FINE-NEEDLE BIOPSY SAMPLE COLLECTION & HANDLING ERRORS

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- Suspected Food Allergy in Dogs: Algorithm
- Step-by-Step Euthanasia Protocols
- Case Report: Pelvic Limb Lameness in a Cat
- Differential Diagnoses for Neutrophilia
Are your patients getting the canine osteoarthritis (OA) pain and inflammation relief they need?

Recommend Galliprant as first-line treatment

- **FIRST-IN-CLASS** non-COX inhibiting NSAID¹
- **MODE OF ACTION** TARGETS canine OA pain and inflammation while reducing the impact on GI, kidney, and liver homeostasis¹,²‡
- **FOR ALL STAGES** of OA from the earliest clinical signs*

*Approved for use in dogs older than 9 months of age and greater than 8 pounds.
‡Monitoring is recommended if used long-term.

INDICATION
Galliprant is an NSAID that controls pain and inflammation associated with osteoarthritis in dogs.

IMPORTANT SAFETY INFORMATION
Not for use in humans. For use in dogs only. Keep this and all medications out of reach of children and pets. Store out of reach of dogs and other pets in a secured location in order to prevent accidental ingestion or overdose. Do not use in dogs that have a hypersensitivity to grapiprant. If Galliprant is used long-term, appropriate monitoring is recommended. Concomitant use of Galliprant with other anti-inflammatory drugs, such as COX-inhibiting NSAIDs or corticosteroids, should be avoided. Concurrent use with other anti-inflammatory drugs or protein-bound drugs has not been studied. The safe use of Galliprant has not been evaluated in dogs younger than 9 months of age and less than 8 lbs (3.6 kg), dogs used for breeding, pregnant or lactating dogs, or dogs with cardiac disease. The most common adverse reactions were vomiting, diarrhea, decreased appetite, and lethargy. For full prescribing information see Galliprant package insert.


Galliprant, Elanco and the diagonal bar logo are trademarks of Elanco or its affiliates. ©2021 Elanco or its affiliates. PM-US-21-1577
For oral use in dogs only
20 mg, 60 mg and 100 mg flavored tablets
A prostaglandin E₂ (PGE₂) EP4 receptor antagonist; a non-cyclooxygenase inhibiting, non-steroidal anti-inflammatory drug

Caution:
Federal (USA) law restricts this drug to use by or on the order of a licensed veterinarian.

Description:
GALLIPRANT (grapiprant tablets) is a prostaglandin E₂ (PGE₂) EP4 receptor antagonist; a non-cyclooxygenase (COX) inhibiting, non-steroidal anti-inflammatory drug (NSAID) in the piptaden family. It is a flavored, oval, biconvex, beige to brown in color, scored tablet debossed with a “G” that contains grapiprant and desiccated pork liver as the flavoring agent. The molecular weight of grapiprant is 491.61 Daltons. The empirical formula is C₂₆H₂₃N₅O₆.S. Grapiprant is a N-[2-[2-(2-Ethyl-4,6-dimethyl-1H-imidazo[4,5-c]pyridin-1-yl)phenyl]ethylamine][carbonil]-4 methylbenzenesulfonamide.

The structural formula is:

\[
\text{Galliprant (grapiprant tablets)}
\]

Indication:
GALLIPRANT (grapiprant tablets) is indicated for the control of pain and inflammation associated with osteoarthritis in dogs.

Dosage and Administration:
Always provide “Information for Dog Owners” Sheet with prescription.
Use the lowest effective dose for the shortest duration consistent with individual response.
The dose of GALLIPRANT (grapiprant tablets) is 0.9 mg/kg (2 mg/kg) once daily.

Dogs less than 8 lbs. (3.6 kgs) cannot be accurately dosed.

Table: Dosing Chart

<table>
<thead>
<tr>
<th>Dose</th>
<th>Weight in pounds</th>
<th>Weight in kilograms</th>
<th>20 mg tablet</th>
<th>60 mg tablet</th>
<th>100 mg tablet</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.9 mg/lb</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(2 mg/kg)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>once daily</td>
<td></td>
<td></td>
<td>0.5</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>8-15</td>
<td>15.1-30</td>
<td>6.9-13.6</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>30.1-45</td>
<td>45.1-75</td>
<td>13.7-20.4</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>75.1-150</td>
<td>34.1-68</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The 100 mg tablet is not scored and should not be broken in half.
Breaking the 100 mg tablet in half will not guarantee that half of the active ingredient is contained within each half of the tablet. For dogs larger than 150 lbs (68 kgs), use a combination of tablet and half tablets to achieve the appropriate dose.

Contraindications:
GALLIPRANT should not be used in dogs that have a hypersensitivity to grapiprant.

Warnings:
Not for use in humans. Keep this and all medications out of reach of children and pets.
Consult a physician in case of accidental ingestion by humans.
For use in dogs only. Store GALLIPRANT out of reach of dogs and other pets in a secured location in order to prevent accidental ingestion or overdose.

Precautions:
The safe use of GALLIPRANT has not been evaluated in dogs younger than 9 months of age and less than 8 lbs (3.6 kgs). Dogs used for breeding, or in pregnant or lactating dogs. Adverse reactions in dogs receiving GALLIPRANT may include vomiting, diarrhea, decreased appetite, mucous, watery or bloody stools, and decreases in serum albumin and total protein. If GALLIPRANT is used long term appropriate monitoring is recommended. Concomitant use with other anti-inflammatory drugs has not been studied. Concomitant use of GALLIPRANT with other anti-inflammatory drugs, such as COX-inhibiting NSAIDs or corticosteroids, should be avoided. If additional pain medication is needed after a daily dose of GALLIPRANT, a non-NSAID/ non-corticosteroid class of analgesic may be necessary. The concomitant use of protein-bound drugs with GALLIPRANT has not been studied. Commonly used protein-bound drugs include cardiac, anticonvulsant and behavioral medications.

Drug compatibility should be monitored in patients requiring adjunctive therapy. Consider appropriate washout times when switching from one anti-inflammatory to another or when switching from corticosteroids or COX-inhibiting NSAIDs to GALLIPRANT use. The use of GALLIPRANT in dogs with cardiac disease has not been studied. It is not known whether dogs with a history of hypersensitivity to sulfonamide drugs will exhibit hypersensitivity to GALLIPRANT. GALLIPRANT is a methylbenzenesulfonamide.

Adverse Reactions:
In a controlled field study, 285 dogs were evaluated for safety when given either GALLIPRANT or a vehicle control (tablet minus grapiprant) at a dose of 2 mg/kg (0.9 mg/lb) once daily for 28 days. GALLIPRANT-treated dogs ranged in age from 2 yrs to 16.75 years. The following adverse reactions were observed:

Table 1. Adverse reactions reported in the field study.

<table>
<thead>
<tr>
<th>Adverse reaction*</th>
<th>GALLIPRANT (grapiprant tablets)</th>
<th>Vehicle control (tablets minus grapiprant)</th>
</tr>
</thead>
<tbody>
<tr>
<td>N = 141</td>
<td>N = 144</td>
<td></td>
</tr>
<tr>
<td>Vomiting</td>
<td>24</td>
<td>9</td>
</tr>
<tr>
<td>Diarrhea, soft stool</td>
<td>17</td>
<td>13</td>
</tr>
<tr>
<td>Anorexia, inappetence</td>
<td>9</td>
<td>7</td>
</tr>
<tr>
<td>Lethargy</td>
<td>6</td>
<td>2</td>
</tr>
<tr>
<td>Buccal ulcer</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Immune mediated hemolytic anemia</td>
<td>1</td>
<td>0</td>
</tr>
</tbody>
</table>

* Dogs may have experienced more than one type or occurrence during the study.

GALLIPRANT was used safely during the field studies with other concurrent therapies, including antibiotics, parasiticides and vaccinations.

To report suspected adverse drug adverse events and/or to obtain a copy of the Safety Data Sheet (SDS) or for technical assistance, call 1-888-545-5973.

For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS or online at http://www.fda.gov/AnimalVetinary/SafetyHealth

Information for Dog Owners:
Owners should be advised of the potential for adverse reactions and be informed of the clinical signs associated with drug intolerance. Adverse reactions may include vomiting, diarrhea, decreased appetite, and decreases albumin and total protein. Appetite and stools should be monitored and owners should be advised to consult with their veterinarian if appetite decreases or stools become abnormal.

Clinical Pharmacology:
Galliprant is a prostaglandin E₂ (PGE₂) EP4 receptor antagonist; a non- cyclooxygenase inhibiting, non-steroidal, anti-inflammatory drug. Grapiprant has a canine EP4 receptor binding affinity (Ki) of 24 nM. Prostaglandins have a wide variety of physiologic effects. Prostaglandin E₂ is a prostanoid that exerts its effects via four receptors, EP1, EP2, EP3, and EP4. PGE₂ is involved in mediating inflammatory pain, vasodilation, increasing vascular permeability; as well as gastrointestinal homeostasis, renal function and reproductive functions. The EP4 receptor is important in mediating pain and inflammation as it is the primary mediator of the PGE₂- elicited sensitization of sensory neurons and PGE₂- elicited inflammation. Grapiprant blocks PGE₂- elicited pain and inflammation by antagonizing the EP4 receptor.

The EP4 receptor, along with the EP1, EP2 and EP3 receptors, is involved in PGE₂, mediated effects on gastrointestinal homeostasis and renal function. PGE₂ effects mediated solely by the EP4 receptor are stimulation of mucus secretion in the stomach and large intestine, stimulation of acid secretion in the stomach, inhibition of small intestine motility and inhibition of cytokine expression in the large intestine. While PGE₂, gastroprotective action is mediated by EP1, the healing- promoting action of PGE₂, in the stomach is mediated by the EP4 receptor. In the kidney, the PGE₂, antinatriuretic effect is mediated by the EP4 receptor. EP4 receptors are abundantly expressed in the heart of dogs; the clinical relevance of which is unknown. The EP4 receptor is not involved in generation of pyrexia. Grapiprant is a non potential inhibitor of CYP1A2, CYP2C9, CYP2C19, CYP2D6, and CYP3A4 mediated metabolism pathways. Grapiprant is a substrate of P-glycoprotein transport. In vitro metabolism with dog liver microsomes identified two oxidative metabolites, M3 (hydroxyl) and M5 (N-dealkylation).

The pharmacokinetic characterization of grapiprant following oral administration of GALLIPRANT tablets to healthy Beagles is provided in the table below.

Table 2. Mean (±SD) Plasma Pharmacokinetic Parameters for Grapiprant in Beagles after single oral dose of GALLIPRANT tablet formulation.

<table>
<thead>
<tr>
<th>Study</th>
<th>Study 1</th>
<th>Study 1</th>
<th>Study 2</th>
<th>Study 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>PK Parameter</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>2 mg/kg</td>
<td>2 mg/kg</td>
<td>6 mg/kg</td>
<td>50 mg/kg</td>
</tr>
<tr>
<td>(n = 10)</td>
<td>(n = 10)</td>
<td>(n = 8)</td>
<td>(n = 8)</td>
<td></td>
</tr>
<tr>
<td>(Fasted)</td>
<td>(Fasted)</td>
<td>(Fasted)</td>
<td>(Fasted)</td>
<td></td>
</tr>
<tr>
<td>Tmax (hr)</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
<td>2.0</td>
</tr>
<tr>
<td>(hr)</td>
<td>(0.5 – 1.03)</td>
<td>(0.5 – 0.97)</td>
<td>(1.0 – 2.0)</td>
<td>(1.0 – 4.0)</td>
</tr>
<tr>
<td>Cmax (mg/mL)</td>
<td>1210</td>
<td>278</td>
<td>5720</td>
<td>88500</td>
</tr>
<tr>
<td>(n = 341)</td>
<td>(n = 179)</td>
<td>(n = 3220)</td>
<td>(n = 13100)</td>
<td></td>
</tr>
<tr>
<td>AUC(0-inf) (mg*hr/mL)</td>
<td>2790</td>
<td>1200</td>
<td>17800</td>
<td>414000</td>
</tr>
<tr>
<td>(n = 522)</td>
<td>(n = 5520)</td>
<td>(n = 73700)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>T1/2 (hr)</td>
<td>4.60</td>
<td>5.67</td>
<td>5.01</td>
<td>5.21</td>
</tr>
<tr>
<td>(n = 19)</td>
<td>(n = 19)</td>
<td>(n = 19)</td>
<td>(n = 19)</td>
<td></td>
</tr>
<tr>
<td>Fed/Fasted Relative Bioavailability Geometric Mean Ratio of AUC</td>
<td>0.37 (0.28 – 0.46)</td>
<td>NA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>90% Confidence Limits</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1 Study 1 was a food effect determination study.
2 Study 2 was a PK bridging study conducted using 60 mg GALLIPRANT tablets at 6 mg/kg dose and 5 X 100 mg GALLIPRANT tablets at 50 mg/kg dose.
3 Median (Range)
Claro® is indicated for the treatment of otitis externa in dogs associated with susceptible strains of yeast (*Malassezia pachydermatis*) and bacteria (*Staphylococcus pseudintermedius*).

**CAUTION:** Federal (U.S.A.) law restricts this drug to use by or on the order of a licensed veterinarian.

**PRECAUTIONS:** For use in dogs only. Do not use in cats (see POST APPROVAL EXPERIENCE). CLARO® has been associated with rupture of the tympanic membrane. Reevaluate the dog if hearing loss or signs of vestibular dysfunction are observed during treatment. Signs of internal ear disease such as head tilt, vestibular signs, ataxia, nystagmus, facial paralysis, and keratoconjunctivitis sicca have been reported (see POST APPROVAL EXPERIENCE) with the use of CLARO®.

Guarantee compliance
- Administer the only FDA-approved single-dose otitis externa treatment and rest your confidence on a 30-day duration of effect

Eliminate the stress of at-home treatments
- The power is in your hands to treat your patient’s ear infection in-clinic

**SAVE THE DAY.** **USE CLARO® FOR YOUR MOST COMMON OTITIS CASES.**

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See page 2 for product information summary.
Providing small animal practitioners and their teams with practical, relevant information on the latest topics in veterinary medicine
CLARO® should be administered by veterinary personnel. Shake before use.

In a well-controlled, double-masked field study, CLARO® was evaluated against a vehicle control in 221 dogs with otitis externa. Of the 183 dogs included in the effectiveness evaluation, 72.5% of dogs administered CLARO® solution were successfully treated, compared to 11.1% of the dogs in the vehicle-control group (p=0.0001).

ADVERSE REACTIONS:
In a field study conducted in the United States (see EFFECTIVENESS), there were no direct adverse effects attributed to administering CLARO®. To report suspected adverse drug events and/or obtain a copy of the Safety Data Sheet (SDS) or for technical assistance, contact Bayer HealthCare at 1-800-422-9874.

PHARMACOLOGY:
CLARO® Otic Solution is a fixed combination of three active substances: florfenicol (antibacterial), terbinafine (antifungal), and mometasone furoate (steroidal anti-inflammatory). Florfenicol is a bacteriostatic antibiotic which acts by inhibiting bacterial protein synthesis. Terbinafine is an antifungal which selectively inhibits the early synthesis of ergosterol. Mometasone furoate is a glucocorticoid with anti-inflammatory activity.

