# Feline Anesthesia & Analgesia: Recent Developments

Kristen Messenger, DVM, Diplomate ACVAA & ACVCP North Carolina State University

**FELINE FRIENDLY ARTICLE** 

There are approximately 74.1 million pet cats in the United States<sup>1</sup> but, despite this popularity, anesthesia and analgesia remain challenging in cats. Surprisingly few anesthetic and analgesic products are approved by the U.S. Food and Drug Administration (FDA) for use in cats, but several new products have become recently available.

### NEW ANESTHETIC PRODUCTS **Airway Device**

The v-gel (docsinnovent.com) is a supraglottic airway device (**Figure 1**) similar to a laryngeal mask airway, and is an alternative to orotracheal intubation.<sup>2,3</sup> The device was designed specifically for use in cats (Figure 2).

**Indications.** The v-gel provides a protected and secured airway, allowing use of positive pressure ventilation and administration of inhalant anesthetics without exposure to staff or the environment. It can also be used for emergency resuscitation if an endotracheal tube is not available.

The v-gel is most commonly used at my institution in cases in which patients may be at high risk for trauma associated with endotracheal intubation or for short procedures that require no manipulation of the head since the device is potentially easy to dislodge.

Positioning. The v-gel should be used with capnometry in order to confirm it is correctly positioned over the airway, especially if the cat is being moved or its head manipulated. The manufacturer provides training for use of this device, which is strongly recommended prior to patient use.

Considerations. The v-gel does not directly contact the larynx or

arytenoid cartilages (Figure 3); therefore, it should not trigger laryngospasm directly. To my knowledge, there are no studies comparing the occurrence of laryngospasm with conventional endotracheal intubation versus v-gel placement.4

#### Alfaxalone

Alfaxalone (jurox.com) was approved by the FDA for use in cats in September 2012 and by the U.S. Drug Enforcement Agency in 2014. However, this drug has been approved for use in several other countries for many years.

**Approved Use.** Alfaxalone is a neurosteroid anesthetic agent that produces general anesthesia through modulation of the GABA-A receptor. This drug is approved for induction of anesthesia in cats at a median IV dose of 4 mg/kg (range, 2.2–9.7), slowly and titrated to effect. It is a Schedule IV controlled substance with a shelf life of 6 hours after broaching the vial because the formulation does not contain a preservative.5

When used according to the FDA-approved label, alfaxalone is more or less interchangeable with propofol. The anesthetic and physiologic effects are clinically similar; both drugs provide smooth and effective induction of anesthesia in cats. Similar to propofol, alfaxalone may also result in apnea;



FIGURE 1. An example of the v-gel for FIGURE 2. Photograph of the cats, which comes in 6 different sizes. v-gel correctly placed in a patient.





FIGURE 3. Anatomic representation showing placement of the v-gel in a feline oropharynx. Note the supraglottic position of the v-gel.

therefore, orotracheal intubation should be used when administering alfaxalone in cats.

**Off-Label Use.** The off-label use of alfaxalone by IM administration provides some additional advantages over current products for sedation, either prior to anesthesia or for minor procedures (eg, ultrasound). While this use is not supported by the drug label in the U.S., it is in other countries (Australia and New Zealand).

At my institution, IM alfaxalone is routinely used at doses of 0.5 mg/kg to 3 mg/kg, in combination with opioids and other sedative drugs, for premedication in cats. IM alfaxalone is particularly useful in feline patients in which additional sedation is necessary to accomplish a procedure but ketamine or dexmedetomidine may be contraindicated.

**Monitoring.** Cats premedicated with alfaxalone should be monitored closely for apnea; flow-by oxygen should be provided and equipment necessary for orotracheal intubation should be available. In healthy (ASA I or II, **Table**) or fractious cats, larger doses (volumes) of alfaxalone may be required, making the practical use of alfaxalone at a single injection site prohibitive, particularly if the drug is used on its own (ie, without other sedatives).

#### **NEW ANALGESIC PRODUCTS**

With the publication and validation of multiple feline-specific pain scales, veterinarians in both practice and academia are rightly paying close attention to the provision of appropriate analgesia to feline patients. Two recently FDA-approved products are now available for use in cats.

#### Buprenorphine

(Simbadol, zoetisus.com) is the only injectable buprenorphine formulation that is FDA-approved

for use in cats in the U.S. This formulation of buprenorphine is a more concentrated formulation (1.8 mg/mL) compared with the standard Buprenex (**rb.com**) injectable (0.3 mg/mL) that most veterinarians are accustomed to using.

