|  |
| --- |
| **TRANQUILIZERS, SEDATIVES, AND OTHER AGENTS** |
| **Drug** | **Dosage and Route** | **Duration of Anesthesia** | **Comments** |
| **Sedatives/Tranquilizers** |
|  Diazepam (Valium®) | 3-5 mg/kg SC (sedation) | Sedation only |  |
|  Midazolam (Versed®) | 1-2 mg/kg SC (sedation) | Sedation only | Pre-anesthetic |
| **Barbiturates** |
| Pentobarbital (Nembutal®) | 40-50 mg/kg IP sedation70-85 mg/kg IP anesthesia | 20-60 min.80-95 minutes | Poor analgesic in rats. Dose sufficient to produce surgical anesthesia may cause severe respiratory depression and death. Give diluted in saline (<10 mg/ml). |
| **Dissociatives** |
| Ketamine (Ketoset®)\* | 50-100 mg/kg IM | Unproven | Poor muscle relaxation and insufficient analgesia for major surgery. Lower doses appropriate for sedation only. |
| Ketamine + Acepromazine (Promace®) | Ket 75-80 mg/kg IM, IP + Ace 2.5 mg/kg IP, IM  | 20-30 min. | Light anesthesia |
| Ketamine + Diazepam (Valium®) | Ket 40-80 mg/kg IP + Diaz 5-10 mg/kg IP | 45-60 min. |  |
| Ketamine + Medetomidine# | Ket 60-75 mg/kg IP + Med 0.25-0.5 mg/kg SC, IP | Surgical anesthesia 20-30 min.; Sleep time 60-120 min. | Light anesthesia.Females more sensitive than males. |
| Ketamine + xylazine# (Rompun®) **Recommended** | Ket 40-80 mg/kg IP + Xyl 5-10 mg/kg IP  | 45-90 min. | Thermal support is crucial. To prolong anesthesia, supplement with 1/3 dose of ketamine only.  |
| Ketamine + xylazine#  + acepromazine (Triple sedative) | Ket 31.25 mg/kg IP, IM + Xyl 6.25 mg/kg IP, IM + Ace 1.25 mg/kg IP, IM (0.04-0.05 ml/100g)  | ~20-30 min.  | Sedative- not appropriate for anesthesia alone- 60-120 min, sleep time, 30-40 min. anesthesia |
| **Other** |
| Telazol®= Tiletamine + zolazepam | 20-40 mg/kg IP or20 mg/kg IM | 30-60 min. | Anesthesia variable. Corneal, pedal and swallowing reflexes remain intact.  |
| Telazol® + Xylazine | Tel 20-40 mg/kg IP +Xyl 5-10 mg/kg IP | 130-200 min.  | Good analgesia but marked cardiovascular depression. |
| Telazol® + Butorphanol | Tel 20-40 mg/kg IP +But 1.25-5 mg/kg IP | 59-140 min. | Good analgesia but transient hypotension, bradycardia, and dose-dependent respiratory depression. |
| Propofol (Diprivan®,Propoflo®) | 7.5-10 mg/kg IV for induction, then 44-55 mg/kg/hr continuous IV infusion | 8-11 min.3 hr. |  |
| Urethane | 1000 mg/kg IP |  | Caution! Prolonged anesthesia; terminal procedures only; carcinogenic and mutagenic |
| **Inhalation** |
| Isoflurane (Forane®, Aerane®) Recommended | 3-4 % 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 | 4-6% induction0.5-3% 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, 0.5 mg/kg IM.

|  |
| --- |
| **Analgesic Drugs** |
| **Drug** | **Dosage** | **Comments** |
| Buprenorphine (Buprenex®)a | 0.01-0.05 mg/kg SC, IP | 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 | 15 mg/kg PO  | 4 hrs |
| Ketoprofen | 5 mg/kg SC, IP | 24 h |
| Meloxicam (Metacam®) | 2 mg/kg SC, IP 5 mg/kg PO | 24 hours |
| Morphine a,b | 2.5 mg/kg SC, IP | 2-4 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.

Neonatal Rat Anesthesia (rat < 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.

|  |
| --- |
| **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 unless an endotracheal tube is already in place. A rubber bulb with attached tubing large enough to fit over the nose may be used to periodically inflate the lungs. Respiratory depression can be treated by the administration of doxapram (Dopram®) 5-10 mg/kg IV or IP. If respiratory depression reoccurs, the doxapram should be administered repeatedly at approximately 10-15 min. intervals. Supportive care for animals which reach too deep a level of anesthesia 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 Rats:

**HR 260-500 beats/min, RR 70-110 breaths/min., Temp. 96.6-99.5oF**

**Buprenorphine Dilution and Dosage Chart**

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

**Dilution for Rat**: 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 rats according to the following chart. Buprenorphine is **light sensitive** so prepare dilution in an **amber bottle** or cover bottle with **foil**.