PHARMACOKINETICS:
The compatibility and additive effect of each of the components in CLARO® solution were determined in a compatibility and non-stability study. In vitro studies of organisms collected from clinical cases of otitis externa in dogs enrolled in the clinical effectiveness study determined that florfenicol and terbinafine hydrochloride inhibit the growth of bacteria and yeast commonly associated with otitis externa in dogs. Terbinafine hydrochloride showed the most significant effect on the bacteria and yeast, an antimicrobial effect that was dose dependent.

ENZYMES:
The compatibility and additive effect of each of the components in CLARO® solution were determined in a compatibility and non-stability study. In vitro studies of organisms collected from clinical cases of otitis externa in dogs enrolled in the clinical effectiveness study determined that florfenicol and terbinafine hydrochloride inhibit the growth of bacteria and yeast commonly associated with otitis externa in dogs. Terbinafine hydrochloride showed the most significant effect on the bacteria and yeast, an antimicrobial effect that was dose dependent.

EFFECTIVENESS:
In a well-controlled, double-masked field study, CLARO® was evaluated against a vehicle control in 221 dogs with otitis externa. Of the 183 dogs included in the effectiveness evaluation, 72.5% of dogs administered CLARO® solution were successfully treated, compared to 11.1% of the dogs in the vehicle-control group (p=0.0001).

CLARO® Otic Solution is supplied in a single-use dropperette in a blister. Each dropperette contains 1 mL dropper.

MANUFACTURED FOR:
Bayer HealthCare LLC, Animal Health Division
P.O. Box 380 Shrewsbury, Mass. 01545 USA.

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NADA 141-440, Approved by FDA
US0182

KAITLIN N. BAHLMANN, DVM, is an associate veterinarian at Exclusively Cats Veterinary Hospital in Waterford, Michigan, and is pursuing board certification in feline practice by the American Board of Veterinary Practitioners. Dr. Bahlmann earned her DVM from the University of Guelph. She has worked as a general practitioner and emergency veterinarian at various clinics across Canada. Her interests are feline internal medicine and complex surgical cases.

CASE IN POINT PAGE 73

STEVEN J. BAILEY, DVM, DABVP (Feline), is the founder, owner, and medical director of Exclusively Cats Veterinary Hospital in Waterford, Michigan. Dr. Bailey’s special interests include complicated medical and surgical cases, as well as advanced dentistry. He and his team at Exclusively Cats Veterinary Hospital were the first to identify feline knees and teeth syndrome, and Bailey has coauthored several articles detailing the condition.

CASE IN POINT PAGE 73

KATHLEEN COONEY, DVM, MS, CHPV, CCFP, is the Director of Education at the Companion Animal Euthanasia Training Academy in Loveland, Colorado, and the Chief Medical Officer of Caring Pathways in Denver, Colorado. Dr. Cooney is a past president of the International Association for Animal Hospice and Palliative Care (IAAHPC), where she designed the Animal Hospice and Palliative Care certification program. She has authored 2 books and numerous articles and book chapters. Dr. Cooney has collaborated in end-of-life training with AVMA, AAHA, NAVC, IAAHPC, Fear Free Program, and Society for Veterinary Medical Ethics. She is a strong advocate for best practices in all aspects of end-of-life care and speaks worldwide. Dr. Cooney is working toward board certification in animal clinical nutrition.

PROCEDURES PRO PAGE 25

ELIZABETH R. DRAKE, DVM, DACVD, is an associate professor of small animal dermatology at University of Tennessee, where she also completed a dermatology residency. Dr. Drake earned her DVM from Texas A&M University. Her main area of concentration is the treatment of otitis in companion animals.

DIAGNOSTIC TREE PAGE 22
Do you dip slides into the stain or drip the stain directly onto slides?

“We always dip, but it makes a huge mess and usually gets on shoes and fingers.” — Stephanie B

“Dripping is awesome. There is no debris, is less waste, and are no more ‘dirty’ and ‘clean’ tubs. Slides are fine.” — Alexis W

“Dip; I never learned the drip.” — Chelsey M

“We dip but have one set of slides for both skin and ears and a separate set for blood smears.” — Ali B

“I always drip; otherwise, stains may be contaminated.” — Sarah D

What is the most unique vein you have used to gain venous access in a patient?

“I used the dorsal coccyegeal vein in a huge snapping turtle and the cephalic vein in a Galapagos tortoise—it took 6 people and a 5-gallon bucket to restrain him!” — Ericka K

“I went in through the tongue in a llama. My employer at the time would not consider the suggestion of going high up the neck.” — Darlene J

“Sublingual in a brown bear” — Christina L

“The scrotum in a horse!” — Lauren G

“Postoccipital sinus in a sea turtle”— Erica F

“Palatine vein in a venomous snake”— Ismar L

Have you ever diagnosed an axial osteosarcoma in a patient?

- 42% Yes
- 58% No

Do you plan on attending in-person continuing education in 2021?

- 15% Yes, but only locally
- 18% Yes, anywhere
- 67% No

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As part of a multimodal treatment, Derm Complete is shown in clinical studies to:

1. Manage itching in dogs with food and/or environmental allergies
2. Reduce licking, scratching, head shaking and skin redness in dogs with environmental allergies

Ask your Hill’s rep about allergy care that’s A STEP AHEAD FOR THEIR BEST LIFE
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Lisa M. Pohlman, DVM, MS, DACVP

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TOP 5 Fine-Needle Biopsy Sample Collection & Handling Errors
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TOP 5 Dermatologic Indications for Pentoxifylline in Dogs
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Robert Kennis, DVM, DACVD, MS

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DIFFERENTIAL DIAGNOSIS
Neutrophilia
Marie Chartier, DVM, DACVIM
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Canine and Feline Vaccines From Boehringer Ingelheim.

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We packed years of research and innovations into each of our vaccines. But it all started with prevention. See how the RECOMBITEK® canine vaccines, PUREVAX® feline vaccines, and IMRAB® rabies vaccines help protect against common dangerous infectious diseases for canines and felines.
ON THE WEB

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PODCAST
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Karen A. Moriello, DVM, DACVD, discusses all angles of dermatophytosis—exposure, diagnostics, species, therapies, and disinfection. brief.vet/dermatophytosis

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Congenital & Heritable Diseases
This course provides expert advice for detecting and treating common congenital and heritable diseases (including hydrocephalus, pectus excavatum, and MDRI mutation) in dogs and cats. brief.vet/congenital-disease

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Articles archived at
digital.cliniciansbrief.com
ROBERT KENNIS, DVM, DACVD, MS, is a professor at Auburn University. He earned his DVM from and completed a residency at Michigan State University. Dr. Kennis earned his MS in veterinary immunology from Texas A&M University. He is the past president of the American Academy of Veterinary Dermatology and has presented numerous continuing education seminars at the state, national, and international levels. Dr. Kennis has received the Pfizer Distinguished Teacher award at both Auburn University and Texas A&M University, as well as the Texas A&M Association of Former Students’ Distinguished Achievement award. His research interests include food allergy, endocrine alopecia, and feline bacterial infections.

SARAH LEWIS, DVM, MS, is a dermatology resident at Auburn University. She earned her MS and DVM at University of Florida and completed an internship in small animal medicine and surgery at The Ohio State University. Dr. Lewis is interested in small animal dermatology, especially hypersensitivity disorders.

LISA M. POHLMAN, DVM, MS, DACVP, is an associate professor of clinical pathology at Kansas State University. She earned her DVM from University of Guelph and her MS in clinical pathology from Auburn University, where she also completed a residency. Dr. Pohlman serves as the president and medical director of the Riley County Humane Society in Manhattan, Kansas, and is an active teacher and mentor of veterinary interns, residents, and graduate students. She enjoys providing CE in clinical pathology through speaking engagements, online courses, and publications. Her research interests include improvement of clinical pathology laboratory methods and identification and characterization of disease in domestic species, particularly in shelter animals, as well as pets owned by individuals who cannot afford routine veterinary care.

ISABELLE SOGA, DVM candidate, is a senior veterinary student (class of 2021) at Kansas State University. She plans to pursue a small animal rotating internship. Her interests are clinical pathology, internal medicine, and animal behavior.

LOOK FOR THESE ARTICLES IN FUTURE ISSUES

- Enteral & Parenteral Nutrition in the Intensive Care Unit
- Image Gallery: Ocular Manifestations of Systemic Disease
- Smoke Inhalation
- Anesthetic Protocols & Concerns in Planned & Emergent Cesarean Sections
- Noncardiogenic Pulmonary Edema in a Puppy
THE IT LIST

NOT THE ITCH LIST

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PROVIDE COMFORT AND RELIEF
Stop the itch with formulations that cleanse and protect the skin.

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Offer a complementary product line with ingredients you know and trust.

SUPPORT A DAILY ROUTINE
Increase compliance with products for bath day and every day in between.

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SHAMPOOS | MOUSSES | WIPES | SPRAYS | OTICS | FLUSHES

The Dechra dermatology collection makes it easy for clients to follow a multimodal management protocol to provide their pets with relief from itchy, uncomfortable skin conditions.

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Cardinalis™

(spironolactone and benazepril hydrochloride chewable tablets)

Cardinalis for oral use in dogs only

Approved by FDA under NADA #141-538

Caution: Federal (USA) law restricts this drug to use by or on the order of a licensed veterinarian.

Description: CARDALIS™ (spironolactone and benazepril hydrochloride chewable tablets) for dogs contains two active ingredients: spironolactone and angiotensin-converting enzyme (ACE) inhibitor benazepril hydrochloride. The empirical formula for spironolactone is C24H28N2O5 · H2O. The molecular weight is 466.5. The chemical name is 7-hydroxy-7a-methyl-5a-11h-7-oxo-4-2,3,4,5-tetrahydro-2-oxo-1H-naphthalene-5-carboxylic acid and the structural formula is shown below.

Spironolactone, and its active metabolites, act as a specific aldosterone antagonist. Spironolactone empirical formula is C24H28N2O5 and the molecular weight is 466.5. The chemical name is 7-hydroxy-7a-methyl-5a-11h-7-oxo-4-2,3,4,5-tetrahydro-2-oxo-1H-naphthalene-5-carboxylic acid and the structural formula is shown below.

Spironolactone is a potassium-sparing diuretic. The clinical pathology parameters associated with renal function were not statistically different between the treatment groups.

Cardinalis™ Adverse Reactions:

The following adverse events were observed in at least 3% of the study animals, in decreasing order: cutaneous ulceration, fluid in abdomen, otitis, weight loss, diaphragmatic hernia, diarrhea, polyuria, polydipsia, vomiting, lethargy, inappetence and anorexia, dizziness, and skin reactions.

Cardinalis™ Animal Safety:

Dogs ranged from 3 to 19 years of age and 5 to 155 lbs (2.3 to 70.5 kg) at enrollment. The most common breeds were mixed breed, Cavalier King Charles Spaniel, Chihuahua, Shih Tzu, Maltese, Dachshund, and Yorkshire Terrier. Smaller dogs demonstrated radiographic evidence of congestive heart failure prior to enrollment on day 1 and exhibited clinical signs associated with left-sided RHF, including increased heart rate and decreased respiratory rate, decreased cardiac output with evidence of left atrial enlargement, moderate to severe respiratory dyspnea, and presence of left sided cardiac murmur. Dogs with acquired heart disease other than left-sided RHF, congested heart defect, current or previous heart failure, or any condition related to heart disease, and dogs intended for breeding or to be pregnant or lactating were excluded. A total of 230 dogs were treated with either CARDALIS (240 dogs) or a dose of 2 mg/kg spironolactone and 2.5 mg/kg benazepril hydrochloride once on cardiac baseline or on day 30. Dogs were chosen to be wasted if any dose or placebo. All dogs were monitored for the presence of any signs or symptoms consistent with congestive heart failure.

The rate of treatment failure was the primary effectiveness variable used to compare CARDALIS to benazepril hydrochloride alone. Treatment failure was defined as cardiac death or euthanasia (including death of unknown cause), recurrence or worsening of pulmonary edema, newly documented cardiac arrhythmia, or clinical signs of congestive heart failure requiring administration of furosemide dosages higher than 5 mg/kg. Failure rates at study days 30, 90, 180, and 270 were also evaluated as secondary outcomes.

The rate of failure in the CARDALIS group exhibited a longer median time-to-failure when compared to the control group. Further, the rate of failure in the CARDALIS group was significantly lower than the group administered benazepril hydrochloride alone at all evaluation periods past study Day 0. The dogs in the CARDALIS group exhibited a longer median time-to-failure when compared to the control group.

Cardinalis™ Effective Parameters for Congenital and TMS on Day 10

<table>
<thead>
<tr>
<th>Parameter</th>
<th>CARDALIS</th>
<th>TMS (n=285)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Feces</td>
<td>100 (100%)</td>
<td>93 (96.8%)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>10 (8.9%)</td>
<td>4 (3.5%)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>19 (16.4%)</td>
<td>20 (17.4%)</td>
</tr>
<tr>
<td>Lethargy</td>
<td>21 (18.0%)</td>
<td>16 (14.0%)</td>
</tr>
<tr>
<td>Weight loss</td>
<td>14 (12.0%)</td>
<td>13 (11.5%)</td>
</tr>
<tr>
<td>Urinary Incontinence</td>
<td>18 (15.6%)</td>
<td>14 (12.6%)</td>
</tr>
</tbody>
</table>
There is a new couple in town

Spironolactone is the essential addition to an ACE inhibitor

The only FDA approved combination drug for the management of congestive heart failure (CHF) in dogs.

- Improved patient acceptance solves owner compliance challenges.
- CARDALIS™ chewable tablets provide half of the ACVIM quad-therapy recommendation for congestive heart failure.*

*In 2019, the ACVIM published new guidelines recommending a quadruple therapy approach for the treatment of CHF in dogs. The safety and efficacy of CARDALIS™ has not been investigated with pimobendan.

**Non-allergenic beef flavoring

See page 10 for product information summary.
The end is near.

Get to the cause of chronic vomiting and diarrhea faster
Only from Antech

To learn more about how Antech can benefit your veterinary organization visit antechdiagnostics.com call 1-800-872-1001

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Canine CE-IBD Assay

Quickly rule in or rule out IBD/chronic enteropathy in your canine patients with this non-invasive assay—letting you arrive at treatment decisions more quickly.

Diagnose and monitor patients with a simple, affordable blood test

Vomiting, diarrhea, and other gastrointestinal (GI) signs are among the most common reasons for a dog to require a visit to the veterinarian. Ascertaining the cause of these signs is often a time-consuming task for clinicians and a frustrating and expensive process for pet owners, especially in the case of a complex condition like chronic enteropathy (commonly referred to as inflammatory bowel disease).

Help your patients get better sooner

The Canine Chronic Enteropathy-Inflammatory Bowel Disease (CE-IBD) Assay is a simple and affordable blood test that makes diagnosing and managing this condition easier than ever before.

