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| **TRANQUILIZERS, SEDATIVES, AND OTHER AGENTS** |
| **Drug** | **Dosage and Route** | **Duration of Anesthesia** | **Comments** |
| **Barbiturates** |
| Thiopental (Pentothal®) | 25-50 mg/kg IV50 mg/kg IP | 10 minutes- unproven | Dose dependent respiratory depression and hypothermia |
| Pentobarbital (Nembutal®) | 40-50 mg/kg IP sedation70-85 mg/kg IP anesthesia | 10-300 minutes | Respiratory depression /poor analgesia |
| **Dissociatives** |
| Ketamine (Ketoset®) | 100-200 mg/kg IP | Unproven | Poor muscle relaxation/mild analgesia |
| Ketamine + Medetomidine\* | 75 mg/kg + 1 mg/kg IP | Surgical anesthesia 20-30 min. | Sleep time 60-120 min. |
| Ketamine + Dexmedetomidine | 50-75 mg/kg + 500 µg/kg IP | 20-30 minutes | May not produce surgical plne of anesthesia for major procedures. If re-dosing, administer ketamine only at ¼ - ½ the original dose. |
| **Ketamine + xylazine\* (Rompun®) Recommended** | 80-120 mg/kg ketamine IP + 5-10 mg/kg xylazine IP | 30-45 minutes | Anesthetic depth varies from sedation to anesthesia |
| Ketamine + xylazine\* + acepromazine (Triple sedative) | 13 mg/kg ketamine + 0.66 mg/kg xylazine + 0.33 mg/kg ace IP (0.01-0.03 ml/100g)  | Unproven | Sedative- not appropriate for anesthesia alone- 60-120 min, sleep time, 30-40 min. anesthesia |
| Ketamine + acepromazine | 44 mg/kg ketamine IP + 0.75 mg/kg ace IP | 20-30 minutes | Sedation only |
| Ketamine + diazepam (Valium®) | 100-200 mg/kg ket IP + 5 mg/kg diaz. IP | 20-30 minutes | Sedation/immobilization |
| Ketamine + midazolam (Versed®) | 100 mg/kg ket IP + 5 mg/kg mid. IP | 20-30 minutes | Immobilization |
| **Other** |
| Propofol (Diprivan®) | 12-26 mg/kg IV | 5-7 minutes | Titrate as needed |
| Urethane | 1000-1500 mg/kg IP |  | **Caution!** Prolonged anesthesia; terminal procedures only; carcinogenic and mutagenic |
| Tribromoethanol (Avertin) | 200-240 mg/kg IP | Use fresh solution (<1 week old).  | May be used for only a single survival procedure. Expect 15-20 min. anesthesia time. (Booster as necessary during procedure). |
| **Inhalation** |
| Isoflurane (Forane®, Aerane®) Recommended | 4-5 % for induction1-2 % for maintenance |  | 300 ul in a 500 ml container- chamber induction for brief anesthesia; maintenance requires use of a calibrated vaporizer |
| Sevoflurane | 5-7% induction3-4% maintenance |  | Requires use of a calibrated vaporizer. |

Subcutaneous (SC), Intaperitoneal (IP), Intravenous (IV)

\*Ketamine alone is not adequate for deep anesthesia or procedures that are painful. It is only to be used for immobilization.

\*Reversal of α2agonists such as xylazine and medetomidine can be accomplished by giving atipamazole (Antisedan®) 1-2.5 mg/kg IM, IP, SC or IV or Yohimbine 0.2 mg/kg IV or 1- 2.1mg/kg IP. Side effects of yohimbine include CNS excitement, muscle tremors, salivation, and increased respiratory rate.

