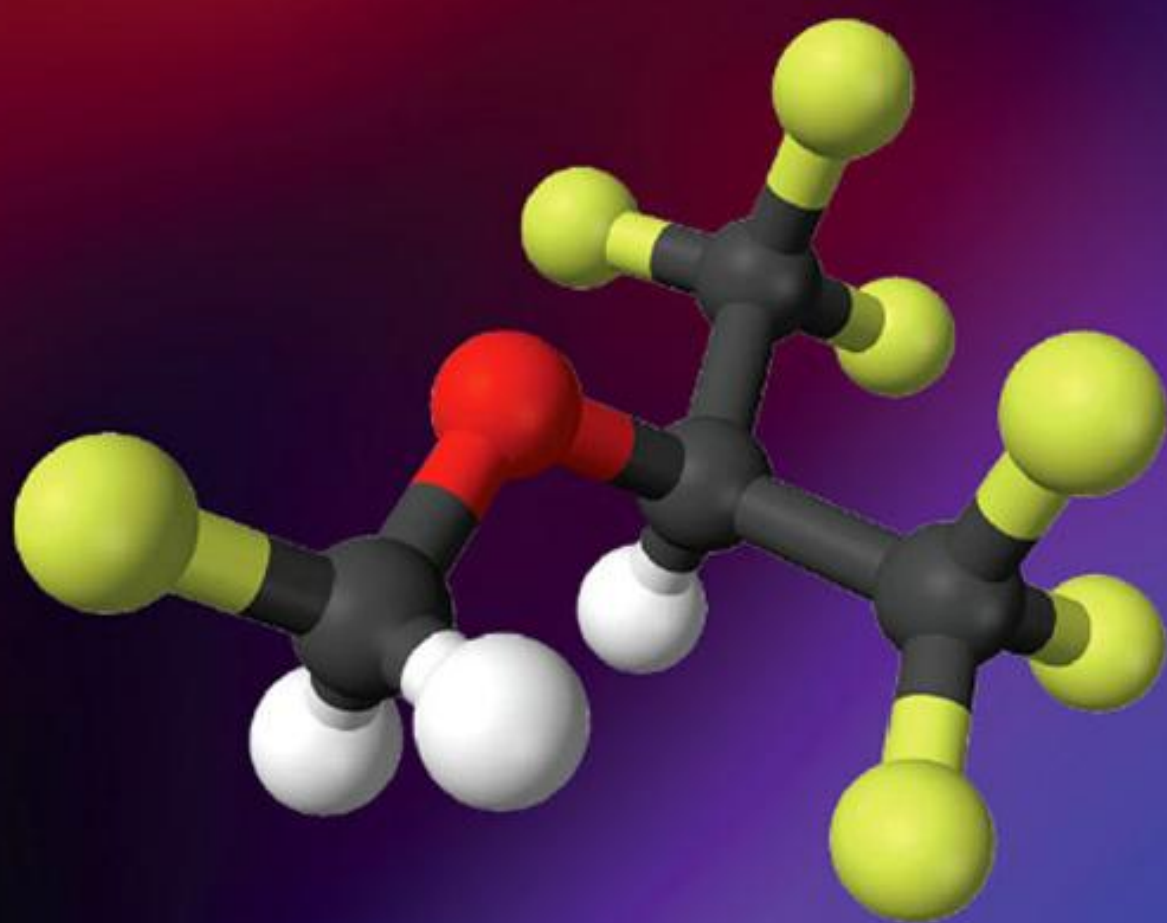


THIRD EDITION

LABORATORY ANIMAL ANAESTHESIA



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Inevitably, a number of specialist terms are used throughout this book and these are defined below.

