

## **Alternatives to Acetaminophen for pain control methods in rats and mice**

Acetaminophen (Tylenol) has long been used by RAR for easily administered pain relief through the drinking water for rats and mice. However, this drug has not been proven to be an effective pain reliever when administered in this manner. Using acetaminophen in the drinking water for pain relief in rodents does not meet current best practices and is not currently acceptable.

## **Current recommendations for analgesia in rats and mice**

### ***Oral:***

Drug name*	Species	Dose	Frequency	Controlled substance?
Aspirin	Rodents	100-400 mg/kg	1-2X per day	No
Meloxicam	Rats	1.0 mg/kg	Daily	No
Buprenorphine	Rodents	0.01-0.02 mg/ml drinking water	Daily	Yes
Buprenorphine	Rodents	0.5 mg/kg in jello	Daily	Yes
Carprofen	Rodents	5-10 mg/kg in water or jello	Daily or once post-operatively	No
Ibuprofen	Mice	30 mg/kg—4.7 ml Children's Motrin in 500 ml water	Daily	No
Ibuprofen	Rats	15 mg/kg—2.35 ml Children's Motrin in 500 ml water	Daily	No
Ketoprofen	Rodents	5 mg/kg	Daily	No

\*Because of its potential for abuse, use of Buprenorphine in water would need to be approved by the Office of Regulatory Affairs and done in accordance with all rules regarding controlled substances

### ***Injectable analgesic options:***

Drug*	Species	Dose	Route	Frequency	Controlled?
Buprenorphine	Rodents	0.05-0.1 mg/kg	IM, SC, IP	Daily	Yes
Butorphanol	Rodents	1-2 mg/kg	SC	Every 4 hours	Yes
Flunixin meglumine(Banamine)	Rodents	2.5 mg/kg	SC	1-2X per day	No

Ketoprofen	Rodent	5 mg/kg	SQ	Daily	No
Morphine	Rodents	5 mg/kg	SQ	Every 2-4 hours	Yes
Carprofen	Rodents	5-10 mg/kg	SQ	Daily	No
Meloxicam	Rats	1.0 mg/kg	SQ	Daily	No

\* Ketoprofen and Buprenorphine are used as injectable drugs with good pain relieving capacities. Please consult an RAR veterinarian with any questions.

### **Standard analgesic drug selection**

Ibuprofen has been recommended for use as a pain reliever with a wide ranging dose of 7.5 to 30 mg/kg (Jenkins, 1987, "Pharmacological Aspects of Analgesic Drugs in Animals: An Overview", JAVMA 191 (10) pp. 1231; Liles, JH and Flecknell, P, 1992 "Use of NSAID for Relief of Pain in Rodents and Rabbits" Lab Animal 26: p. 241-255). Accordingly, RAR will begin using this drug more routinely as an additive to water to treat mild to moderately painful conditions such as skin lesions, fight wounds and eye abscesses. Carprofen will also be available for use in water as an alternative. Other drugs should be used when severe pain is anticipated. A neophobic response has been documented when adding drugs to water of rats which can cause weight loss but is usually temporary. ("Regarding the Inadvisability of administering postoperative analgesics in the drinking water of rats (*Rattus norvegicus*)" Speth, Robert C., Smith, Susan, Brogan, Rebecca S. Contemporary Topics In Laboratory Animal Science, 40 (6), 15., Nov. 2001).

### **Additional characteristics of chosen analgesic drugs**

#### **Ibuprofen**

Ibuprofen has anti-inflammatory, analgesic and an anti-pyretic (fever) activity. Ibuprofen is a non-specific COX inhibitor resulting in decreased prostaglandin formation. It is well absorbed orally and the majority is excreted in the urine within 24 hours with a small amount also excreted through the stool. Excretion is virtually 100% within 24 hours of the last dose. Possible side effects include gi ulceration, blood thinning effects (avoid use with blood thinning drugs), decrease in efficacy of blood pressure lowering drugs, and an interference with secretion of lithium and aminoglycosides that can result in increased blood levels of those drugs. At higher doses, some renal effects may be seen as well. No studies of effects in pregnancy have been completed (pregnant humans only use it on advice from their doctors) and it is excreted in small amounts into milk.

#### **Carprofen**

Carprofen (Rimadyl) is a relatively new drug which has been used in water but has not been scientifically proven to be effective in this route.. (It has, however,

been shown to be effective when delivered in jello – Flexnell, 1999 “Comparison of the Effects of Oral or Subcutaneous Carprofen or Ketoprofen in Rats Undergoing Laparotomy” Veterinary Record 144(3): 65-7). Carprofen is a NSAID and has a much more selective effect than Ibuprofen (inhibits COX 2 while allowing COX 1 activity) which protects the GI system while still being effective in lowering pain. In normal dogs, doses up to 10X the recommended dose resulted in little adversity. Animals with chronic disease appear to be most at risk for developing toxicity with this drug. Effects such as gi problems, hepatocellular damage, renal disease, blood thinning effects on platelets activity, and hypoalbuminemia have been reported. Recommended dose is 5-10 mg/kg orally (Plumb Veterinary Drug Handbook, 4<sup>th</sup> Edition, 2002).

### **Meloxicam**

Another new NSAID that is available for oral use is Meloxicam. It is expensive and thus may not be practical for every day use but it also shows a more selective inhibition of COX 2. A dose of 1.0 mg/kg orally or subcutaneously once a day for rats has been given.

### **Jello formulation and use**

Jello is used as a way to get an effective dose in all at once for pain relief. Since rats and mice are neophobic, they must be introduced to it for several days before it is needed. Once they try it, they like it. The jello is prepared according to the package directions for Jigglers (with the appropriate amount of drug mixed into the water added) and can be poured into ice cube trays to solidify.

Jello recipes:

Drug name	Species	Amount of drug	Amount of water	Dose per animal
Carprofen	Rat	100 mg crushed	500 cc	Yields 0.2 mg Carprofen /ml--at 5 mg dose give 7.5 ml (1.5 tsp) jello cube, at 10 mg dose give 15 ml (1 Tbsp) jello cube
Buprenorphine*	Mouse	0.3 mg (one ml vial)	15 ml water	Give 1 cubic ml BID
Buprenorphine*	Rat	0.3 mg (one ml vial)	3 ml water	Give 4 cubic ml cube BID

\*Buprenorphine is a controlled narcotic drug. Because of its potential for abuse, use of Buprenorphine in jello would need to be approved by the Office of Regulatory Affairs and done in accordance with all rules regarding controlled substances.

### **Other resources:**

1. National Institute of Health, Office of Animal Care and Use: “Guidelines on Use of Analgesic Drugs”  
[http://oacu.od.nih.gov/ARAC/painresprecall\\_table2.htm](http://oacu.od.nih.gov/ARAC/painresprecall_table2.htm)

2. Huerkamp, Michael J., "The Use of Analgesic in Rodents and Rabbits"  
Emory University, website, updated 2/16/2000.  
[http://www.emory.edu/WHSC/MED/DAR/Analgesic\\_drugs.htm](http://www.emory.edu/WHSC/MED/DAR/Analgesic_drugs.htm)
3. Flecknell P.A. 1996. Anaesthesia and analgesia for rodents and rabbits. In:  
**Handbook of Rodent and Rabbit Medicine**, Laber-Laird K, Swindle MM  
and Flecknell PA, eds., Pergammon Press, Butterworth-Heineman, Newton,  
MA, pp. 219-37.