.5 g in 250 ml** NS/D5 = **10 mg/ml**; syringe 500 mg in 50 ml
- Example: 70 kg at 100 mcg/kg/min = 7 mg/min = 42 ml/h of 10 mg/ml

Dose adjustment — renal, hepatic and other conditions

Renal	No dose change; acid metabolite accumulates in renal failure (clinically minor)
Hepatic	No adjustment
Other	Avoid in decompensated heart failure, cardiogenic shock, high-grade AV block, severe bradycardia; cocaine toxicity (relative)

Cautions and adverse effects

- Hypotension (most common), bradycardia, heart block
- Bronchospasm (less than non-selective)
- Phlebitis and skin necrosis at concentrations >10 mg/ml
- Worsening heart failure

Antidote / reversal

Stop infusion (offset 10–20 min). Severe toxicity: **glucagon** 3–10 mg IV then 1–5 mg/h, high-dose insulin euglycaemia, calcium, pacing.

ICU PEARL The safe trial of β-blockade in a fragile heart — if it does not tolerate esmolol, it will not tolerate metoprolol.

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Metoprolol

Cardioselective β1-adrenoceptor blocker (class II)

Drug and class

Metoprolol — Cardioselective β1-adrenoceptor blocker (class II).

Mechanism of action

Competitive β1 antagonist reducing heart rate, AV conduction, contractility and renin release; no intrinsic sympathomimetic activity. Hepatic CYP2D6 metabolism; IV half-life 3–4 h.

Dose in ICU

- **IV rate control (AF/SVT) or ACS:** 2.5–5 mg IV over 2 min, repeat every 5 min to max 15 mg
- **Oral/NG:** 25–100 mg 12-hourly (tartrate); 25–200 mg daily (succinate)
- **Post-MI / HFrEF:** start low (12.5–25 mg) once stable

Drug dilution and infusion

- Ampoule 1 mg/ml (5 ml = 5 mg); give undiluted slow IV
- Not used as infusion

Dose adjustment — renal, hepatic and other conditions

Renal	No adjustment
Hepatic	Reduce dose (extensive hepatic metabolism)
Other	CYP2D6 inhibitors (fluoxetine, paroxetine, amiodarone) increase levels; avoid IV in early STEMI with heart failure or shock risk

Cautions and adverse effects

- Bradycardia, AV block, hypotension, cardiogenic shock in acute HF
- Bronchospasm (dose-dependent loss of selectivity)
- Masks hypoglycaemia; fatigue
- Abrupt withdrawal → rebound ischaemia/tachycardia

Antidote / reversal

Glucagon 3–10 mg IV over 1 min, then 3–5 mg/h; high-dose insulin euglycaemia therapy; calcium; atropine; pacing.

ICU PEARL Before IV metoprolol, look for signs of heart failure — β-blockade turns compensated low output into shock.

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Propranolol

Non-selective β-adrenoceptor blocker (class II)

Drug and class

Propranolol — Non-selective β-adrenoceptor blocker (class II).

Mechanism of action

Blocks β1 and β2 receptors (reduces HR, contractility, renin, portal pressure via splanchnic vasoconstriction); membrane-stabilising activity; inhibits peripheral T4 → T3 conversion. Lipophilic — crosses blood–brain barrier.

Dose in ICU

- **IV:** 0.5–1 mg over 1 min, repeat every 2 min to max 0.1 mg/kg (≈5–10 mg)
- **Thyroid storm:** 60–80 mg orally/NG every 4 h (or 0.5–1 mg IV; esmolol preferred if unstable)
- **Variceal bleeding prophylaxis:** 20–40 mg 12-hourly titrated to HR 55–60
- **Burns hypermetabolism / TBI sympathetic storm:** 10–40 mg 6-hourly titrated to HR reduction 15–20%

Drug dilution and infusion

- Ampoule 1 mg/ml; give undiluted slowly or diluted in 10 ml NS
- Oral tablets 10/40 mg crushed via NG

Dose adjustment — renal, hepatic and other conditions

Renal	No adjustment
Hepatic	Reduce dose (high first-pass metabolism, increased bioavailability in cirrhosis)
Other	Refractory ascites, SBP <90, Na <130 or AKI in cirrhosis — reduce or stop

Cautions and adverse effects

- **Bronchospasm** — avoid in asthma/COPD
- Bradycardia, heart block, hypotension, heart failure
- Masks hypoglycaemia symptoms; impairs glucose recovery
- Overdose: seizures, wide QRS (Na^+ channel blockade)

Antidote / reversal

Glucagon 3–10 mg IV then 3–5 mg/h; high-dose insulin; **sodium bicarbonate** for QRS widening; lipid emulsion in refractory overdose.

ICU PEARL The β-blocker of choice for portal hypertension and thyroid storm — avoid it in the wheezy patient.

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Digoxin

Cardiac glycoside — rate control and weak inotrope

Drug and class

Digoxin — Cardiac glycoside — rate control and weak inotrope.

Mechanism of action

Inhibits myocardial Na^+/K^+-ATPase → increased intracellular Ca^{2+} (positive inotropy) and enhanced vagal tone (slows SA rate and AV-node conduction). Narrow therapeutic index; renally excreted; half-life 36–48 h.

Dose in ICU

- **IV loading (AF rate control):** 0.25–0.5 mg IV, then 0.25 mg every 6 h to total 0.75–1.5 mg (8–12 mcg/kg) in 24 h
- **Maintenance:** 0.0625–0.25 mg daily (IV or oral), by renal function
- **Target level** 0.5–0.9 ng/ml (sample ≥6 h after dose)
- Useful in AF with hypotension or heart failure where β-blockers are limited

Drug dilution and infusion

- Ampoule 0.25 mg/ml (2 ml = 0.5 mg)
- Give slowly over 10–20 min undiluted or in 10–50 ml NS/D5
- Not given IM (painful, erratic)

Dose adjustment — renal, hepatic and other conditions

Renal	**Reduce** maintenance: CrCl 30–50 — 0.125 mg/day; <30 — 0.0625 mg daily or alternate days; ESRD — reduce loading dose by 25–50%; not dialysed
Hepatic	No adjustment
Other	**Hypokalaemia, hypomagnesaemia, hypercalcaemia**, hypothyroidism and hypoxia increase toxicity; amiodarone, verapamil, diltiazem, macrolides raise levels — halve dose

Cautions and adverse effects

- **Toxicity**: nausea, vomiting, confusion, xanthopsia, bradycardia, AV block, atrial tachycardia with block, bidirectional VT, hyperkalaemia (acute)
- Avoid in WPW with AF, HOCM, second/third-degree block
- DC cardioversion in toxicity → VF risk

Antidote / reversal

Digoxin-specific antibody (Fab) fragments: each 40 mg vial binds ≈0.5 mg digoxin; acute ingestion unknown — 10 vials; chronic toxicity — 3–6 vials. Correct K^+/Mg^{2+}; avoid calcium bolus if possible.

ICU PEARL In AKI, stop digoxin first and check the level — most ICU digoxin toxicity is renal.

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Procainamide

58

Class Ia antiarrhythmic (Na^+ and K^+ channel blocker)

Drug and class

Procainamide — Class Ia antiarrhythmic (Na^+ and K^+ channel blocker).

Mechanism of action

Blocks fast Na^+ channels (slows conduction, widens QRS) and K^+ channels (prolongs repolarisation); slows conduction through accessory pathways. Acetylated to N-acetylprocainamide (NAPA, class III, renally cleared).

Dose in ICU

- **Loading:** 20–50 mg/min (or 100 mg every 5 min) until arrhythmia suppressed, hypotension, QRS widens >50% or 17 mg/kg (≈1 g) given
- **Maintenance:** 1–4 mg/min
- **Indications:** stable monomorphic VT, **pre-excited AF (WPW)**, AF/flutter cardioversion
- Limited availability in India

Drug dilution and infusion

- Vial 100 mg/ml
- Loading: 1 g in 50 ml NS/D5 = 20 mg/ml; maintenance 2 g in 500 ml = **4 mg/ml**

Dose adjustment — renal, hepatic and other conditions

Renal	Reduce maintenance (CrCl <50: 25–50%) — NAPA accumulates; monitor levels
Hepatic	Reduce maintenance dose
Other	Heart failure: reduce loading and maintenance; monitor QRS and QTc

Cautions and adverse effects

- Hypotension (ganglionic blockade), especially with rapid infusion
- QRS widening, QT prolongation, torsades de pointes; avoid with prolonged QT
- Long-term: drug-induced lupus, agranulocytosis

Antidote / reversal

Sodium bicarbonate 1–2 mmol/kg for QRS widening; magnesium for TdP; overdrive pacing.

ICU PEARL The drug of choice for the irregular broad-complex tachycardia of WPW-AF when the patient is stable.

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Sotalol

59

Class III antiarrhythmic with non-selective β-blockade (class II)

Drug and class

Sotalol — Class III antiarrhythmic with non-selective β-blockade (class II).

Mechanism of action

Non-selective β-blocker (d,l-isomer) and potassium-channel (IKr) blocker prolonging repolarisation and refractoriness; dose-dependent QT prolongation. Renally excreted unchanged.

Dose in ICU

- **Oral:** 80 mg 12-hourly, increase to 120–160 mg 12-hourly after ≥3 days
- **IV (where available):** 75 mg over 5 h, then per renal function; IV loading regimens to reach oral steady state
- **Indications:** maintenance of sinus rhythm in AF, ventricular arrhythmias
- Start in hospital with continuous ECG for ≥3 days (5–6 doses)

Drug dilution and infusion

- Oral tablets 40/80 mg
- IV: 15 mg/ml — dilute to 120 ml in NS/D5 and infuse over 5 h

Dose adjustment — renal, hepatic and other conditions

Renal	CrCl 40–60: every 24 h; <40: **contraindicated** for AF (ventricular use — specialist dosing)
Hepatic	No adjustment
Other	Contraindicated if baseline QTc >450 ms, K^+ <4, Mg^{2+} low, bradycardia, asthma, decompensated HF

Cautions and adverse effects

- **Torsades de pointes** (dose and renal dependent) — check QTc 2–4 h after each dose; stop if QTc >500 ms
- Bradycardia, hypotension, heart failure
- Bronchospasm

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Antidote / reversal

TdP: **magnesium sulfate** 2 g IV, correct K^+, isoprenaline or overdrive pacing; β-blocker toxicity: glucagon.

ICU PEARL Sotalol is a β-blocker with a QT problem — calculate creatinine clearance before every dose change.

Ibutilide

60

Class III antiarrhythmic (pure IKr blocker / slow Na^+ current activator)

Drug and class

Ibutilide — Class III antiarrhythmic (pure IKr blocker / slow Na^+ current activator).

Mechanism of action

Prolongs atrial and ventricular action potential and refractoriness by blocking the rapid delayed rectifier K^+ current and enhancing the slow inward Na^+ current — pharmacological cardioversion of recent-onset AF and atrial flutter (flutter ≈60–75%).

Dose in ICU

- **Weight ≥60 kg:** 1 mg IV over 10 min; repeat once 10 min after end of first infusion if no conversion
- **Weight <60 kg:** 0.01 mg/kg over 10 min, repeat once
- Pre-treat with **magnesium sulfate 1–2 g IV** (reduces TdP, improves conversion)
- Stop infusion once rhythm converts or QT lengthens markedly

Drug dilution and infusion

- Vial 0.1 mg/ml (10 ml = 1 mg)
- Give undiluted or diluted in 50 ml NS/D5 over 10 min

Dose adjustment — renal, hepatic and other conditions

Renal	No adjustment
Hepatic	No adjustment; prolonged monitoring
Other	Avoid if QTc >440 ms, K^+ <4, Mg^{2+} low, LVEF <30%, recent class I/III drug

Cautions and adverse effects

- **Torsades de pointes** (2–4%, mostly within 1 h) — continuous ECG for ≥4 h and defibrillator ready
- Bradycardia, heart block, hypotension
- Limited availability in India

Antidote / reversal

TdP: magnesium 2 g IV, correct K^+, overdrive pacing/defibrillation.

ICU PEARL Ibutilide works best on flutter — but monitor for four hours, because TdP follows the drug, not the rhythm.

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Verapamil

Non-dihydropyridine calcium-channel blocker (class IV) — phenylalkylamine

Drug and class

Verapamil — Non-dihydropyridine calcium-channel blocker (class IV) — phenylalkylamine.

Mechanism of action

Blocks L-type Ca^{2+} channels in the SA and AV node and myocardium → slows AV conduction, reduces heart rate and contractility; arterial vasodilation. Terminates AV-nodal re-entry and controls ventricular rate in AF/flutter.

Dose in ICU

- **SVT / AF rate control:** 2.5–5 mg IV over 2–3 min; repeat 5–10 mg every 15–30 min to max 20 mg
- **Infusion (rarely):** 5–10 mg/h (0.005 mg/kg/min)
- **Oral:** 40–120 mg 8-hourly
- Alternative to adenosine in asthma

Drug dilution and infusion

- Ampoule 2.5 mg/ml; give undiluted slowly over ≥2 min (3 min in elderly)
- Infusion: 50 mg in 50 ml NS = 1 mg/ml

Dose adjustment — renal, hepatic and other conditions

Renal	No adjustment (monitor in severe impairment)
Hepatic	Reduce dose by 20–50% — high first-pass metabolism
Other	**Contraindicated**: WPW-AF, broad-complex tachycardia of unknown origin, HFrEF, hypotension, sick sinus, recent IV β-blocker

Cautions and adverse effects

- Hypotension, bradycardia, AV block, asystole
- Negative inotropy — precipitates heart failure
- Constipation; raises digoxin and other CYP3A4 substrate levels

Antidote / reversal

Calcium chloride 1 g (10 ml 10%) or gluconate 3 g IV, repeat; **high-dose insulin euglycaemia** 1 U/kg bolus then 1–10 U/kg/h; vasopressors; lipid emulsion; pacing/ECMO.

