Enhancing Feline Pain Management Strategies

Experience Exchange Panel Participant Materials

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Krista Rose

- Krista has a bachelor’s degree from the Pennsylvania State University.
- She spent 10 years with Ciba-Geigy and Novartis as a Sales Manager, Training Specialist and Sales Representative in the Northeast and Midwest. For the past 19 years, she and her husband have run a cow-calf operation.
- Krista joined Beck Ag in 1999 and has moderated and managed projects across a variety of crops and disciplines, including livestock and companion animal. She has also been involved in writing and serves as Implementation Leader for Market Instruction.
Panel Series Members Include:

Michael Petty, DVM, CVPP, DMVA, CCRT, DAAPM
Arbor Pointe Veterinarian Hospital and Animal Pain Center, Canton, MI

Ralph Harvey, DVM, MS, DACVAA
Associate Professor of Anesthesiology, University of Tennessee College of Veterinary Medicine

Tammy Grubb, DVM, PhD, DACVAA
Assistant Clinical Professor of Anesthesia and Analgesia, Washington State University

Robin A. Downing, DVM, MS, DACVSMR, DAAPM, CVPP, CCRP
Hospital Director, Windsor Veterinary Clinic, P.C., The Downing Center for Animal Pain Management, LLC, Windsor, CO

Sheilah A. Robertson, BVMS (Hons), PhD, DACVAA, DECVAA, DACAW, DECAWBM (WSEL), MRCVS
Associate Professor, Department of Small Animal Clinical Sciences, Michigan State University

Daniel Edge, DVM, MBA
Manager, US Companion Animal Veterinary Specialty Operations, Veterinary Medical Lead: Pain, Oncology, Specialty, Zoetis

Not all panelists will attend every discussion.
To Join the Discussion

To ask questions during the discussion:

1. Press Star 1 on your touchtone phone and the operator will open your line so you can ask your question directly to the panelists.

2. For webinar participants: Type in a question online and the moderator will present your question to the panelists.
Importance of Feline Pain Management

- Pain management is central to veterinary practice\(^1\)
  - Professional obligation
  - Key contributor to successful case outcomes and enhancement of the veterinarian-client-patient relationship

- Treating pain can significantly speed healing and recovery\(^1\)
  - Pain can have immediate and long-term detrimental effects on health
  - Uncontrolled pain is a major biologic stressor, affecting numerous aspects of physical health
    - Wound healing
    - Resistance to infectious disease
  - Sudden-onset pain not managed properly can lead to pain that lasts for months or longer

- Cats without proper pain management will be frightened and stressed during future veterinary visits\(^2\)


Feline Pain: Limited Treatment Options

FDA-approved Treatment Options:
- NSAIDS: meloxicam, robenacoxib
- Opioids: butorphanol

Limitations of current options include:
- Some are one dose only
- Some are administered orally
- Most must be given multiple times within a 24-hour period for continuous pain control
Assessment of Feline Pain is Evolving

Only recently have validated feline pain scales become available for assessing surgical pain\(^1,2,3\)

1. Assess patient prior to procedure
2. Evaluate patient from a distance
3. Approach and interact with patient
4. Palpate incision
5. Physiological changes
   a. Increased systemic arterial blood pressure, decreased appetite\(^1\)
6. Behavioral/posture changes
   a. Hunched posture, ears out to side, whiskers down
   b. Hiding
   c. Reluctant to interact, lie down, move or sleep
   d. Protecting or excessive grooming of incision, reacts to palpation
7. Vocalization

**Appropriate pain management relies on regular and frequent assessment**


\(^3\) Colorado State University Feline Acute Pain Scale: [https://csuanimalcancercenter.org/assets/files/csualcuentvcalpain_scale_feline.pdf](https://csuanimalcancercenter.org/assets/files/csualcuentvcalpain_scale_feline.pdf)
Tenets and Strategies of Pain Management

1. Establish policies and procedures that support pain management
   • Vet team buy-in
2. Initial pain assessment followed by treatment
   • Provide copy of pain scale to owner
   • Pain scales simple, easy to use
3. On-going pain assessment
   • Evaluate response to therapy and make adjustments
4. Re-evaluation and treatment until patient is back to “normal”