THIS NOVEL ASSAY PROVIDES INFORMATION THAT IS USEFUL FOR DIAGNOSIS, TREATMENT, AND MONITORING:

• A panel of three gastrointestinal biomarkers helps determine if a dog with chronic GI signs is likely to have chronic enteropathy
• Results are actionable when interpreted alongside other routine diagnostics:
  • Direction on whether or not additional diagnostics should be performed
  • Insight into which therapeutic diet to select for a dietary trial

To download the diagnostic algorithm and learn more about the Canine CE-IBD Assay visit q-r.to/brief-ibd
Get to the cause of chronic vomiting and diarrhea faster

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VISIT qr.to/brief-ibd

To learn more about how Antech can benefit your veterinary organization
VISIT antechdiagnostics.com CALL 1-800-872-1001

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TOP 5 DERMATOLOGIC INDICATIONS FOR PENTOXIFYLLINE IN DOGS

Sarah Lewis, DVM, MS
Robert Kennis, DVM, DACVD, MS
Auburn University
Pentoxifylline is a methylxanthine derivative that inhibits phosphodiesterase to raise intracellular cyclic adenosine monophosphate levels; this can have many global effects, including improved circulation and reduced inflammation. Pentoxifylline inhibits RBC deformability, microvascular constriction, and thrombus formation; decreases proinflammatory cytokine production, neutrophil degranulation, natural killer cell activity, leukocyte adhesion, chemotaxis, and adherence to keratinocytes; and stimulates fibroblasts to produce collagenase and promote wound healing. Cytokines inhibited by pentoxifylline include tumor necrosis factor-α, interferon-γ, interleukin-1 (IL-1), IL-6, IL-8, and IL-10.
TOP 5 DERMATOLOGIC INDICATIONS FOR PENTOXIFYLLINE

1. Cutaneous Vasculitis
2. Canine Familial Dermatomyositis
3. Other Ischemic Dermatopathies
4. Allergic Contact Dermatitis
5. Atopic Dermatitis

Pentoxifylline (10-30 mg/kg PO every 8 to 12 hours) has a reported elimination half-life of 24 to 404 minutes that supports 8-hour administration.4-6 In dogs, oral bioavailability is variable and reported to be 15% to 50%.5,6 Pentoxifylline is available as a 400-mg extended-release tablet and is commonly halved or quartered to achieve the intended dosage.5,6 No controlled studies have directly investigated the pharmacokinetic effects of breaking the extended-release tablet. Pentoxifylline is generally well-tolerated in dogs, and GI upset is the most commonly reported adverse effect.5,6 Anecdotal reported use in veterinary medicine is vast; however, peer-reviewed studies evaluating its efficacy for the treatment of specific diseases are limited and generally retrospective. Based on anecdotal evidence in human and veterinary medicine, there is believed to be a lag in onset to clinical effect that may last several months.6-8 Previously, concerns about cost limited the use of pentoxifylline in veterinary medicine, but affordable generic formulations are now available.

Following are 5 common uses of pentoxifylline in veterinary dermatology according to the authors.

1. Cutaneous Vasculitis

Cutaneous vasculitis refers to inflammation of the blood vessels in the skin (Figure 1) that results in altered blood flow and ischemic necrosis of the skin (Figure 2).9 The condition may be idiopathic or caused by adverse drug reaction, infection, insect bite, or neoplasia.8 Treatment should address the underlying cause and repair tissue damage.9 Pentoxifylline is an ideal treatment (regardless of cause) because of its effect on perfusion and inflammation.

Because pentoxifylline has a potential delayed onset of effect, it is often combined with other drugs (eg, glucocorticoids).9 In a retrospective study,10 9 of 19 dogs with vasculitis were treated with pentoxifylline (10-20 mg/kg PO every 12 hours) alone (1 dog) or in combination (8 dogs) with prednisone (1.5-3 mg/kg/day) with variable success. Six dogs had complete resolution, 2 had

**FIGURE 1** Multifocal to coalescing erythematous macules on the ventral abdomen of a dog with cutaneous vasculitis. Because the lesion does not blanch on diascopy, it is likely due to vasculitis or hemorrhage. *Image courtesy of Amelia White, Auburn University*

**FIGURE 2** Full-thickness dermal necrosis on the hock of a patient with a neutrophilic necrotizing vasculitis suspected to be secondary to a spider bite. Pentoxifylline (25 mg/kg PO every 12 hours) and open wound management were provided. *Image courtesy of Karly Hicks, Auburn University*
partial resolution, and 1 failed to respond. Of the 6 dogs with complete resolution, 3 relapsed when prednisone was tapered, suggesting that pentoxifylline may be insufficient when used alone to treat vasculitis. Insufficient dosage and frequency could explain the limited success and lack of response in 3 dogs. Despite reports of variable success, pentoxifylline is often used for the treatment of vasculitis.

**2 Canine Familial Dermatomyositis**
Canine familial dermatomyositis (CFD) is an inherited, ischemic disease of the skin, blood vessels, and muscle that predominately affects Shetland sheepdogs and collies; however, other dog breeds can also be affected. Lesions occur in the first few months of life and can vary from minor alopecia (Figure 3) to severe dermal ulceration and muscle atrophy. CFD is incurable; many treatments have been attempted with limited success. In a study, 10 dogs with CFD had partial or complete resolution of cutaneous lesions after receiving pentoxifylline (25 mg/kg PO every 12 hours for 12 weeks). The median time to initial response was 6 weeks, supporting a lag in onset of effect. No adverse effects, including clinicopathologic abnormalities, were observed, further supporting the relative safety of pentoxifylline as compared with other therapeutic options.

**3 Other Ischemic Dermatopathies**
Ischemic dermatopathy refers to several clinical syndromes characterized by overall nutrient and oxygen deficiency in the skin, including CFD, rabies-vaccine–induced vasculitis, vaccine-associated ischemic dermatopathy, familial cutaneous vasculopathy in German shepherd dogs, pinnal vasculitis (Figure 4), and idiopathic ischemic dermatopathy. In a study, 3 dogs with rabies-vaccine–induced vasculitis had partial to complete hair regrowth 12 to 16 weeks after receiving pentoxifylline (15 mg/kg PO every 12 hours) combined with prednisone (0.8-3 mg/kg/day PO). In a retrospective study of 177 dogs with ischemic dermatopathy, the majority of dogs (91.3%) were treated with either pentoxifylline alone or as adjunctive therapy, with a mean dosage of 47.12 mg/kg/day PO (range, 18-112.5 mg/kg/day PO). Despite common use, no difference was found between dogs treated and dogs not treated with pentoxifylline. It was concluded that the retrospective nature of the study and variability in dosing regimens could explain this finding. Additional prospective, placebo-controlled studies are needed to determine the effectiveness of pentoxifylline in the treatment of ischemic dermatopathies. Despite limited evidence in the literature, the hemorrhologic properties of pentoxifylline could be favorable for the management of ischemic dermatopathies.
4 Allergic Contact Dermatitis

Allergic contact dermatitis (ACD) is a type IV hypersensitivity reaction.\(^8,14\) Reported causes of ACD in dogs include ingestion of plants, topical medications, detergents, cleansers, fibers, and plastic.\(^8,14\) Pentoxifylline inhibits tumor necrosis factor-\(\alpha\), which is a critical mediator of ACD.\(^1,14\) Pentoxifylline (10 mg/kg PO every 12 hours) was protective in preventing clinical signs in 3 dogs with known contact allergy to plants in the Commelinaceae family.\(^14\) A clinical effect was observed within 2 days of onset of therapy and persisted for 7 days following discontinuation of therapy.\(^14\) Treatment duration was limited to 3 to 5 weeks due to the cost of therapy.\(^14\) Pentoxifylline has become less cost-prohibitive; thus, it can be a reasonable choice for prevention of clinical signs of ACD when avoidance is not possible. Major limitations of this study were the few number of dogs included and its retrospective nature. Additional investigations are required to determine the effectiveness of pentoxifylline in the treatment of ACD.

5 Atopic Dermatitis

Canine atopic dermatitis (CAD) is a common allergic dermatosis characterized by hypersensitivity to environmental allergens, primarily mediated by immunoglobulin E (IgE).\(^15\) CAD can be challenging for the patient, pet owner, and clinician despite available pharmacologic management options. Although pentoxifylline is not considered a mainstay for management of CAD, limited research suggests it may have value as adjunctive therapy.\(^16,17\) One study in normal dogs demonstrated that pentoxifylline inhibited late-phase inflammation by inhibiting IgE-mediated mast cell degranulation and eosinophil recruitment at the site’s wheal formation.\(^18\) These findings suggest pentoxifylline may have some effect in managing IgE-mediated inflammatory diseases. A double-blinded, placebo-controlled, crossover study of 10 atopic dogs showed that pentoxifylline (10 mg/kg PO every 12 hours) reduced pruritus scores by 50% in one-third of dogs over 4 weeks.\(^16\) Dexamethasone and pentoxifylline have an in vitro synergistic effect on cytokine production via human leukocytes.\(^19\) Pentoxifylline may have use as a steroid-sparing agent in dogs with CAD, but further studies are warranted to confirm its efficacy.\(^15,16\)

In addition to these indications, anecdotal evidence suggests pentoxifylline may be useful for treatment of vesicular cutaneous lupus erythematosus, erythema multiforme, acral lick dermatitis, and metatarsal fistulae in German shepherd dogs.\(^8\) Recent evidence evaluating the use of pentoxifylline in the treatment of dermal arteritis of the nasal philtrum and symmetric lupoid onychodystrophy suggests this drug may be an effective sole or adjunctive treatment in the management of these diseases.\(^20,21\) Controlled clinical studies regarding the efficacy of pentoxifylline are lacking. Because of its relatively affordable cost and minimal adverse effects, pentoxifylline may be a useful adjunct therapeutic for dermatologic conditions in which improved microcirculation and reduced inflammation are desired.\(^8\)

Although pentoxifylline is not considered a mainstay for management of CAD, limited research suggests it may have value as adjunctive therapy.\(^16,17\)
We Help the Biggest Hearts

Detect Heart Disease in Minutes

The only in-clinic NT-proBNP biomarker test for the quantitative and precise detection of heart disease in dogs and cats is available from Bionote’s Vcheck line of affordable diagnostic tests. For use in routine care, pre-operatively or in response to patient symptoms, Vcheck’s canine and feline NT-proBNP tests allow for identification of the cardiac pro-hormone biomarker within minutes. Without the need for an outside reference lab, the in-clinic NT-proBNP tests allow veterinarians to detect indicators for heart disease quickly while reducing the potential for sample degradation.
Many dogs are susceptible to developing dirty or infected ears. When they get an ear infection, this can complicate treatment. By recommending T8 Keto® Flush as treatment support, you can help keep your patients’ ears healthy.

**Common ear issues:**
- Presence of dirt and debris
- Too much moisture
- Unpleasant odors
- Yeast or bacterial infections
- Waxy, crusty or gooey buildup

T8 Keto offers Tris-EDTA and ketoconazole in a patented alkaline, water-based formulation combined with mild surfactants for gentle cleansing and flushing of patients’ ears. When infections strike, this bacteria-potentiating product raises the pH of the ear, priming it for other topical treatments.

**Tris-EDTA** to damage harmful bacteria  
**Ketoconazole** for proven activity against fungus

**Bacteria Potentiating Tris-EDTA**
Tris-EDTA damages and destabilizes bacterial cell walls, especially gram-negatives. This, in turn, increases susceptibility of bacteria to antimicrobial therapies, particularly fluoroquinolones, aminoglycosides and silver sulfadiazine.1,4

**Kills Microorganisms Fast**
T8 Keto provides 60-second rapid kill of common ear pathogens such as *Malassezia pachydermatis* and *Pseudomonas aeruginosa* in vitro.1,7 It also has demonstrated in vitro activity against *Staphylococcus* spp, *Staphylococcus pseudintermedius*, *Proteus* and *B-hemolytic streptococcus*.2

**Non Irritating, pH- Appropriate Base**
T8 Keto has an alkaline (pH 8.5) base. This helps maximize Tris-EDTA’s activity. And because fluoroquinolones and aminoglycosides work better in an alkaline environment, it helps set your treatment protocol up for success.3

**Ceruminolytic Activity**
Common pathogens actively work against your treatment protocol by actively creating debris, wax and other discharge that act as a barrier. The cleaning action of T8 Keto flush breaks apart and removes:
- Excessive wax and ceruminous discharge
- Inflammatory debris
- Biofilms and pus

This allows topical medications to reach deep into the ear canal, including the horizontal canal where most of the infection typically resides.

T8 Keto promotes ear health and the normalization of the ear canal, including epithelial migration, which is key to restoring the cell layer that helps prevent the entry of pathogens and leakage of fluids.

**Pseudomonas** triggers a purulent, supportive discharge and is a potent biofilm producer.

**Malassezia** leads to excessive ceruminous production and wax buildup.

In addition, benzyl alcohol provides a number of benefits. It helps prevent product contamination after repeated use in infected ears. It also provides antiseptic activity against Gram-positive cocci and Gram-negative rods.2

This formula does not sting or burn, making it potentially more pleasant for the patient, aiding in compliance.

**To learn more about adding T8 Keto to compliment your treatment regimen, contact your Elanco Sales Representative or Customer Service at (800) 633-3796.**

**CAUTION:** For topical use on dogs, cats and horses. Avoid contact with eyes. If eye contact occurs or skin irritation develops, rinse thoroughly with water, discontinue use and contact your veterinarian. Available through licensed veterinarians only.

---

MORE THAN JUST AN EAR CLEANER

Gently cleans while penetrating wax and buildup

Contains Ketoconazole and Tris-EDTA

Kills common pathogens within one minute in vitro¹

Call Customer Service at 1-800-633-3796 or contact your sales representative.


CAUTION: Federal law restricts this drug to use by or on the order of a licensed veterinarian. For topical use on dogs, cats and horses. Avoid contact with eyes. If eye contact occurs or skin irritation develops, rinse thoroughly with water, discontinue use and contact your veterinarian.

SUSPECTED FOOD ALLERGY IN DOGS

Elizabeth R. Drake, DVM, DACVD
University of Tennessee

SUSPECTED FOOD ALLERGY
(CUTANEOUS ADVERSE REACTION TO FOOD)

Is the patient pruritic?

NO

Recurrent skin or ear infections?