ICU PEARL Never give verapamil to a broad-complex tachycardia — assume VT until proven otherwise.

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Diltiazem

Non-dihydropyridine calcium-channel blocker (class IV) — benzothiazepine

Drug and class

Diltiazem — Non-dihydropyridine calcium-channel blocker (class IV) — benzothiazepine.

Mechanism of action

L-type Ca^{2+} channel blockade in nodal tissue and myocardium — slows AV conduction and heart rate with less negative inotropy and less vasodilation than verapamil; CYP3A4 inhibitor.

Dose in ICU

- **AF/flutter rate control:** 0.25 mg/kg IV over 2 min (≈15–20 mg); if inadequate after 15 min, 0.35 mg/kg (≈20–25 mg)
- **Infusion:** 5–15 mg/h (start 5–10 mg/h) titrated to heart rate
- **Oral:** 30–90 mg 6–8 hourly (convert from infusion: [rate (mg/h) × 3 + 3] × 10 = daily oral dose)

Drug dilution and infusion

- Vial 5 mg/ml (refrigerate) or lyophilised 25/100 mg
- Infusion: **125 mg in 125 ml** NS/D5 = **1 mg/ml** (or 100 mg in 100 ml)
- Bolus undiluted over 2 min

Dose adjustment — renal, hepatic and other conditions

Renal	No adjustment
Hepatic	Reduce dose; prolonged half-life
Other	Contraindicated: WPW-AF, broad-complex tachycardia, decompensated HFrEF, hypotension, second/third-degree block

Cautions and adverse effects

- Hypotension, bradycardia, AV block
- Worsening heart failure in reduced LVEF
- **CYP3A4 inhibition**: raises tacrolimus, ciclosporin, midazolam, fentanyl, statins, apixaban/rivaroxaban levels

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Antidote / reversal

Calcium chloride 1 g / gluconate 3 g IV; high-dose insulin euglycaemia; vasopressors; pacing.

ICU PEARL In AF with a preserved ejection fraction, diltiazem controls rate faster than amiodarone — check the LVEF first.

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CHAPTER 6 · CLASS SUMMARY

Antiarrhythmics and Cardiac Medications — At a Glance

Rate and rhythm control, bradycardia and tachyarrhythmia drugs

Drug	ICU dose	Dilution / infusion	Renal / hepatic / other	Key cautions	Antidote
Amiodarone	Arrest 300 mg then 150 mg; 150–300 mg load, then 900 mg/24 h	D5 only; 900 mg/500 ml; central if >2 mg/ml	No renal adj; caution hepatic	Hypotension, QT, thyroid, lung, liver	None
Adenosine	6 mg, then 12 mg, then 12 mg rapid push + flush	Undiluted 3 mg/ml; large vein	Start 3 mg central/transplant	Asystole, bronchospasm; no WPW-AF	Aminophylline
Lidocaine (Lignocaine)	Arrest 1–1.5 mg/kg (max 3 mg/kg); infusion 1–4 mg/min	1 g/250 ml = 4 mg/ml	↓50% hepatic failure/HF/shock	LAST — seizures, arrhythmia	Lipid emulsion 20%
Atropine	Bradycardia 1 mg q3–5 min (max 3 mg); OP doubling doses	Undiluted; OP infusion 10–20% of load/h	No adjustment	Anticholinergic toxicity; ineffective infranodal	Physostigmine
Esmolol	Load 500 mcg/kg; 50–300 mcg/kg/min	2.5 g/250 ml = 10 mg/ml	No adjustment	Hypotension, bradycardia, phlebitis	Glucagon; HDIE
Metoprolol	IV 2.5–5 mg q5 min (max 15 mg); oral 25–100 mg BD	Undiluted 1 mg/ml	↓ in hepatic failure	Bradycardia, HF, bronchospasm	Glucagon; HDIE
Propranolol	IV 0.5–1 mg q2 min (max 0.1 mg/kg); oral 10–80 mg	Undiluted 1 mg/ml	↓ in hepatic failure	Bronchospasm, hypoglycaemia masking	Glucagon; bicarbonate (QRS)
Digoxin	Load 0.75–1.5 mg/24 h; maintenance 0.0625–0.25 mg/day	Slow IV over 10–20 min	↓ maintenance by CrCl; ↑ toxicity with ↓K^+/↓Mg^{2+}	Narrow index, AV block, VT	Digoxin Fab fragments
Procainamide	Load 20–50 mg/min to 17 mg/kg; maintenance 1–4 mg/min	2 g/500 ml = 4 mg/ml	↓ in renal (NAPA) & hepatic failure	Hypotension, QT/TdP, lupus	Sodium bicarbonate
Sotalol	Oral 80–160 mg BD; IV 75 mg over 5 h	IV in 120 ml over 5 h	CrCl 40–60 q24h; <40 avoid	TdP, bradycardia	Magnesium; glucagon
Ibutilide	≥60 kg 1 mg over 10 min, repeat once; <60 kg 0.01 mg/kg	Undiluted or 50 ml over 10 min	No adjustment	TdP — monitor ≥4 h	Magnesium
Verapamil	2.5–5 mg IV, then 5–10 mg (max 20 mg)	Undiluted 2.5 mg/ml slow	↓20–50% in hepatic failure	Hypotension, HF; no WPW/VT	Calcium; HDIE
Diltiazem	0.25 mg/kg, then 0.35 mg/kg; infusion 5–15 mg/h	125 mg/125 ml = 1 mg/ml	↓ in hepatic failure	Hypotension, HF, CYP3A4	Calcium; HDIE

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Nitroglycerin (Glyceryl Trinitrate)

Organic nitrate vasodilator (predominant venodilator)

Drug and class

Nitroglycerin (Glyceryl Trinitrate) — Organic nitrate vasodilator (predominant venodilator).

Mechanism of action

Converted to nitric oxide in vascular smooth muscle → cGMP → relaxation. Low doses dilate veins (reduce preload), higher doses dilate arteries and coronary arteries (reduce afterload, relieve ischaemia).

Dose in ICU

- **Infusion:** start 5–10 mcg/min, increase by 5–10 mcg/min every 3–5 min; usual 10–200 mcg/min (up to 400)
- **Acute pulmonary oedema with hypertension (SCAPE):** high-dose boluses 400–800 mcg IV or 100–200 mcg/min
- **Sublingual:** 0.4 mg every 5 min ×3 (ACS)
- **Indications:** ACS with ongoing pain/hypertension, acute heart failure, peri-operative hypertension

Drug dilution and infusion

- Ampoule 5 mg/ml
- Infusion: **50 mg in 50 ml** NS/D5 = **1 mg/ml** (1000 mcg/ml); 10 mcg/min = 0.6 ml/h
- Use glass or non-PVC syringe/tubing (adsorption to PVC)

Dose adjustment — renal, hepatic and other conditions

Renal	No adjustment
Hepatic	No adjustment
Other	Hypovolaemia: severe hypotension — correct first

Cautions and adverse effects

- Hypotension, reflex tachycardia, headache
- **Contraindicated**: PDE-5 inhibitors (sildenafil 24 h, tadalafil 48 h), RV infarction, severe aortic stenosis, HOCM, raised ICP, SBP <90
- Tolerance after 24–48 h continuous use
- Methaemoglobinaemia at high doses

Antidote / reversal

Hypotension: stop infusion (half-life 2–3 min), elevate legs, fluids. Methaemoglobinaemia: **methylene blue** 1–2 mg/kg IV.

ICU PEARL Ask about sildenafil before the first dose — the combination can be lethal.

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Sodium Nitroprusside

Direct-acting balanced arterial and venous vasodilator (nitric oxide donor)

Drug and class

Sodium Nitroprusside — Direct-acting balanced arterial and venous vasodilator (nitric oxide donor).

Mechanism of action

Spontaneously releases nitric oxide (and cyanide) in blood → cGMP-mediated relaxation of arterial and venous smooth muscle; onset seconds, offset 1–2 min — the most titratable antihypertensive.

Dose in ICU

- **Infusion:** start 0.25–0.5 mcg/kg/min, titrate every 5 min; usual 0.5–2 mcg/kg/min
- **Maximum 10 mcg/kg/min for ≤10 min**; keep ≤2 mcg/kg/min to limit cyanide
- **Indications:** hypertensive emergency (with arterial line), acute severe MR/AR with heart failure, aortic dissection (after β-blockade)

Drug dilution and infusion

- Vial 50 mg powder — reconstitute with 2–3 ml D5
- Infusion: **50 mg in 50 ml D5** = **1 mg/ml** (or 50 mg in 250 ml = 200 mcg/ml)
- **Protect from light** (wrap syringe and tubing); discard if blue/green; invasive BP monitoring

Dose adjustment — renal, hepatic and other conditions

Renal	**Thiocyanate accumulates** — limit dose/duration; monitor levels if >72 h (toxic >10 mg/dl)
Hepatic	Cyanide accumulates (reduced rhodanese) — avoid high doses
Other	Pregnancy (fetal cyanide) — avoid; vitamin B12 deficiency, Leber's optic atrophy

Cautions and adverse effects

- Precipitous hypotension; reflex tachycardia; rebound hypertension
- **Cyanide toxicity**: metabolic (lactic) acidosis, high venous O_2 saturation, confusion, arrhythmia
- Thiocyanate toxicity: confusion, psychosis, seizures, hypothyroidism
- Coronary steal; raises ICP; worsens hypoxaemia (inhibits HPV)

Antidote / reversal

Cyanide: **hydroxocobalamin 5 g IV** over 15 min (repeat once) or **sodium thiosulfate** 12.5 g IV; prophylactic thiosulfate 10:1 ratio with high doses.

ICU PEARL Rising lactate on nitroprusside is cyanide until proven otherwise.

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Nicardipine

Dihydropyridine calcium-channel blocker (IV arterial vasodilator)

Drug and class

Nicardipine — Dihydropyridine calcium-channel blocker (IV arterial vasodilator).

Mechanism of action

Highly vascular-selective L-type Ca^{2+} channel blocker → arteriolar dilation (systemic, coronary and cerebral) with minimal negative inotropy or AV-nodal effect; predictable, titratable BP reduction (onset 5–15 min).

Dose in ICU

- **Infusion:** start 5 mg/h, increase by 2.5 mg/h every 5–15 min to max 15 mg/h
- Reduce to 3 mg/h once target reached
- **Indications:** hypertensive emergency, acute ischaemic stroke/ICH BP control, pre-eclampsia, post-operative hypertension

Drug dilution and infusion

- Ampoule 2.5 mg/ml (10 ml = 25 mg)
- Infusion: 25 mg in 240 ml NS/D5 = **0.1 mg/ml** (premixed 20 mg/200 ml); syringe 25 mg in 50 ml = 0.5 mg/ml (central line)
- Peripheral line: change site every 12 h (phlebitis)

Dose adjustment — renal, hepatic and other conditions

Renal	No major adjustment; titrate
Hepatic	Reduce starting dose; prolonged effect
Other	Advanced aortic stenosis — avoid; CYP3A4 substrate (and inhibitor — raises ciclosporin/tacrolimus)

Cautions and adverse effects

- Hypotension, reflex tachycardia, headache, flushing
- Phlebitis at infusion site
- Myocardial ischaemia from reflex tachycardia (caution in ACS)

Antidote / reversal

No antidote; stop infusion (offset 30–40 min); fluids, vasopressors; calcium for severe overdose.

ICU PEARL The easiest titratable drug for stroke BP targets — start at 5 mg/h and change the cannula every 12 hours.

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Clevidipine

Ultra-short-acting dihydropyridine calcium-channel blocker

66

Drug and class

Clevidipine — Ultra-short-acting dihydropyridine calcium-channel blocker.

Mechanism of action

Arterial-selective L-type Ca^{2+} channel blocker metabolised by blood and tissue esterases (half-life ≈1 min) — rapid, organ-independent onset and offset; no effect on venous capacitance or myocardial contractility.

Dose in ICU

- **Infusion:** start 1–2 mg/h; double every 90 s initially, then smaller increments every 5–10 min
- Usual 4–6 mg/h; maximum 32 mg/h (≤21 mg/h average over 24 h because of lipid load)
- **Indications:** hypertensive emergency, peri-operative hypertension, aortic dissection, ICH

Drug dilution and infusion

- Ready-to-use lipid emulsion **0.5 mg/ml** — do not dilute
- Strict asepsis; discard open vial after 12 h; 2 kcal/ml (lipid) — include in nutrition
- Limited availability in India

Dose adjustment — renal, hepatic and other conditions

Renal	No adjustment
Hepatic	No adjustment
Other	Max lipid ≈1000 ml/24 h; contraindicated in severe aortic stenosis and defective lipid metabolism (pancreatitis, hyperlipidaemia)

Cautions and adverse effects

- Hypotension, reflex tachycardia, atrial fibrillation
- **Contraindicated** in soy or egg allergy
- Rebound hypertension if not transitioned to oral agents

Antidote / reversal

No antidote; stop infusion (offset 5–15 min).

ICU PEARL Behaves like nitroprusside without cyanide — but it is a lipid emulsion, so count the calories.

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Labetalol

Combined α1- and non-selective β-adrenoceptor blocker

Drug and class

Labetalol — Combined α1- and non-selective β-adrenoceptor blocker.

Mechanism of action

Competitive β1/β2 and α1 antagonist (β:α ratio ≈7:1 IV) — reduces SVR without reflex tachycardia while maintaining cardiac output and cerebral/coronary flow.