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| **Analgesic Drugs** |
| Drug | Dosage | Comments |
| Buprenorphine (Buprenex®)a,c | 0.05-0.1 (2 mg/kg) mg/kg SC or IV | 6-12 hrs |
| Buprenorphine SR | 1-1.2 mg/kg SC | Lasts for 3 days |
| Carprofen (Rimadyl®) | 5 mg/kg SC or IP, 10 mg/kg PO | 24 hours |
| Flunixin (Banamine®) | 2.5 mg/kg SC | 12-24 hours |
| Ibuprofen | 7.5-40 mg/kg PO (0.2 mg/ml water) |  |
| Ketoprofen | 5 mg/kg SC | 24 h |
| Meloxicam (Metacam®) | 2 mg/kg SC, 5 mg/kg PO | 12-24 hours |
| Morphine a,b | 2-5 mg/kg SC | 1-4 hrs |
| Tramadol | 5 mg/kg SC, IP |  |
| Lidocaine 1% | 4 mg/kg (0.4 ml/kg) | 1.5-2 hours |
| Bupivacaine 0.25% | 1-2 mg/kg (0.4-0.8 ml/kg) | 4-12 hours |

Subcutaneous (SC), Intraperitoneal (IP), Intravenous (IV), oral (PO)

a In addition to being an analgesic, this drug also acts as a sedative. If this drug is administered as an animal is recovering from anesthesia, the animal must be observed carefully for cumulative sedative effects of the anesthetics and analgesics.

b  This drug has a broad range of recommended doses. It is recommended that the animal be given the lowest dose in the range and be observed for signs of pain or discomfort. Additional analgesics may be administered if necessary at the next scheduled dosing time.

c Naloxone 0.01-0.1 mg/kg IV, IP can be given as opiod reversal agent once as needed to reverse respiratory depression. Note that reversal will also remove the analgesic effect of the opioid.

Mouse Neonatal Anesthesia (mouse < 10 days of age)

Hypothermia- can only be performed in neonatal rodents < 6 days old and should not be used for procedures lasting longer than 30 minutes.

1. Place neonates either on a latex covered bed of crushed ice, in a cut off finger of a latex glove and place in ice water (animal’s head must be held above water to prevent water aspiration and death) or a paper lined test tube and placing in crushed ice/ice water.
2. Animals have reached proper plane of anesthesia when pedal reflex is lost (animal does not respond to toe pinch).
3. Once proper plane is reached, animals are removed from ice bath and placed on a chilled cold pack or bed of ice.
4. Use fiber optic light during procedure because incandescent bulbs can warm surgical field.
5. Following anesthesia animal should be rewarmed slowly. Rapid warming can cause tissue damage. Patient can be rewarmed on a circulating water heating pad (40oC) or in an incubator (33oC).
6. Pups can be returned to dam once they are able to crawl.

Inhalant Anesthetics

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| Stage of Anesthesia | Route | Oxygen (L/min.) | Isoflurane (%) |
| Induction | Mask or Chamber | 0.5-1 | 4-5 |
| Maintenance | Mask or intubation | 0.5-1 | 1-2 |

**Recommended Injectable Anesthetics**

Ketamine + Xylazine- Mice >7 days, 50-150 mg/kg Ketamine + 5-10 mg/kg xylazine

1. Intraperitoneal (IP)- 27 g needle, 1 ml syringe; maximum volume- 0.5 ml
2. Subcutaneous (SC)- 27 g needle, 1 ml syringe; maximum volume- 1 ml

Emergency Situations

Attempts at resuscitating mice that have received an excessive dose of anesthetic or are experiencing cardiac or respiratory arrest for any reason, are typically unrewarding. Chest compressions often do not restore circulation, and artificial ventilation is difficult in the mouse. Respiratory depression can be treated by the administration of doxapram (Dopram®) 5-10 mg/kg IV or IP administered repeatedly at approximately 10-15 min. intervals. Supportive care includes raising body temperature to normal, providing supplemental oxygen through a facemask or nosecone, and administering reversal agents if available (e.g. Yohimbine at 2.1 mg/kg IP or atipamazole 1-2.5 mg/kg IP or SC as needed to reverse xylazine or medetomidine).

Normal Values for Mice:

**HR 310-840 beats/min, RR 163 breaths/min., Temp. 98.8-99.3o**

**Buprenorphine Dilution and Dosage Chart**

**Buprenorphine (Buprenex®)** 0.3 mg/ml in boxes of 5 1 ml vials

**Dilution for Mice**: 1.0 ml Buprenorphine (0.3 mg buprenorphine/ml) + 9.0 D5W (5% dextrose in water) for injection to make a final concentration of 0.03 mg/ml. Using this dilution, dose mice according to the following chart. Buprenorphine is **light sensitive** so prepare dilution in an **amber bottle** or cover bottle with **foil**.