Re-evaluation is key to successful pain management

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2 Grubb T. Spotlight on acute pain in cats: Improving your assessment, treatment, and prevention of pain in feline patients Feb 02, 2015
SIMBADOL™
(buprenorphine injection)

- FDA-Approved, Once-Daily, 24-Hour, Continuous Surgical Pain Control for Cats
- Novel concentration and dose of buprenorphine
- Immediate release – onset of effect within one hour of injection
- Safety demonstrated in over 200 cats
IMPORTANT SAFETY INFORMATION: Due to serious human safety and abuse concerns, including physical or psychological dependence, life-threatening respiratory depression and additive CNS depressant effects, read the full prescribing information before using this drug, including the complete Boxed Warning. Not for use in humans. Hospital staff should be trained in the handling of potent opioids and should avoid accidental exposure. SIMBADOL has not been evaluated in breeding, pregnant, or lactating cats, in cats younger than 4 months of age or moribund cats. Do not use in cats with known hypersensitivity to buprenorphine hydrochloride or any of the components of SIMBADOL, or known intolerance to opioids. Use with caution in cats with impaired hepatic function. Adverse reactions may include hyperthermia, tachycardia, hypotension, hypertension, hypothermia, anorexia, and hyperactivity. For more safety information, refer to the full Prescribing Information enclosed or at www.Simbadol.com/PI
SIMBADOL™ blocks pain within the brain and spinal cord.

Buprenorphine is a partial mu agonist with high binding affinity and avidity to mu receptors, such that its receptor disassociation is slow.

24-hour analgesia is a combined effect of:
- SIMBADOL Dosage
- Opioid receptor binding capacity
- Slow hepatic metabolism of buprenorphine
Efficacy/Safety Demonstrated in >200 Cats

Studies Included:

<table>
<thead>
<tr>
<th>Study Title</th>
<th>Number of Cats Treated with SIMBADOL™</th>
</tr>
</thead>
<tbody>
<tr>
<td>Target Animal Safety Study</td>
<td>24 Cats</td>
</tr>
<tr>
<td>Soft Tissue Clinical Field Study</td>
<td>109 Cats</td>
</tr>
<tr>
<td>Orthopedic Clinical Field Study</td>
<td>115 Cats</td>
</tr>
<tr>
<td>Blood Pressure Study</td>
<td>8 Cats</td>
</tr>
</tbody>
</table>
Once daily SC injections of SIMBADOL up to 1.2 mg/kg for 9 days\(^{1,2}\)*

Observations in SIMBADOL Treated Cats Included:

- Difficulty handling, hyperactivity, slight disorientation, agitation, dilated pupils and respiratory sinus arrhythmia – 1-1x cat, day 4; 1-3x cat, day 2
- Lower incidence of urination, abnormal oral dryness
- Elevated body temperature all groups (max was 103.8° F; mean was 102° F)
- Weight loss in 5x group; weight gain in all other groups
- Vocalization upon injection – either moderate or severe at 1-5 time points
- Elevated creatinine kinase (3x and 5x) due to inflammation at injection site

*Zoetis does not recommend administering SIMBADOL at higher than label dose (0.24 mg/kg) or for longer than 3 consecutive days


\(^{2}\)SIMBADOL Freedom of Information Summary NADA 141-434; July 18,2014.

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Blood Pressure Study Design

- Prospective, single center, randomized, blinded, active control study
- Exploratory laparotomy with either meloxicam (0.3 mg/kg) or SIMBADOL™ (0.24 mg/kg)
- BP, HR, RR, BT, ECG, ETCO₂, oxygen saturation, PE, BW, adverse reactions, clinical observations
- Conducted to assess correlation of direct verses indirect BP measurements

