



## POST-OPERATIVE ANALGESIA AND DRUG FORMULARIES

An integral component of any animal protocol is the prevention or alleviation of pain or distress, such as that associated with surgical and other procedures. *Pain must be relieved not only during surgical procedures, but during the post-operative period as well.* Anesthetic agents render an animal unconscious without loss of vital function and are required for most surgical procedures. In contrast, **analgesic agents** reduce or relieve pain *without loss of consciousness* and their use is required in the post-operative period. Stress induced by post-operative pain can lead to weight loss, deficiencies in the immunological response, impairment of wound healing, self-mutilation, and other issues that have negative effects on the animal. In addition to being a moral imperative, the prevention and alleviation of pain and distress in laboratory animals makes for better science!

The most commonly used analgesics are opioids and non-steroidal anti-inflammatory drugs (NSAIDs). While the ultimate selection of drugs must be based on the experimental objectives, the IACUC will not approve an animal protocol that omits the use of appropriate analgesics to reduce post-operative pain unless very compelling scientific justification is provided. The objective of the use of analgesics is always to minimize pain and distress as much as possible without compromising the scientific integrity of the research. Toward this objective, it is recommended that post-surgical analgesics be administered to the animal *prior to or shortly after inducing anesthesia* (“preemptive” use) and then post-operatively *as needed* at a frequency based on the duration of action of the agent and depending on the clinical symptoms.

Appropriate choice of analgesic agent to use includes consideration of both the predicted level of pain and discomfort that a given surgical procedure will cause, and evaluation of individual animals post-operatively for signs of pain/distress. The detection of pain/distress requires a good working knowledge of both normal behavior and appearance and signs of pain and distress in the species of laboratory animal that one is working with.

### **Signs of pain or distress in laboratory animals include:**

- immobility, lethargy, reluctance to move
- decreased grooming resulting in a rough hair coat
- staining of the periorbital and nasal region which appears as a black or reddish-brown discharge (porphyrin, in rodents)
- vocalizing, often with an altered pitch
- postural and gait abnormalities; guarding a limb
- aggression
- change in respiratory rate
- changes in appetite or excretion

A rule of thumb is that major survival surgical procedures will require more post-operative analgesia than minor procedures (48 hrs vs. 24 hrs). Administration of local anesthetics/ analgesics such as lidocaine and bupivacaine at incision points is recommended for major surgeries and may be useful for biopsies and other minor procedures. Analgesia (as well as anesthesia) plans for all surgical protocols should be discussed with a veterinarian during the planning stages of protocol preparation.

- ***Major survival procedures should incorporate a minimum of 48 hr of analgesia; this will typically require several doses of analgesic (e.g. buprenorphine every 6-12 hrs or a single preemptive dose of buprenorphine followed by subsequent administrations of a NSAID).***
- ***Minor surgical procedures should incorporate a minimum of 24 hr of analgesia.***

## FORMULARIES FOR ANALGESIA BY SPECIES

**Abbreviations used:** *IH:* Inhaled agent; *IP:* Intraperitoneal injection; *:* subcutaneous injection; *IV:* intravenous injection; *IM:* intramuscular injection; *PO:* oral delivery; **CS:** *controlled substance regulated by the Drug Enforcement Agency. Special licensing required to procure; appropriate record keeping logs required.*

### MICE

Drug Name	DOSE (mg/kg) and Route	FREQUENCY	NOTES
*Buprenorphine (CS - opioid)	0.05 - 0.1 SC or IP	Used pre-operatively for preemptive analgesia and post-operatively every 6-12 hr	For major procedures this requires more frequent dosing than 12 hr intervals. Consider multi-modal analgesia with NSAID. SR formulation may be useful for abdominal procedures at 0.5-1 mg/kg single dose SC. <i>*Note: If buprenorphine is diluted to a stock solution with a more workable concentration, the dilution MUST be stored in a sterile multidose glass vial rather than in a plastic syringe or vial, to avoid significant loss of potency over time (Den Herder et al. 2017)</i>
Carprofen (NSAID)	5-10 SC	Used pre-operatively for preemptive analgesia and post-operatively every 12-24 hr	Depending on the procedure, may be used as sole analgesic, or as multi-modal analgesia with buprenorphine.
Meloxicam (NSAID)	~0.2-1 SC	Used pre-operatively for preemptive analgesia and post-operatively every 12-24 hr	Depending on the procedure, may be used as sole analgesic, or as multi-modal analgesia with buprenorphine.
Flunixin meglumine (NSAID)	2-2.5 SC	Used pre-operatively for preemptive analgesia and post-operatively every 12-24 hr	Depending on the procedure may be used as sole analgesic, or as multi-modal analgesia with buprenorphine.
Ketoprofen (NSAID)	2-5 SC	Used pre-operatively for preemptive analgesia and post-operatively every 12-24 hr	Depending on the procedure may be used as sole analgesic, or as multi-modal analgesia with buprenorphine.