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| **Mouse** | **Dosage** |
| **Weight** | **0.05 mg/kg** | **0.075 mg/kg** | **0.1 mg/kg** |
| 15 g | 0.025 ml | 0.04 ml | 0.05 ml |
| 20 g | 0.03 ml | 0.05 ml | 0.07 ml |
| 25 g | 0.04 ml | 0.06 ml | 0.08 ml |
| 30 g | 0.05 ml | 0.08 ml | 0.1 ml |
| 35 g | 0.06 ml | 0.09 ml | 0.12 ml |
| 40 g | 0.07 ml | 0.1 ml | 0.13 ml |
| 45 g | 0.08 ml | 0.11 ml | 0.15 ml |
| 50 g | 0.08 ml | 0.12 ml | 0.17 ml |

Stable for up to 30 d at 21oC or 4oC- Jappinen A, Kokki H, Naaranlahti TJ, Rasi AS. Stability of buprenorphine, haloperidol and glycopyrrolate mixture in 0.9% sodium chloride solution. Pharm World Sci. 1999: 21(6): 272-4.

**Dilution for Carprofen**

**Carprofen (Rimadyl®)** 50 mg/ml 10 ml bottle

**Diluent:** 5% Dextrose (D5W)

**Stability:** stable up to 7 days stored at 4oC, protected from light (amber vials).

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| **Mouse** | **Dosage** |
| Weight | 5 mg/kg |
| 15 g | 0.08 ml |
| 20 g | 0.1 ml |
| 25 g | 0.12 ml |
| 30 g | 0.15 ml |
| 35 g | 0.18 ml |
| 40 g | 0.2 ml |
| 45 g | 0.22 ml |
| 50 g | 0.25 ml |

**Dilution for Mice:** 1.0 ml carprofen (50 mg/ml) + 49.0 ml D5W (5% dextrose) to make a final concentration of 1 mg/ml. Using this dilution, dose mice according to the following chart. Solutions stable for **1 week** refrigerated at 4oC.

**Ketamine/Xylazine Dilution for Rodents**

**Ketamine (Ketaset®)** 100 mg/ml in 10 ml vial

**Xylazine (Rompun®, Anased®)** 20 mg/ml or 100 mg/ml 20 ml vial

**Diluent:** 5% Dextrose (D5W) or normal saline (0.9% NaCl)

**Stability:** stable for 28 days stored under ambient conditions and at 4oC, protected from light (amber bottle).

**Mouse Anesthetic Dose**

Ketamine (100 mg/kg) + Xylazine (10 mg/kg)

* 1. **ml Ketamine (100 mg/ml) + 0.5 ml xylazine (20 mg/ml) + 8.5 ml D5W or normal saline for injection OR + 0.1 ml xylazine (100 mg/ml) + 8.9 ml for injection**

**Mice receive 0.1 ml/10 g body weight**

Ketamine and xylazine diluted as above with D5W (5% dextrose) or normal saline are chemically and physically stable after storage for 28 days under ambient conditions of 4oC protected from light.

**Triple Sedative (Ketamine + Xylazine + Acepromazine)**

4 ml Ketamine 100 mg/ml + 1 ml Xylazine (20 mg/ml) + 1 ml Acepromazine (10 mg/ml)=

66.66 mg/ml Ketamine + 3.33 mg/ml Xylazine + 1.66 mg/ml Acepromazine

**0.01-0.03 ml/100g mouse**

**Ketamine/Xylazine/Acepromazine** (alternate recipe) for IP administration:

Ketamine 65 mg/kg

Xylazine 13 mg/kg

Acepromazine 2.0 mg/kg

To prepare cocktail:

Ketamine (100 mg/ml) 1.0 ml

Xylazine (20 mg/ml) 1.0 ml

Acepromazine (10 mg/ml) 0.3 ml

Sterile water or saline 7.7 ml

Cocktail total volume: 10.0 ml

Dose anesthetic cocktail based upon individual mouse body weight:

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| Mouse Body Weight (g) | Volume of cocktail (ml) |
| 20 g | 0.13 ml |
| 25 g | 0.16 ml |
| 30 g | 0.20 ml |
| 35 g | 0.23 ml |

This cocktail is useful for longer more invasive surgical procedures in mice. It provide anesthesia for 45-60 minutes. If the acepromazine is eliminated, the anesthesia will be shorter and the recovery faster.