NO

DIAGNOSIS
Not allergic

DIFFERENTIAL
Sarcoptic mange

- Selamectin (FDA approved)
- Moxidectin, imidacloprid (FDA approved)
- Lime sulfur dip (FDA approved)
- Isoxazolines (extra-label)

DIFFERENTIAL
Flea allergy dermatitis
- Lesion distribution caudodorsal

- Topical parasite preventive
- Antipruritic treatment
- Treat secondary pyoderma

DIFFERENTIAL
Atopic dermatitis
- Seasonal pruritus or nonseasonal pruritus with seasonal flare

- Diagnosis of exclusion

DIFFERENTIAL
Food allergy
- Nonseasonal pruritus
- Recurrent secondary skin infections (eg, otitis externa/pyoderma)

- Treat and resolve secondary infection

YES

GI signs?
- Regurgitation/vomiting/nausea
- Diarrhea
- ≥3 bowel movements per day

NO

DIFFERENTIAL
Sarcoptic mange

YES

TREATMENT
Diagnosis of exclusion

- Regurgitation/vomiting/nausea
- Diarrhea
- ≥3 bowel movements per day

- Treat and resolve secondary infection
INVESTIGATION
Choose which elimination diet trial (e.g., hydrolyzed, novel protein, home-cooked) will be given
- Diet should be readily available and easy to obtain (to minimize trial interruptions)
- Diet should be palatable
- Diagnosis can be made with any of these diet types, providing all potential variables (e.g., no flavored medications, prevent ingestion of other animals’ feces) are addressed
- Subsequent diet trial with a different type of diet may be needed if the first trial fails but food allergy remains a top differential diagnosis
- Diet should also be based on life stage (e.g., growth formula for young dogs)
- Treat options
  - Vegetables (choose only one)

TREATMENT
Topical heartworm/intestinal helminth/flea/tick preventive

Pruritus/clinical signs improved ≥50% after 4 weeks?

NO

Continue diet trial

Follow up after 4 weeks

Pruritus/clinical signs improved ≥50%?

NO

Continue diet trial

YES

Diet challenge with prior diet

Patient pruritic?

NO

YES

DIAGNOSIS
Cutaneous adverse food reaction
- Consider which individual ingredient to challenge

DIAGNOSIS
After 12 weeks, not food allergy/cutaneous adverse food reaction OR Diet trial is not valid
- Identify reason for lack of improvement
HEARTGARD® Plus Chewables


References

HEARTGARD® Plus (ivermectin/pyrantel) should be administered orally at monthly intervals during the period of the year when mosquitoes (vectors), potentially carrying infective heartworm larvae, are active. The initial dose must be given within a month (30 days) after the dog’s first exposure to mosquitoes. The final dose must be given within a month (30 days) after the dog’s last exposure to mosquitoes. When replacing another heartworm preventive product in a heartworm disease preventive program, the first dose of HEARTGARD Plus must be given within a month (30 days) of the last dose of the former medication.

If the interval between doses exceeds a month (30 days), the efficacy of ivermectin can be reduced. Therefore, for optimal performance, the chewable must be given once a month (30 days) or about the same day of the month. If treatment is delayed, whether by a few days or many, immediate treatment with HEARTGARD Plus and resumption of the recommended dosing regimen will minimize the opportunity for the development of adult heartworms.

Monthly treatment with HEARTGARD Plus also provides effective treatment and control of ascariids (T. canis, T. ferimenti) and hookworms (A. caninum, U. stenocephala, A. braziliensis). Clients should be advised of measures to be taken to prevent reinfection with intestinal parasites.

EFFICACY: HEARTGARD Plus Chewables, orally using the recommended dose and regimen, are effective against the tissue larval stage of D. immitis for a month (30 days) after infection and, as a result, prevent the development of the adult stage. HEARTGARD Plus Chewables are also effective against canine ascariids (T. canis, T. ferimenti) and hookworms (A. caninum, U. stenocephala, A. braziliensis). Clients should be advised of measures to be taken to prevent reinfection with intestinal parasites.

ACCEPTABILITY: In acceptability and field trials, HEARTGARD Plus was shown to be an acceptable oral chewable for dogs that was consumed at first offering by the majority of dogs.

PRECAUTIONS: All dogs should be tested for existing heartworm infection before starting treatment with HEARTGARD Plus which is not effective against D. immitis. Infected dogs must be treated to remove adult heartworms before initiating a program with HEARTGARD Plus. While some microlarynx may be killed by the ivermectin in HEARTGARD Plus at the recommended dose level, HEARTGARD Plus is not effective for microlarynx clearance. A mild hypersensitivity type reaction, presumably due to dead or dying microlarynx and particular involving a transient diarrhea, has been observed in clinical trials with microlarynx alone after treatment of some dogs that have circulating microlarynx.

Keep this and all drugs out of the reach of children.

CAUTION: Federal (U.S.A.) law restricts this drug to use by or on the order of a licensed veterinarian.

INDICATIONS: For use in dogs to prevent canine heartworm disease by eliminating the tissue stage of heartworm larvae (Dirofilaria immitis) for a month (30 days) after infection and for the treatment and control of ascariids (Toxocara canis). Toxocara species) and hookworms (Ancylostoma caninum, Uncinaria stenocephala, Ancylostoma braziliense). The dose regimens of HEARTGARD Plus and HEARTGARD are the same with regard to ivermectin. Studies with ivermectin indicate that certain dogs of the Collie breed are more sensitive to the effects of ivermectin administered at elevated dose levels (more than 16 times the target use level) than dogs of other breeds. At elevated doses, sensitive dogs showed adverse reactions which included mydriasis, depression, ataxia, tremors, drooling, paresis, recumbency, excitability, stupor, coma and death. HEARTGARD demonstrated no signs of toxicity at 10 times the recommended dose (80 mcg/kg) in sensitive Collies. Based on results of these trials and bioequivalency studies, the safety of HEARTGARD products in dogs, including Collies, when used as recommended.

HEARTGARD Plus has shown a wide margin of safety at the recommended dose level in dogs, including pregnant or breeding bitches, stud dogs and puppies aged 6 or more weeks. In clinical trials, many commonly used flea collars, dips, shampoo, anthelminthic, antibiotics, vaccines and steroid preparations have been administered with HEARTGARD Plus in a heartworm disease prevention program.

In one trial, where some dogs had parvovirus, there was a marginal reduction in efficacy against intestinal nematodes, possibly due to a change in intestinal transit time.

HOW SUPPLIED: HEARTGARD Plus is available in three dosage strengths (see DOSAGE section) for dogs of different weights. Each strength comes in convenient cartons of 6 and 12 chewables. Marketed by Boehringer Ingelheim Animal Health USA Inc.

Distributed in the USA by Boehringer Ingelheim Animal Health USA Inc.

Made in U.S.A.

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US-PET-0196-2020

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TOP 5 ➤ DERMATOLOGY ➤ CONTINUED FROM PAGE 18
WHAT CLIENTS SEE.

Get clinic support at HEARTGARDClinic.com

IMPORTANT SAFETY INFORMATION: HEARTGARD® Plus (ivermectin/pyrantel) is well tolerated. All dogs should be tested for heartworm infection before starting a preventive program. Following the use of HEARTGARD Plus, digestive and neurological side effects have rarely been reported. For more information, please see full prescribing information or visit www.HEARTGARDClinic.com.

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YOU SEE THIS
INVISIBLE
THREAT.
YOUR CLIENTS DON'T.

HEARTGARD® Plus (ivermectin/pyrantel) has tools available to help you educate your clients about the real risks of heartworm disease. With HEARTGARD Plus, you're recommending:

- Safe and trusted heartworm disease prevention that's still #1 after 33 years¹
- The #1 dog-preferred, real-beef chew that makes compliance enjoyable for pets and pet owners²
- Highly effective control of five species of common intestinal parasites³,⁴
- Prevention backed by the HEARTGARD Plus Satisfaction Guarantee

Get clinic support at HEARTGARDClinic.com

IMPORTANT SAFETY INFORMATION: HEARTGARD® Plus (ivermectin/pyrantel) is well tolerated. All dogs should be tested for heartworm infection before starting a preventative program. Following the use of HEARTGARD Plus, digestive and neurological side effects have rarely been reported. For more information, please see full prescribing information or visit www.HEARTGARDClinic.com.

Euthanasia is a medical procedure to end life, typically via IV administration of a pentobarbital anesthetic overdose or with select organ injection in anesthetized patients. Euthanasia is chosen for a variety of reasons when continued life is deemed unacceptable, including to end suffering in patients with physical and/or emotional problems that lead to a significant decrease in quality of life and well-being. Veterinary professionals must evaluate what is in the best interest of the patient. If euthanasia is not deemed necessary, an alternative approach to maintain quality of life is recommended.

Guidelines are available for euthanasia procedures in animals, including with IV and intraorgan administration of a pentobarbital anesthetic. It is imperative that any euthanasia technique deliver a pain- and stress-free death. Different euthanasia techniques can result in shorter or longer times to death depending on the absorption rate of pentobarbital in the body and, ultimately, the brain (Table, page 27). Multiple techniques are available, and it is important to quickly modify techniques if necessary. Choice of technique depends on the signalment and physical condition of the patient, requirement for pre-euthanasia sedation or anesthesia, availability of required supplies, clinician comfort and skill, and possible need for postmortem examination.

Successful euthanasia procedures involve use of the correct supplies, attention to patient comfort, and knowledge of administration methodology. A sedative or
anesthetic agent should be given prior to euthanasia to reduce the risk for pain and stress. Common pre-euthanasia sedatives include benzodiazepines (eg, midazolam), opioids (eg, butorphanol), $\alpha_2$ agonists (eg, dexmedetomidine), and phenothiazines (eg, acepromazine). Common pre-euthanasia anesthetics include dissociatives (eg, ketamine), hypnotics (eg, propofol), neurosteroids (eg, alfaxalone), and anesthetic gases (eg, isoflurane).

Clinicians are required to pronounce death by auscultating the heart and verifying apnea. Additional indicators include lack of corneal reflex and onset of rigor mortis.

**Injection Site/Needle Placement**
The most common euthanasia techniques in dogs and cats require the euthanasia solution be injected into the venous system; this can be done via administration of solution directly in the vein or in areas of the body (eg, intraorgan) where the venous system moves the drug to the brain to induce death. Decisions about ideal technique should be based on patient signalment. Injection techniques described in this article can be used in cats and dogs.

**Intravenous Injection**
For IV injection, the preferred injection sites are the cephalic veins of the thoracic limbs, the medial (cats) and lateral saphenous (dogs) veins of the pelvic limbs, and the dorsal pedal vein of the foot. It is common to inject near the distal end of the vein, moving proximally as needed. All veins are acceptable to use if patent and easy to locate without causing additional stress to the patient or pet owner. Needle size varies from 18- to 22-gauge.

**Intracardiac Injection**
In most dogs and cats, the heart is between the third to sixth intercostal space and approximately one-third the distance dorsally to the thorax from the sternum. When auscultating for the heart, the loudest region (also called the point of maximum intensity [PMI]) should be identified. The thoracic limb can also be used to help identify the injection site. Combining the location of the PMI with the position of the elbow and visualizing the intercostal spaces can help ensure accurate placement of the needle directly in the heart. Needle length should be long enough to reach any heart chamber (ventricles are preferred); a 1- to 3-inch needle is usually sufficient for most dog and cat breeds. The syringe should be large enough to hold both the pentobarbital solution and the blood obtained on aspiration during needle placement. Needle size is typically 18-gauge. This technique requires the patient be unconscious.

**Intrarenal Injection**
For intrarenal injection, either kidney may be used. If time of death appears prolonged, another injection may be administered in either kidney. Needle size is typically 18-gauge. This technique requires the patient be unconscious.
Intrahepatic Injection
For intrahepatic injection, the xyphoid process should be located; the liver is typically dorsal to the xyphoid process. If time of death appears prolonged, another injection may be administered. Needle size is typically 18-gauge. This technique requires the patient be unconscious.

Intraperitoneal Injection
Pure pentobarbital solution is commonly administered intraperitoneal to conscious patients, but care should be taken to prevent the solution from entering neighboring organs, as intraorgan injection is painful. Use of pre-euthanasia sedation or anesthesia can help prevent injection pain or discomfort. Intraperitoneal injection results in a longer time to death, as the solution must be absorbed across serosal linings to enter the blood stream. Abdominal fluid and fat may slow absorption further. Needle size varies from 18- to 22-gauge.

Alternative Methods
Oral administration of pentobarbital and use of nonpentobarbital drug choices (when safe body disposition is unavailable) are gaining popularity as alternative euthanasia methods. Oral pentobarbital (255 mg/kg) can be a viable option for some patients, including those that have tendencies toward aggression or that are highly aversive to needles. Pentobarbital appears to have an unpleasant taste and is best hidden in food or drug capsules. Nonpentobarbital drug choices include overdoses of other anesthetics (eg, propofol).

**TABLE**

**PENTOBARBITAL DOSE FOR DIFFERENT INJECTION TECHNIQUES**

<table>
<thead>
<tr>
<th>Route of Administration</th>
<th>Dose* (per 10-lb [4.5-kg] body weight)</th>
<th>Time to Death</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intravenous</td>
<td>85 mg/kg</td>
<td>&lt;1 minute</td>
</tr>
<tr>
<td></td>
<td>1 mL</td>
<td></td>
</tr>
<tr>
<td>Intracardiac</td>
<td>85 mg/kg</td>
<td>&lt;1 minute</td>
</tr>
<tr>
<td></td>
<td>1 mL</td>
<td></td>
</tr>
<tr>
<td>Intrarenal</td>
<td>255 mg/kg</td>
<td>&lt;1 minute</td>
</tr>
<tr>
<td></td>
<td>3 mL</td>
<td></td>
</tr>
<tr>
<td>Intrahepatic</td>
<td>170 mg/kg</td>
<td>&lt;5 minutes</td>
</tr>
<tr>
<td></td>
<td>2 mL</td>
<td></td>
</tr>
<tr>
<td>Intraperitoneal</td>
<td>255 mg/kg</td>
<td>&lt;15 minutes</td>
</tr>
<tr>
<td></td>
<td>3 mL</td>
<td>(highly variable)</td>
</tr>
</tbody>
</table>

*These doses are based on a 390 mg/mL pentobarbital concentration. A greater volume of solution may be needed if exact patient weight is unknown.

PMI = point of maximum intensity

Continues
**WHAT YOU WILL NEED**

- Pentobarbital solution
- Sedative or anesthetic drugs
- 18- to 27-gauge needle
- 1- to 35-mL syringe
- IV or butterfly, 20- to 24-gauge catheter
- Tourniquet
- Clippers (optional)
- Adhesive tape (optional)
- Male adapters (optional)
- Extension sets (optional)

**STEP-BY-STEP EUTHANASIA PROTOCOLS**

**INTRAVENOUS INJECTION**

**STEP 1**

Administer a sedative or anesthetic agent.

**STEP 2**

Place the sedated/anesthetized patient in lateral recumbency. Clip the hair from the area of the injection site, place a secure tourniquet, and massage the area to increase blood in the vein for better visibility and accessibility.

**STEP 3**

Using a needle and syringe, a butterfly catheter, or a secured indwelling IV catheter, directly administer the pentobarbital solution at a rate of 1 mL/second (conscious patient) or 0.1 mL/second (heavily sedated/anesthetized patient).

**STEP 4**

Following injection, flush the catheter with saline to remove the pentobarbital solution.

**STEP 5**

Check for signs of death; if not present, readminister the injection.

**AUTHOR INSIGHT**

A slower rate of administration in sedated patients can reduce active signs of death.
**INTRACARDIAC INJECTION**

**STEP 1**
Administer an anesthetic agent to induce unconsciousness.

**STEP 2**
Place the anesthetized patient in lateral recumbency to identify the injection site. If auscultating the heart, identify the PMI. Grasp the antebrachium and press the elbow up to the chest wall to simulate its position as if the patient were standing. Insert the needle at the point where the elbow meets the chest.