Indications. The specific dose for this buprenorphine formulation is 0.24 mg/kg SC Q 24 H, which is vastly different from the traditional use of the human injectable buprenorphine formulation (SC administration is not recommended). Simbadol dosed at approximately 12× the customary dose of 0.02 mg/kg leverages the ceiling effect of buprenorphine, whereby the higher doses do not elicit greater analgesia, but do extend duration of action. The label recommends Simbadol administration 1 hour prior to surgery, and injections can be repeated every 24 hours for a total of 3 doses.

**Considerations.** Clinical signs of euphoria may be observed after Simbadol administration, which include purring and kneading the forepaws.

The reader is referred to the package insert for further information on safety and adverse effects of Simbadol, which includes a warning that this product should not be dispensed for administration at home by the pet owner.<sup>6,7</sup>

Simbadol is not an extended or sustained release form of buprenorphine and should not be confused with such products.

#### Robenacoxib

Nonsteroidal anti-inflammatory drugs (NSAIDs) are among the most widely used analgesic drugs in veterinary medicine, and when used at appropriate doses in otherwise healthy animals, these drugs are remarkably safe and effective. Robenacoxib is a cyclooxygenase-2, (COX-2) selective NSAID that has

TABLE.

American Society of Anesthesiologists

Physical Status Classification System

ASA I	Normal healthy patient
ASA II	Patient with mild systemic disease
ASA III	Patient with severe systemic disease
ASA IV	Patient with severe systemic disease that is a constant threat to life
ASA V	Moribund patient who is not expected to survive without surgery
ASA VI	Declared brain-dead patient whose organs are being removed for donor purposes

Adapted from ASA Physical Status Classification System, available at asahq.org/resources/clinical-information/asaphysical-status-classification-system



## Read

Purr-fect Feline Anesthesia in the March/April 2016 issue of Today's Veterinary Technician, available with the print edition of Today's Veterinary Practice or at todaysveterinary technician.com. been previously available for use in cats as an orally administered tablet.

Cats have unique (deficient) metabolic pathways for some NSAIDs (ie, those requiring glucuronidation). Only approved NSAIDs should be used in cats, such as meloxicam and robenacoxib, which do not undergo metabolism by this pathway.

**Indications.** The approved label recommendation for the new injectable formulation, Onsior Injectable (**us.onsior.com/en/**), is 2 mg/kg SC Q 24 H for a maximum of 3 days. It can be administered prior to surgery (30 minutes is recommended by the manufacturer). Veterinarians can choose to follow the injection with robenacoxib, 1 mg/kg PO Q 24 H if desired for 2 days. The total robenacoxib dose should not exceed 3 total dose administrations (ie, 1 injection and 2 tablets).<sup>8</sup>

**Long-Term Use.** No NSAIDs are approved for chronic use in cats in the U.S.; however, in several other countries approval exists for chronic low-dose NSAID use.<sup>9</sup> Published studies on the off-label use of meloxicam at low doses (0.01–0.03 mg/kg PO Q 24 H) would suggest that long-term use at a low dose is both efficacious and safe in most cats.<sup>10-12</sup> A recent publication on chronic administration of robenacoxib at 1 to 2.4 mg/kg PO Q 24 H also suggests that long-term (30-day) use of this NSAID may be well tolerated in cats.<sup>9</sup>

Use in Cats with Comorbidities. Cats with comorbidities, such as hypovolemia, dehydration, and/or chronic kidney disease (CKD), may not be the best candidates for NSAID therapy predominantly due to the antiprostaglandin effects of these drugs. <sup>13</sup> Despite this warning, several studies have reported the use of long-term (1–6 months) administration of NSAIDs in cats with CKD, and general conclusions from these studies are that long-term use of NSAIDs is well tolerated in cats with carefully managed CKD. <sup>9-11</sup> In these patients, client education and close monitoring for NSAID-related adverse effects on the kidneys and other organs is highly recommended.

#### EXTRA-LABEL DRUG USE IN CATS

Extra-label drug use (ELDU) is the use of an approved drug but not according to the FDA-approved drug label. <sup>14</sup> ELDU is legal in the U.S., under the Animal Medicinal Drug Use Clarification Act (AMDUCA) of 1994, and commonplace in feline medicine due to a lack of approved medications.