Anaesthesia a state of controllable, reversible insensibility in which sensory perception and motor responses are both markedly depressed

Analgesia the temporary abolition or diminution of pain perception

Analeptic drug which stimulates respiration

Anoxia complete deprivation of oxygen for tissue respiration

Apnoea temporary cessation of breathing

Arrhythmia (cardiac) alteration in the normal rhythm of the heart

Asystole lack of cardiac muscle contractions

Ataxia lack of co-ordination, 'wobbliness'

BMR basal metabolic rate

Bradycardia slowing of the heart rate

CNS central nervous system

CNS depressant any agent which modifies function by depressing sensory or motor responses in the CNS

Cyanosis blue or purple colouring of the skin or visible membranes due to the presence of an increased concentration of reduced haemoglobin in capillary blood, symptomatic of hypoxia

Dosages mg of drug per kg body weight (mg/kg) except for the neuroleptanalgesic combinations which are more conveniently expressed as ml of commercial or diluted premixed solution per kg body weight (ml/kg)

Dosage schedules u.i.d. – once daily

b.i.d. – twice daily

t.i.d. – three times daily

q.i.d. – four times daily

Dyspnoea laboured breathing

ECG electrocardiogram

Hypercapnia elevated blood carbon dioxide content

Hyperpnoea fast or deep breathing

Hypertension elevated (arterial) blood pressure

Hypnotic a drug which induces a state resembling deep sleep, but usually with little analgesic effect

Hypocapnia reduced blood carbon dioxide content

Hypopnoea slow or shallow breathing

Hypotension a fall in (arterial) blood pressure

Hypothermia a fall in body temperature

Hypovolaemia a fall in circulating blood volume

Hypoxia depressed levels of oxygen

Induction (of anaesthesia) the initial establishment of a state of anaesthesia

Injection routes iv – intravenous

im – intramuscular

ip – intraperitoneal

sc – subcutaneous

Laryngospasm spasm of the vocal cords, producing complete or partial obstruction of the airway

Minute volume the volume of gas breathed in 1 minute, that is, the product of tidal volume and respiratory rate

Narcosis a state of insensibility or stupor from which it is difficult to arouse the animal

Normovolaemic having a normal circulating blood volume

PCO₂ partial pressure of carbon dioxide

Per os by mouth

PO₂ partial pressure of oxygen

Polypnoea rapid, panting breathing

Pulmonary ventilation the mechanical expansion and contraction of the lungs in order to renew alveolar air with fresh atmospheric air

Tachycardia an increase in heart rate

Tachypnoea rapid respiration

Tidal volume the volume of gas expired with each breath

TABLE 5.4 Pain-Related Behaviour Following Abdominal Surgery in Rats, Mice and Rabbits.

Species	Behaviours
Rat	Back arching (vertical stretch from crouched position as in felines upon waking); belly-press (muscular contraction where the ventral abdomen is pressed upon bedding – occurs immediately prior to or during ambulation); fall/stagger (stagger or fall during ambulation – a rapid transition to crouch from high or low rear. More often a partial loss of balance during grooming, resulting in lateral lying position from which recovery to balanced crouched posture occurs almost immediately); writhing (writhing involving lateral contortion of flank abdominal muscles, usually when crouching but also during transient break in walking or grooming); twitch (brief, seemingly spasmodic contraction, usually of the muscles of the back, travelling in an anterior–posterior direction)
Mouse	Writhing (slow contraction of abdominal muscles); rear-leg lift (momentary lifting of rear paw, often associated with writhe or press); belly-press (pressing of abdomen to cage floor, often associated with hindlimb extension); flinching (rapid contraction of muscles of back, as in twitching, but also involving other areas of the body)
Rabbit	Twitch (rapid movement of fur on back); wince (rapid movement backwards in a rocking motion, accompanied by eye closing and swallowing); stagger (partial loss of balance); flinch (body jerks upwards for no apparent reason); press (abdomen pushed towards floor, usually before walking); writhe (contraction of the abdominal muscles)

For further details, see Roughan and Flecknell (2003, 2004), Wright-Williams et al. (2007) and Leach et al. (2009).