Dose in ICU

- **IV bolus:** 20 mg over 2 min, then 40–80 mg every 10 min to max 300 mg
- **Infusion:** 0.5–2 mg/min (some up to 3 mg/min), titrated
- **Pre-eclampsia/eclampsia:** 20 mg, then 40, 80, 80 mg every 10 min (max 220–300 mg)
- **Acute stroke / ICH, aortic dissection, hypertensive emergency**

Drug dilution and infusion

- Ampoule 5 mg/ml (20 ml = 100 mg)
- Infusion: **undiluted 5 mg/ml** by syringe pump, or 200 mg in 200 ml NS/D5 = 1 mg/ml
- Example: 2 mg/min = 120 mg/h = 24 ml/h of 5 mg/ml

Dose adjustment — renal, hepatic and other conditions

Renal	No adjustment
Hepatic	Reduce dose (extensive hepatic metabolism); rare hepatotoxicity
Other	Avoid in asthma/COPD with bronchospasm, bradycardia, heart block, decompensated heart failure; caution in cocaine toxicity

Cautions and adverse effects

- Bradycardia, heart block, orthostatic hypotension
- Bronchospasm, heart failure
- Scalp tingling, nausea; neonatal bradycardia/hypoglycaemia after maternal use

Antidote / reversal

Glucagon 3–10 mg IV then infusion; atropine; high-dose insulin euglycaemia; vasopressors.

ICU PEARL First choice in hypertensive emergencies of pregnancy and stroke — check for wheeze and bradycardia first.

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Hydralazine

Direct-acting arteriolar vasodilator (phthalazine)

Drug and class

Hydralazine — Direct-acting arteriolar vasodilator (phthalazine).

Mechanism of action

Directly relaxes arteriolar smooth muscle (interferes with IP3-mediated Ca^{2+} release, opens K^+ channels) → reduced afterload with reflex tachycardia, increased renin and fluid retention. Onset 10–20 min, unpredictable duration 2–12 h.

Dose in ICU

- **Severe hypertension in pregnancy:** 5 mg IV over 2 min, then 5–10 mg every 20–30 min (max 20–30 mg)
- **Other hypertensive urgency/emergency:** 10–20 mg IV every 4–6 h
- **Oral (heart failure with nitrate, HFrEF):** 25–75 mg 8-hourly

Drug dilution and infusion

- Ampoule 20 mg powder — reconstitute with 1 ml water; dilute to 10 ml NS for slow IV
- Infusion rarely used

Dose adjustment — renal, hepatic and other conditions

Renal	Increase dosing interval (8–12 h if CrCl <30)
Hepatic	Reduce dose
Other	Slow acetylators — higher levels and lupus risk

Cautions and adverse effects

- Reflex tachycardia, myocardial ischaemia — **avoid in ACS and aortic dissection** unless β-blocked
- Unpredictable, prolonged hypotension (stacking doses)
- Headache, flushing, fluid retention
- Drug-induced lupus with chronic use (>200 mg/day)

Antidote / reversal

No antidote; fluids and vasopressors for hypotension.

ICU PEARL Hydralazine's effect lasts much longer than its dosing interval suggests — wait before you repeat.

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Enalaprilat

Intravenous angiotensin-converting enzyme inhibitor (active metabolite of enalapril)

69

Drug and class

Enalaprilat — Intravenous angiotensin-converting enzyme inhibitor (active metabolite of enalapril).

Mechanism of action

Inhibits ACE, reducing angiotensin II (vasoconstriction, aldosterone) and increasing bradykinin → arterial and venous dilation and natriuresis. Onset 15 min, peak 1–4 h, duration ≈6 h — not suitable for rapid titration.

Dose in ICU

- **Hypertension:** 1.25 mg IV over 5 min every 6 h; may increase to 5 mg every 6 h
- **On diuretics, hypovolaemia or CrCl <30:** start 0.625 mg
- Convert to oral enalapril 5 mg/day when possible
- Availability limited in India

Drug dilution and infusion

- Ampoule 1.25 mg/ml
- Give undiluted over 5 min or diluted in 50 ml NS/D5

Dose adjustment — renal, hepatic and other conditions

Renal	CrCl <30: 0.625 mg every 6 h; dialysed
Hepatic	No adjustment
Other	Contraindicated in pregnancy, history of angioedema, bilateral renal artery stenosis; avoid in AKI and hyperkalaemia

Cautions and adverse effects

- First-dose hypotension, especially in hypovolaemia/high renin states
- Hyperkalaemia, acute kidney injury
- Angioedema (bradykinin-mediated)
- Fetal toxicity

Antidote / reversal

No specific antidote. Hypotension: fluids (± angiotensin II); angioedema: airway management, consider icatibant or fresh frozen plasma.

ICU PEARL Not an emergency drug — its slow onset makes it a bridge to oral therapy, not a rescue.

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CHAPTER 7 · CLASS SUMMARY

Antihypertensives and Vasodilators — At a Glance

Titratable IV agents for hypertensive emergencies, heart failure and aortic dissection

Drug	ICU dose	Dilution / infusion	Renal / hepatic / other	Key cautions	Antidote
Nitroglycerin (Glyceryl Trinitrate)	5–200 mcg/min (up to 400); SCAPE boluses	50 mg/50 ml = 1 mg/ml; non-PVC	No adjustment	Hypotension; no PDE-5/RV infarct	Methylene blue (MetHb)
Sodium Nitroprusside	0.25–2 mcg/kg/min (max 10 for ≤10 min)	50 mg/50 ml D5 = 1 mg/ml; protect from light	Thiocyanate ↑ renal; cyanide ↑ hepatic	Cyanide toxicity, hypotension	Hydroxocobalamin; thiosulfate
Nicardipine	5–15 mg/h titrated by 2.5 mg/h	25 mg in 250 ml = 0.1 mg/ml	↓ in hepatic failure	Reflex tachycardia, phlebitis	None
Clevidipine	1–2 mg/h, double q90 s; usual 4–6, max 32 mg/h	Ready 0.5 mg/ml emulsion	No adjustment; lipid limit	Reflex tachycardia, soy/egg allergy	None
Labetalol	20 mg then 40–80 mg q10 min (max 300 mg); 0.5–2 mg/min	Undiluted 5 mg/ml or 1 mg/ml	↓ in hepatic failure	Bradycardia, bronchospasm	Glucagon
Hydralazine	5–10 mg IV q20–30 min (pregnancy); 10–20 mg q4–6h	20 mg in 10 ml slow IV	Longer interval if CrCl <30; ↓ hepatic	Reflex tachycardia, unpredictable	None
Enalaprilat	1.25 mg IV q6h (up to 5 mg q6h)	Undiluted over 5 min	0.625 mg if CrCl <30	Hypotension, ↑K^+, AKI, angioedema	None

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Furosemide

Loop diuretic (sulfonamide derivative)

70

Drug and class

Furosemide — Loop diuretic (sulfonamide derivative).

Mechanism of action

Inhibits the Na^+-K^+-$2Cl^-$ co-transporter in the thick ascending limb of the loop of Henle after secretion into the tubular lumen (needs renal blood flow and is albumin-bound) — potent natriuresis; IV venodilation precedes diuresis.

Dose in ICU

- **Acute heart failure:** 20–40 mg IV in diuretic-naïve; on oral loop — 1–2.5 × the total daily oral dose IV (DOSE trial), bolus or infusion
- **Infusion:** 40 mg bolus then 5–40 mg/h (max ≈240 mg/day in normal renal function; higher in CKD)
- **Furosemide stress test (AKI):** 1 mg/kg (1.5 mg/kg if on loop diuretic); <200 ml urine in 2 h predicts progression
- Target urine Na >50–70 mmol/L at 2 h or urine output >100–150 ml/h in the first 6 h

Drug dilution and infusion

- Ampoule 10 mg/ml
- Infusion: **250 mg in 50 ml** = 5 mg/ml, or undiluted 10 mg/ml (500 mg/50 ml)
- Bolus rate ≤4 mg/min for doses >120 mg (ototoxicity); protect from light; incompatible with milrinone, dobutamine (precipitation) — separate line

Dose adjustment — renal, hepatic and other conditions

Renal	Higher doses needed (reduced secretion): CrCl <30 may need 80–200 mg boluses; ineffective in anuria
Hepatic	Cirrhosis: may precipitate hepatic encephalopathy, hypokalaemia and hepatorenal syndrome — combine with spironolactone
Other	Hypoalbuminaemia reduces delivery — albumin co-administration debated; correct hypokalaemia/hypomagnesaemia

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Cautions and adverse effects

- Hypovolaemia, pre-renal AKI, hypotension
- **Hypokalaemia, hypomagnesaemia, hyponatraemia**, hypochloraemic metabolic alkalosis, hyperuricaemia
- Ototoxicity (high dose, rapid bolus, with aminoglycosides)
- Sulfonamide allergy (cross-reactivity low); pancreatitis

Antidote / reversal

No antidote. Over-diuresis: stop, replace volume and electrolytes.

ICU PEARL Measure the response at 2 and 6 hours — if the urine sodium is low, double the dose, do not repeat it.

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Torsemide (Torasemide)

Loop diuretic (pyridine-sulfonylurea)

71

Drug and class

Torsemide (Torasemide) — Loop diuretic (pyridine-sulfonylurea).

Mechanism of action

Inhibits the Na^+-K^+-$2Cl^-$ co-transporter in the thick ascending limb; high and predictable oral bioavailability (80–100%), longer duration (6–8 h) and mild anti-aldosterone/anti-fibrotic effects. Mainly hepatic clearance.

Dose in ICU

- **Oral/IV:** 10–20 mg once daily, double as needed to max 200 mg/day
- **Infusion:** 20 mg bolus then 5–20 mg/h
- **Equivalence:** torsemide 20 mg ≈ furosemide 40 mg IV / 80 mg oral ≈ bumetanide 1 mg
- Useful when oral furosemide absorption is unreliable (gut oedema)

Drug dilution and infusion

- Ampoule 10 mg/ml (where available); tablets 10/20/100 mg
- IV bolus over 2 min; infusion 100 mg in 50 ml NS = 2 mg/ml

Dose adjustment — renal, hepatic and other conditions

Renal	No dose change but larger doses needed for effect; not dialysed
Hepatic	Hepatically metabolised — caution; precipitates encephalopathy in cirrhosis
Other	Elderly — start 5–10 mg

Cautions and adverse effects

- Hypokalaemia, hypomagnesaemia, hypovolaemia, metabolic alkalosis
- Ototoxicity (less than furosemide)
- Hyperglycaemia, hyperuricaemia; sulfonamide-type allergy

Antidote / reversal

No antidote; volume and electrolyte replacement.

ICU PEARL In gut oedema, switching oral furosemide to torsemide fixes the absorption problem.

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Bumetanide

Loop diuretic (potent, short-acting)

Drug and class

Bumetanide — Loop diuretic (potent, short-acting).

Mechanism of action

Na^+-K^+-$2Cl^-$ co-transporter inhibitor ≈40 times as potent as furosemide by weight, with near-complete oral bioavailability and partial hepatic clearance.

Dose in ICU

- **IV/IM:** 0.5–1 mg, repeat every 2–3 h to max 10 mg/day
- **Infusion:** 1 mg bolus then 0.5–2 mg/h
- **Equivalence:** 1 mg bumetanide ≈ 40 mg IV furosemide
- Useful in furosemide allergy or resistance

Drug dilution and infusion

- Ampoule 0.25 mg/ml (2 ml = 0.5 mg)
- IV bolus over 1–2 min undiluted; infusion 5 mg in 50 ml NS = 0.1 mg/ml

Dose adjustment — renal, hepatic and other conditions

Renal	Larger doses needed; avoid with nephrotoxins
Hepatic	Caution — hepatic encephalopathy, hypokalaemia in cirrhosis
Other	Elderly: start low

Cautions and adverse effects

- Hypovolaemia, hypokalaemia, hypomagnesaemia, alkalosis
- **Myalgia and muscle cramps** at high doses
- Ototoxicity (less than furosemide), thrombocytopenia (rare)

Antidote / reversal

No antidote; supportive.

ICU PEARL Count micrograms carefully: a 'furosemide-sized' dose of bumetanide is a 40-fold overdose.

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Mannitol

Osmotic diuretic / hyperosmolar agent (six-carbon sugar alcohol)

Drug and class

Mannitol — Osmotic diuretic / hyperosmolar agent (six-carbon sugar alcohol).

Mechanism of action

Freely filtered, non-reabsorbed osmotic agent: raises plasma osmolality drawing water from brain parenchyma (lowers ICP within 15–30 min); immediate plasma expansion reduces blood viscosity and improves cerebral microcirculation; produces osmotic diuresis.

Dose in ICU

- **Raised ICP / impending herniation:** 0.25–1 g/kg IV over 15–20 min (20% solution: 1 g/kg = 5 ml/kg); repeat every 4–6 h as needed
- **Hold if serum osmolality >320 mOsm/kg or osmolar gap >20** (gap better reflects mannitol accumulation)
- Insert urinary catheter; replace urine losses to avoid hypovolaemia

Drug dilution and infusion

- 20% solution = 200 mg/ml (100 ml = 20 g); 10% also available
- Use an **in-line filter**; inspect for crystals — warm to redissolve
- Peripheral administration acceptable

Dose adjustment — renal, hepatic and other conditions

Renal	**Contraindicated in anuria**; avoid in established AKI (osmotic nephrosis) — prefer hypertonic saline
Hepatic	No adjustment
Other	Heart failure/pulmonary oedema: initial volume expansion — avoid; hypovolaemia worsened by diuresis

Cautions and adverse effects

- Hypovolaemia and hypotension after diuresis; acute kidney injury
- Electrolyte disturbance: initial dilutional hyponatraemia, then hypernatraemia, hypo-/hyperkalaemia
- Pulmonary oedema; rebound intracranial hypertension with prolonged use (leak through damaged BBB)
- Extravasation causes tissue injury

Antidote / reversal

No antidote; haemodialysis removes mannitol in toxicity.