|  |  |
| --- | --- |
| **Rat** | **Dosage** |
| **Weight** | **0.01 mg/kg** | **0.03 mg/kg** | **0.05 mg/kg** |
| 100 g | 0.03 ml | 0.1 ml | 0.17 ml |
| 125 g | 0.04 ml | 0.12 ml | 0.21 ml |
| 150 g | 0.05 ml | 0.15 ml | 0.25 ml |
| 175 g | 0.06 ml | 0.18 ml | 0.29 ml |
| 200 g | 0.07 ml | 0.20 ml | 0.33 ml |
| 225 g | 0.08 ml | 0.22 ml | 0.38 ml |
| 250 g | 0.08 ml | 0.25 ml | 0.42 ml |
| 275 g | 0.09 ml | 0.28 ml | 0.46 ml |
| 300 g | 0.1 ml | 0.30 ml | 0.50 ml |
| 325 g | 0.11 ml | 0.32 ml | 0.54 ml |
| 350 g | 0.12 ml | 0.35 ml | 0.58 ml |
| 375 g | 0.12 ml | 0.38 ml | 0.62 ml |
| 400 g | 0.13 ml | 0.40 ml | 0.67 ml |
| 450 g  | 0.15 ml | 0.45 ml | 0.75 ml |
| 500 g | 0.17 ml | 0.50 ml | 0.83 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).

**Dilution for Rats:** 1.0 ml carprofen (50 mg/ml) + 9.0 ml D5W (5% dextrose) to make a final concentration of 5 mg/ml. Using this dilution, dose mice according to the following chart.

|  |  |
| --- | --- |
| **RATS** | **Dosage** |
| Weight | 5 mg/kg |
| 100 g | 0.10 ml |
| 125 g | 0.12 ml |
| 150 g | 0.15 ml |
| 175 g | 0.18 ml |
| 200 g | 0.20 ml |
| 225 g | 0.22 ml |
| 250 g | 0.25 ml |
| 275 g | 0.28 ml |
| 300 g | 0.30 ml |
| 325 g | 0.32 ml |
| 350 g | 0.35 ml |
| 375 g | 0.38 ml |
| 400 g | 0.40 ml |
| 450 g | 0.45 ml |
| 500 g | 0.50 ml |

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).

**Rat Anesthetic Dose**

Ketamine (40-90 mg/kg) + Xylazine (10 mg/kg)

* 1. **ml Ketamine (100 mg/ml) + 2.5 ml xylazine (20 mg/ml) + 3.75 ml D5W or normal saline for injection OR + 0.5 ml xylazine (100 mg/ml) + 5.75 ml water for injection**

**Rats receive 0.2 ml/100 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

**0.04-0.05 ml/100g rat**

**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 Rats**

**2 ml atipamezole (5 mg/ml) + 8 ml sterile saline** to make final concentration of **1 mg/ml** solution. This makes a 10 ml dilution of atipamezole which is enough to reverse medetomidine or xylazine in approximately 25-30 rats weighing between 300-400 g.Using this dilution,dose rats at **0.1 ml solution/100 g body weight SC** according to the following chart.Dose is administered as **1 mg/kg** atipamezole SC.

|  |  |
| --- | --- |
| **Rat** | **Dosage** |
| **Weight** | **1 mg/kg** |
| 100 g | 0.10 ml |
| 125 g | 0.12 ml |
| 150 g | 0.15 ml |
| 175 g | 0.18 ml |
| 200 g | 0.20 ml |
| 225 g | 0.22 ml |
| 250 g | 0.25 ml |
| 275 g | 0.28 ml |
| 300 g | 0.30 ml |
| 325 g | 0.32 ml |
| 350 g | 0.35 ml |
| 375 g | 0.38 ml |
| 400 g | 0.40 ml |
| 450 g | 0.45 ml |
| 500 g | 0.50 ml |

**Bupivicaine Dilution for Rodents**

**Bupivicaine (Sensorcaine®, Marcaine®)** 0.5% (50 mg/ml) 20 ml bottle?= $3.32

**Dilution for Rats**

0.2 ml bupivacaine (50 mg/ml) + 9.8 ml 0.9% saline to make a final concentration of 1 mg/ml solution. Using this dilution, dose rats according to the following chart. Dose is administered as **1-2 mg/kg** bupivacaine SC.

|  |  |
| --- | --- |
| **Rat** | **Dosage** |
| **Weight** | **1 mg/kg** | **2 mg/kg** |
| 100 g | 0.1 ml | 0.20 ml |
| 125 g | 0.12 ml | 0.25 ml |
| 150 g | 0.15 ml | 0.30 ml |
| 175 g | 0.18 ml | 0.35 ml |
| 200 g | 0.20 ml | 0.40 ml |
| 225 g | 0.22 ml | 0.45 ml |
| 250 g | 0.25 ml | 0.50 ml |
| 275 g | 0.28 ml | 0.55 ml |
| 300 g | 0.30 ml | 0.60 ml |
| 325 g | 0.32 ml | 0.65 ml |
| 350 g | 0.35 ml | 0.70 ml |
| 375 g | 0.38 ml | 0.76 ml |
| 400 g | 0.40 ml | 0.80 ml |
| 450 g | 0.45 ml | 0.9 ml |
| 500 g | 0.50 ml | 1.0 ml |