TABLE 5.5 Suggested Dose Rates for Non-steroidal Anti-inflammatory Drugs in Laboratory Animals.

Drug	Mouse	Rat	Guinea pig	Rabbit	Ferret
Aspirin	120 mg/kg per os	100 mg/kg per os	87 mg/kg per os	100 mg/kg per os	200 mg/kg per os
Carprofen	5 mg/kg sc	5 mg/kg sc	4 mg/kg sc ? once daily	1.5 mg/kg per os u.i.d., 4 mg/ kg sc u.i.d.	4 mg/kg sc u.i.d.
Diclofenac	8 mg/kg per os	10 mg/kg per os	2.1 mg/kg per os	–	–
Flunixin	2.5 mg/kg sc or im ?12 hourly	2.5 mg/kg sc or im ?12 hourly	2.5 mg/kg sc or im ?12 hourly	1–2 mg/kg sc im ? 12 hourly	0.5–2 mg/ kg sc 12– 24 hourly
Ibuprofen	30 mg/kg per os	15 mg/kg per os	10 mg/kg im ?4 hourly	10 mg/kg iv ? 4 hourly	–
Indomethacin	1 mg/kg per os	2 mg/kg per os	8 mg/kg per os	12.5 mg/kg per os	–
Ketoprofen	5 mg/kg sc	5 mg/kg sc	–	3 mg/kg im	3 mg/kg im
Meloxicam	5 mg/kg sc or per os	1 mg/kg sc or per os	0.1–0.3 mg/ kg sc or per os every 24 h	0.6–1 mg/ kg sc or per os	0.1–0.2 mg/ kg sc or per os
Paracetamol (acetaminophen)	200 mg/kg per os	200 mg/kg per os	–	–	–

Note that considerable individual and strain variation in response may be encountered and that it is therefore essential to assess the analgesic effect in each individual animal

TABLE 5.7 Suggested Dose Rates for Opioid Analgesics in Laboratory Animals.

Drug	Mouse	Rat	Guinea pig	Rabbit	Ferret
Buprenorphine	0.05–0.1 mg/kg sc 12 hourly	0.01–0.05 mg/kg sc or iv, 8–12 hourly 0.1–0.25 mg/kg per os, 8–12 hourly	0.05 mg/kg sc, 8–12 hourly	0.01–0.05 mg/kg sc or iv, 8–12 hourly	0.01–0.03 mg/ kg iv, im or sc, 8–12 hourly
Butorphanol	1–2 mg/kg sc, 4 hourly	1–2 mg/kg sc, 4 hourly	1–2 mg/kg sc, 4 hourly	0.1 – 0.5 mg/kg iv, 4 hourly	0.4 mg/kg im, 4–6 hourly
Hydromorphone	–	–	–	0.1–0.2 mg/kg ? 6–8 hourly	0.1–0.2 mg/kg ?6–8 hourly
Morphine	2.5 mg/kg sc, 2–4 hourly	2.5 mg/kg sc, 2–4 hourly	2–5 mg/kg sc or im, 4 hourly	2–5 mg/kg sc or im, 2–4 hourly	0.5–2 mg/kg im or sc, 6 hourly
Nalbuphine	2–4 mg/kg im ?4 hourly	1–2 mg/kg im, 3 hourly	1–2 mg/kg iv, ip or im	1–2 mg/kg iv, 4–5 hourly	–
Oxymorphone	0.2–0.5 mg/kg sc ?4 hourly	0.2–0.5 mg/kg sc ?4 hourly	0.2–0.5 mg/kg sc ? 4 hourly	0.05–0.2 mg/kg sc ?6–8 hourly	0.05–0.2 mg/kg sc ?6–8 hourly
Pentazocine	5–10 mg/kg sc 3–4 hourly	5–10 mg/kg sc, 3–4 hourly	–	5–10 mg/kg sc, im or iv, 4 hourly	–
Pethidine (Meperidine)	10–20 mg/kg sc or im, 2–3 hourly	10–20 mg/kg sc or im, 2–3 hourly	10–20 mg/kg sc or im, 2–3 hourly	5–10 mg/kg sc or im, 2–3 hourly	5–10 mg/kg im or sc, 2–4 hourly
Tramadol	5 mg/kg sc, ip ?	5 mg/kg sc, ip ?	–	–	–