#### **Propofol**

PropoFlo 28 (zoetisus.com) is a formulation of propofol containing the preservative benzyl alcohol, which was developed to give this product a 28-

day shelf life after broaching the vial. The product is FDA-approved for use in dogs in the U.S., but not cats due to concerns over toxicity of the benzyl alcohol preservative. <sup>15</sup> However, studies using PropoFlo 28 in cats at recommended anesthetic doses (ie, 4–6 mg/kg IV for induction of anesthesia) have shown that this drug is not associated with any adverse effects related to the benzyl alcohol preservative. <sup>15,16</sup>

#### **Tramadol**

Unlike most, if not all dogs, cats produce the major M1 metabolite of tramadol (O-desmethyltramadol), which is responsible for producing the opioid analgesic effects of this drug. <sup>17</sup> There are both anecdotal reports and prospectively designed research studies identifying positive analgesic effects following tramadol administration to cats. <sup>18,19</sup>

Doses of 2 to 4 mg/kg PO Q 6 to 12 H are recommended. <sup>18</sup> Tramadol may result in dysphoria in cats; therefore, doses and/or dose frequency may be reduced if cats experience dysphoria after receiving tramadol. <sup>20</sup> Other potential side effects include ataxia, if extrapyramidal effects occur, or hypersalivation, which occurs due to the bitter taste of the tramadol tablet.

#### Gabapentin

In humans, gabapentin is frequently used to treat both chronic and acute pain,<sup>21</sup> although it appears to be most efficacious for neuropathic pain.

There are anecdotal reports on the successful use of gabapentin for the treatment of pain in cats, <sup>19,22,23</sup> but a prospective research study was unable to detect an analgesic effect of gabapentin following a thermal noxious stimulus.<sup>24</sup>

Reported doses for orally administered gabapentin in cats are approximately 10 to 20 mg/kg PO Q 8 H, although these doses are extrapolated from pharmacokinetic studies and case reports. 19,22,24,25 The doses recommended for analgesia above are likely to result in sedation; anecdotally, gabapentin can be started at lower doses and slowly increased to minimize sedation.

Liquid formulations of gabapentin for humans contain xylitol, a known toxin in dogs.<sup>26</sup> There have not been reports of xylitol toxicity in cats; however, commercially available gabapentin solutions often contain flavoring agents that can result in hypersalivation.

#### COMPOUNDED MEDICATION USE IN CATS

I strongly discourage the use of compounded medications, with very few exceptions. Compounded

formulations do not undergo the rigorous testing and manufacturing procedures as do FDA-approved formulations; therefore, drugs can vary from batch to batch. Extensive reviews on veterinary compounding are available for further information. <sup>27,28</sup>

A possible concern in cats is the use of compounded formulations of buprenorphine. With the approval of Simbadol, the use of any compounded buprenorphine is difficult to justify under AMDUCA guidelines. There is one publication on use of a compounded formulation of buprenorphine in cats; however, the sustained-release formulation of buprenorphine was only studied in a small number of healthy cats.<sup>29</sup>

#### **IN SUMMARY**

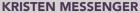
The goal of this review article is to provide relevant clinical updates on new products and pharmaceuticals used for feline anesthesia and analgesia. It is likely that veterinarians will continue to see more research in feline pain management over the next 5 years, which will strengthen our ability to treat this unique patient population.

AMDUCA = Animal Medicinal Drug Use Clarification Act; CKD = chronic kidney disease; COX = cyclooxygenase; ELDU = extra-label drug use; FDA = U.S. Food and Drug Administration; NSAID = nonsteroidal anti-inflammatory drug

Photos courtesy Docsinnovent, Ltd.

#### References

- American Veterinary Medical Association. U.S. Pet Ownership and Demographics Sourcebook. Schaumburg, IL: American Veterinary Medical Association, 2012.
- Van Oostrom H, Krauss MW, Sap R. A comparison between the v-gel supraglottic airway device and the cuffed endotracheal tube for airway management in spontaneously breathing cats during isoflurane anaesthesia. Vet Anaesth Analg 2013; 40(3):265-271.
- Prasse SA, Schrack J, Wenger S, Mosing M. Clinical evaluation
  of the v gel supraglottic airway device in comparison with a
  classical laryngeal mask and endotracheal intubation in cats during
  spontaneous and controlled mechanical ventilation. Vet Anaesth
  Analg 2015 (epub ahead of print).
- 4. Sheppard D. Personal communication, 2015.
- NADA Alfaxan freedom of information summary. Rockville, MD: NADA, 2014, pp 141-342.
- NADA Simbadol freedom of information summary. Rockville, MD: NADA, 2014, pp 141-434.
- 7. Simbadol package insert (2015) Simbadol (buprenorphine



Kristen Messenger, DVM, Diplomate ACVAA & ACVCP, is an assistant professor of anesthesiology at North Carolina State University (NCSU), where she oversees the Comparative Pharmacology and Anesthesiology Laboratory. Her research interests include the pharmacokinetics and pharmacodynamics of analgesic drugs in veterinary species. Dr. Messenger received her DVM and completed a residency at NCSU.