**STEP 3**
Keep the needle in a perpendicular position to the chest wall and insert it between the ribs. Maintain negative pressure on the syringe as the needle advances, until blood is freely aspirated, then inject the solution.

**STEP 4**
Remove the needle slowly after all solution has been administered.

**STEP 5**
Check for signs of death; if not present, readminister the injection.

**AUTHOR INSIGHT**
If the owner is present, consider use of a small extension set to shield blood from view. Curl the extension set in the palm of the hand and keep the syringe low and out of sight.2

PMI = point of maximum intensity
**INTRARENAL INJECTION**

**STEP 1**
Administer an anesthetic agent to induce unconsciousness.

**STEP 2**
Place the anesthetized patient in lateral recumbency and gently run hands along the abdomen to locate the kidneys; check that no muscle tensing or resistance to palpation is evident.

**STEP 3**
Using fingertips, cup the kidney and raise it so that it is parallel with the spine. Ensure the kidney remains immobile during the entire procedure.

**STEP 4**
Using a needle with a length that can reach the kidney (1-1.5–inch, depending on patient size), insert the needle tip into the renal cortical or medullary tissue, and slowly inject the solution. Palpate for swelling of the kidney. Continue injecting until the syringe is empty.

**STEP 5**
If swelling is not palpated during the injection, redirect the needle slightly in multiple directions to fill the kidney.

**STEP 6**
Check for signs of death; if not present, readminister the injection.

**AUTHOR INSIGHT**
When injecting the solution, the kidney should swell with the pressure of the solution against the renal capsule. Kidney swelling does not guarantee immediate death, but it does increase the possibility for a shorter time to death. Death may occur before completion of the injection.
INTRAHEPATIC INJECTION

STEP 1
Administer an anesthetic agent to induce unconsciousness.

STEP 2
Place the anesthetized patient in lateral recumbency and locate the xyphoid process.

STEP 3
Using a 1- to 3-inch needle, depending on patient size, insert the needle tip on either side of the xyphoid process at a 45-degree angle cranially.

STEP 4
Slowly inject the solution into the liver region. Redirect the needle as needed to infuse the solution in more of the hepatic tissue.

STEP 5
After administration, slowly remove the needle.

STEP 6
Check for signs of death; if not present, readminister the injection.

Continues ▶
**INTRAPERITONEAL INJECTION**

**STEP 1**
Administer a sedative or anesthetic agent.

**STEP 2**
Locate the injection site either slightly caudal and to the right of the umbilicus or midabdomen in the flank region.

**STEP 3**
Insert a 1- to 1.5-inch needle through the abdominal wall. Pull the syringe plunger to aspirate for negative pressure.

**STEP 4**
If no blood or fluid is aspirated, administer the solution.

**STEP 5**
Check for signs of death. If the patient remains breathing after 10 to 15 minutes, readminister the injection or change to an intraorgan injection with the patient in an unconscious state.

**AUTHOR INSIGHT**
When giving intraorgan injections, it is recommended to slowly administer a small amount of solution (up to 0.5 mL) in the area to assess depth of sleep (eg, no response to stimuli). If no immediate response is observed, the remainder of the solution can be administered to effect.

**References**

**Suggested Reading**
Help Pets with Adverse Food Reactions
with comprehensive nutrition management from
BLUE Natural Veterinary Diet.

BLUE Natural Veterinary Diet™ HF
Hydrolyzed for Food Intolerance
features highly digestible salmon hydrolysate (a novel protein with a mean molecular weight of 2,000 daltons).

BLUE Natural Veterinary Diet™ NP
Novel Protein – Alligator
features a single novel animal protein, alligator, which is not typically associated with adverse food reactions.

Provide an Ideal Dietary Approach for Dogs and Cats
with Adverse Food Reactions.

• BLUE HF and NP diets are pure formulations that undergo ELISA-TEK and PCR testing to ensure they show no evidence of contaminating proteins

• High levels of omega-3 fatty acids help reduce skin cell inflammation

• Rich in antioxidants and fermentable fibers

Learn more at bluebuffalo.com/dermatology
The diagnosis of food allergy unfortunately is not performed by a quick laboratory test. There is no simple blood or skin test that can accurately make the diagnosis. Attempts have been made via skin testing, IgG/IgE serum testing, and hair and saliva testing all to no avail. In fact, we keep coming back to the elimination diet and provocative challenge as the “gold standard” for accurately assessing food allergy in our patients. It has been shown that 90% of food allergy cases in either dogs or cats require a restrictive diet fed for 8 weeks; 80% of food allergic dogs may respond within 5 weeks and in cats, 6 weeks. But did you know that by also feeding a prescription hypoallergenic food to your atopic patients, you may be helping to reduce their atopic flareups?

First, a bit of collective information on food allergy and how it differs in dogs and cats. Food allergy incidence in dogs is unknown, possibly due to not being recognized by owners, use of inappropriate diets, lack of compliance, and/or inadequate length of a diet trial. It is reported to occur in 1-2% of the canine population and in 14-33% of dogs with skin disease. Some dogs (33%) have clinical signs at <1 year of age. There is no breed predilection, but German Shepherds, West Highland White Terriers, and Labrador and Golden Retrievers account for 40% of affected dogs. Food allergy in cats may occur in 3-6% of cats with skin disease and in up to 21% of cats with pruritus, with the age of onset from 6 months to 12 years of age. There is no breed predilection, but one study found a third of food allergic cats to be Siamese or Siamese crosses.

Dermatological clinical signs in dogs with food allergy may include pruritus of the face, feet, axilla, and perineum; recurrent pyoderma; and otitis externa (25% unilateral). Non-cutaneous signs such as gastrointestinal issues to include vomiting, abdominal discomfort, frequent stools, and flatulence, as well as seizures, erythema multiforme, lupoid onychodystrophy, vasculitis, and pemphigus may also be attributed to food allergy. In addition to pruritus, cats may experience eosinophilic granuloma lesions, miliary dermatitis, seborrhea, pyoderma (bacterial or Malassezia), and/or otitis. Non-cutaneous signs may include flatulence, diarrhea, vomiting, salivation, conjunctivitis, and/or sneezing.

Since food allergy and atopy in both species can have the same clinical signs and often exist together, making a diagnosis may be difficult. A recent study found 10 of 53 dogs with nonseasonal atopic dermatitis managed with a hydrolyzed prescription food and a 2-week course of prednisolone flared when challenged with their former diet after being weaned off prednisolone. This resulted in a diagnosis of “food-induced atopic dermatitis.” Evidence in humans and now in dogs suggests that foods may trigger symptoms of atopy. Cross-reactivity has been shown between certain pollens and foods as well as unrelated allergens such as house dust mite and shellfish. Cross-reactivity also exists between certain food proteins (e.g., beef and venison, duck and other avian), but the clinical relevance to daily practice remains unknown. Due to cross-reactivity between pollens and foods, it may be prudent to advise a prescription hypoallergenic food for your atopic patients. A study of dogs allergic to house dust mites showed that they had fewer flareups when fed such a food (Hill’s z/d).

Choosing an elimination diet for food allergy testing requires knowledge of what the pet has eaten in the past, particularly if using a novel protein diet. Obtaining a thorough dietary history from the owner is essential and if former diets are unknown (such as in a rescued pet), a hydrolyzed protein diet may be the better option. Also, one needs to consider the age of the pet, as only a few prescription elimination foods are labelled for growth: for cats, Royal Canin PR dry, PD dry, PV dry; Rayne rabbit maintenance; and Blue Buffalo NP; for dogs, Royal Canin HP dry and PD dry, Rayne rabbit maintenance, and Blue Buffalo NP. Over-the-counter (OTC) “limited ingredient” diets are not suitable for use as elimination diets because up to 83% may contain ingredients not listed on the label. Raw diets are also not suitable, as one study showed 78% of canine diets and 56% of feline diets contained other meat species. For owners wanting to feed a vegetarian diet, Royal Canin Vegetarian was helpful in eliminating pruritus in 3 food allergic dogs that previously reacted to animal protein-containing diets. Insect-based (mealworm) diets fed for 12 weeks in 7 dogs not only helped with pruritus, but also reduced transepidermal water loss, demonstrating improved skin barrier function.
SO, WHAT CAN YOU DO?

• Consider a prescription elimination food in atopic patients to reduce flare-ups and achieve better control of clinical signs overall, but don't forget that food allergy can play a role in other systemic conditions.

• Choose a prescription elimination food, whether novel or hydrolyzed protein, or a supervised home-cooked diet and feed it for 8 weeks for food allergy diagnosis. When challenged with the offending protein or former diet, cats and dogs will flare immediately or within 7 or 14 days, respectively.

• OTC “limited ingredient” diets and raw diets are not suitable for food allergy testing.

• In young, growing patients, be sure the prescription food is labeled for growth.

• It is not worthwhile to advise an owner to avoid a certain protein when feeding OTC foods or treats, as up to 83% may contain ingredients not listed on the label.

There is now a plethora of commercial novel prescription elimination foods to choose from. Most manufacturers, including Blue Buffalo, Royal Canin, and Rayne, perform PCR or ELISA-TEK testing during manufacturing and of the final product to detect contaminant proteins in their diets. Benefits of a novel protein diet include convenience, appropriate for feeding long-term, owners being able to obtain meats such as venison or rabbit to use as “treats” or supplement the commercially available product, multiple products available with the same novel protein if palatability of one product is an issue, and some owner’s opinion that a novel protein diet is more “natural” than a hydrolyzed diet. Disadvantages may include availability and sustainability of the novel protein, many OTC diets now containing novel proteins so the pet has already been exposed to what was formerly “novel” for that pet, and undeclared proteins being found in one study of novel prescription foods.

Hydrolyzed protein diets, in which the long-chain proteins are cleaved to reduce allergenicity, are either soy (Purina HA, Royal Canin HP), salmon (Blue Buffalo HF), chicken (Hill’s z/d), or poultry-feather (Royal Canin Ultamino)-based. However, up to 50% of chicken- or soy-allergic patients may still react to hydrolyzed protein diets containing either of those 2 proteins.19 The benefits of a hydrolyzed protein diet include reduced allergenicity due to small molecular size (most are < 8kDa and <10kDa is preferred), convenience, and an ideal option when the dietary history is unknown. For Ultamino, 99% of peptides are < 6kDa; for z/d, average peptide size is < 1kDa, with 7% > 5kDa; for HF, 97.3% < 2kDa; and for HA, 8KDa. Disadvantages of hydrolyzed foods may include a reported incidence of diarrhea in 10% of patients on hydrolyzed diets and a bitter taste of the diet due to the pH of the hydrolysis process. Studies show that novel protein diets have the same efficacy as hydrolyzed diets, so the choice between the two remains one of veterinarian and owner preference. Home-cooked elimination diets using a novel protein are also suitable if done under veterinary supervision, as one study showed that when owners composed the diets, protein, minerals, and omega-3 levels were deficient and the calcium: phosphorus ratio was incorrect.20

References:
11. Faverot C, et al. The usefulness of short course prednisolone during the initial phase of an elimination diet trial in dogs with food induced atopic dermatitis. Vet Derm 2019;30(6), 496 e149.
12. Faverot C, et al. The usefulness of short course prednisolone during the initial phase of an elimination diet trial in dogs with food induced atopic dermatitis. Vet Derm 2019;30(6), 496 e149.
Leptospirosis is the most common infectious zoonotic disease worldwide and is considered to be a re-emerging disease and significant threat to canine health in all regions of the United States.\(^1\) Although veterinarians are commonly educated on the acute presentations of canine leptospirosis (eg, inappetence, vomiting, fever, lethargy), many may not be aware of the chronic carrier state that can produce idiopathic polyuria/polydipsia or result in no clinical signs at all.\(^2\) These chronic carriers pose a risk to humans in their household, veterinary teams, and other dogs in the community.\(^2\)

Prevention of disease is best achieved through an understanding of how a patient becomes infected and the pathophysiology of the organism. Direct transmission of *Leptospira* spp occurs when dogs come in contact with infected urine or ingest infected tissue. Once infection ensues, the spirochetes travel the bloodstream for several days, creating leptospiremia; after this phase, they can infect and set up residence in other organs, including the kidneys.\(^3\) This can create a carrier state. Shedding of leptospires in the urine (ie, leptospiruria) can persist for ≤3 months if there is inappropriate or absence of appropriate treatment.\(^4\)

The significance of the chronic carrier state in the canine population could easily be underestimated, since these dogs may show no clinical signs of disease. In one study, PCR testing demonstrated that 8% of dog from a group of 500 seen at a veterinary teaching hospital excreted leptospires in the urine.\(^5\) Only 10% of the shedding dogs had clinical signs of leptospirosis.

These chronic carriers pose a substantial hidden risk for transmission within homes, dog parks, kennels, and daycares. In our role as public health officers, it is imperative to choose a vaccine that prevents not only mortality but also leptospiremia and subsequent leptospiruria and urinary shedding. At the 2016 International Society for Companion Animal Infectious Diseases meeting, researchers presented a set of challenge studies that were conducted using 2 groups of puppies: those appropriately vaccinated as compared with a placebo group and then challenged. Urine samples were evaluated over 35 days and blood samples over 10 days. Results indicated no evidence of leptospiremia or leptospiruria in any of the vaccinated puppies, firmly supporting the claim of prevention of urinary shedding.\(^6\) Choosing this vaccination strategy provides the best chance for protection for patients, pet parents, and veterinary team members.

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Designed to bridge the gap between research pages and daily practice protocol, the following pearls offer tips and techniques to grow the general practitioner’s clinical excellence.

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Effective Treatment of Snake Mites

Sara J. Sokolik, DVM
Dan H. Johnson, DVM, DABVP (ECM)
Avian and Exotic Animal Care
Raleigh, North Carolina

In the literature

FROM THE PAGE …

Ophionyssus natricis is a common mite that affects captive snakes. Mite infestations can lead to irregularities in the scales, dyscecdysis, anemia, and clinical signs such as lethargy and decreased appetite. O natricis may also be a vector for the arenavirus responsible for boid encephalitis. Ophionyssus natricis can also be a vector for the arenavirus responsible for boid encephalitis.

Afoxolaner is a commonly used oral treatment for fleas and ticks in dogs. This study evaluated the effectiveness of afoxolaner in the treatment of 2 Burmese pythons with O natricis mite infestation. Both snakes were treated with a single dose of afoxolaner (2 mg/kg body weight PO) through an orogastric tube. There was no evidence of live O natricis in either snake within 3 days, indicating rapid onset of action. Dead mites were found in the snake enclosures for up to 30 days. No adverse effects were observed.

IMOXI™ Topical Solution for Dogs and for Cats (imidaclopird + moxidectin)
BRIEF SUMMARY: Before using IMOXI™ Topical Solution for Dogs (imidacloprid + moxidectin) or IMOXI™ Topical Solution for Cats (imidacloprid + moxidectin), please consult the product insert, a summary of which follows:
CAUTION: Federal (U.S.A.) Law restricts this drug to use by or on the order of a licensed veterinarian.

