

## Ketamine Combinations for Rodent Anesthesia

The combination of ketamine and xylazine is popular for the anesthesia of many species including mice. Ketamine, a class III controlled substance<sup>1</sup>, is an anesthetic that produces a trance-like state with muscle rigidity and twitching when used alone. Combined with a second drug like the sedative xylazine, complete surgical levels of anesthesia may be attained. The most effective dose varies with strain, sex, and age of the animal. The following recommendations are approximations, and adjustments are sometimes necessary based on the animal details and the nature of the procedure.

The responsible anesthetist must determine if sufficient levels and duration of anesthesia have been obtained (such as by evaluating a toe pinch), since underdosing may result in unnecessary pain and overdosing may result in death of the animal. The LASP veterinary staff may assist in determination of the optimal injectable ketamine combination for use in experimental animals.

A suggested, common starting dose for mice is **100 mg/kg ketamine combined with 10 mg/kg xylazine**, which gives about 20+ minutes of surgical anesthesia. The drugs are diluted in sterile water or sterile saline and the volume to be injected intraperitoneally (IP) is based on the mouse's body weight. Dilution is important to ensure adequate dosing and distribution. Dilution may affect a drug's stability, and diluted drugs are typically considered stable for up to one week unless otherwise indicated from applicable reference material. Therefore the mix date should be written on the diluted vial.

	Drug stock concentration <sup>1</sup> (mg/ml)	Volume used for cocktail	Volume of cocktail administered to mouse per 10 g body weight	Dose administered to mouse
Ketamine	100 mg/ml	1.0 ml	-	<b>100 mg/kg</b>
Xylazine	20 mg/ml	0.5 ml	-	<b>10 mg/kg</b>
Saline	Sterile, isotonic	8.5 ml	-	-
<b>Combination Cocktail</b>		10 ml total	<b>0.10 ml / 10 g</b>	-

Intraperitoneal injection of this combination (using 1 ml syringe, 25-27 gauge needle) may result in 1-2 hours of sedation, following surgical levels of anesthesia. Additional anesthesia may be achieved by re-dosing with half the quantity of ketamine (only). Supplementation with vaporizer-delivered isoflurane also works well. Providing supplemental warmth and warm saline subcutaneously, post-operatively shortens the recovery time and can prevent deaths due to hypothermia.

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<sup>1</sup> Controlled substance storage and use must be consistent with NIH Manual 1345: [Handling and Safeguarding of Controlled Substances for Nonhuman Use](#)

Use of pharmaceutical grade saline or sterile water, which comes in disposable plastic stopper vials, is required (see image below). Laboratory-prepared saline or PBS for parenteral injections does not meet this standard. Any use of non-pharmaceutical grade products because of scientific necessity or unavailability of pharmaceutical grade products must be reviewed and approved by the NCI ACUC, as specified in the NIH ARAC Guideline on Pharmaceutical Grade Compounds. Parenteral injections to study animals must be sterile and used prior to the labeled expiration date.



Other suggested combinations for mice that provide either a longer duration of surgical anesthesia or different levels of analgesia include:

	<b>Drug stock concentration<sup>1</sup> (mg/ml)</b>	<b>Volume used for cocktail</b>	<b>Volume of cocktail administered to mouse</b>	<b>Dose administered to mouse</b>
Ketamine	100 mg/ml	0.8 ml	-	<b>80 mg/kg</b>
Xylazine	20 mg/ml	0.3 ml	-	<b>6 mg/kg</b>
Acepromazine	10 mg/ml	0.1 ml		<b>1 mg/kg</b>
Saline	Sterile, isotonic	8.8 ml	-	-
<b>Combination Cocktail</b>		10 ml total	<b>0.10 ml / 10 g</b>	-

	<b>Drug stock concentration<sup>1</sup> (mg/ml)</b>	<b>Volume used for cocktail</b>	<b>Volume of cocktail administered to mouse</b>	<b>Dose administered to mouse</b>
Ketamine	100 mg/ml	0.8 ml	-	<b>80 mg/kg</b>
Xylazine	20 mg/ml	0.3 ml	-	<b>6 mg/kg</b>
Buprenorphine	0.3 mg/ml	1.7 ml		<b>0.5 mg/kg</b>
Saline	Sterile, isotonic	7.2 ml	-	-

<b>Combination Cocktail</b>	10 ml total	<b>0.10 ml / 10 g</b>	-
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**Mouse Sample Recipe for KETAMINE and DEXmedetomidine (Must be reversed with atipamazole)**

	<b>Drug stock concentration<sup>1</sup> (mg/ml)</b>	<b>Volume used for cocktail</b>	<b>Volume of cocktail administered to mouse</b>	<b>Dose administered to mouse</b>
Ketamine	100 mg/ml	0.3 ml	-	<b>75 mg/kg</b>
Dexmedetomidine	0.5 mg/ml	0.8 ml	-	<b>1.0 mg/kg</b>
Saline	Sterile, isotonic	6.9 ml	-	-
<b>Combination Cocktail</b>		8 ml total	<b>0.2 ml / 10 g</b>	-

**Reversal**

Ketamine is not reversible following injection, but must be metabolized; however both xylazine and DEXmedetomidine are reversible with the injectible product atipamazole (Antisedan, 5 mg/ml). Inject 0.1 to 1.0 mg/kg either subcutaneously (SC) or IP for reversal of the sedative and analgesic effects.

Because of prolonged recovery from anesthesia and marked bradycardia, medetomidine and DEXmedetomidine reversal is **strongly recommended**.

**Rat Anesthesia**

Suggested starting dose for rat anesthesia is 80 mg/kg ketamine and 10 mg/kg xylazine.

**Pre-operative Considerations**

Fasting rodents is not necessary and is not recommended. Ophthalmic ointment should be applied to the eyes to prevent drying of the corneas, as ketamine anesthesia suppresses the blink reflex.

**Post-operative Considerations**

- The animals should be kept dry, insulated, or warmed to prevent excessive loss of body heat. Hypothermia is typical during and following surgery and can contribute to mortality.

- Surgical records for research rodents **must be maintained** and should be individual or cage specific. The record should reflect the procedure performed and date, dates and doses of anesthetics and analgesics delivered, and the initials of the person administering them. LASP recommends keeping this data on the back of the cage card and has templates available.