#### Local anesthetic/analgesics:

Lidocaine hydrochloride	Dilute to 0.5%, do not exceed 7 mg/kg total dose, SC or intra-incisional	Use locally before making surgical incision, or before final skin closure. Place 2-3 drops in ear canal prior to mounting animal in stereotaxic apparatus	Faster onset than bupivacaine but shorter (<1 hr) duration of action
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Bupivacaine	Dilute to 0.25%, do not exceed 8 mg/kg total dose, SC or intra-incisional	Use locally before making surgical incision, or before final skin closure. Place 2-3 drops in ear canal prior to mounting animal in stereotaxic apparatus	Slower onset than lidocaine but longer (~ 4-8 hr) duration of action
Lidocaine and bupivacaine combination	May be mixed in same syringe.	<i>Contact veterinarian for formulation, dosages and precautions</i>	Fast onset, longer duration
EMLA (eutectic mixture of lidocaine and prilocaine)	Thick cream with 25 mg/mL of each	Apply to skin surface as a thick layer; useful for small biopsies	Usually left on for 30 to 60 min.

### RAT

Drug Name	DOSE (mg/kg) and Route	FREQUENCY	NOTES
*Buprenorphine (CS - opioid)	0.01 - 0.05 SC or IP	Used pre-operatively for preemptive analgesia and post-operatively every 6-12 hr	Major procedures require more frequent dosing than 12 hr intervals. Consider multi-modal analgesia with NSAID. High doses of buprenorphine may lead to pica behavior. <i>*Note: If buprenorphine is diluted to a stock solution with a more workable concentration, the dilution MUST be stored in a sterile multidose glass vial rather than in a plastic syringe or vial, to avoid significant loss of potency over time (Den Herder et al. 2017)</i>
Carprofen (NSAID)	4-5 SC	Used pre-operatively for preemptive analgesia and post-operatively every 24 hr	Depending on the procedure, this may be used as sole analgesic, or as multi-modal analgesia with buprenorphine. <i>Recently shown to be ineffective for post-operative pain (Waite, 2015).</i>
Ketoprofen (NSAID)	2-5 SC	Used pre-operatively for preemptive analgesia and post-operatively every 12-24 hr	Depending on the procedure may be used as sole analgesic, or as multi-modal analgesia with buprenorphine. High doses may cause GI bleeding and ulceration. <i>Recently shown to be ineffective for post-operative pain (Waite 2015).</i>
Meloxicam (NSAID)	0.2 - 1 SC	Used pre-operatively for preemptive analgesia and post-operatively every 12-24 hr	Depending on the procedure may be used as sole analgesic, or as multi-modal analgesia with buprenorphine.
Flunixin meglumine (NSAID)	2-2.5 SC	Used pre-operatively for preemptive analgesia and post-operatively every 12-24 hr	Depending on the procedure, can be used as sole analgesic, or used with buprenorphine.

**Local anesthetic/analgesics:**

Lidocaine hydrochloride	Dilute to 0.5%; do not exceed 7 mg/kg total dose, <b>SC</b> or intra-incisional	Use locally before making surgical incision. Place 2-3 drops in ear canal prior to mounting animal on stereotaxic apparatus	Faster onset than bupivacaine but shorter (<1 hr) duration of action
Bupivacaine	May dilute to 0.25%, do not exceed 8 mg/kg total dose, <b>SC</b> or intra-incisional	Use locally before making surgical incision. Place 2-3 drops in ear canal prior to mounting animal on stereotaxic apparatus	Slower onset than lidocaine but longer (~ 4-8 hr) duration of action
Lidocaine and bupivacaine combination	May be mixed in same syringe.	<i>Contact veterinarian for formulation, dosages and precautions</i>	Fast onset, longer duration
EMLA (eutectic mixture of local anesthetics)	Thick cream with 25 mg/mL each of lidocaine and prilocaine	Apply to skin surface as a thick layer; useful for small biopsies	Usually left on for 30 to 60 min

**SWINE**

**Opioids:**

Drug Name	DOSE (mg/kg) and Route	FREQUENCY	NOTES
Buprenorphine (CS)	0.005-0.1 <b>SC</b> (typically .05- 0.1 is used with major surgery)	Used pre-operatively for preemptive analgesia and given post-operatively every 6-12 hr	For major procedures, may require more frequent dosing than 12 hr intervals. Consider multi-modal analgesia with NSAID;. Sustained release (SR) formulations are manufactured but may be difficult to obtain due to purchasing restrictions. Dosage is 0.12-0.24 mg/kg.
Butorphanol (CS)	0.1-0.3 <b>IM, SC</b>	Used pre-operatively for preemptive analgesia and post-operatively every 4-6 hr	Depending on the procedure may be used as sole analgesic, or as multi-modal analgesia with buprenorphine.
Oxymorphone (CS)	0.01-0.02 <b>SC</b>	Used pre-operatively for preemptive analgesia and post-operatively every 3-4 hr. Also used as 'rescue analgesia' when buprenorphine is not enough.	More potent but shorter duration than buprenorphine or butorphanol.
Fentanyl patch (CS)	50 µg/hr <b>patch</b> for up to 40 kg body weight	Place patch 24 hrs in advance of surgery and maintain for up to 3 days	When severe post-surgical pain is anticipated.