*Note that considerable individual and strain variation in response may be encountered, and that it is therefore essential to assess the analgesic effect in each animal.
? = duration of action uncertain.*

TABLE 6.1 Sedatives, Tranquillizers and Other Pre-anaesthetic Medication for Use in the Rat.

Drug	Dose rate	Comments
Acepromazine	2.5 mg/kg im, ip	Light sedation
Atropine	0.05 mg/kg ip, sc	Anticholinergic
Diazepam	2.5–5.0 mg/kg ip, im	Light sedation
Fentanyl/dropiderol (Innovar-Vet)	0.3–0.5 ml/kg im	Immobilization/analgesia
Fentanyl/fluanisone (Hypnorm)	0.2–0.5 ml/kg im	Light/moderate sedation, moderate analgesia
	0.3–0.6 ml/kg ip	
Glycopyrrolate	0.5 mg/kg im	Anticholinergic
Ketamine	50–100 mg/kg im, ip	Deep sedation, immobilization, mild to moderate analgesia
Medetomidine	30–100 µg/kg sc, ip	Light to heavy sedation, mild to moderate analgesia
Midazolam	5 mg/kg ip	Light sedation
Xylazine	1–5 mg/kg im, ip	Light to heavy sedation, mild to moderate analgesia

Considerable variation in effect occurs between different strains.

TABLE 6.2 Anaesthetic Dose Rates in the Rat.

Drug	Dose rate	Effect	Duration of anaesthesia (minutes)	Sleep time (minutes)
Alphaxalone/alphadolone	10–12 mg/kg iv	Surgical anaesthesia	5	10
Chloral hydrate	400 mg/kg ip	Light/surgical anaesthesia	60–120	120–180
Alpha-chloralose	55–65 mg/kg ip	Light anaesthesia	480–600	Non-recovery only
Etorphine/methotrimeprazine (Immobilon) + midazolam	0.5 ml/kg sc*	Surgical anaesthesia	60–70	120–240
Fentanyl/fluanisone + diazepam	0.6 ml/kg ip + 2.5 mg/kg ip	Surgical anaesthesia	20–40	120–240
Fentanyl/fluanisone/ midazolam	2.7 ml/kg ip†	Surgical anaesthesia	30–40	120–240
Fentanyl/medetomidine	300 µg/kg + 200 µg/kg ip	Surgical anaesthesia	60–70	240–360
Inactin (thiobutobarbital)	80 mg/kg ip	Surgical anaesthesia	60–240	120–300
Ketamine/acepromazine	75 mg/kg + 2.5 mg/kg ip	Light anaesthesia	20–30	120
Ketamine/diazepam	75 mg/kg + 5 mg/kg ip	Light anaesthesia	20–30	120
Ketamine/medetomidine	75 mg/kg + 0.5 mg/kg ip	Surgical anaesthesia	20–30	120–240
Ketamine/midazolam	75 mg/kg + 5 mg/kg ip	Light anaesthesia	20–30	120
Ketamine/xylazine	75–100 mg/kg + 10 mg/kg ip	Surgical anaesthesia	20–30	120–240
Ketamine/xylazine/ acepromazine	40–50 mg/kg + 2.5 mg/kg + 0.75 mg/kg im			
Methohexital	10–15 mg/kg iv	Surgical anaesthesia	5	10
Pentobarbital	40–50 mg/kg ip	Light anaesthesia	15–60	120–240
Propofol	10 mg/kg iv	Surgical anaesthesia	5	10
Thiopental	30 mg/kg iv	Surgical anaesthesia	10	15
Tiletamine/zolezepam	40 mg/kg ip	Light anaesthesia	15–25	60–120
Urethane	1000 mg/kg ip	Surgical anaesthesia	360–480	Non-recovery only

Duration of anaesthesia and sleep time (loss of righting reflex) are provided only as a general guide, since considerable between-animal variation occurs. For recommended techniques, see text.