ICU PEARL Check the osmolar gap, not just osmolality — the gap tells you how much mannitol is still in the blood.

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Hypertonic Saline (3% NaCl)

Hyperosmolar sodium chloride solution (osmotherapy and sodium replacement)

Drug and class

Hypertonic Saline (3% NaCl) — Hyperosmolar sodium chloride solution (osmotherapy and sodium replacement).

Mechanism of action

3% NaCl contains 513 mmol/L Na^+ (osmolality ≈1027 mOsm/L). Raises serum sodium and osmolality, drawing water out of brain cells (lowers ICP) and expanding intravascular volume; corrects symptomatic hyponatraemia.

Dose in ICU

- **Severe symptomatic hyponatraemia** (seizure, coma): 100–150 ml 3% IV over 10–20 min, repeat up to 3 times until symptoms improve or Na^+ rises 4–6 mmol/L
- **Raised ICP:** 2–5 ml/kg (≈150–250 ml) of 3% over 15–20 min, or 30 ml of 23.4% via central line; maintenance 0.5–1 ml/kg/h targeting Na^+ 145–155
- **Correction limit in hyponatraemia:** ≤10 mmol/L in 24 h (≤8 if high risk: alcohol, malnutrition, hypokalaemia, liver disease)
- Check Na^+ every 2–4 h during therapy

Drug dilution and infusion

- Commercial 3% NaCl (513 mmol/L) bottles — use ready-made solution, do not prepare at the bedside unless protocol exists
- 3% may be given peripherally (large vein); 23.4% only via central line
- Expected rise ≈ 1 mmol/L per 1 ml/kg of 3%

Dose adjustment — renal, hepatic and other conditions

Renal	Caution — fluid and chloride load; monitor Na^+ closely
Hepatic	Cirrhosis: high ODS risk — slow correction
Other	Heart failure: volume overload; stop if Na^+ >155–160 or osmolality >320 in ICP therapy

Cautions and adverse effects

- **Osmotic demyelination syndrome** with over-rapid correction of chronic hyponatraemia
- Hyperchloraemic metabolic acidosis, volume overload, pulmonary oedema
- Hypokalaemia; phlebitis; rebound cerebral oedema if stopped abruptly

Antidote / reversal

Over-correction: **re-lower Na^+** with 5% dextrose (3–6 ml/kg/h) and **desmopressin 2–4 mcg IV** every 6–8 h.

ICU PEARL For hyponatraemic seizures: 150 ml of 3% now, then think about the cause.

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Spironolactone

Potassium-sparing diuretic (mineralocorticoid receptor antagonist)

Drug and class

Spironolactone — Potassium-sparing diuretic (mineralocorticoid receptor antagonist).

Mechanism of action

Competitive antagonist of aldosterone at mineralocorticoid receptors in the distal tubule and collecting duct — natriuresis with K^+ and H^+ retention; anti-fibrotic cardiac effects. Onset 2–3 days (active metabolite canrenone).

Dose in ICU

- **Cirrhotic ascites:** 100 mg daily with furosemide 40 mg (ratio 100:40), increase every 3–5 days to max 400 mg spironolactone / 160 mg furosemide
- **HFrEF:** 12.5–25 mg daily (max 50 mg) if K^+ <5.0 and eGFR >30
- **Primary hyperaldosteronism / resistant hypertension:** 25–100 mg daily
- IV potassium canrenoate 200–400 mg/day where available

Drug dilution and infusion

- Oral tablets 25/50/100 mg — crush via NG
- No IV spironolactone (canrenoate IV in some countries)

Dose adjustment — renal, hepatic and other conditions

Renal	eGFR 30–50: 12.5–25 mg daily or alternate days; **avoid if eGFR <30 or K^+ >5.0**
Hepatic	Used in cirrhosis — monitor K^+, Na^+ and renal function; may precipitate encephalopathy with electrolyte shifts
Other	Avoid with ACE inhibitor + ARB combination, potassium supplements, trimethoprim; AKI — stop

Cautions and adverse effects

- **Hyperkalaemia** (especially with AKI, ACEi/ARB, NSAIDs, diabetes, elderly)
- Hyponatraemia, AKI, metabolic acidosis
- Gynaecomastia, menstrual disturbance (anti-androgen)

Antidote / reversal

No antidote; treat hyperkalaemia (calcium, insulin–dextrose, salbutamol, binders, dialysis).

ICU PEARL In the ICU, stop spironolactone on the first day of AKI — hyperkalaemia follows quickly.

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Acetazolamide

Carbonic anhydrase inhibitor diuretic (sulfonamide)

76

Drug and class

Acetazolamide — Carbonic anhydrase inhibitor diuretic (sulfonamide).

Mechanism of action

Inhibits carbonic anhydrase in the proximal tubule — bicarbonate, Na^+ and water excretion (alkaline urine, hyperchloraemic acidosis); reduces aqueous humour and CSF production; stimulates ventilation via metabolic acidosis.

Dose in ICU

- **Metabolic alkalosis (diuretic-induced, post-hypercapnic):** 250–500 mg IV/oral 8–12 hourly for 1–2 doses, repeat by pH/HCO_3^-
- **Acute heart failure (ADVOR):** 500 mg IV daily with loop diuretic
- **Idiopathic intracranial hypertension / CSF leak:** 250–500 mg 12-hourly
- **Acute mountain sickness prophylaxis:** 125–250 mg 12-hourly; acute angle-closure glaucoma 500 mg IV

Drug dilution and infusion

- Vial 500 mg powder — reconstitute with 5 ml water = **100 mg/ml**; give slowly IV over 2–5 min or in 50 ml NS
- Avoid IM (painful, alkaline)

Dose adjustment — renal, hepatic and other conditions

Renal	CrCl 10–50: every 12 h; <10: **avoid** (ineffective, acidosis)
Hepatic	**Avoid in cirrhosis** — increases ammonia, precipitates encephalopathy
Other	Hypokalaemia and hyperchloraemic acidosis: correct K^+ first; COPD with severe hypercapnia — may worsen acidosis

Cautions and adverse effects

- Hypokalaemia, hyperchloraemic metabolic acidosis
- Paraesthesia, drowsiness, renal stones
- Sulfonamide allergy, aplastic anaemia (rare), Stevens–Johnson syndrome

Antidote / reversal

No antidote; supportive; bicarbonate for severe acidosis.

ICU PEARL Use acetazolamide for the alkalaemic patient who cannot wean — but never in liver failure.

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Potassium Chloride (KCl)

Electrolyte replacement — potassium salt

77

Drug and class

Potassium Chloride (KCl) — Electrolyte replacement — potassium salt.

Mechanism of action

Replaces total body potassium (98% intracellular), restoring resting membrane potential of nerve and muscle and preventing arrhythmias. Chloride corrects associated hypochloraemic alkalosis.

Dose in ICU

- **Mild (K^+ 3.0–3.5):** oral 40–80 mmol/day in divided doses, or IV 10 mmol/h
- **Moderate–severe (K^+ <3.0, or arrhythmia):** 10–20 mmol/h IV; each 10 mmol raises K^+ ≈0.1 mmol/L
- **Life-threatening (arrhythmia, paralysis):** up to 40 mmol/h via central line with continuous ECG and hourly K^+
- Recheck K^+ after every 40–60 mmol; correct magnesium simultaneously

Drug dilution and infusion

- Ampoule 15% KCl 10 ml = 1.5 g = **20 mmol** — **never give undiluted or as bolus (fatal)**
- Peripheral: ≤40 mmol/L (e.g., 20 mmol in 500 ml NS) at ≤10 mmol/h
- Central: 20 mmol in 50–100 ml NS over 1 h (≤20 mmol/h routinely); use infusion pump only; mix bag thoroughly

Dose adjustment — renal, hepatic and other conditions

Renal	Reduce dose and rate in AKI/CKD/oliguria; monitor K^+ every 2–4 h
Hepatic	No adjustment; hypokalaemia worsens hepatic encephalopathy — correct
Other	**Refractory hypokalaemia — correct Mg^{2+}**; DKA: give K^+ before insulin if K^+ <3.3; avoid dextrose diluent in severe hypokalaemia (insulin release)

Cautions and adverse effects

- **Hyperkalaemia and cardiac arrest** with rapid or undiluted administration
- Phlebitis and pain with peripheral concentrations >40 mmol/L; extravasation injury
- Oral KCl: GI irritation, ulceration

Antidote / reversal

Hyperkalaemia: **calcium gluconate 10% 30 ml**, insulin 10 U + dextrose 25 g, salbutamol nebulised 10–20 mg, stop K^+, dialysis.

ICU PEARL Concentrated KCl ampoules belong in a locked cupboard — never on the ward trolley.

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Magnesium Sulfate

78

Electrolyte replacement / antiarrhythmic / anticonvulsant (in eclampsia) / bronchodilator

Drug and class

Magnesium Sulfate — Electrolyte replacement / antiarrhythmic / anticonvulsant (in eclampsia) / bronchodilator.

Mechanism of action

Physiological calcium antagonist: stabilises excitable membranes, blocks NMDA receptors and presynaptic acetylcholine release, relaxes smooth muscle (bronchial, vascular), shortens early afterdepolarisations (TdP). Cofactor for Na^+/K^+-ATPase.

Dose in ICU

- **Hypomagnesaemia:** 1–2 g IV over 15–60 min; severe/symptomatic 2–4 g over 1–2 h; up to 8 g/24 h
- **Torsades de pointes:** 2 g IV over 1–2 min (arrest) or over 15 min (with pulse); repeat once
- **Eclampsia / severe pre-eclampsia:** 4 g IV over 15–20 min, then 1 g/h for 24 h (Zuspan); or Pritchard: 4 g IV + 5 g IM each buttock, then 5 g IM every 4 h
- **Acute severe asthma:** 2 g IV over 20 min; **AF rate control adjunct:** 2 g over 20 min

Drug dilution and infusion

- 50% solution = 500 mg/ml (2 ml = 1 g = 4 mmol); 1 g = 4 mmol = 8 mEq
- Dilute to ≤20% for IV: e.g., 2 g in 50–100 ml NS; eclampsia 4 g in 100 ml over 15–20 min; maintenance 20 g in 500 ml NS at 25 ml/h = 1 g/h

Dose adjustment — renal, hepatic and other conditions

Renal	**Reduce dose by 50%** and check levels in AKI/oliguria (eclampsia: reduce maintenance to 0.5 g/h, check Mg^{2+})
Hepatic	No adjustment
Other	Myasthenia gravis — avoid (worsens weakness); potentiates NMBAs and CCBs

Cautions and adverse effects

- Toxicity: loss of patellar reflexes (Mg^{2+} >3.5–5 mmol/L), respiratory depression (>5–6.5), heart block and cardiac arrest (>7.5)
- Flushing, hypotension with rapid infusion
- Monitor reflexes, respiratory rate (≥12/min) and urine output (≥30 ml/h) hourly in eclampsia

Antidote / reversal

Calcium gluconate 10% 10–20 ml IV over 10 min; ventilatory support; dialysis.

ICU PEARL Before replacing potassium in a refractory case, replace magnesium.

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Calcium Gluconate / Calcium Chloride

Electrolyte replacement / membrane stabiliser

Drug and class

Calcium Gluconate / Calcium Chloride — Electrolyte replacement / membrane stabiliser.

Mechanism of action

Restores ionised calcium needed for excitation–contraction coupling, coagulation and neuromuscular function; raises the threshold potential, antagonising the cardiac membrane effects of hyperkalaemia within minutes. Calcium chloride gives ≈3 times more elemental calcium.

Dose in ICU

- **Hyperkalaemia with ECG changes:** calcium gluconate 10% 30 ml (3 g) IV over 5–10 min, or calcium chloride 10% 10 ml (1 g) via central line; repeat after 5 min if ECG unchanged
- **Symptomatic hypocalcaemia:** 10% gluconate 10–20 ml over 10 min, then infusion 0.5–1.5 mg/kg/h elemental (e.g., 100 ml 10% gluconate in 1 L D5 at 50 ml/h)
- **CCB / β-blocker toxicity:** CaCl 10% 10–20 ml or gluconate 30–60 ml, repeat every 10–20 min ×3, then infusion
- **Massive transfusion:** keep ionised Ca^{2+} >1.1 mmol/L (≈1 g CaCl per 4 units blood)

Drug dilution and infusion

- 10% calcium gluconate 10 ml = 2.2 mmol (93 mg elemental); 10% calcium chloride 10 ml = 6.8 mmol (272 mg elemental)
- Gluconate may be given peripherally; **chloride via central or large vein** only
- **Never mix with bicarbonate or phosphate** (precipitates); flush line; not with ceftriaxone in neonates

Dose adjustment — renal, hepatic and other conditions

Renal	CKD: monitor Ca^{2+} × phosphate product; avoid over-correction
Hepatic	Liver failure/massive transfusion: citrate not metabolised — chloride preferred
Other	Correct magnesium in refractory hypocalcaemia; digoxin toxicity — calcium bolus traditionally avoided (give slowly if essential)

Cautions and adverse effects

- Bradycardia, arrhythmias with rapid injection
- **Extravasation** → severe tissue necrosis and calcinosis (especially chloride)
- Hypercalcaemia; vasoconstriction; venous irritation

Antidote / reversal

No antidote. Extravasation: stop, aspirate, elevate; hyaluronidase infiltration may help.

ICU PEARL In hyperkalaemia, calcium buys you minutes, not hours — insulin–dextrose and K^+ removal must follow.

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Sodium Bicarbonate

Alkalinising agent / systemic buffer

80

Drug and class

Sodium Bicarbonate — Alkalinising agent / systemic buffer.