IMOXI™ Topical Solution for Dogs:
• DO NOT ADMINISTER THIS PRODUCT ORALLY.
• For the first 30 minutes after application ensure that dogs cannot lick the product from application sites on themselves or other treated animals.
• Children should not come in contact with application sites for two (2) hours after application.
• Do not administer this product orally. (See WARNINGS)

INDICATIONS:
IMOXI™ Topical Solution for Dogs is indicated for the prevention of heartworm disease caused by Dirofilaria immitis and the treatment of Dirofilaria immitis circulating microfilariae in heartworm-positive dogs. IMOXI™ Topical Solution for Dogs kills adult Rees and is indicated for the treatment of flea infestations (Ctenocephalides felis). IMOXI™ Topical Solution for Dogs is indicated for the treatment and control of sarcoptic mange caused by Sarcopes scabiei var. canis. IMOXI™ Topical Solution for Dogs is also indicated for the treatment and control of the following intestinal parasites species: Hookworms (Ancylostoma caninum) (Circinastris ctenocephalidea), Roundworms (Toxocara canis) (Toxocara canis) and Whiptails (Tachyura suis).

IMOXI™ Topical Solution for Cats is indicated for the prevention of heartworm disease caused by Dirofilaria immitis. IMOXI™ Topical Solution for Cats kills adult Rees (Ctenocephalides felis) and is indicated for the treatment of flea infestations. IMOXI™ Topical Solution for Cats is also indicated for the treatment and control of ear mite (Ophionyssus cynotis) infestations and the intestinal parasites species Hookworm (Ancylostoma batioides) and Roundworm (Toxocara cati).

CONTRAINDICATIONS:
Do not administer this product orally. (See WARNINGS)
Do not use the Dog product (containing 2.5% moxidectin) on cats.

WARNINGS:
IMOXI™ Topical Solution for Dogs: For the first 30 minutes after application:
Ensure that dogs cannot lick the product from application sites on themselves or other treated dogs, and separate treated dogs from one another and from other pets to reduce the risk of accidental ingestion.

IMOXI™ Topical Solution for Cats: For the first 30 minutes after application:
Ensure that dogs cannot lick the product from application sites on themselves or other treated dogs, and separate treated dogs from one another and from other pets to reduce the risk of accidental ingestion.

ADVERSE REACTIONS:
For the first 30 minutes after application:
Do not use the Dog product (containing 2.5% moxidectin) on cats.

Do not use this product on dogs that are less than 9 weeks of age or less than 2 lbs. body weight.

IMOXI™ Topical Solution for Dogs: Do not use on sick, debilitated, or underweight cats.
IMOXI™ Topical Solution for Cats: Do not use on sick, debilitated, or underweight cats.

IMOXI™ Topical Solution for Dogs is indicated for the prevention of heartworm disease caused by Dirofilaria immitis and the treatment of Dirofilaria immitis circulating microfilariae in heartworm-positive dogs. IMOXI™ Topical Solution for Dogs kills adult Rees and is indicated for the treatment of flea infestations (Ctenocephalides felis). IMOXI™ Topical Solution for Dogs is indicated for the treatment and control of sarcoptic mange caused by Sarcopes scabiei var. canis. IMOXI™ Topical Solution for Dogs is also indicated for the treatment and control of the following intestinal parasites species: Hookworms (Ancylostoma caninum) (Circinastris ctenocephalidea), Roundworms (Toxocara canis) (Toxocara canis) and Whiptails (Tachyura suis).
THE PROTECTION PETS NEED AGAINST
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CAUTION: Federal (U.S.A) law restricts this drug to use by or on the order of a licensed veterinarian.

Dogs: WARNING: DO NOT ADMINISTER THIS PRODUCT ORALLY. For the first 30 minutes after application, ensure that dogs cannot lick the product from application sites on themselves or other treated animals. Children should not come in contact with the application sites for two (2) hours after application. (See Contraindications, Warnings, Human Warnings and Adverse Reactions for more information.) Cats: Do not use on sick, debilitated, or underweight cats. Avoid oral ingestion. For additional safety information see brief on page 38 or visit www.vetoquinnolusa.com/imoxi-info.
Dogs that withdrew from the masked field study could enter an unmasked study where all dogs in the APOQUEL group remained within the normal range. Mean lymphocyte counts were transiently increased at Day 14 (one dog), and increased cholesterol and lipase compared to the placebo group but group means did not differ from the normal range. In the 283 dogs that received APOQUEL, the following additional clinical signs were reported after beginning APOQUEL: percentage of dogs with at least one report of the clinical sign as a non-pre-existing finding: pyoderma (12.0%), non-specified dermal lumps (12.5%), citrull (9.9%), vomiting (9.3%), diarrhea (8.0%), histiocytoma (9.9%), cysts (3.5%), anorexia (3.2%), lethargy (2.8%), yeast skin infections (2.5%), pododermatitis (2.5%), Ipioma (2.1%), polydipsia (1.4%), lymphadenopathy (1.1%), nausia (1.1%), increased appetite (1.1%), aggression (1.1%), and weight loss (0.7). Warnings:

APOQUEL is not for use in dogs less than 12 months of age (see Animal Safety). Adverse Reactions:

APOQUEL modulates the immune system. APOQUEL may increase susceptibility to infection, including demodicosis, and exacerbation of neoplastic conditions (see Precautions, Adverse Reactions, Post-Approval Experience and Animal Safety).

New neoplastic conditions (benign and malignant) were observed in dogs treated with APOQUEL during clinical studies and have been reported in the post-approval period (see Adverse Reactions and Post-Approval Experience).

Consider the risks and benefits of treatment prior to initiating APOQUEL in dogs with a history of recurrent serious infections or recurrent demodicosis or neoplasia (see Adverse Reactions, Post-Approval Experience, and Animal Safety).

Keep APOQUEL in a secure location out of reach of dogs, cats, and other animals to prevent accidental ingestion or overdose.

Human Warnings:

This product is not for human use. Keep this and all drugs out of reach of children. For use in dogs only. Wash hands immediately after handling the tablets. In case of accidental eye contact, flush immediately with water or saline for at least 15 minutes and then seek medical attention. In case of accidental ingestion, seek medical attention immediately. Wash hands immediately after handling the tablets.

In case of accidental eye contact, flush immediately with water or saline for at least 15 minutes and then seek medical attention. In case of accidental ingestion, seek medical attention immediately. Do not use in breeding dogs, or pregnant or lactating bitches.

Adverse Reactions:

Control of Atopic Dermatitis

In a masked field study to assess the effectiveness and safety of oclacitinib for the control of atopic dermatitis in dogs, 152 dogs treated with APOQUEL and 147 dogs treated with placebo (vehicle control) were evaluated for safety. The majority of dogs in the placebo group withdrew from the 112-day study by Day 16. Adverse reactions reported (and percent of dogs affected) during Days 0-16 included diarrhea (4.6% APOQUEL, 3.4% placebo), vomiting (5.9% APOQUEL, 4.1% placebo), anorexia (0.5% APOQUEL, 0% placebo), new cutaneous or subcutaneous lumps (2.6% APOQUEL, 2.7% placebo), and lethargy (0.2% APOQUEL, 0.4% placebo). In most cases, diarrhea, vomiting, anorexia, and lethargy spontaneously resolved with continued dosing. Dogs on APOQUEL had decreased leukocytes (neutrophil, eosinophil, and monocyte counts) and serum globulin, and increased cholesterol and lipase compared to the placebo group but group means remained within the normal range. Mean lymphocyte counts were transiently increased at Day 14 in the APOQUEL group. Dogs that withdrew from the masked field study could enter an unmasked study where all dogs received APOQUEL. Between the masked and unmasked study, 283 dogs received at least one dose of APOQUEL. Of these 283 dogs, two were withdrawn from study due to suspected treatment-related adverse reactions: one dog that had an intense flare-up of dermatitis and severe secondary pyoderma after 19 days of APOQUEL administration, and one dog that developed generalized demodicosis after 28 days of APOQUEL administration. Two other dogs on APOQUEL were withdrawn from study due to suspected or confirmed malignant neoplasia and subsequently euthanized, including one dog that developed signs associated with a heart base mass after 21 days of APOQUEL administration, and one dog that developed a Grade III mast cell tumor after 60 days of APOQUEL administration.

One of the 147 dogs in the placebo group developed a Grade I mast cell tumor and was withdrawn from the masked study. Additional dogs receiving APOQUEL were hospitalized for diagnosis and treatment of pneumonia (one dog), transient bloody vomiting and stool (one dog), and cystitis with urolithiasis (one dog).

In the 283 dogs that received APOQUEL, the following additional clinical signs were reported after beginning APOQUEL: percentage of dogs with at least one report of the clinical sign as a non-pre-existing finding: pyoderma (12.0%), non-specified dermal lumps (12.5%), citrull (9.9%), vomiting (9.3%), diarrhea (8.0%), histiocytoma (9.9%), cysts (3.5%), anorexia (3.2%), lethargy (2.8%), yeast skin infections (2.5%), pododermatitis (2.5%), Ipioma (2.1%), polydipsia (1.4%), lymphadenopathy (1.1%), nausia (1.1%), increased appetite (1.1%), aggression (1.1%), and weight loss (0.7).
The road to itch relief felt like a long one, until APOQUEL

Trusted for over 7 years, APOQUEL® (oclacitinib tablet) has been prescribed to more than 9 million dogs in need of fast and effective allergic itch relief.1-4

INDICATIONS
Control of pruritus associated with allergic dermatitis and control of atopic dermatitis in dogs at least 12 months of age.

IMPORTANT SAFETY INFORMATION
Do not use APOQUEL in dogs less than 12 months of age or those with serious infections. APOQUEL may increase the chances of developing serious infections, and may cause existing parasitic skin infestations or pre-existing cancers to get worse. Consider the risks and benefits of treatment in dogs with a history of recurrence of these conditions. New neoplastic conditions (benign and malignant) were observed in clinical studies and post-approval. APOQUEL has not been tested in dogs receiving some medications including some commonly used to treat skin conditions such as corticosteroids and cyclosporines. Do not use in breeding, pregnant, or lactating dogs. Most common side effects are vomiting and diarrhea. APOQUEL has been used safely with many common medications including parasiticides, antibiotics and vaccines.

See accompanying Brief Summary of Prescribing Information


2 best-in-class options for allergic itch relief:

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**Osurnia**

(florfenicol, terbinafine, betamethasone acetate)

**DISC gel**

For Otic Use in Dogs Only

Do not use in cats

**CAUTION:** Federal (USA) law restricts this drug to use by or on the order of a licensed veterinarian.

**BRIEF SUMMARY** (for full prescribing information, see package insert):

**DESCRIPTION:** OSURNIA contains 10 mg florfenicol, 10 mg terbinafine and 1 mg betamethasone acetate per mL, and the inactive ingredients propylene carbonate, glycerol, formaldehyde, phenylalcohol, saline acid and BHT in an off-white to slightly yellow transparent gel.

**INDICATION:** OSURNIA is indicated for the treatment of otitis externa in dogs associated with susceptible strains of bacteria (*Staphylococcus pseudintermedius* and *Streptococcus* *pseudotuberculosis*) and yeast (*Malassezia* *pachydermatis*).

**DOSE AND ADMINISTRATION:** OSURNIA should be administered in the clinic. Clean and dry the external ear canal before administering the initial dose of the product. Administer one dose (1 tube) per affected ear(s) and repeat administration in 7 days. Do not clean the ear canal for 45 days after the initial administration to allow contact of the gel with the ear canal. Cleaning the ear may affect product effectiveness (see Effectiveness in the product insert). If alternative oral therapies are required it is recommended to clean the ear(s) prior to application. Open tube by twisting the soft tip. Insert the flexible tip into the affected ear canal(s) and squeeze entire tube contents into the external ear canal(s). After administration, gently and slowly lower the base of the ear to allow the gel to penetrate to the lower part of the ear canal.

**CONTRAINdications:** Do not use in dogs with known tympanic perforation (see Precautions in the product insert). Do not use in dogs with a hypersensitivity to florfenicol, terbinafine, or corticosteroids.

**WARNINGS:**

**Human Safety Warning:**

OSURNIA may cause eye irritation and irritation Not for use in humans. Keep this and all medications out of reach of children. Consult a physician in case of accidental ingestion by humans. In case of accidental skin contact, wash area thoroughly with water. Avoid contact to the eyes. In case of accidental eye contact, flush thoroughly with water for at least 15 minutes. If symptoms develop, seek medical advice.

**PRECAUTIONS:** Wear eye protection when administering OSURNIA and restrain the dog to minimize post-application head shaking. Reducing the potential for splatter of product will help prevent accidental eye exposure in people and dogs and help to prevent outer ear injury. Do not administer orally. The use of OSURNIA in dogs with perforated tympanic membranes has not been evaluated. The integrity of the tympanic membrane should be confirmed before administering this product. Reevaluate the dog if hearing loss or signs of vestibular dysfunction are observed during treatment. Use of topical otic corticosteroids has been associated with adenocarcinoma/pseudosquamous and hyperammoniamonocytomas in dogs (see Animal Safety in the product insert). Use with caution in dogs with impaired hepatic function (see Animal Safety and Adverse Reactions in the product insert). The safe use of OSURNIA in dogs used for breeding purposes, for non-therapeutic purposes, for pregnant or lactating bitches, has not been evaluated.

**ADVERSE REACTIONS:** The following adverse reactions were reported during the course of a US field study for treatment of otitis externa in dogs treated with OSURNIA, in decreasing order: elevated liver enzymes, vomiting, weight loss (>10% body weight) and hearing loss. To report suspected adverse events, for technical assistance or to obtain a copy of the SIDS, contact Dechra Veterinary Products at (866) 363-2472. For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS or online at [http://www.fda.gov/AnimalVeterinary/SafetyHealth](http://www.fda.gov/AnimalVeterinary/SafetyHealth).

**POST-APPROVAL EXPERIENCE:** In humans, accidental exposure leading to corneal ulcers and other ocular injuries such as eye irritation, burning, stinging, and itchiness have been reported to occur when the dog shook its head after application of OSURNIA. In dogs, the adverse events reported for OSURNIA are presented below in decreasing order of reporting frequency: Otorhea, ear discharge, ocular irritation and pain, vomiting, head shaking, head tilt, ataxia, vocalization, contact anhidrosis, lacrimation, ocular and facial pain.

**INFORMATION FOR DOG OWNERS:** Owners should be aware that adverse reactions may occur following administration of OSURNIA and should observe dog for signs such as deafness, ear pain and irritation, vomiting, head shaking, head tilt, incoordination, eye pain and ocular discharge (see Animal Safety and Post-Approval Experience in the product insert). Owners should be advised to contact their veterinarian if any of the above signs are observed. Owners should also be informed that splatter may occur if the dog shakes its head following administration of OSURNIA which may lead to ocular exposure. As a result, eye injuries in humans and dogs have been reported including corneal ulcers.