**Dose in millilitres per kilogram of a mixture of one part 'Immobilon', one part midazolam (5 mg/ml initial concentration) and two parts water for injection.*

†Dose in millilitres per kilogram of a mixture of one part 'Hypnorm' plus two parts water for injection, and one part midazolam (5 mg/ml initial concentration).

TABLE 6.3 Antagonists to Anaesthetic Regimens for Use in Rodents and Rabbits.

Compound	Anaesthetic regimen	Dose rate	Comments
Atipamezole	Any regimen using xylazine or medetomidine	0.1–1 mg/kg im, ip, sc or iv	Highly specific alpha2 adrenoreceptor antagonist; dose required varies depending on dose of xylazine or medetomidine administered
Buprenorphine	Any regimen using μ opioids (e.g. fentanyl)	See Table 14c	Slower onset than butorphanol and nalbuphine, but longer-acting analgesia
Doxapram	All anaesthetics	5–10 mg/kg im, iv or ip	General respiratory stimulant
Flumaznil	Benzodiazepine (e.g. midazolam)	0.1–10 mg/kg	Dose varies depending upon dose of benzodiazepine; resedation may occur
Butorphanol	Any regimen using μ opioids (e.g. fentanyl)	See Table 14c	Almost as rapid-acting as naloxone, maintains post-operative analgesia
Naloxone	Any regimen using μ opioids (e.g. fentanyl)	0.01–0.1 mg/kg iv, im or ip	Reverses analgesia as well as respiratory depression
Yohimbine	Any regimen using xylazine or medetomidine	0.2 mg/kg iv 0.5 mg/kg im	Relatively non-specific antagonist; not recommended

TABLE 6.4 Sedatives, Tranquillizers and Other Pre-anaesthetic Medication for Use in the Mouse.

Drug	Dose rate	Comments
Acepromazine	2–5 mg/kg ip, sc	Light sedation
Atropine	0.04 mg/kg sc	Anticholinergic
Diazepam	5 mg/kg im, ip	Light sedation
Fentanyl/dropiderol (Innovar-Vet)	0.5 ml/kg im	Immobilization, analgesia
Fentanyl/fluanisone (Hypnorm)	0.1–0.3 ml/kg ip	Light sedation, moderate analgesia
Ketamine	100–200 mg/kg im	Deep sedation, mild to moderate analgesia
Medetomidine	30–100 µg/kg sc	Light to deep sedation, mild to moderate
Midazolam	5 mg/kg im, ip	Light to moderate sedation
Xylazine	5–10 mg/kg ip	Light sedation, mild to moderate analgesia

Considerable variation in effects occurs between different strains.

TABLE 6.5 Anaesthetic Dose Rates in the Mouse.