Mechanism of action

Bicarbonate combines with H^+ to form carbonic acid → CO_2 + water, raising pH (CO_2 must be ventilated off). Provides sodium load that reverses Na^+-channel blockade (TCAs) and alkalinises urine (ion trapping of weak acids).

Dose in ICU

- **Severe metabolic acidosis with AKI** (pH ≤7.20): 4.2% 125–250 ml over 30 min, repeat to pH >7.30 (BICAR-ICU); not for lactic acidosis/DKA routinely
- **TCA / Na^+-channel blocker toxicity** (QRS >100 ms): 1–2 mmol/kg IV bolus, repeat until QRS narrows; target pH 7.45–7.55
- **Urine alkalinisation** (salicylate, rhabdomyolysis): 150 mmol in 1 L D5 at 150–250 ml/h, target urine pH 7.5–8.5 (keep K^+ normal)
- **Hyperkalaemia with acidosis:** 50–100 mmol over 5–10 min (adjunct only); deficit = 0.5 × weight × (24 − HCO_3^-)

Drug dilution and infusion

- 8.4% = **1 mmol/ml** (hyperosmolar, 2000 mOsm/L); 4.2% = 0.5 mmol/ml
- Give 8.4% via central/large vein; isotonic 1.26–1.4% (150 mmol/L) for infusion: 150 ml 8.4% in 850 ml D5
- Incompatible with calcium, catecholamines (inactivated); flush line

Dose adjustment — renal, hepatic and other conditions

Renal	Sodium and volume load — caution in oliguria; renal replacement therapy preferred in severe AKI with overload
Hepatic	No adjustment
Other	Adequate ventilation essential (CO_2 load → intracellular acidosis); correct hypokalaemia and hypocalcaemia first

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Cautions and adverse effects

- Hypernatraemia, hyperosmolality, volume overload
- Hypokalaemia, fall in ionised calcium (tetany, arrhythmia), metabolic alkalosis
- Rising $PaCO_2$ and paradoxical intracellular/CSF acidosis
- Extravasation necrosis

Antidote / reversal

No antidote; stop; correct electrolytes; acetazolamide or dialysis for severe alkalosis.

ICU PEARL Bicarbonate is a drug for TCA toxicity and AKI-acidosis — for lactic acidosis, treat the cause.

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CHAPTER 8 · CLASS SUMMARY

Diuretics and Fluid / Electrolyte Management — At a Glance

Loop, osmotic and other diuretics, hyperosmolar therapy and electrolyte replacement

Drug	ICU dose	Dilution / infusion	Renal / hepatic / other	Key cautions	Antidote
Furosemide	20–40 mg IV or 1–2.5× oral dose; infusion 5–40 mg/h	250 mg/50 ml = 5 mg/ml; ≤4 mg/min	↑ dose in CKD; caution cirrhosis	↓K^+/↓Mg^{2+}, alkalosis, ototoxicity	None
Torsemide (Torasemide)	10–20 mg daily (max 200 mg); infusion 5–20 mg/h	Bolus over 2 min	Larger doses in CKD; caution cirrhosis	↓K^+, ototoxicity	None
Bumetanide	0.5–1 mg q2–3h (max 10 mg/day); infusion 0.5–2 mg/h	0.1 mg/ml infusion	Larger doses in CKD	Myalgia, ↓K^+	None
Mannitol	0.25–1 g/kg over 15–20 min q4–6h	20% (200 mg/ml) with filter	Avoid anuria/AKI; hold if osm >320 or gap >20	Hypovolaemia, AKI, rebound ICP	None (HD in toxicity)
Hypertonic Saline (3% NaCl)	Hypo-Na: 100–150 ml bolus ×3; ICP: 2–5 ml/kg	Ready 3% (513 mmol/L); peripheral OK	Slow correction in liver disease	ODS, hyperchloraemia, overload	D5W + desmopressin (over-correction)
Spironolactone	Ascites 100–400 mg/day; HF 12.5–50 mg/day	Oral/NG only	Avoid eGFR <30 or K^+ >5	Hyperkalaemia, gynaecomastia	None (treat ↑K^+)
Acetazolamide	250–500 mg IV/oral q8–12h (1–2 doses)	500 mg + 5 ml = 100 mg/ml	CrCl 10–50 q12h; avoid <10, cirrhosis	↓K^+, acidosis, sulfonamide	None
Potassium Chloride (KCl)	10–20 mmol/h (max 40 central); 10 mmol ↑K^+ ≈0.1	Peripheral ≤40 mmol/L; central 20 mmol/100 ml/h	↓ in renal failure; fix Mg^{2+}	Fatal if bolus; phlebitis	Calcium, insulin–dextrose
Magnesium Sulfate	Deficiency 1–2 g; TdP 2 g; eclampsia 4 g then 1 g/h; asthma 2 g	Dilute to ≤20%; 1 g = 4 mmol	↓50% in renal failure; check levels	Areflexia, resp depression, block	Calcium gluconate
Calcium Gluconate / Calcium Chloride	Hyper-K: gluconate 30 ml / chloride 10 ml; hypo-Ca: 10–20 ml then infusion	Gluconate peripheral; chloride central	Liver failure → chloride; fix Mg^{2+}	Extravasation necrosis, bradycardia	None
Sodium Bicarbonate	4.2% 125–250 ml (AKI acidosis); TCA 1–2 mmol/kg; urine alkalinisation	8.4% = 1 mmol/ml central	Na^+/volume load in AKI	↑Na^+, ↓K^+, ↓iCa^{2+}, CO_2	None

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Meropenem

Carbapenem β-lactam antibiotic

Drug and class

Meropenem — Carbapenem β-lactam antibiotic.

Mechanism of action

Binds penicillin-binding proteins inhibiting cell-wall synthesis — bactericidal; time-dependent killing (%fT>MIC). Stable to most β-lactamases including ESBL and AmpC; not active against MRSA, E. faecium, Stenotrophomonas; inactivated by carbapenemases.

Dose in ICU

- **Severe sepsis / HAP / VAP:** 1 g IV every 8 h
- **Meningitis, Pseudomonas, MDR organisms, high MIC:** 2 g IV every 8 h
- **Extended infusion** over 3 h (or continuous infusion after a 1–2 g loading dose) improves target attainment
- Give first dose within 1 h of recognising septic shock

Drug dilution and infusion

- Reconstitute 1 g with 20 ml water; dilute in 50–100 ml NS
- Stability: NS ≈ 8 h at room temperature (shorter in D5) — for 3-h extended infusion prepare fresh; bolus over 5 min possible

Dose adjustment — renal, hepatic and other conditions

Renal	CrCl 26–50: 1 g q12h; 10–25: 500 mg q12h; <10: 500 mg q24h; HD: 500 mg q24h after HD; CRRT: 1 g q8–12h (2 g q8h for high MIC)
Hepatic	No adjustment
Other	Augmented renal clearance (CrCl >130, young trauma/burns): 2 g q8h extended infusion

Cautions and adverse effects

- **Valproate interaction** — reduces valproate levels by 60–90% within 24 h (seizures): avoid or change antiepileptic
- Seizures (less than imipenem), C. difficile, candidiasis
- Hypersensitivity (low cross-reactivity with penicillin)
- Selection of carbapenem-resistant organisms — de-escalate early

Antidote / reversal

No antidote; dialysable.

ICU PEARL Prolonged infusions and full loading doses matter more in ICU than the choice between 1 g and 2 g.

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Vancomycin

Glycopeptide antibiotic (gram-positive including MRSA)

Drug and class

Vancomycin — Glycopeptide antibiotic (gram-positive including MRSA).

Mechanism of action

Binds D-Ala-D-Ala terminus of peptidoglycan precursors, blocking cell-wall synthesis — slowly bactericidal; AUC/MIC-dependent. Active against MRSA, coagulase-negative staphylococci, streptococci, enterococci (not VRE), C. difficile (oral).

Dose in ICU

- **Loading:** 25–30 mg/kg IV (actual body weight, max 3 g) in critically ill
- **Maintenance:** 15–20 mg/kg every 8–12 h, adjusted to **AUC 400–600 mg·h/L** (trough 15–20 mg/L if AUC unavailable)
- **Continuous infusion:** 30–40 mg/kg/day after loading, target steady-state 20–25 mg/L
- **C. difficile:** 125 mg orally 6-hourly (IV ineffective)

Drug dilution and infusion

- Reconstitute 500 mg with 10 ml water; dilute to **≤5 mg/ml** (1 g in 200–250 ml NS/D5)
- Infuse at ≤10 mg/min (≥1 h per gram) to prevent infusion reaction; central line allows 10 mg/ml

Dose adjustment — renal, hepatic and other conditions

Renal	Dose interval by CrCl and levels: CrCl 30–50 q24h; <30 — level-guided; HD: 25 mg/kg load, then 500–1000 mg after each session; CRRT: 15–20 mg/kg q24h
Hepatic	No adjustment
Other	Obesity: load on actual weight (max 3 g); augmented renal clearance needs q8h; avoid combination nephrotoxins

Cautions and adverse effects

- **Nephrotoxicity** (higher with piperacillin–tazobactam, aminoglycosides, high troughs)
- Vancomycin infusion reaction (flushing, pruritus, hypotension) — slow the rate, antihistamine
- Ototoxicity; neutropenia and thrombocytopenia with prolonged therapy; DRESS

Antidote / reversal

No antidote; haemodialysis (high-flux) removes it.

ICU PEARL Load properly — under-dosing on day 1 is the commonest vancomycin error in the ICU.

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Piperacillin–Tazobactam

Antipseudomonal ureidopenicillin + β-lactamase inhibitor

Drug and class

Piperacillin–Tazobactam — Antipseudomonal ureidopenicillin + β-lactamase inhibitor.

Mechanism of action

Piperacillin inhibits cell-wall synthesis (PBP binding); tazobactam irreversibly inhibits many class A β-lactamases. Broad gram-negative (including Pseudomonas), gram-positive and anaerobic activity; unreliable against ESBL bacteraemia (MERINO) and AmpC producers.

Dose in ICU

- **Standard:** 4.5 g IV every 6 h (q8h for less severe infections)
- **Extended infusion:** 4.5 g over 4 h every 8 h, after first dose over 30 min
- **Continuous infusion:** 4.5 g load, then 13.5–18 g/24 h

Drug dilution and infusion

- Reconstitute 4.5 g with 20 ml water/NS; dilute in 100 ml NS/D5
- Infuse over 30 min (standard) or 4 h (extended); stable 24 h at room temperature

Dose adjustment — renal, hepatic and other conditions

Renal	CrCl 20–40: 4.5 g q8h (or 3.375 g q6h); <20: 4.5 g q12h (or 2.25 g q6h); HD: 2.25 g q8h + 0.75 g after HD; CRRT: 4.5 g q8h
Hepatic	No adjustment
Other	Sodium load ≈11 mmol per 4.5 g — caution in heart failure; augmented renal clearance — extended/continuous infusion

Cautions and adverse effects

- Hypersensitivity (penicillin allergy)
- AKI risk increased with vancomycin (monitor creatinine)
- Hypokalaemia, thrombocytopenia, neutropenia with prolonged use, C. difficile
- Encephalopathy/seizures at high levels in renal failure

Antidote / reversal

No antidote; dialysable.

ICU PEARL For proven ESBL bloodstream infection, switch to a carbapenem — pip–taz is not equivalent.

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Cefepime

Fourth-generation cephalosporin (antipseudomonal)

84

Drug and class

Cefepime — Fourth-generation cephalosporin (antipseudomonal).

Mechanism of action

β-lactam inhibiting cell-wall synthesis with zwitterionic structure allowing rapid gram-negative penetration; stable to AmpC β-lactamases; active against Pseudomonas, Enterobacterales (non-ESBL) and MSSA/streptococci.

Dose in ICU

- **Severe infection, Pseudomonas, febrile neutropenia:** 2 g IV every 8 h
- **Moderate infection:** 1–2 g every 12 h
- **Extended infusion** over 3–4 h improves time above MIC

Drug dilution and infusion

- Reconstitute 1 g with 10 ml water; dilute in 50–100 ml NS/D5
- Infuse over 30 min (or 3–4 h extended)

Dose adjustment — renal, hepatic and other conditions

Renal	CrCl 30–60: 2 g q12h; 11–29: 2 g q24h; ≤10: 1 g q24h; HD: 1 g on day 1, then 1 g q24h (after HD); CRRT: 2 g q12h
Hepatic	No adjustment
Other	Elderly with reduced CrCl — highest neurotoxicity risk

Cautions and adverse effects

- **Cefepime neurotoxicity**: encephalopathy, myoclonus, non-convulsive status epilepticus — especially with renal failure or excess dose
- Hypersensitivity, C. difficile, positive Coombs test
- Not reliable against ESBL producers

Antidote / reversal

No antidote; stop drug; **haemodialysis** removes it in severe neurotoxicity; benzodiazepines/EEG for NCSE.

ICU PEARL New confusion in a renal patient on cefepime — get an EEG and check the dose.

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Ceftriaxone

Third-generation cephalosporin

Drug and class

Ceftriaxone — Third-generation cephalosporin.

Mechanism of action

β-lactam inhibiting cell-wall synthesis; long half-life (8 h) permits once-daily dosing; excellent CSF penetration. Active against streptococci (incl. penicillin-resistant pneumococcus), Neisseria, H. influenzae, most community Enterobacterales; no antipseudomonal or anti-enterococcal activity.