**EFFECTIVENESS:** Effectiveness was evaluated in 235 dogs with otitis externa. The study was a double-masked field study with a placebo control (vehicle without the active ingredients). One hundred and fifty-nine dogs were treated with OSURNIA and seventy-six dogs were treated with the placebo control. All dogs were evaluated for safety. **TREATMENT:** (1 mL) was administered to the affected ear(s) and repeated 7 days later. Prior to the first administration, the ear(s) were cleaned with saline but not prior to the Day 7 administration. Six clinical signs associated with otitis externa were evaluated: pain, erythema, edema, swelling, odor and ulceration. Total clinical scores were assigned for a dog based on the severity of each clinical sign on Days 0, 1, 4, 7, 14, 30 and 45. Success was determined by clinical improvement at Day 45. The success rates of the two groups were significantly different (p=0.0094); 64.78% of dogs administered OSURNIA were successfully treated, compared to 43.2% of the dogs in the placebo control group.

**STORAGE CONDITIONS:** OSURNIA should be stored under refrigerated conditions between 36° - 46° F (2° - 8° C). To facilitate control during administration, OSURNIA may be brought to room temperature and stored for up to three months.

**MANUFACTURED FOR:**

Dechra Veterinary Products
7015 College Boulevard, Suite 525
Overland Park, KS 66211 USA

Product of Great Britain

Approved by FDA under NADA # 141-437

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R 03 2021

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**Reference**


**Suggested Reading**


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Because this is a single-dose treatment option, it allows for reduced stress due to less handling, lessened chance of toxicity, and elimination of risks associated with compliance failure of at-home treatments. In addition, measuring and administering an oral treatment is typically a more specific administration method as compared with topically applying drugs. Resistance has been reported with older acaricides but not with afoxolaner.

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**… TO YOUR PATIENTS**

Key pearls to put into practice:

1. **It is important to verify *O* *nativis* mite infestation with morphometric identification under a microscope.**

2. **Care should be taken when tube-feeding oral medication to snakes. Staff should be comfortable with the procedure, and pet owners should be educated about possible risks, which include mucosal damage, esophageal perforation, regurgitation, and aspiration. When medicating via tube, it is important to flush the tube with enough food or fluid so the intended dose is fully administered to the patient (ie, none of the oral dose remains in the tube).**

3. **Rechecks should be performed 1 month following treatment to ensure no mites remain.**
Two reasons to recheck.

1. Important Safety Information

Canine otitis externa treatment is only successful when you’re confident your treatment is working. That’s why the follow-up appointment is so important. Resolve the infection with 2-dose Osurnia, use the follow-up to monitor the response to treatment and trust the Dechra dermatology portfolio to help you manage the underlying problem. To order or schedule a lunch and learn, call your Dechra representative or call (866) 683-0660.

Osurnia®
(florfenicol-terbinafine-betamethasone acetate)

Osurnia should be administered by a veterinary professional. Do not use in dogs with known tympanic perforation or a hypersensitivity to florfenicol, terbinafine or corticosteroids. **Osurnia may cause eye injury and irritation. Wear eye protection when administering Osurnia and restrain the dog** to minimize post-application head shaking. **Do not use in cats.** Refer to the prescribing information for complete details or visit www.dechra-us.com.

For Veterinary Technical Support, Contact Dechra Veterinary Products at:
866-933-2472  |  www.dechra-us.com  |  support@dechra.com

Important Safety Information
As with all drugs, side effects may occur. In field studies and post-approval experience the most common side effects reported were vomiting, increased liver enzymes and loss of hearing. Other signs reported were ear discharge, ear irritation and pain, vomiting, head shaking, head tilt, ataxia, vocalization, corneal ulcer, keratoconjunctivitis sicca, nystagmus, tympanic rupture, and facial paralysis.

Osurnia® is a registered trademark of Dechra Limited. Dechra is a registered trademark of Dechra Pharmaceuticals PLC.

See page 42 for product information summary.
**Blastomyces dermatitidis** 

from a Needlestick Injury

Radford G. Davis, DVM, MPH, DACVPM  
Iowa State University

In the literature


FROM THE PAGE …

Many occupational hazards (including animal bites, scratches, crushing and kicking injuries, and needlestick and other sharps injuries) can affect clinicians and veterinary staff. Needlestick injuries (NSIs) appear to be underdocumented but are common in the clinic, with most clinicians reporting at least 1 NSI, if not more, in their career. Consequences of an NSI can include infection, local inflammation, localized necrosis, skin slough, nerve damage, allergic reaction, miscarriage, systemic effects, and/or even death. Zoonoses transmission via needlestick and sharps injuries has been associated with *Bartonella* spp, *Brucella abortus* RB51 vaccine, and *Blastomyces* spp, among others. *Blastomyces dermatitidis* has also been transmitted via dog bites.

In this case, a clinician suffered an NSI to the right index finger from a 21-gauge needle after aspirating fluid from a subcutaneous cystic mass in a dog with systemic blastomycosis. Swelling, tenderness, erythema, pain, and limited range of motion of the distal interphalangeal joint ensued. Purulent exudate was expressed from the finger during surgery, and biopsies were taken. Staining of tissues revealed broad-based budding between mother and daughter cells consistent with *B dermatitidis*, which was confirmed via isolation.

The usual method of infection in humans with *B dermatitidis* is via inhalation of the conidia, which transforms into the yeast phase and can spread hematogenously throughout the body. Humans may have no clinical signs, show nonspecific signs (eg, cough, fever, malaise, fatigue, weight loss), or develop more severe disease. Pneumonia is the most common manifestation of blastomycosis in humans, with skin lesions being next most common. Abscesses frequently form in the skin and subcutaneous tissues, but they can also form in the brain, bones, prostate, or other organs.

Dogs and, less commonly, cats can develop *B dermatitidis* infection. Young, male dogs of sporting breeds are most commonly affected by blastomycosis. Signs may include dyspnea, tachypnea, fever, lethargy, weight loss, skin abscesses, uveitis, and pulmonary nodules.
... TO YOUR PATIENTS

Key pearls to put into practice:

1. NSI can result in zoonotic transmission or injection of substances (e.g., vaccines, antimicrobials, chemotherapy, euthanasia solution).

2. Performing fine-needle aspiration or necropsy on a dog with Blastomyces spp infection can result in human infection if there is a needlestick or sharps injury.

3. Staff should be educated on safe sharps handling and possible adverse health outcomes.1,2 All NSIs should be recorded, and staff should be trained in human first aid and blood-borne pathogen awareness.

References


Brief Summary: Before using NexGard® (afoxolaner) Chewables, please consult the product insert, a summary of which follows.

CAUTION: Federal (USA) law restricts this drug to use by or on the order of a licensed veterinarian.

Description: NexGard is a soft chewable for oral administration to dogs and puppies according to their weight. Each chewable is formulated to provide a minimum afoxolaner dosage of 1.14 mg/lb (2.5 mg/kg).

Indications: NexGard kills adult fleas and is indicated for the treatment and prevention of flea infestations (Ctenocephalides felis), and the treatment and control of lice, scabies, Demodex, and Amblyomma americanum, and Rhipicephalus sanguineus infestations in dogs and puppies 8 weeks of age and older, weighing 4 pounds of body weight or greater, for one month. NexGard is indicated for the prevention of Borna virus infections as a direct result of killing Ixodes scapularis vector ticks.

Dosage and Administration: NexGard is given orally once a month, at the minimum dosage of 1.14 mg/lb (2.5 mg/kg). See full product insert for dosing table and details.

Warnings: Not for use in humans. Keep this and all drugs out of the reach of children. In case of accidental ingestion, contact a physician immediately. Keep NexGard in a secure location out of reach of dogs, cats, and other animals to prevent accidental ingestion or overdose.

Precautions: Afoxolener is a member of the isoxazoline class. This class has been associated with neurologic adverse reactions including tremors, ataxia, and seizures. Seizures have been reported in dogs receiving isoxazoline class drugs, even in dogs without a history of seizures. Use with caution in dogs with a history of seizures or neurologic disorders.

The safe use of NexGard in breeding, pregnant or lactating dogs has not been evaluated.

Adverse Reactions: In a well-controlled US field study, which included a total of 333 households and 415 treated dogs (415 administered afoxolaner; 200 administered active control), no serious adverse reactions were observed with NexGard. Over the 90-day study period, all observations of potential adverse reactions were recorded. The most frequent reactions reported at an incidence of > 1% within any of the three months of observations are presented in the following table.

Table 1. Dogs with Adverse Reactions

<table>
<thead>
<tr>
<th>Treatment Group</th>
<th>Afoxolaner Oral active control</th>
</tr>
</thead>
<tbody>
<tr>
<td>% (n=475)</td>
<td>% (n=200)</td>
</tr>
<tr>
<td>Vomiting (with and without blood)</td>
<td>17</td>
</tr>
<tr>
<td>Dry/Itchy Skin</td>
<td>13</td>
</tr>
<tr>
<td>Lethargy (with and without blood)</td>
<td>13</td>
</tr>
<tr>
<td>Anorexia</td>
<td>7</td>
</tr>
<tr>
<td>1 Number of dogs in the afoxolaner treatment group with the identified abnormality.</td>
<td></td>
</tr>
<tr>
<td>2 Number of dogs in the control group with the identified abnormality.</td>
<td></td>
</tr>
</tbody>
</table>

In the US field study, one dog with a history of seizures experienced a seizure on the same day after receiving the first dose and on the same day after receiving the second dose of NexGard. This dog experienced a third seizure one week after receiving the third dose. The dog remained enrolled and completed the study. Another dog with a history of seizures had a seizure 19 days after the third dose of NexGard. The dog remained enrolled and completed the study. A third dog with a history of seizures received NexGard and experienced no seizures throughout the study.

Post-Approval Experience (July 2018): Following adverse events are based on postapproval adverse drug experience reporting. Not all adverse events are reported to FDA/CVM. It is not always possible to reliably estimate the adverse event frequency or establish a causal relationship to product exposure using these data.

The following adverse events reported for dogs are listed in decreasing order of reporting frequency for NexGard: Vomiting, pruritus, lethargy, diarrhea (with and without blood), anorexia, seizures, hyperactivity/restlessness, panting, ataxia, dermatis (including rash, papules), allergic reactions (including hives, swelling), and tremors.

Effectiveness: See full product insert for details regarding Effectiveness.

Animal Safety: In a margin of safety study, NexGard was administered orally to 8 to 9-week-old Beagle puppies at 1, 3, and 5 times the maximum exposure dose for a total of six treatments. There were no clinically-relevant effects related to treatment on physical examination, body weight, food consumption, clinical pathology (hematology, clinical chemistries, or coagulation tests), gross pathology, histopathology or organ weights. Vomiting occurred throughout the study, with a similar incidence in the treated and control groups, including one dog in the 5x group that vomited four hours after treatment.

In a well-controlled field study, no adverse reactions were observed from the concurrent use of NexGard with other medications.

Contact Information: For a copy of the Safety Data Sheet (SDS) or to report suspected adverse drug events, contact Boehringer Ingelheim Animal Health USA Inc. at 1-888-637-4251. For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS or www.fda.gov/reportanimalae. The information provided here is not comprehensive. The full FDA-approved product insert is available at www.nexgardfordogs.com. Consult your veterinarian for further information.

Product approved by FDA under NADA # 141-406

Marketed by: Frontline Vet Labs™, a Division of Boehringer Ingelheim Animal Health USA Inc. Duluth, GA 30096

NexGard® is a registered trademark and FRONTLINE VET LABS™ is a trademark of the Boehringer Ingelheim Group.

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Reference package insert: 1050-4893-09 Rev. 11/2019

Brief summary preparation date: 08/2020

US-PET-0735-2020
In Clinic.

Thank you for trusting NexGard® (afoxolaner)...

- **Kills fleas and ticks** all month long and prevents flea infestations.
- **FDA-approved** to prevent *Borrelia burgdorferi* infections by killing black-legged ticks.

NexGard® (afoxolaner) Chewables

**IMPORTANT SAFETY INFORMATION:** NexGard® is for use in dogs only. The most frequently reported adverse reactions include vomiting, pruritus, lethargy, diarrhea and lack of appetite. The safe use of NexGard in pregnant, breeding, or lactating dogs has not been evaluated. Use with caution in dogs with a history of seizures or neurologic disorders. For more information, see the full prescribing information or visit NexGardClinic.com.

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**Research Note:**

**Body Temperature Measurement in Guinea Pigs**

Body temperature is an important clinical indicator. In guinea pigs, the physical restraint required for taking a rectal temperature can cause stress and may induce hyperthermia. Less invasive methods for obtaining a temperature in this species have been examined; the present study assessed whether body temperatures taken in the axillary (AT) or inguinal (IT) areas were as accurate as rectal temperature (RT). Temperatures were measured in duplicate using a commercially available digital thermometer according to a standardized method over a short (<3 minute) period. AT and IT were consistently significantly lower than RT by 0.58°F (0.32°C) and 1.31°F (0.73°C), respectively. RT was not unduly stressful, and no patients were injured. Given these findings, the authors concluded that rectal temperature should remain the gold standard for temperature measurement in guinea pigs.

**Source**

Research Note: 
Mineral Content in Cat Foods

Studies suggest that high dietary phosphorus (P) and low calcium:phosphorus (Ca:P) ratios may contribute to the development of chronic kidney disease (CKD) in cats. Although feline dietary minimums exist for P, Ca, and magnesium (Mg), there are no available maximums. This study evaluated P, Ca, and Mg in 82 commercial, nonprescription cat foods and examined discrepancies between reported and analyzed quantities. Of the foods tested, 81 had an Association of American Feed Control Officials nutritional adequacy statement on the label. However, 33% contained phosphorus levels $\geq 3.6 \text{ g/1000 kcal ME}$, which is in the range of levels experimentally shown to cause renal dysfunction in healthy cats. Nine percent of the foods had P levels $\geq 4.8 \text{ g/1000 kcal ME}$, which has been shown to cause rapid renal decline in adult cats when most P was provided by inorganic P sources. Sixteen percent of the foods had low Ca:P ratios. These results suggest pet food regulatory reform should be considered.

Source
Gastric Dilation & GI Obstruction in Rabbits

David Eshar, DVM, DABVP (ECM), DECZM (SM & ZHM)
Kansas State University

In the literature

FROM THE PAGE …

GI stasis is one the most common health issues in pet rabbits and often occurs secondary to an underlying medical issue.1 With the exception of physiologic ileus (eg, from a low-fiber diet), common primary problems that occur with GI stasis include gastric dilation and GI obstruction, typically of either the pylorus or duodenum. In most cases, a small ingested hair pellet is the cause of the intestinal obstruction.2 Stomach outflow

▲ FIGURE Right lateral radiograph of a 1-year-old, intact male Holland lop rabbit presented with a history of reduced activity, anorexia, and no fecal output since the previous day. Blood glucose was 328 mg/dL (reference range, 110-160 mg/dL). The stomach appears distended and fluid-filled with a gas cap, and an abnormal gas pattern can be seen in the small intestines. The combination of history, clinical signs, physical examination, hyperglycemia, and radiographic findings is highly suggestive of intestinal obstruction.
Deploy Nutritional Strategies to Manage Patients With Feline LUTD

Q What does the research tell us about the problem of lower urinary tract disease (LUTD) in cats?