Drug	Dose rate	Effect	Duration of anaesthesia (minutes)	Sleep time (minutes)
Alphachloralose	100–120 mg/kg ip	Light anaesthesia	300–420	Non-recovery only
Alphaxalone/alphadolone	10–15 mg/kg iv	Surgical anaesthesia	5	10
Chloral hydrate	400 mg/kg ip	Light anaesthesia	30	60–90
Fentanyl/fluanisone (Hypnorm) + diazepam	0.4 ml/kg ip + 5 mg/kg ip	Surgical anaesthesia	30–40	120–240
Fentanyl/fluanisone (Hypnorm)/midazolam	10.0 ml/kg ip*	Surgical anaesthesia	30–40	120–240
Ketamine/acepromazine	100 mg/kg + 5 mg/kg ip	Immobilization/anaesthesia	20–30	40–120
Ketamine/diazepam	100 mg/kg + 5 mg/kg ip	Immobilization/anaesthesia	20–30	60–120
Ketamine/medetomidine	75 mg/kg + 1.0 mg/kg ip	Surgical anaesthesia	20–30	60–120
Ketamine/midazolam	100 mg/kg + 5 mg/kg ip	Immobilization/anaesthesia	20–30	60–120
Ketamine/xylazine	80–100 mg/kg + 10 mg/kg ip	Surgical anaesthesia	20–30	60–120
Ketamine/xylazine/acepromazine	80–100 mg/kg + 10 mg/kg ip + 3 mg/kg ip	Surgical anaesthesia	30–40	60–120
Methohexital	10 mg/kg iv	Surgical anaesthesia	5	10
Metomidate/fentanyl	60 mg/kg + 0.06 mg/kg sc	Surgical anaesthesia	40–60	90–120
Pentobarbital	40–50 mg/kg ip	Immobilization/anaesthesia	20–40	120–180
Propofol	26 mg/kg iv	Surgical anaesthesia	5–10	10–15
Thiopental	30–40 mg/kg iv	Surgical anaesthesia	5–10	10–15
Tiletamine/zolezepam	80 mg/kg ip	Immobilization		60–120
Tribromoethanol	240 mg/kg ip	Surgical anaesthesia	15–45	60–120

Duration of anaesthesia and sleep time (loss of righting reflex) are provided only as a general guide, since considerable between-animal variation occurs. For recommended techniques, see text.

*Dose in millilitres per kilogram of a mixture of one part 'Hypnorm' plus two parts water for injection, and one part midazolam (5 mg/ml initial concentration).

TABLE 6.12 Sedatives, Tranquillizers and Other Pre-anaesthetic Medication for Use in the Rabbit.

Drug	Dose rate	Comments
Acepromazine	1 mg/kg im	Moderate sedation
Acepromazine + butorphanol	1 mg/kg + 1 mg/kg im	Moderate to heavy sedation, moderate analgesia
Alphaxalone/ alphadolone	9–12 mg/kg im	Moderate to heavy sedation, little analgesia
Atropine	0.05 mg/kg im	Very short acting in some rabbits
Diazepam	0.5–2.0 mg/kg iv, im, ip	Light to moderate sedation
Fentanyl/dropiderol (Innovar-Vet)	0.22 ml/kg im	Immobilization, analgesia
Fentanyl/fluanisone (Hypnorm)	0.2–0.5 ml/kg im	Light to heavy sedation, light to deep analgesia
Glycopyrrolate	0.01 mg/kg iv, 0.1 mg/kg im sc	Anticholinergic
Ketamine	25–50 mg/kg im	Moderate to heavy sedation, mild to moderate analgesia
Medetomidine	0.1–0.5 mg/kg im, sc	Light to heavy sedation, mild to moderate analgesia
Midazolam	0.5–2 mg/kg iv, im, ip	Light to moderate sedation
Xylazine	2–5 mg/kg im	Light to moderate sedation, mild to moderate analgesia

Considerable variation in effects occurs between different strains.

TABLE 6.13 Anaesthetic Dose Rates in the Rabbit.