Dose in ICU

- **Community-acquired pneumonia / sepsis:** 1–2 g IV every 24 h
- **Bacterial meningitis:** 2 g IV every 12 h
- **Enteric fever, SBP, pyelonephritis:** 2 g daily
- Give with dexamethasone before/with first dose in suspected pneumococcal meningitis

Drug dilution and infusion

- Reconstitute 1 g with 10 ml water; IV push over 2–4 min, or dilute in 50–100 ml NS/D5 over 30 min
- **Do not mix with calcium-containing solutions** (Ringer's lactate) in the same line

Dose adjustment — renal, hepatic and other conditions

Renal	No adjustment (dual biliary and renal elimination)
Hepatic	No adjustment alone; **combined renal and hepatic failure: max 2 g/day**
Other	Neonates with hyperbilirubinaemia — avoid (bilirubin displacement); calcium co-infusion in neonates fatal

Cautions and adverse effects

- Biliary pseudolithiasis/sludge, pancreatitis
- C. difficile, hypersensitivity, haemolytic anaemia (immune)
- Encephalopathy (rare, renal failure)
- Ceftriaxone–calcium precipitates in neonates

Antidote / reversal

No antidote; not significantly dialysed.

ICU PEARL The one cephalosporin you never need to renally adjust — but double the dose for meningitis.

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Ciprofloxacin

Fluoroquinolone antibiotic

86

Drug and class

Ciprofloxacin — Fluoroquinolone antibiotic.

Mechanism of action

Inhibits bacterial DNA gyrase (topoisomerase II) and topoisomerase IV — concentration-dependent bactericidal activity (AUC/MIC). Active against gram-negatives including Pseudomonas, atypicals (moderate); poor streptococcal activity; excellent oral bioavailability (70–80%).

Dose in ICU

- **IV:** 400 mg every 8–12 h (q8h for Pseudomonas/severe infection)
- **Oral/NG:** 500–750 mg every 12 h
- Use oral route when gut works (same exposure, lower cost)

Drug dilution and infusion

- Premixed 2 mg/ml (200 mg/100 ml; 400 mg/200 ml) — infuse over 60 min into a large vein
- NG: separate from enteral feeds, Ca^{2+}, Mg^{2+}, Fe, Zn, antacids by ≥2 h (chelation)

Dose adjustment — renal, hepatic and other conditions

Renal	CrCl 30–50: 400 mg IV q12h (oral 250–500 q12h); <30: 400 mg IV q24h (oral 250–500 q24h); HD: dose after dialysis
Hepatic	No adjustment
Other	Elderly, steroids, transplant: higher tendon rupture risk

Cautions and adverse effects

- **QT prolongation**, arrhythmias; dysglycaemia (hypo- and hyperglycaemia)
- Tendinopathy/rupture, aortic aneurysm/dissection, peripheral neuropathy
- Delirium, seizures, exacerbation of **myasthenia gravis**
- C. difficile; CYP1A2 inhibition (theophylline, clozapine, warfarin interactions)

Antidote / reversal

No antidote; magnesium for TdP; supportive.

ICU PEARL Ciprofloxacin is a gram-negative drug — do not rely on it for pneumococcal pneumonia.

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Amphotericin B

Polyene antifungal (deoxycholate and lipid formulations)

87

Drug and class

Amphotericin B — Polyene antifungal (deoxycholate and lipid formulations).

Mechanism of action

Binds ergosterol in fungal cell membranes forming pores → leakage of ions and cell death; fungicidal, broadest spectrum (Candida, Cryptococcus, Aspergillus, Mucorales, endemic fungi, Leishmania). Also binds cholesterol in human cells — causes toxicity.

Dose in ICU

- **Liposomal amphotericin B:** 3–5 mg/kg IV daily; **mucormycosis** 5–10 mg/kg daily
- **Conventional (deoxycholate):** 0.7–1 mg/kg IV daily (max 1.5 mg/kg) — never exceed (fatal overdose confusion with liposomal)
- **Cryptococcal meningitis:** liposomal 3–4 mg/kg (or single 10 mg/kg) with flucytosine
- Check formulation and mg/kg dose before every infusion

Drug dilution and infusion

- **Dilute in D5 only** — precipitates with NS; flush line with D5 before and after
- Conventional: 0.1 mg/ml in D5 over 2–6 h; liposomal: reconstitute with water, dilute to 0.2–2 mg/ml in D5, over 2 h (1 h if tolerated)
- Use 5-micron filter (liposomal); protect conventional from light

Dose adjustment — renal, hepatic and other conditions

Renal	No dose reduction, but **nephrotoxicity** — prefer liposomal; saline loading 500 ml NS before and after (prehydration)
Hepatic	No adjustment
Other	Monitor K^+, Mg^{2+} (daily), creatinine; avoid other nephrotoxins

Cautions and adverse effects

- **AKI**, distal renal tubular acidosis, **hypokalaemia, hypomagnesaemia**
- Infusion reactions: fever, rigors, hypotension, bronchospasm (premedicate: paracetamol, antihistamine, hydrocortisone; pethidine 25 mg for rigors)
- Anaemia, phlebitis, arrhythmia from hypokalaemia

Antidote / reversal

No antidote; not dialysed. Replace K^+ and Mg^{2+}; supportive care.

ICU PEARL Confusing conventional and liposomal doses kills — 5 mg/kg of the conventional drug is a fatal overdose.

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Fluconazole

Triazole antifungal

88

Drug and class

Fluconazole — Triazole antifungal.

Mechanism of action

Inhibits fungal CYP450 lanosterol 14-α-demethylase, blocking ergosterol synthesis — fungistatic against Candida (not C. krusei; reduced against C. glabrata) and Cryptococcus; no mould activity. Excellent oral bioavailability and CSF penetration.

Dose in ICU

- **Loading:** 800 mg (12 mg/kg) IV/oral, then **400 mg (6 mg/kg) daily**
- **Invasive candidiasis** (non-severe, susceptible species) or step-down from an echinocandin
- **Cryptococcal consolidation:** 400–800 mg daily
- Echinocandin preferred first-line in septic shock/candidaemia

Drug dilution and infusion

- Premixed 2 mg/ml (200 mg/100 ml) — infuse at ≤10 ml/min (over 1–2 h)
- Oral/NG route equivalent when gut functioning

Dose adjustment — renal, hepatic and other conditions

Renal	Give full loading dose; CrCl ≤50: 50% of maintenance dose; HD: full dose after each session; CRRT: 400–800 mg daily (higher clearance)
Hepatic	Use with caution; monitor LFTs
Other	Strong **CYP2C9/3A4/2C19 inhibitor**: raises warfarin, phenytoin, midazolam, fentanyl, tacrolimus, ciclosporin, statins

Cautions and adverse effects

- QT prolongation and TdP (especially with other QT drugs, hypokalaemia)
- Hepatotoxicity
- Resistance in C. glabrata and C. krusei; C. auris often resistant

Antidote / reversal

No antidote; dialysable.

ICU PEARL Fluconazole is a step-down drug — start an echinocandin in the shocked candidaemic patient.

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Acyclovir (Aciclovir)

Antiviral — guanosine nucleoside analogue

Drug and class

Acyclovir (Aciclovir) — Antiviral — guanosine nucleoside analogue.

Mechanism of action

Phosphorylated by viral thymidine kinase then host kinases to acyclovir triphosphate, which inhibits viral DNA polymerase and terminates chain elongation — active against HSV-1, HSV-2 and VZV (less against CMV/EBV).

Dose in ICU

- **HSV encephalitis:** 10 mg/kg IV every 8 h for 14–21 days (start on suspicion)
- **Disseminated / severe VZV, immunocompromised zoster:** 10 mg/kg every 8 h
- **Severe mucocutaneous HSV:** 5 mg/kg every 8 h
- Dose on **ideal body weight** in obesity

Drug dilution and infusion

- Vial 250/500 mg — reconstitute and dilute to **≤7 mg/ml** (usually 5 mg/ml) in NS/D5
- Infuse over 1 h; alkaline (pH 11) — phlebitis/extravasation injury
- Maintain good hydration (urine output >100 ml/h) to prevent crystal nephropathy

Dose adjustment — renal, hepatic and other conditions

Renal	CrCl 25–50: 10 mg/kg q12h; 10–25: q24h; <10: 5 mg/kg q24h; HD: dose after dialysis; CRRT: 5–10 mg/kg q12–24h
Hepatic	No adjustment
Other	Obesity: ideal body weight; elderly: neurotoxicity risk

Cautions and adverse effects

- **Crystal nephropathy / AKI** (rapid infusion, dehydration, high dose)
- **Neurotoxicity** (confusion, tremor, hallucinations, coma) — mainly in renal failure
- Phlebitis, nausea, raised transaminases

Antidote / reversal

No antidote; haemodialysis removes acyclovir in neurotoxicity.

ICU PEARL Start acyclovir with the first antibiotic in suspected encephalitis — and run fluids with it.

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CHAPTER 9 · CLASS SUMMARY

Antimicrobials — Antibiotics, Antifungals and Antivirals — At a Glance

Broad-spectrum ICU antimicrobials: dosing, infusion strategy and renal adjustment

Drug	ICU dose	Dilution / infusion	Renal / hepatic / other	Key cautions	Antidote
Meropenem	1–2 g q8h; extended 3-h infusion	1 g in 50–100 ml NS	CrCl-based (500 mg q24h <10)	Valproate interaction, seizures	None
Vancomycin	Load 25–30 mg/kg; 15–20 mg/kg q8–12h; AUC 400–600	≤5 mg/ml; ≥1 h/g	Interval by CrCl + levels	Nephrotoxicity, infusion reaction	None
Piperacillin–Tazobactam	4.5 g q6h; extended 4-h q8h	4.5 g in 100 ml	CrCl-based (4.5 g q12h <20)	AKI with vanco, ↓K^+, allergy	None
Cefepime	2 g q8h (severe); 1–2 g q12h	1 g in 50–100 ml	CrCl-based (1 g q24h ≤10)	Neurotoxicity/NCSE in AKI	None (HD removes)
Ceftriaxone	1–2 g q24h; meningitis 2 g q12h	1 g in 10 ml push or 50–100 ml	No renal adj; max 2 g if renal+hepatic	Biliary sludge, Ca^{2+} precipitates	None
Ciprofloxacin	400 mg IV q8–12h; oral 500–750 mg q12h	Premixed 2 mg/ml over 60 min	CrCl <30: 400 mg q24h	QT, tendons, aorta, myasthenia	None
Amphotericin B	Liposomal 3–5 (mucor 5–10) mg/kg/day; conventional 0.7–1 mg/kg	D5 only; flush with D5	Nephrotoxic — NS prehydration	AKI, ↓K^+/↓Mg^{2+}, infusion reactions	None
Fluconazole	Load 800 mg, then 400 mg daily	Premixed 2 mg/ml over 1–2 h	CrCl ≤50: 50% maintenance	QT, hepatotoxicity, interactions	None
Acyclovir (Aciclovir)	10 mg/kg q8h (encephalitis/VZV); 5 mg/kg q8h	≤7 mg/ml over 1 h	CrCl-based (5 mg/kg q24h <10)	Crystal AKI, neurotoxicity	None (HD removes)

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Hydrocortisone

90

Short-acting glucocorticoid with mineralocorticoid activity (cortisol)

Drug and class

Hydrocortisone — Short-acting glucocorticoid with mineralocorticoid activity (cortisol).

Mechanism of action

Binds intracellular glucocorticoid receptors altering gene transcription — anti-inflammatory and immunosuppressive effects, increased vascular responsiveness to catecholamines, gluconeogenesis; significant mineralocorticoid (Na^+ retention) effect at high doses.

Dose in ICU

- **Septic shock** (norepinephrine ≥0.25 mcg/kg/min for ≥4 h): 200 mg/day — 50 mg IV every 6 h or 200 mg/24 h infusion ± fludrocortisone 50 mcg daily; stop when vasopressors off (taper optional)
- **Adrenal crisis:** 100 mg IV bolus, then 200 mg/24 h (infusion or 50 mg 6-hourly) with IV fluids; taper over 1–3 days
- **Peri-operative stress dosing** (chronic steroid users): 50–100 mg IV at induction, then 50 mg 6–8 hourly for 24–48 h
- **Thyroid storm:** 300 mg IV load, then 100 mg every 8 h

Drug dilution and infusion

- Vial 100 mg powder — reconstitute with 2 ml water (50 mg/ml)
- Bolus over 1–10 min; infusion: **200 mg in 50 ml NS** = 4 mg/ml at 2.1 ml/h (200 mg/24 h)

Dose adjustment — renal, hepatic and other conditions

Renal	No adjustment
Hepatic	No adjustment
Other	Monitor glucose, Na^+, K^+; CYP3A4 inducers (rifampicin, phenytoin) increase requirement

Cautions and adverse effects

- Hyperglycaemia, hypernatraemia, hypokalaemia, fluid retention
- Infection risk, impaired wound healing, GI bleeding (with NSAIDs)
- ICU-acquired weakness/myopathy (with NMBAs), delirium
- Adrenal suppression after prolonged use — taper

Antidote / reversal

No antidote. Treat complications (insulin, potassium); taper slowly after >2–3 weeks to avoid adrenal crisis.

ICU PEARL Hydrocortisone does not cure septic shock — it shortens the time on vasopressors.

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Methylprednisolone

Intermediate-acting synthetic glucocorticoid (minimal mineralocorticoid effect)

Drug and class

Methylprednisolone — Intermediate-acting synthetic glucocorticoid (minimal mineralocorticoid effect).

Mechanism of action

Glucocorticoid receptor agonist ≈5 times as potent as hydrocortisone, with little Na^+ retention; high-dose pulses act via non-genomic membrane effects to suppress inflammation rapidly.