*Minimum 14 days
Blood Pressure Study Results

1. No differences between blood pressure measurements in the meloxicam and SIMBADOL™ treated groups

2. Indirect blood pressure measurements and direct blood pressure measurements were closely correlated

3. During and postoperatively, SIMBADOL cats had higher HR

4. During surgery, SIMBADOL cats had lower RR

5. Postoperatively, SIMBADOL cats had higher body temperature; highest temperature was 104.5° F

6. One SIMBADOL cat had hemoglobin saturation < 90%
Soft Tissue & Orthopedic Clinical Trial Summary

**Soft Tissue Surgeries**

- Age: 0.33-16 y
- Weight: 1.2-9.1 kg
- 109 SIMBADOL™; 112 placebo

**Orthopedic Surgeries**

- Age: 0.33-10 y
- Weight: 1.5-9.0 kg
- 115 SIMBADOL™; 114 placebo

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**Soft Tissue Surgeries Diagram**

- Ovario-hysterectomy (OHE) - 41%
- Lumpectomy - 18%
- Cystotomy - 7%
- Perineal urethrostomy - 8%
- Enucleation - 6%
- Other - 20%

**Orthopedic Surgeries Diagram**

- Onychectomy + orchiectomy - 15%
- Onychectomy + OHE - 23%
- Onychectomy - 62%

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- Isoflurane use: 91%
- Glycopyrrolate use: 18%
- IV fluid use: 57%
- Duration: ≤ 60 m in majority of cases

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Understanding and Setting Expectations

Veterinary Healthcare Team¹

- Most cats tolerated injection with a few mild to moderate reactions
- Expect dilated pupils & euphoric behavior
- Euphoria does not preclude use of sedatives or anxiolytics
- Postop temperature may be 103–105°F; intervention typically not required
- Most cats will eat after surgery
- Additional analgesia dependent upon patient, procedure, assessment

Pet Owner²

- Dilated pupils and playful, friendly, loopy cat
- Normal to possibly increased appetite
- The cat should be comfortable and not experiencing pain
- Call if they have concerns

1) SIMBADOL Freedom of Information Summary NADA 141-434; July 18, 2014.
2) SIMBADOL Consumer Tear Pad SIM-0047R, Zoetis, Inc.
All trademarks are the property of Zoetis Services LLC or a related company or a licensor unless otherwise noted. © 2016 Zoetis Services LLC. All rights reserved.
### Indication
- Control of postoperative pain associated with surgical procedures in cats

### Dosage Administration
- 0.24 mg/kg SC
- 1 hour prior to surgery; q 24 hours for up to 3 total doses (72 hours)

### Formulation Storage
- Proprietary 1.8 mg/mL buprenorphine
- 10 mL vial
- Room temperature; 28 day in-use shelf life

### Safety and Efficacy
- Demonstrated in >200 cats for approval
- Margin of safety is 5x label dosage
INDICATION:
SIMBADOL is indicated for the control of postoperative pain associated with surgical procedures in cats.

DOSEAGE AND ADMINISTRATION:
The dosage of SIMBADOL is 0.24 mg/kg (0.11 mg/pound) administered subcutaneously once daily, for up to 3 days. Administer the first dose approximately 1 hour prior to surgery. Do not discontinue SIMBADOL for administration at home by the pet owner.

CONTRAINDICATIONS:
SIMBADOL is contraindicated in cats that are receiving other opioid because of the risk of respiratory depression and bone marrow depression.

WARNINGS:
For subcutaneous (SQ) injection in Human Safety Warning:
- Adult Human User Safety while performing SQ injection:
  - Mucus membrane or eye contact:
  - Direct contact of SIMBADOL with skin or mucous membranes could result in adverse reactions. If accidental contact is made during administration, a physician should be consulted immediately.
  - Skin contact during administration:
  - If skin irritations or sensitizations are noted, discontinue administration of SIMBADOL and consult with a veterinarian.

HUMAN SAFETY WARNING
Abuse Potential
SIMBADOL contains buprenorphine (1.8 mg/mL), an opioid agonist and Schedule III controlled substance with an abuse potential similar to other Schedule III opioids. Buprenorphine has certain opioid properties that in humans may lead to dependence of the morphine type. Abuse of buprenorphine may lead to physical dependence or psychological dependence. The risk of abuse by humans should be considered when storing, administering, and disposing of SIMBADOL. Persons at increased risk for opioid abuse include those with a personal or family history of substance abuse (including drug or alcohol abuse or addiction) or mental illness (suicidal depression).