Drug	Dose rate	Effect	Duration of anaesthesia (minutes)	Sleep time (minutes)
Alphaxalone/alphadolone	6–9 mg/kg iv	Light anaesthesia	5–10	10–20
Alpha-chloralose	80–100 mg/kg iv	Light to surgical anaesthesia	360–600	Non-recovery only
Etorphine/methotrimeprazine (Immobilon SA)	0.025–0.05 ml/kg im	Immobilization, analgesia	60 (analgesia)	120–240
Etorphine/methotrimeprazine (Immobilon SA) + midazolam	0.05 ml/kg im + 1 mg/kg iv	Surgical anaesthesia (severe respiratory depression, see text)	50–100	180–240
Fentanyl/fluanisone (Hypnorm) + diazepam	0.3 ml/kg im + 1–2 mg/kg iv, im or ip	Surgical anaesthesia	20–40	60–120
Fentanyl/fluanisone (Hypnorm) + midazolam	0.3 ml/kg im + 1–2 mg/kg iv or ip	Surgical anaesthesia	20–40	60–120
Fentanyl + medetomidine	8 µg/kg iv + 330 µg/kg iv		30–40	60–120
Ketamine/acepromazine	50 mg/kg im + 1 mg/kg im	Surgical anaesthesia	20–30	60–90
Ketamine/diazepam	25 mg/kg im + 5 mg/kg im	Surgical anaesthesia	20–30	60–90
Ketamine/medetomidine	15 mg/kg im + 0.25 mg/kg sc, im	Surgical anaesthesia	20–30	60–90

(Continued)

TABLE 6.13 (Continued)

Drug	Dose rate	Effect	Duration of anaesthesia (minutes)	Sleep time (minutes)
Ketamine/xylazine	35 mg/kg im + 5 mg/kg im	Surgical anaesthesia	25–40	60–120
	10 mg/kg iv + 3 mg/kg iv	Surgical anaesthesia	20–30	60–90
Ketamine/xylazine/acepromazine	35 mg/kg im + 5 mg/kg im + 1.0 mg/kg im, sc	Surgical anaesthesia	45–75	100–150
Ketamine/xylazine/butorphanol	35 mg/kg im + 5 mg/kg im + 0.1 mg/kg im	Surgical anaesthesia	60–90	120–180
Methohexital	10–15 mg/kg iv	Surgical anaesthesia	4–5	5–10
Pentobarbital	30–45 mg/kg iv	Light to medium anaesthesia	20–30	60–120
Propofol	10 mg/kg iv	Light anaesthesia	5–10	10–15
Thiopental	30 mg/kg iv	Surgical anaesthesia	5–10	10–15
Urethane	1000–2000 mg/kg iv	Surgical anaesthesia	360–480	Non-recovery only

Duration of anaesthesia and sleep time (loss of righting reflex) are provided only as a general guide, since considerable between-animal variation occurs. For recommended techniques, see text.

TABLE 6.26 Anaesthetic, Sedative and Analgesic Drugs for Use in Birds.

Drug	Dose rate	Effect	Duration of anaesthesia (minutes)	Sleep time (minutes)
Alphaxalone/alphadolone	10–14 mg/kg iv	Light anaesthesia	10–15	20–60
Buprenorphine	0.01–0.05 mg/kg im	Analgesia		
Butorphanol	2–4 mg/kg im	Analgesia		
Equithesin*	2.5 ml/kg im	Light to medium anaesthesia	20–30	60–120
Flunixin	1–10 mg/kg im	Analgesia		
Ketamine > 1 kg	15–20 mg/kg im	Immobilization, some analgesia	20–30	30–90
Ketamine < 1 kg	30–40 mg/kg im			
Ketamine/diazepam	20–40 mg/kg im + 1–1.5 mg/kg im	Medium surgical anaesthesia	20–30	30–90
Ketamine/midazolam	20–40 mg/kg im + 4 mg/kg im	Medium surgical anaesthesia	20–30	30–90
Ketamine/xylazine	5–30 mg/kg im + 0.2–5 mg/kg im	Light to medium surgical anaesthesia	10–30	30–60
Ketamine/medetomidine	5–10 mg/kg im + 0.05–0.1 mg/kg im	Light to medium surgical anaesthesia	10–30	30–60
Ketoprofen	2 mg/kg sc	Analgesia		
Metomidate	10–20 mg/kg im	Immobilization	10–30	30–60
Propofol	5–10 mg/kg iv	Medium surgical anaesthesia	10	20

Duration of anaesthesia and sleep time (loss of righting reflex) are provided only as a general guide, since considerable species variation occurs. For recommended techniques, see text.

**See Appendix 3.*