Dose in ICU

- **Pulse therapy** (vasculitis, SLE, transplant rejection, autoimmune encephalitis, MS relapse): 500–1000 mg IV daily for 3–5 days
- **ARDS (early, moderate–severe):** 1 mg/kg/day infusion, then taper over ≈4 weeks (avoid starting after day 14)
- **Severe CAP with shock (selected):** 0.5 mg/kg every 12 h for 5–7 days
- **Acute severe asthma / COPD exacerbation:** 40–60 mg IV daily (asthma up to 1 mg/kg every 6–12 h)
- **Post-extubation stridor prevention:** 20 mg IV every 4 h for 12 h before extubation (high-risk cuff leak)

Drug dilution and infusion

- Vials 40/125/500/1000 mg powder — reconstitute with supplied diluent
- Doses ≤250 mg: IV over 5 min; pulse doses: dilute in 100–250 ml NS/D5 over ≥30–60 min (rapid pulses → arrhythmias)

Dose adjustment — renal, hepatic and other conditions

Renal	No adjustment
Hepatic	No adjustment
Other	Equivalence: methylprednisolone 4 mg = prednisolone 5 mg = hydrocortisone 20 mg = dexamethasone 0.75 mg

Cautions and adverse effects

- Hyperglycaemia, hypertension, fluid retention, hypokalaemia
- Infection (including reactivation of TB, strongyloides hyperinfection — consider ivermectin)
- Arrhythmias and sudden death with rapid pulse infusion; psychosis, myopathy, GI bleeding
- Adrenal suppression

Antidote / reversal

No antidote; supportive; taper after prolonged course.

ICU PEARL Before pulse steroids in a patient from an endemic area, think strongyloides.

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Dexamethasone

92

Long-acting potent synthetic glucocorticoid (no mineralocorticoid effect)

Drug and class

Dexamethasone — Long-acting potent synthetic glucocorticoid (no mineralocorticoid effect).

Mechanism of action

Glucocorticoid receptor agonist ≈25–30 times as potent as hydrocortisone with a 36–72 h biological half-life and no Na^+ retention — reduces vasogenic oedema, airway oedema and inflammation; induces CYP3A4.

Dose in ICU

- **Vasogenic cerebral oedema (tumour, abscess):** 10 mg IV, then 4 mg every 6 h
- **Bacterial meningitis:** 0.15 mg/kg (10 mg) IV every 6 h for 4 days, first dose before or with the first antibiotic
- **COVID-19 on oxygen:** 6 mg daily for up to 10 days
- **ARDS (DEXA-ARDS regimen):** 20 mg daily ×5 days, then 10 mg daily ×5 days
- **Airway oedema / post-extubation stridor:** 4–5 mg IV every 6 h for 24 h; **antiemetic** 4–8 mg

Drug dilution and infusion

- Ampoules 4 mg/ml (8 mg/2 ml)
- Give slowly IV over 1–5 min (rapid push → perineal burning/itching) or in 50 ml NS over 15 min

Dose adjustment — renal, hepatic and other conditions

Renal	No adjustment
Hepatic	No adjustment
Other	**Do not use in traumatic brain injury** (CRASH — increased mortality), ischaemic stroke or ICH oedema; CYP3A4 inducer (lowers levels of many drugs)

Cautions and adverse effects

- Marked hyperglycaemia; infection; GI bleeding
- Psychosis, insomnia, delirium; myopathy
- Adrenal suppression (long half-life)
- Tumour lysis in lymphoma (steroid-sensitive tumours)

Antidote / reversal

No antidote; supportive.

ICU PEARL Dexamethasone helps tumour oedema, meningitis and hypoxic COVID — and harms traumatic brain injury.

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CHAPTER 10 · CLASS SUMMARY

Corticosteroids and Anti-inflammatory Agents — At a Glance

Glucocorticoids for shock, adrenal crisis, airway, cerebral oedema and inflammatory disease

Drug	ICU dose	Dilution / infusion	Renal / hepatic / other	Key cautions	Antidote
Hydrocortisone	Septic shock 200 mg/day; adrenal crisis 100 mg then 200 mg/24 h	200 mg/50 ml infusion	No adjustment	Hyperglycaemia, ↑Na^+, ↓K^+, infection	None
Methylprednisolone	Pulse 500–1000 mg ×3–5 d; ARDS 1 mg/kg/day; asthma 40–60 mg	Pulse in 100–250 ml over ≥30–60 min	No adjustment	Hyperglycaemia, infection, arrhythmia (rapid pulse)	None
Dexamethasone	Cerebral oedema 10 mg then 4 mg q6h; meningitis 10 mg q6h ×4 d; COVID 6 mg	Slow IV or 50 ml over 15 min	No adjustment; NOT in TBI	Hyperglycaemia, psychosis, infection	None

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Heparin Sodium (Unfractionated Heparin)

Indirect thrombin and factor Xa inhibitor (glycosaminoglycan anticoagulant)

Drug and class

Heparin Sodium (Unfractionated Heparin) — Indirect thrombin and factor Xa inhibitor (glycosaminoglycan anticoagulant).

Mechanism of action

Binds antithrombin, accelerating its inactivation of thrombin (IIa) and factor Xa ≈1000-fold. Short half-life (60–90 min), fully reversible with protamine, not renally cleared — the anticoagulant of choice when bleeding risk is high or renal function is poor.

Dose in ICU

- **VTE treatment:** 80 U/kg IV bolus, then 18 U/kg/h; adjust to aPTT 1.5–2.5 × control (≈60–85 s) or anti-Xa 0.3–0.7 IU/ml, check 6 h after each change
- **ACS (with fibrinolysis/PCI):** 60 U/kg bolus (max 4000 U), then 12 U/kg/h (max 1000 U/h)
- **Prophylaxis:** 5000 U SC every 8–12 h
- **CRRT circuit:** 5–10 U/kg/h pre-filter (if citrate not used)

Drug dilution and infusion

- Vials 5000 U/ml (check — also 1000 U/ml)
- Infusion: **25,000 U in 50 ml NS** = **500 U/ml** (or 25,000 U in 250 ml = 100 U/ml)
- Example: 70 kg at 18 U/kg/h = 1260 U/h = 2.5 ml/h of 500 U/ml

Dose adjustment — renal, hepatic and other conditions

Renal	No adjustment — preferred in AKI/CKD/dialysis
Hepatic	No adjustment; caution with coagulopathy and varices
Other	Obesity: bolus/infusion on actual weight (cap bolus 10,000 U, initial rate 2000 U/h); antithrombin deficiency → heparin resistance (use anti-Xa monitoring)

Cautions and adverse effects

- Bleeding — check platelets, Hb, aPTT
- **Heparin-induced thrombocytopenia**: platelet fall >50% at day 5–10 or thrombosis — stop all heparin, 4T score, switch to argatroban/bivalirudin/fondaparinux
- Hyperkalaemia (aldosterone suppression); osteoporosis with long use

Antidote / reversal

Protamine sulfate 1 mg per 100 U given in previous 2–3 h (max 50 mg), slow IV.

ICU PEARL Count platelets every 2–3 days on heparin — HIT presents with thrombosis, not bleeding.

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Enoxaparin

Low-molecular-weight heparin (indirect factor Xa > IIa inhibitor)

Drug and class

Enoxaparin — Low-molecular-weight heparin (indirect factor Xa > IIa inhibitor).

Mechanism of action

Binds antithrombin and predominantly inhibits factor Xa (anti-Xa:anti-IIa ≈4:1). Predictable SC bioavailability, longer half-life (4–6 h), renally cleared; lower HIT risk than UFH; only partially reversed by protamine.

Dose in ICU

- **VTE prophylaxis:** 40 mg SC daily (BMI >40: 40 mg 12-hourly; trauma: 30 mg 12-hourly)
- **VTE treatment:** 1 mg/kg SC every 12 h (or 1.5 mg/kg once daily)
- **NSTE-ACS:** 1 mg/kg SC every 12 h; **STEMI with fibrinolysis** (<75 y): 30 mg IV + 1 mg/kg SC 12-hourly; ≥75 y: no bolus, 0.75 mg/kg 12-hourly

Drug dilution and infusion

- Prefilled syringes 100 mg/ml (20, 40, 60, 80 mg); no dilution SC
- IV bolus 30 mg undiluted

Dose adjustment — renal, hepatic and other conditions

Renal	**CrCl <30:** treatment 1 mg/kg once daily; prophylaxis 20–30 mg daily; avoid in dialysis/unstable AKI (use UFH); monitor anti-Xa
Hepatic	Caution — coagulopathy, thrombocytopenia
Other	Obesity, pregnancy, renal impairment, extremes of weight: anti-Xa 4 h post-dose (treatment 0.6–1.0 IU/ml; prophylaxis 0.2–0.5)

Cautions and adverse effects

- Bleeding; accumulation in renal failure
- **Neuraxial haematoma**: wait 12 h after prophylactic / 24 h after therapeutic dose before neuraxial block or catheter removal
- HIT (less than UFH); hyperkalaemia; injection-site haematoma

Antidote / reversal

Protamine 1 mg per 1 mg enoxaparin if given within 8 h (0.5 mg per 1 mg if 8–12 h) — neutralises ≈60% of anti-Xa activity; andexanet alfa where available.

ICU PEARL In ICU AKI, switch enoxaparin to unfractionated heparin — reversible, titratable and not renally cleared.

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Alteplase (tPA)

Recombinant tissue plasminogen activator — fibrinolytic

95

Drug and class

Alteplase (tPA) — Recombinant tissue plasminogen activator — fibrinolytic.

Mechanism of action

Fibrin-selective serine protease converting fibrin-bound plasminogen to plasmin, which lyses fibrin clot. Short half-life (4–6 min) — requires bolus plus infusion.

Dose in ICU

- **Acute ischaemic stroke** (≤4.5 h): 0.9 mg/kg (max 90 mg) — 10% IV bolus over 1 min, remainder over 60 min
- **Massive (high-risk) PE:** 100 mg IV over 2 h; cardiac arrest from PE — 50 mg bolus (repeat 50 mg after 15 min)
- **STEMI (accelerated):** 15 mg bolus, 0.75 mg/kg (max 50 mg) over 30 min, then 0.5 mg/kg (max 35 mg) over 60 min
- **Catheter occlusion:** 2 mg (2 ml) instilled, dwell 30–120 min

Drug dilution and infusion

- Vial 50 mg powder — reconstitute with 50 ml sterile water = **1 mg/ml**; swirl gently, do not shake
- Give undiluted or dilute to ≥0.5 mg/ml with NS; dedicated line; use within 8 h

Dose adjustment — renal, hepatic and other conditions

Renal	No adjustment
Hepatic	No dose adjustment; severe liver disease — high bleeding risk (relative contraindication)
Other	Stroke: BP must be <185/110 before and <180/105 for 24 h; no antiplatelet/anticoagulant for 24 h; glucose must be 50–400 mg/dl

Cautions and adverse effects

- **Intracranial haemorrhage** and major bleeding — screen contraindications (recent surgery/trauma, prior ICH, active bleeding, platelets <100,000, INR >1.7)
- Orolingual angioedema (higher with ACE inhibitors)
- Reperfusion arrhythmias; cholesterol embolisation
- Neuro checks every 15 min during infusion and 2 h after

Antidote / reversal

Stop infusion; **cryoprecipitate 10 U** (target fibrinogen >150–200 mg/dl), **tranexamic acid** 1 g IV over 10 min; platelets if on antiplatelets; neurosurgical review for ICH.

ICU PEARL Time is brain and lung: do the contraindication checklist in minutes, not hours.

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Insulin (Regular / Soluble)

Short-acting human insulin — glycaemic control and potassium shift

96

Drug and class

Insulin (Regular / Soluble) — Short-acting human insulin — glycaemic control and potassium shift.

Mechanism of action

Binds insulin receptors (tyrosine kinase) promoting glucose uptake (GLUT-4), glycogen synthesis and lipogenesis, suppressing ketogenesis and gluconeogenesis; stimulates Na^+/K^+-ATPase shifting K^+ into cells. IV half-life ≈5–10 min.

Dose in ICU

- **DKA:** fixed-rate 0.1 U/kg/h IV (K^+ must be ≥3.3 mmol/L first); when glucose <250 mg/dl add D5–D10 and reduce to 0.02–0.05 U/kg/h; continue until ketones cleared; overlap SC basal insulin 1–2 h before stopping
- **HHS:** 0.05 U/kg/h after fluids have started to lower glucose
- **ICU hyperglycaemia:** variable-rate protocol targeting **140–180 mg/dl** (avoid <110)
- **Hyperkalaemia:** 10 U IV with 25 g dextrose (50 ml D50 or 250 ml D10); glucose hourly ×6 h
- **CCB/β-blocker toxicity (HIET):** 1 U/kg bolus, then 1–10 U/kg/h with dextrose and K^+

Drug dilution and infusion

- Vial 100 U/ml
- Infusion: **50 U in 50 ml NS = 1 U/ml**; prime/flush tubing with 20 ml (adsorption)
- Example: 70 kg DKA at 0.1 U/kg/h = 7 ml/h

Dose adjustment — renal, hepatic and other conditions

Renal	Reduced clearance — lower doses, higher hypoglycaemia risk; hyperkalaemia regimen: 5 U if eGFR <30 (or give dextrose infusion)
Hepatic	Reduced gluconeogenesis — hypoglycaemia; lower doses
Other	Steroids, sepsis, catecholamines increase requirement; stopping enteral feed — reduce or stop insulin

Cautions and adverse effects

- **Hypoglycaemia** (hourly glucose on infusion)
- **Hypokalaemia** and hypophosphataemia (check K^+ every 2 h in DKA)
- Cerebral oedema with over-rapid glucose fall (children)
- Concentration/units errors — always write 'units' in full

Antidote / reversal

Hypoglycaemia: **dextrose 25 g IV** (D50 50 ml or D10 250 ml), repeat by glucose; glucagon 1 mg IM if no IV access.

ICU PEARL Never start insulin in DKA until you know the potassium.

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Pantoprazole

Proton-pump inhibitor (substituted benzimidazole)

Drug and class

Pantoprazole — Proton-pump inhibitor (substituted benzimidazole).

