UBC ANIMAL CARE COMMITTEE
TECH 18 – Analgesia for Adult Mice and Rats
Ketoprofen SOP

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PURPOSE:

- To describe the procedure for administering a non-steroidal anti-inflammatory drug (NSAID) in adult mice and rats to provide pain relief (analgesia) and/or reduce inflammation in cases of mild to moderate pain.
- This Standard Operating Procedure (SOP) describes the use of one type of NSAID, Ketoprofen (brand name: Anafen®).
- This SOP follows the UBC Surgical Class and Analgesia Guidelines and is in keeping with the Canadian Council on Animal Care (CCAC) current guidelines on the use of analgesics.

RESPONSIBILITY:

- Those trained UBC Persons listed on an approved Animal Care Committee (ACC) Animal Care Protocol who are responsible for performing procedures requiring the administration of Ketoprofen.
- All animal users performing analgesic injections in rodents must have successfully completed the UBC Animal Care Services (or equivalent) Introduction to Working with Rodents in Research (IWRR), and Rodent Restraint/SQ/IP injections (RSCIP) courses.

MATERIALS: (*can be purchased from Animal Care Services*)

- Ketoprofen injectable (100 mg/ml) (i.e.: Anafen®)
- Sterile needles (25-27g, 1/2" or smaller)
- Sterile syringes (0.3-1 ml)
- Sterile amber multi-use vial for diluted solutions (protect from light)
- Sterile 0.9% normal saline (Sodium chloride, NaCl; for dilution)
- Sharps container
- Weigh scale.
- Sterile Lactated Ringer's solution or 0.9% sterile saline (if giving subcutaneous (SQ) fluids for dehydration)
- Sterile 1-10 ml syringes (if giving SQ fluids for dehydration)

Table 1 - DOSE FOR MICE AND RATS:

Species	Dose	Concentration to Dilute To	Frequency and Duration
Rat	5 mg/kg	10 mg/ml	Once every 24 hours for 1-3 days
Mouse	5 mg/kg	1 mg/ml	Once every 24 hours for 1-3 days

See next page for dilution instructions.

PROCEDURE:

1. Weigh animal(s) to be treated.
2. Calculate the dose and volume in ml of Ketoprofen required (refer to Table 1).
    a. See instructions on how to calculate below.
    b. Injectable formulation requires dilution to dose accurately.
    c. Dose is based on animal's weight and drug concentration (see examples in Table 2 below).
3. Draw up the calculated dose in a sterile syringe.
    a. Use a new sterile syringe and needle for each animal.
4. Gently restrain the mouse or rat appropriately for a subcutaneous injection.
5. Administer the dose of injectable Ketoprofen subcutaneously in the loose skin at the base of the neck or over the rump (hips) of the animal.
6. If animal(s) are, or may become dehydrated, administer sterile 0.9% sodium chloride or Lactated Ringers solution subcutaneously (SQ).
    a. See UBC ACC Guidelines and SOP for the Maintenance of Fluid Homeostasis in Animals for details. A useful starting point is 20 ml/kg SQ.
7. Reassess for signs of pain at least every 12 hours.
    a. If still painful, then alternative analgesics may be required (e.g. Buprenorphine).
    b. Note: Ketoprofen should only be given once in a 24 hour period.
    c. If no improvement is observed after administration of analgesia, contact the Principal Investigators and/or the facility's Clinical Veterinarian.

DILUTION INFORMATION:

Ketoprofen (100 mg/ml) requires dilution to accurately dose mice and rats.

- **Rats:** Prepare a 1:10 dilution of 100 mg/ml Ketoprofen with sterile 0.9% saline.
    - Final concentration will be 10 mg/ml.
    - Add 1 part Ketoprofen (100 mg/ml) to 9 parts sterile 0.9% saline for a total volume of 10 parts of diluted solution.
        - E.g. Add 1.0 ml of Ketoprofen (100 mg/ml) to 9.0 ml of sterile 0.9% saline for a total volume of 10 ml of diluted solution.
- **Mice:** Prepare a 1:100 dilution of 100 mg/ml Ketoprofen with sterile 0.9% saline.
    - Final concentration will be 1 mg/ml.
    - Add 1 part Ketoprofen (100 mg/ml) to 99 parts sterile 0.9% saline for a total volume of 100 parts of diluted solution.
        - E.g. Add 0.1 ml Ketoprofen (100 mg/ml) to 9.9 ml sterile 0.9% saline for a total volume of 10 ml of diluted solution.
- Label vial with drug name, concentration and date of dilution. It is suggested to also add the initials of the person who made the dilution.
- Store diluted solution aseptically in a sterile, amber, multi-dose vial and protect from light.