Life-Threatening Respiratory Depression
Respiratory depression, including fatal cases, may occur with abuse of SIMBADOL.

Additive CNS Depressant Effects
SIMBADOL has additive CNS depressant effects when used with alcohol, other opioids, or illicit drugs that cause central nervous system depression.

Accidental Exposure
Because of the potential for adverse reactions associated with accidental injection, SIMBADOL should only be administered by veterinarians or veterinary technicians who are trained in the handling of potent opioids.

See Human Safety for detailed information.
Label Review – Human Safety

HUMAN SAFETY WARNING

INDICATION:
SIMBADOL is indicated for the control of postoperative pain associated with surgical procedures in cats.

DOSEAGE AND ADMINISTRATION:
The dosage of SIMBADOL is 0.24 mg/kg (0.11 mg/lb) administered subcutaneously once daily, for up to 5 days. Administer the first dose approximately 1 hour prior to surgery. Do not disperse SIMBADOL for administration at home by the pet owner (see Human Safety).

CONTRAINDICATIONS:
SIMBADOL is contraindicated in cats with known hypersensitivity to buprenorphine hydrochloride or any of the components of SIMBADOL, or known intolerance to opioids.

WARNINGS:
For subcutaneous (SQ) injectable use in cats.

Human Safety:

Adult Human Safety while handling SIMBADOL in the hospital:
Mucous membrane or eye contact during administration:
Direct contact of SIMBADOL with the eyes, oral or other mucous membranes could result in absorption of buprenorphine and the potential for adverse reactions. If accidental eye, oral or other mucous membrane contact is made during administration, flush the area with water and contact a physician.

Skin contact during administration:
If human skin is accidentally exposed to SIMBADOL, wash the exposed areas with soap and water and contact a physician. Accidental exposure could result in absorption of buprenorphine and the potential for adverse reactions.

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Information for physician:
SIMBADOL injectable solution is a mu opioid partial agonist (1.8 mg buprenorphine/mL). In the case of an emergency, provide the physician with the package insert. Naloxone may not be effective in reversing respiratory depression produced by buprenorphine. The onset of naloxone effect may be delayed by 30 minutes or more. Doxapram hydrochloride has also been used as a respiratory stimulant.
Contraindications, Warnings & Precautions

1. Contraindicated in cats with known hypersensitivity to buprenorphine hydrochloride or any of the components of SIMBADOL or known intolerance to opioids

2. Store, record usage and discard according to state and federal regulations

3. Due to the concentration of SIMBADOL™, it needs to be administered by or at the direction of a veterinarian and is not to be administered by the pet owner

4. Hyperactivity has been observed up to 8 h after anesthetic recovery

5. Safety has not been evaluated in moribund cats; use in such cases should be based on the risk benefit assessment of the veterinarian

6. Use with caution in cats with impaired hepatic function

7. SIMBADOL has not been evaluated in breeding, pregnant or lactating cats or in cats younger than 4 months of age

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SIMBADOL™: Convenient, Effective, Safe and Cost-Effective¹

- First FDA-approved buprenorphine for cats
- Provides 24 hours continuous postoperative pain control
- Immediate release formulation of buprenorphine
- Proprietary formulation of 1.8 mg/mL, 10 mL vial
- Dosage is 0.24 mg/kg SC; 5 kg cat receives 0.67 mL; therefore 1 vial treats ~15–5 kg cats
- Proven effective and safe for postoperative pain for both soft tissue and orthopedic surgeries in >200 cats
  - Reactions reported at higher incidence than controls: Hypertension and tachycardia
  - Typical feline buprenorphine or opioids reactions: Dilated pupils, hyperactivity, elevated body temperatures
  - Reactions similar to control group: Hypotension, anorexia, hypothermia

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For More Information

- Contact your local Zoetis Representative
- www.zoetis.com

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