**Atipamazole (Antisedan®) Dilution and Dosage Chart**

To Reverse Medetomidine (Dormitor®) or Xylazine (Rompun®)

**Atipamazole (Antisedan®)** 5 mg/ml 10 ml vial

**Diluent:** normal saline (0.9% NaCl)

**Stability:** stable for 28 days under ambient conditions and at 4oC, protected from light (amber bottles).

**Dilution for Mice**

**0.2 ml atipamezole (5 mg/ml) + 4.8 ml sterile saline** to make final concentration of **0.2 mg/ml** solution. This makes a 5 ml dilution of atipamezole which is enough to reverse medetomidine in approximately 25-35 mice weighing between 25-40 g.Using this dilution,dose mice at **0.05 ml solution/10 g body weight SC** according to the following chart.Dose is administered as **1 mg/kg** atipamezole SC.

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| **Mouse** | **Dosage** |
| **Weight** | **1 mg/kg** |
| 10 g | 0.05 ml |
| 15 g | 0.08 ml |
| 20 g | 0.10 ml |
| 25 g | 0.13 ml |
| 30 g | 0.15 ml |
| 35 g | 0.18 ml |
| 40 g | 0.2 ml |
| 45g | 0.22 ml |

**Bupivicaine Dilution for Rodents**

**Bupivicaine (Sensorcaine®, Marcaine®)** 0.5% (5 mg/ml) 20 ml bottle?= $3.32

**Dilution for Mice**

1.0 ml bupivacaine (5 mg/ml) + 19 ml 0.9% saline to make a final concentration of 0.25 mg/ml solution. Using this dilution, dose mice at 0.1 ml solution/mouse (25 g). Dose is administered as **1-2 mg/kg** bupivacaine.

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| **Mouse** | **Dosage** |
| **Weight** | **1 mg/kg** | **2 mg/kg** |
| 10 g | 0.04 ml | 0.08 ml |
| 15 g | 0.06 ml | 0.12 ml |
| 20 g | 0.08 ml | 0.16 ml |
| 25 g | 0.1 ml | 0.2 ml |
| 30 g | 0.12 ml | 0.24 ml |
| 35 g | 0.14 ml | 0.28 ml |
| 40 g | 0.16 ml | 0.32 ml |
| 45 g | 0.18 ml | 0.36 ml |

**Tribromoethanol (Avertin) recipe:**

**100% stock solution:**

Dissolve 10 g 2, 2, 2-tribromoethanol in 10ml amylene hydrate (tertiary amyl alcohol, 2 methyl-2-butanol). Make sure fully dissolved, heat up to 50o C. Solution s should be clear. Store wrapped in foil (light sensitive solution, ok to use brown glass bottle), at -20oC. Date and label bottle. Stock solution can be kept for up to one year.

**1.25% working solution (12.5 mg/ml):**

Mix 0.5 ml of stock solution with 39.5 ml sterile isotonic saline. Recommended to be used the same day it is prepared, but can be stored at 4oC or frozen at -20oC for up to a week, in a foil wrapped container or brown bottle. Use the frozen aliquots the same day after thawed to 37o C and shaken; discard frozen aliquots after 1 week. Date and label all bottles. Recheck pH prior to use. If pH <5, the solution becomes discolored or if precipitate is present after shaking, these are indicators that the solution has decomposed. If any of these are noted in the solution, do not use and discard.

In keeping with IACUC policy, tribromoethanol must be prepared, sterilized with a 0.2-micron

filter, stored and used with aseptic technique.

Dosing from working solution: 200mg/kg-240mg/kg

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| Mouse Body Weight (g) | Volume (ml) working solution |
| 20 g | 0.3-0.4 ml |
| 25 g | 0.4-0.5 ml |
| 30 g | 0.5-0.6 ml |
| 35 g | 0.6-0.7 ml |