**Non-steroidal anti-inflammatory analgesics (NSAID):**

Flunixin meglumine (NSAID)	1-2 <b>SC</b>	Used pre-operatively for preemptive analgesia and post-operatively every 12-24 hr	Depending on the procedure may be used as sole analgesic, or as multi-modal analgesia with buprenorphine.
Carprofen (NSAID)	2-4 <b>SC or PO</b>	Used pre-operatively for preemptive analgesia and post-operatively every 24 hr for up to 4 days.	Depending on the procedure may be used as sole analgesic, or as multi-modal analgesia with buprenorphine.
Meloxicam (NSAID)	0.2-0.3 <b>PO, IM or SC</b>	Used pre-operatively for preemptive analgesia and post-operatively every 24 hr for up to 4 days.	Depending on the procedure may be used as sole analgesic, or as multi-modal analgesia with buprenorphine.
Ketoprofen (NSAID)	~ 1.0-2.0 <b>SC, IM</b>	Used pre-operatively for preemptive analgesia and post-operatively every 24 hr for up to 4 days	Depending on the procedure may be used as sole analgesic, or as multi-modal analgesia with buprenorphine.

**Local anesthetic/analgesics:**

Lidocaine hydrochloride	Dilute to 0.25-0.5% <b>SC</b> or intra-incisional	Used locally before making surgical incision, or before final skin closure.	Faster onset than bupivacaine but shorter (<1 hr) duration of action
Bupivacaine	Dilute to 0.25-0.5% <b>SC</b> or intra-incisional use	Use locally before making surgical incision, or before final skin closure.	Slower onset than lidocaine but longer (~ 4-8 hr) duration of action
Lidocaine and bupivacaine combination	May be mixed in same syringe	Contact veterinarian for formulation, dosages and precautions	Fast onset, longer duration
EMLA (eutectic mixture of local anesthetics)	Thick cream with 25 mg/mL each of lidocaine and prilocaine	Apply to skin surface as a thick layer.	Usually left on for 30 to 60 minutes.

**RABBITS**

**Opioids:**

Drug Name	DOSE (mg/kg) and Route	FREQUENCY	NOTES
Buprenorphine (CS - opioid)	0.01-0.05 <b>IM, SC, IV</b>	6-12 hr	Major procedures may require more frequent dosing than 12 hr intervals. Consider multi-modal analgesia with NSAID
Morphine (CS)	2-5 <b>IM, SC</b>	Every 4 hr	

**Non-steroidal anti-inflammatory analgesics (NSAID):**

Carprofen (NSAID)	4 - SC 1.5 - PO	Every 12 hr for up to 4 days	Depending on the procedure may be used as sole analgesic, or as multi-modal analgesia with buprenorphine.
Flunixin meglumine (NSAID)	1.0 SC	Every 12-24 hours for up to 4 days	Depending on the procedure may be used as sole analgesic, or as multi-modal analgesia with buprenorphine.
Ketoprofen (NSAID)	3 SC	Every 24 hours for up to 4 days	Depending on the procedure may be used as sole analgesic, or as multi-modal analgesia with buprenorphine.
Meloxicam (NSAID)	0.1-0.3 PO, IM or SC	24 hours	Depending on the procedure may be used as sole analgesic, or as multi-modal analgesia with buprenorphine.

**Local anesthetic/analgesics:**

Lidocaine hydrochloride	Dilute to 0.25-0.5% SC or intra-incisional	Use locally before making surgical incision, or before final skin closure.	Faster onset than bupivacaine but shorter (<1 hr) duration of action
Bupivacaine	Dilute to 0.25-0.5% SC or intra-incisional	Used locally before making surgical incision, or before final skin closure.	Slower onset than lidocaine but longer (~ 4-8 hr) duration of action
Lidocaine and bupivacaine combination	May be mixed in same syringe.	Contact veterinarian for formulation, dosages and precautions	Fast onset, longer duration
EMLA (eutectic mixture of local anesthetics)	Thick cream with 25 mg/mL each of lidocaine and prilocaine	Apply to skin surface as a thick layer.	Usually left on for 30 to 60 minutes.

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