Mechanism of action

Prodrug activated in the acid parietal-cell canaliculus; irreversibly inhibits H^+/K^+-ATPase, suppressing basal and stimulated acid secretion; raising gastric pH >6 stabilises clot in bleeding ulcers.

Dose in ICU

- **Stress-ulcer prophylaxis** (high risk: ventilation >48 h with coagulopathy, shock, chronic liver disease, prior GI bleed): 40 mg IV/NG daily
- **Upper GI bleed (after endoscopic haemostasis):** 80 mg IV bolus, then 8 mg/h for 72 h, or 40 mg IV 12-hourly (equivalent)
- **Before endoscopy:** 80 mg IV bolus
- Switch to oral once eating; stop when risk factors resolve

Drug dilution and infusion

- Vial 40 mg powder — reconstitute with 10 ml NS (4 mg/ml); bolus over 2–5 min or in 100 ml NS over 15 min
- Infusion: **80 mg in 100 ml NS** = 0.8 mg/ml at 10 ml/h (8 mg/h); stable 12 h

Dose adjustment — renal, hepatic and other conditions

Renal	No adjustment
Hepatic	Severe impairment: max 20–40 mg daily (prolonged half-life)
Other	Clopidogrel interaction less than omeprazole

Cautions and adverse effects

- **C. difficile infection**, possibly ventilator-associated pneumonia
- Hypomagnesaemia (prolonged use), acute interstitial nephritis
- Thrombocytopenia (rare); masks symptoms of gastric malignancy
- Continuing unnecessarily after ICU discharge

Antidote / reversal

No antidote.

ICU PEARL Write a stop date: stress-ulcer prophylaxis is for the ICU stay, not for life.

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Haloperidol

Typical (first-generation) butyrophenone antipsychotic

98

Drug and class

Haloperidol — Typical (first-generation) butyrophenone antipsychotic.

Mechanism of action

Potent dopamine D2-receptor antagonist in mesolimbic and mesocortical pathways — rapidly controls agitation and psychotic symptoms with little respiratory depression or hypotension; extrapyramidal effects from nigrostriatal D2 blockade.

Dose in ICU

- **Agitated / hyperactive delirium with distress or danger:** 0.5–2 mg IV/IM (elderly 0.25–0.5 mg); repeat every 15–30 min, doubling if needed (usual max ≈20 mg/day)
- **Scheduled:** 0.5–5 mg IV every 6–12 h for persistent agitation (short-term)
- **Antiemetic:** 0.5–1 mg IV
- PADIS: not recommended routinely to treat or prevent delirium — use for distressing symptoms; treat the cause

Drug dilution and infusion

- Ampoule 5 mg/ml (lactate) — IV use is off-label; give undiluted slowly over 1–2 min or diluted in 10 ml NS
- Decanoate (depot) is IM only — never IV

Dose adjustment — renal, hepatic and other conditions

Renal	No adjustment
Hepatic	Reduce dose (hepatic metabolism)
Other	Elderly, dementia: lowest dose; avoid in Parkinson's disease and Lewy body dementia; QTc >500 ms or rising >60 ms — hold

Cautions and adverse effects

- **QT prolongation and torsades de pointes** (IV, high dose, hypokalaemia/hypomagnesaemia) — baseline and daily ECG
- Extrapyramidal effects: acute dystonia, akathisia, parkinsonism
- **Neuroleptic malignant syndrome**: rigidity, hyperthermia, autonomic instability, raised CK
- Lowers seizure threshold; hypotension (rare)

Antidote / reversal

Dystonia: **promethazine 25–50 mg IV** or benztropine 1–2 mg; TdP: magnesium 2 g IV; NMS: stop, cool, dantrolene/bromocriptine.

ICU PEARL Haloperidol calms the agitated patient — it does not cure delirium; find the cause.

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Quetiapine

Atypical (second-generation) dibenzothiazepine antipsychotic

Drug and class

Quetiapine — Atypical (second-generation) dibenzothiazepine antipsychotic.

Mechanism of action

Antagonist at D2 (low affinity, fast dissociation), 5-HT2A, H1 and α1 receptors — sedating antipsychotic with low extrapyramidal risk; used for agitated delirium and to aid sleep and weaning from sedatives.

Dose in ICU

- **ICU delirium / agitation:** 25–50 mg enterally 12-hourly (12.5–25 mg in elderly); increase by 50 mg/day to max 200 mg 12-hourly
- **Night-time sedation / sedative weaning:** 25–50 mg at night
- **Stop** on resolution of delirium (taper over 2–3 days) — do not continue after ICU/hospital discharge

Drug dilution and infusion

- Oral tablets 25/50/100 mg — crush and give via NG with water flush
- No IV form

Dose adjustment — renal, hepatic and other conditions

Renal	No adjustment
Hepatic	Start 25 mg/day, increase by 25–50 mg/day
Other	CYP3A4 inhibitors (azoles, macrolides) raise levels — reduce dose; elderly/dementia: lowest dose

Cautions and adverse effects

- Sedation, orthostatic hypotension (α1 blockade), tachycardia
- QT prolongation (less than haloperidol IV); anticholinergic effects
- Metabolic effects (hyperglycaemia) with long use; NMS (rare)

Antidote / reversal

No antidote; supportive care for overdose (fluids, vasopressors for hypotension).

ICU PEARL Quetiapine at night helps sleep and sedative weaning — but write the stop plan the day you start it.

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Acetylcysteine (N-Acetylcysteine)

100

Antidote for paracetamol poisoning / mucolytic (thiol)

Drug and class

Acetylcysteine (N-Acetylcysteine) — Antidote for paracetamol poisoning / mucolytic (thiol).

Mechanism of action

Glutathione precursor that replenishes hepatic glutathione, detoxifying the reactive paracetamol metabolite NAPQI; also directly conjugates NAPQI, improves microcirculation and oxygen delivery in established liver failure. Mucolytic by breaking disulphide bonds in mucus.

Dose in ICU

- **Paracetamol overdose — 21-h regimen:** 150 mg/kg in 200 ml D5 over 60 min, then 50 mg/kg in 500 ml over 4 h, then 100 mg/kg in 1000 ml over 16 h (weight capped at 100–110 kg)
- **SNAP 12-h regimen:** 100 mg/kg over 2 h, then 200 mg/kg over 10 h
- Start if level above treatment line (100 or 150 mg/L at 4 h), staggered/unknown-time ingestion, or abnormal LFTs; continue if INR/ALT still rising
- **Non-paracetamol acute liver failure:** 150 mg/kg over 1 h, 12.5 mg/kg/h ×4 h, then 6.25 mg/kg/h ×67 h
- **Mucolytic:** nebulised 3–5 ml of 10–20% 6–8 hourly with a bronchodilator

Drug dilution and infusion

- Ampoule 200 mg/ml (10 ml = 2 g)
- Dilute in D5 (or NS) as above; reduce volumes in children and fluid-restricted adults

Dose adjustment — renal, hepatic and other conditions

Renal	No adjustment
Hepatic	No adjustment — continue in liver failure
Other	Obesity: dose capped at 100–110 kg; heart failure/children — reduce fluid volume

Cautions and adverse effects

- **Anaphylactoid reactions** (flushing, urticaria, bronchospasm, hypotension) — commonest in the first hour, less with 12-h regimen
- Fluid overload and hyponatraemia (large D5 volumes)
- Nausea, vomiting; bronchospasm with nebulised use; mild INR prolongation

Antidote / reversal

Reactions: stop infusion, antihistamine (chlorpheniramine), salbutamol; restart at slower rate when settled.

ICU PEARL When in doubt in paracetamol poisoning, start acetylcysteine — the harm of a reaction is far less than the harm of liver failure.

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CHAPTER 11 · CLASS SUMMARY

Anticoagulants, Thrombolytics and Other ICU Agents — At a Glance

Anticoagulation and thrombolysis, glycaemic control, stress-ulcer prophylaxis, delirium and antidote therapy

Drug	ICU dose	Dilution / infusion	Renal / hepatic / other	Key cautions	Antidote
Heparin Sodium (Unfractionated Heparin)	VTE 80 U/kg then 18 U/kg/h; ACS 60/12 U/kg; SC 5000 U q8–12h	25,000 U/50 ml = 500 U/ml	None — preferred in renal failure	Bleeding, HIT, ↑K^+	Protamine
Enoxaparin	Prophylaxis 40 mg daily; treatment 1 mg/kg q12h	Prefilled 100 mg/ml SC	CrCl <30: once daily; avoid HD	Bleeding, accumulation, spinal haematoma	Protamine (partial)
Alteplase (tPA)	Stroke 0.9 mg/kg (max 90); PE 100 mg/2 h; STEMI accelerated	50 mg + 50 ml water = 1 mg/ml	No adjustment	ICH, bleeding, angioedema	Cryoprecipitate, tranexamic acid
Insulin (Regular / Soluble)	DKA 0.1 U/kg/h; ICU target 140–180 mg/dl; hyper-K 10 U + 25 g dextrose	50 U/50 ml = 1 U/ml	↓ in renal & hepatic failure	Hypoglycaemia, ↓K^+, ↓PO_4	Dextrose; glucagon
Pantoprazole	SUP 40 mg daily; GI bleed 80 mg then 8 mg/h ×72 h (or 40 mg BD)	40 mg/10 ml; infusion 80 mg/100 ml	Severe hepatic: max 20–40 mg	C. difficile, ↓Mg^{2+}, AIN	None
Haloperidol	0.5–2 mg IV/IM (elderly 0.25–0.5), repeat q15–30 min	Undiluted 5 mg/ml slow IV (off-label)	↓ hepatic; avoid Parkinson's	QT/TdP, EPS, NMS	Promethazine; magnesium; dantrolene
Quetiapine	25–50 mg NG BD; max 200 mg BD	Oral/NG only	Start 25 mg in hepatic failure	Sedation, hypotension, QT	None (supportive)
Acetylcysteine (N-Acetylcysteine)	21-h: 150 mg/kg/1 h, 50 mg/kg/4 h, 100 mg/kg/16 h (or SNAP 12-h)	200 mg/ml in D5 (200/500/1000 ml)	No adjustment; cap weight 100–110 kg	Anaphylactoid, fluid overload	Antihistamine for reactions

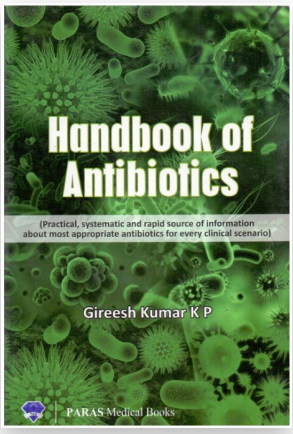
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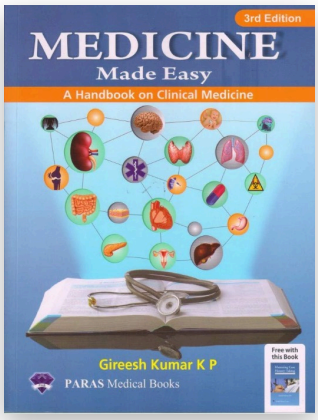
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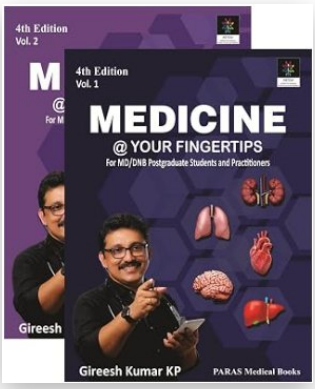
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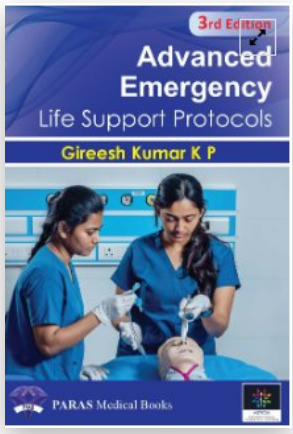
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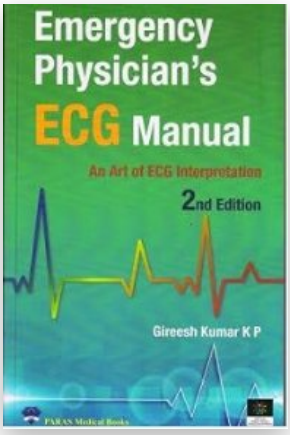
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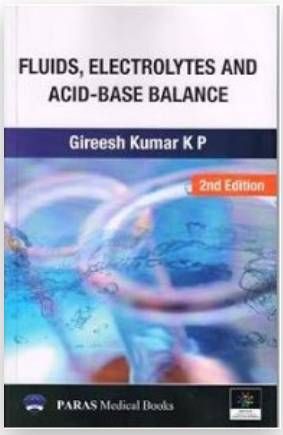
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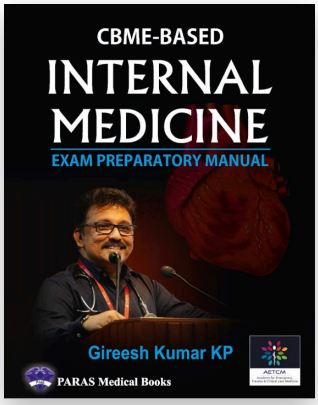
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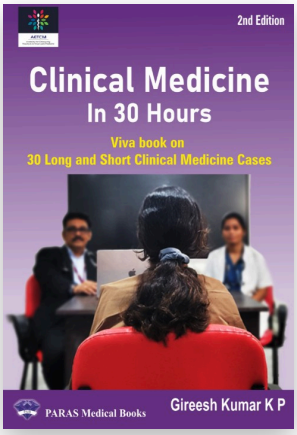
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