- Diluted solutions must be discarded within 30 days from date of dilution.

CALCULATING DRUG VOLUME (IN ML) TO BE ADMINISTERED:

- Convert animal's weight from grams to kilograms
  - Divide the weight in grams by 1000
  - E.g. 25g mouse ÷ 1000 = 0.025kg
- Calculate the volume to give in ml
  - = [dose (mg/kg) x weight of animal (kg)] ÷ concentration of drug (mg/ml)
  - E.g. For a 25g mouse getting a dose of 5 mg/kg of 1 mg/ml Ketoprofen
    Volume (ml) = (5 mg/kg of Ketoprofen x 0.025 kg) ÷ 1 mg/ml = **0.12 ml**

Table 2 - Examples of Dosing

Weight of **Rat**	Ketoprofen **diluted to <u>10 mg/ml</u>** Dose: 5 mg/kg
250 g (0.25 kg)	0.12 ml
350 g (0.35 kg)	0.18 ml
450 g (0.45 kg)	0.22 ml
550 g (0.55 kg)	0.28 ml

Weight of **Mouse**	Ketoprofen **diluted to <u>1 mg/ml</u>** Dose: 5 mg/kg
25 g (0.025 kg)	0.12 ml
35 g (0.035 kg)	0.18 ml
45 g (0.045 kg)	0.22 ml
55 g (0.055 kg)	0.28 ml

IMPORTANT NOTES:

- Ketoprofen has been associated with life threatening ulcerative gastritis, especially in rats. Meloxicam (a different NSAID) is preferred. Discuss the use of Ketoprofen with a UBC Clinical Veterinarian before using it in rats.
- When possible, pain must be treated pre-emptively (before the cause).
- An adequate analgesic plan must be described in the approved Animal Care Protocol for prevention and treatment of pain associated with the experimental procedures.
- For spontaneous or unexpected pain, Principal Investigators and the Clinical Veterinarian should be consulted immediately and prior to administration of analgesics so that an appropriate pain management plan can be devised.
- Use with caution in animals with pre-existing renal, cardiovascular, gastro-intestinal or blood clotting/coagulation disorders. Use in animals that may be or may become dehydrated can increases the risk of both kidney damage and gastrointestinal ulceration. Ensure animals are well hydrated by administering 20 ml/kg subcutaneously of sterile 0.9% sodium chloride or Lactated Ringers solution (see UBC ACC Guidelines and SOP for the Maintenance of Fluid Homeostasis in Animals).

- Do not treat for more than 3 days with NSAIDs without consulting a UBC Clinical Veterinarian.
- Do not use phosphate buffered saline (PBS) when diluting; PBS is not equivalent to normal saline.

COMPLICATIONS:

- Ulcerative gastroenteritis
    - ***Cause:*** Damage to the mucosal layer of the stomach and intestines.
    - ***Clinical signs***: Weight loss, abdominal pain, pale extremities, diarrhea (sometimes dark due to digested blood which is called melena) and decreased activity.
    - ***Response:*** Discontinue drug, provide 20 ml/kg subcutaneous fluids (Lactated Ringer's Solution or 0.9% Sodium Chloride) and safe supplemental heat. Contact a Clinical Veterinarian.

- Kidney damage
    - ***Cause:*** Decrease in prostaglandins which decreases renal plasma flow which causes damage to the kidneys.
    - ***Clinical signs*****:** Weight loss, dehydration (sunken eyes, loss of skin elasticity), and increased or decreased urine production.
    - ***Response:*** Discontinue drug, provide 20 ml/kg subcutaneous fluids (Lactated Ringer's Solution or 0.9% Sodium Chloride) and safe supplemental heat. Contact a Clinical Veterinarian.

REFERENCES: (https://animalcare.ubc.ca/animal-care-committee/sops-policies-and-guidelines)

- UBC SOP Subcutaneous Injections in Rats and Mice
- UBC Rodent Anesthesia and Analgesia Formulary and General Drug Information
- UBC Surgical Class and Analgesia Guidelines
- UBC ACC Guidelines and SOP for the Maintenance of Fluid Homeostasis in Animals