- injection). Available at zoetisus.com/products/cats/simbadol/pdf/prescribing\_information.pdf.
- NADA Onsior freedom of information summary. Rockville, MD: NADA, 2015, pp 141-443.
- King JN, King S, Budsberg SC, et al. Clinical safety of robenacoxib in feline osteoarthritis: Results of a randomized, blinded, placebo-controlled clinical trial. *J Feline Med Surg* 2015 (epub ahead of print).
- Gunew MN, Menrath VH, Marshall RD. Long-term safety, efficacy and palatability of oral meloxicam at 0.01–0.03 mg/kg for treatment of osteoarthritic pain in cats. *J Feline Med Surg* 2008; 10(3):235-241.
- Gowan RA, Lingard AE, Johnston L, et al. Retrospective casecontrol study of the effects of long-term dosing with meloxicam on renal function in aged cats with degenerative joint disease. *J Feline Med Surg* 2011; 13(10):752-761.
- Gruen ME, Griffith EH, Thomson AE, et al. Criterion validation testing of clinical metrology instruments for measuring degenerative joint disease associated mobility impairment in cats. *PloS One* 2015; 10(7):e0131839.
- Whitehouse W, Viviano K. Update in feline therapeutics: Clinical use of 10 emerging therapies. J Feline Med Surg 2015; 17(3):220-234
- Modric S. Regulatory framework for the availability and use of animal drugs in the United States. Vet Clin North Am Small Anim Prac 2013; 43(5):1005-1012.
- Griffenhagen GM, Rezende ML, Gustafson DL. Pharmacokinetics and pharmacodynamics of propofol with or without 2% benzyl alcohol following a single induction dose administered intravenously in cats. Vet Anaesth Analg 2015; 42(5):472-483.
- Taylor PM, Chengelis CP, Miller WR, et al. Evaluation of propofol containing 2% benzyl alcohol preservative in cats. J Feline Med Surg 2012; 14(8):516-526.
- Pypendop BH, Ilkiw JE. Pharmacokinetics of tramadol, and its metabolite O-desmethyl-tramadol, in cats. V Vet Pharmacol Ther 2008; 31(1):52-59.
- Pypendop BH, Siao KT, Ilkiw JE. Effects of tramadol hydrochloride on the thermal threshold in cats. Am J Vet Res 2009; 70(12):1465-1470.
- Steagall PV, Monteiro-Steagall BP. Multimodal analgesia for perioperative pain in three cats. *J Feline Med Surg* 2013; 15(8):737-743.
- Steagall PV, Taylor PM, Brondani JT, et al. Antinociceptive effects of tramadol and acepromazine in cats. J Feline Med Surg 2008; 10(1):24-31.
- Straube S, Derry S, Moore RA, et al. Single dose oral gabapentin for established acute postoperative pain in adults. *Cochrane Database Syst Rev* 2010; 12(5): doi: 10.1002/14651858.
   CD008183.pub2.
- Vettorato E, Corletto F. Gabapentin as part of multi-modal analgesia in two cats suffering multiple injuries. Vet Anaesth Analg 2011; 38(5):518-520.
- Lorenz ND, Comerford EJ, Iff I. Long-term use of gabapentin for musculoskeletal disease and trauma in three cats. *J Feline Med Surg* 2013: 15(6):507-512.
- Pypendop BH, Siao KT, Ilkiw JE. Thermal antinociceptive effect of orally administered gabapentin in healthy cats. Am J Vet Res 2010: 71(9):1027-1032.
- Siao KT, Pypendop BH, Ilkiw JE. Pharmacokinetics of gabapentin in cats. Am J Vet Res 2010; 71(7):817-821.
- Dunayer EK, Gwaltney-Brant SM. Acute hepatic failure and coagulopathy associated with xylitol ingestion in eight dogs. JAVMA 2006; 229(7):1113-1117.
- Davidson G. The compounding controversy: What veterinarians should know to protect themselves and their patients. *JAAHA* 2003; 39(1):13-17.
- Boothe DM. Veterinary compounding in small animals: A clinical pharmacologist's perspective. Vet Clin North Am Small Anim Pract 2006; 36(5):1129-1173.
- 29. Catbagan DL, Quimby JM, Mama KR, et al. Comparison of the efficacy and adverse effects of sustained-release buprenorphine hydrochloride following subcutaneous administration and buprenorphine hydrochloride following oral transmucosal administration in cats undergoing ovariohysterectomy. Am J Vet Res 2011; 72:461-466.