A LUTD is certainly a nagging problem in cats. One study found that the proportional morbidity rates of cats developing LUTD irrespective of cause was 8 in 100 cats. Here’s what we know:

It’s a weighty matter. One study showed that cats with feline idiopathic cystitis (FIC) were significantly more likely to be overweight compared to both healthy cats in the same household and a control population of clinically healthy cats.

Neutering is associated with the development of LUTD. Another study showed that castrated males had increased risk for each cause of LUTD except urinary tract infection (UTI) and incontinence, while spayed females had increased risk for urocystolithiasis, UTI and neoplasia.

Since so many pets in the U.S. are spayed or neutered, and the number of overweight or obese pets increases every year, LUTD in cats may be on the rise. However, we’re also more aware of how to diagnose these conditions and manage these patients. So whether prevalence is increasing or we are now more proactive in diagnosing LUTD is an open question.

Q How can diet play a role in reducing clinical signs of LUTD?

A Cats have a lower physiological thirst drive than dogs, so identifying other strategies to boost fluid intake is key. Increasing dietary moisture can increase urine volume and promote a more-dilute urine. This dilution decreases the opportunity for crystals to form.

The 2016 ACVIM consensus statement on the treatment and prevention of uroliths in dogs and cats suggests that urine dilution is probably one of the best ways to help reduce the risk of urolith formation. We can help owners accomplish this in a variety of ways, such as by recommending use of water fountains, adding water to dry food—which often doesn’t go very well with cats—and feeding a canned diet, introduced gradually to help avoid gastrointestinal upset. For cats with FIC, feeding a canned diet and/or increasing liquid intake is the optimal way to achieve a lower urine specific gravity. A hydration supplement can also help.

For example, Purina® Pro Plan® Veterinary Supplements Hydra Care® is a nutrient-enriched water that promotes hydration in cats. It contains nutritional osmolytes, which are intended to aid in the absorption of water at a cellular level. Sometimes as veterinarians we don’t think about incorporating a hydration supplement into our patient plan—we think about subcutaneous fluids or canned food. But if the cat accepts it, a supplement can be a good way to help decrease a patient’s urine specific gravity.

Additionally, it may be a good idea to encourage owners to expose their cats to a variety of texture preferences when they are young, as opposed to when they are older and have to try eating a canned diet to increase moisture intake. That’s not to say that rotating diets throughout a cat’s lifetime is necessary, only that exposing them to different types of food textures at a young age is a good way to get them comfortable and hopefully promote acceptance.

Q What’s the difference between a dissolution diet and a diet formulated to prevent development of struvite and calcium oxalate crystals—and is it important?

A Dissolution diets, such as Purina® Pro Plan® Veterinary Diets UR Urinary® St/Ox Feline Formulas, are formulated to dissolve uroliths—primarily struvite uroliths. Calcium oxalate stones cannot be dissolved, regardless of diet. Some non-dissolution therapeutic diets have undergone relative supersaturation (RSS) testing to ensure they promote a urinary environment that is unfavorable to the development of struvite and calcium oxalate crystals. However, these diets do not help dissolve struvite uroliths. Purina UR St/Ox formulas both help dissolve struvite uroliths and reduce the risk of struvite and calcium oxalate urolith recurrence.

Sterile struvite uroliths in cats may dissolve as early as one to two weeks after transitioning to a therapeutic dissolution diet. Provided the cat doesn't appear to be too uncomfortable, veterinarians can initiate pain management, start the patient on a urinary diet, monitor progress, and then determine next steps based on radiographs and abdominal ultrasound.
Keeping Cats Calm
How Environmental Enrichment Can Reduce Stress in Cats with FIC

Two cats live in the same household. One is healthy, but the other has been diagnosed with feline idiopathic cystitis (FIC). Because FIC is believed to be brought on by stress in cats that are prone to lower urinary tract disease, one key to managing patients with FIC is to identify stress triggers, then work with the owner to develop a multimodal environmental modification (MEMO) plan that addresses them.

The essence of environmental enrichment is to give cats choices. By analyzing the following aspects of the home environment, owners can identify multiple ways to modify the FIC cat’s environment to help reduce their stress triggers.

**Water sources**

Cats with FIC often produce less urine and urinate less frequently than normal cats, so encouraging them to drink is essential. Rather than giving cats a single bowl of water, encourage owners to provide several drinking options in different locations, e.g., a water bowl and a water fountain or a bowl of water and a bowl of a hydration supplement such as Purina® Pro Plan® Veterinary Supplements Hydra Care®.

**Hidden hangouts**

Whether they need to escape from other pets or simply seek a little solitude, cats feel calmer when they have hiding places to conceal themselves while still keeping an eye on their surroundings.

**Prey play**

Cats’ natural behaviors include stalking, chasing and playing with ‘prey.’ Hiding food in different locations, providing a selection of toys and engaging in interactive activities can help them express these natural behaviors.

**Sleeping spots**

Indoor cats spend a lot of time snoozing and need more than one cozy place to stretch out. Many cats enjoy moving spots throughout the day and a warm spot in the sun is often their preferred location.

**Cuddling and companionship**

Cats are often viewed as independent pets that can be capricious when it comes to owner interaction. However, most cats are actually quite social and crave time with their human companions. Spending time each day playing with owners and being petted or brushed by them is important to a cat’s emotional well-being.

**Lofty lookouts**

Cats are both predator and prey. They thus feel safer and more in control of their environment. Cat trees are good options, and a perch near a window with a view can provide an important visual connection to the outside world.

While stress alone is not the cause of FIC, it is clear that cats that suffer from FIC are particularly susceptible to stress triggers. This suggests that these cats have a reduced sense of control over their environment, which leads to chronic stress. A MEMO plan that expands the cat’s choices and assuages stress triggers can be key to managing this troubling condition.

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Managing Cats with LUTD in a Shelter Setting

Lesli Groshong, DVM, DABVP (Shelter Medicine)
Chief Shelter Veterinarian
Humane Society of Boulder Valley
Boulder, Colorado

Lower urinary tract disease (LUTD), including bladder stones and feline idiopathic cystitis (FIC), is a common health issue we see in cats at our shelter. These issues don't necessarily begin in the shelter setting. Typically, we discover them by interviewing the people who surrender the cats to us and by reviewing the surrender profiles they complete. An indication of litter box misuse automatically triggers us to collect a urine sample.

We try to tease out certain information, e.g., if there are other cats in the home, number of litter boxes, type of litter used, etc., to help determine if this is a behavioral issue or a medical issue for the cat.

We recommended several months later, Mrs. Kitty was returned to the shelter because she wasn’t using her litter box. A urinalysis revealed hematuria but an x-ray showed no bladder stones, so Mrs. Kitty was diagnosed with FIC. Mrs. Kitty was managed with Purina UR St/Ox and a five-day course of Cerenia. She was also moved to the shelter’s administrative offices, which was quieter and less stressful.

Two weeks later, a urinalysis revealed no hematuria and she was successfully adopted.

Using diet to manage FIC

“Mrs. Kitty” was a 10-year-old spayed cat who was surrendered to the shelter by an owner who was moving and couldn’t take the cat with her. She was quickly adopted by a family with a dog and small children.

Several months later, Mrs. Kitty was returned to the shelter because she wasn’t using her litter box. A urinalysis revealed hematuria but an x-ray showed no bladder stones, so Mrs. Kitty was diagnosed with FIC. Mrs. Kitty was managed with Purina UR St/Ox and a five-day course of Cerenia. She was also moved to the shelter’s administrative offices, which were quieter and less stressful.

Two weeks later, a urinalysis revealed no hematuria and she was successfully adopted.

LUTD diagnostic protocol

At the Humane Society of Boulder Valley, we have a standard protocol for diagnosing cats with clinical signs of LUTD.

STEP 1 Collect urine using non-absorbent pellets (NoSorb).

STEP 2 Perform a urinalysis. If hematuria is present, take x-rays.

STEP 3 If x-rays do not indicate bladder stones and other causes of LUTD have been ruled out, assume diagnosis is FIC. Transition cat to Purina Pro Plan Veterinary Diets UR Urinary St/Ox Feline Formulas to promote increased urine volume. Also begin a five-day trial of maropitant (Cerenia) for pain control since it prevents the binding of Substance P to receptors in the bladder.

STEP 4 If bladder stones are detected, transition cat to Purina UR St/Ox as a diagnostic and therapeutic tool to help dissolve suspected struvite uroliths. Also place the cat on Cerenia for five days.

STEP 5 If the cat just had hematuria, five to seven days later, perform a second urinalysis. If there is blood in the urine, continue feeding Purina UR St/Ox for two more weeks and then recheck the urine for blood.

STEP 6 If the cat was diagnosed with uroliths, repeat the x-ray two weeks later. If stones are still present, we would be more suspicious of calcium oxalate uroliths and would likely make the decision to proceed with surgery.

Dissolving stones through diet

I believe the struvite cystolith dissolution study out of Colorado State University was a game changer. It showed that Purina UR St/Ox dry formula can successfully dissolve cystoliths that are likely struvite and may lessen the risk of recurrence of struvite and calcium oxalate cystoliths. Prior to that, we assumed that because it would take many weeks to dissolve struvite cystoliths in a number of cases, we would have to do surgery, which can be traumatic and sometimes dangerous for cats. I was thrilled that the results of that study indicated that struvite stones can be dissolved by feeding Purina UR St/Ox for as little as one or two weeks, and we’ve used that management strategy on a dozen or so cats at our shelter.

Once cats with urinary issues have been adopted, we always stress to adopters the need to develop a relationship with a veterinarian if they don’t already have one and to keep the cat on a therapeutic urinary diet. We also connect them with online tools, such as the Ohio State University’s Indoor Pet Initiative website, that can help them and their new cats be successful.

Key Takeaways

- Cats have a lower physiological thirst drive than dogs, so it’s important to have other strategies to boost fluid intake. Increasing dietary moisture can increase urine volume and promote a more-dilute urine. This dilution decreases the opportunity for crystals to form.

- Developing a multimodal environmental modification (MEMO) plan built around offering cats choices can be key to reducing the stress that contributes to feline idiopathic cystitis (FIC).

- A Colorado State University study found that surgery to remove struvite uroliths can potentially be avoided by feeding Purina Pro Plan Veterinary Diets UR Urinary St/Ox Feline Formulas.

Using Purina Pro Plan Veterinary Diets, the decision to proceed with surgery is avoided by feeding Purina Pro Plan Veterinary Diets UR Urinary St/Ox Feline Formulas.
WHAT IF...
WE COULD DISSOLVE STRUVITE STONES AS EARLY AS TWO WEEKS?

When it comes to urinary stones, every day matters. In a Purina study, Purina® Pro Plan® Veterinary Diets UR Urinary® St/Ox® dry appeared to dissolve presumed struvite cystoliths within two weeks.*

Promotes a urinary environment unfavorable to the development of both struvite uroliths (undersaturated, RSS<1) and calcium oxalate uroliths (metastable RSS<12)

Helps dissolve struvite uroliths

Helps reduce the risk of both struvite and calcium oxalate urolith recurrence


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obstruction can lead to caudal vena cava compression, cranial displacement of the diaphragm, activation of the sympathetic nervous system, severe pain, and reduced respiratory lung volume and heart preload. If the stomach outflow obstruction is left untreated, the pathophysiology changes continue to worsen, leading to debilitating pain, hypovolemia, hypotension, hypothermia, disseminated intravascular coagulation, and acidosis.3-9

In addition to diagnostic imaging, clinical pathology (ie, CBC, serum chemistry profile, blood gas analysis) is important for determining a patient’s health status.3-11 For example, hyponatremia is considered a negative prognostic factor,4 and severe hyperglycemia can occur due to severe pain and stress, which can affect treatment and management decisions.5 As in other species with severe GI disturbances, blood gas analysis and acid-base status can be useful in determining appropriate treatment.

In this study of pet rabbits with gastric dilation and suspected obstruction, the authors evaluated acid-base status, electrolytes, and blood gas values, as well as how both time of presentation and therapy influenced these parameters. Prospective data from 30 rabbits were included. The resulting data suggest that acid-base balance disturbances due to gastric dilation can worsen over time without treatment. Specifically, partial pressure of carbon dioxide, partial pressure of bicarbonate, and base excess were significantly lower in rabbits presented 12 hours after the owner first noticed signs of illness as compared with rabbits presented within 6 hours. These findings strongly suggest the need for immediate veterinary care in rabbits showing reduced activity, dysphagia, and changes in fecal output.

... TO YOUR PATIENTS

Key pearls to put into practice:

1. Survey radiography—including ventrodorsal, dorsoventral, and lateral views—is important in the initial screening and diagnosis of any rabbit showing GI or nonspecific clinical signs.11

2. Elevated blood glucose can indicate severe pain and help in the evaluation of efficacy of provided analgesics.5

3. Rectal temperature should always be obtained during physical examination of rabbits. Increased rectal temperature at presentation has been shown to be a poor prognostic factor in rabbits with signs of GI dysfunction, particularly those with a temperature ≤97.9°F (36.6°C).7

References


Outcomes of Dogs with Splenic Mass Rupture

Timothy M. Fan, DVM, PhD, DACVIM (Oncology, Internal Medicine)
University of Illinois at Urbana-Champaign

In the literature

FROM THE PAGE …

The spleen is an accessory organ responsible for physiologic functions that include extramedullary hematopoiesis and immune activities.1,2 Because the spleen is highly cellular and vascular in nature, it can be predisposed to anatomic anomalies, including the development of proliferative mass effects. Splenic masses can remain physically undetectable and clinically inconsequential in some patients; however, in a subset of affected dogs, rupture of an occult splenic mass can manifest as a spontaneous and life-threatening hemoabdomen.

The underlying pathology responsible for a ruptured splenic mass can be benign or malignant and significantly influences emergent treatment decisions by pet owners and long-term survival outcomes of affected dogs. Benign causes of splenic mass can include nodular lymphoid hyperplasia, focal extramedullary hematopoiesis, and hematomas. Malignant causes of splenic mass include hemangiosarcoma (HSA), other aggressive sarcomas (eg, histiocytic, undifferentiated), lymphoma, mast cell tumor, and metastatic solid tumors.3,4

HSA is a malignant neoplasm that originates from either vascular endothelium or hemangioblast lineage. The spleen remains the most common anatomic site of primary HSA development and has been reported to be the most common cause of spontaneous hemoabdomen associated with splenic mass rupture.5-7 However, these studies have been retrospective and are prone to bias that can influence reported results.8 Although splenic HSA is commonly considered a primary differential in dogs presented with a splenic mass and hemoabdomen, this assumed diagnosis can negatively influence owner decisions to pursue potentially life-saving interventions. There is significant justification for improving presurgical accuracy in the identification of dogs actually afflicted with HSA as the underlying pathology of hemoabdomen.9 In addition, prospective studies less prone to bias are needed to help form the foundational knowledge base used to guide owner decisions when the likely outcome of dogs with splenic mass and hemoabdomen is prognosticated.

This report* describes the findings derived from a prospective, observational study of 40 dogs with splenic mass rupture and spontaneous hemoabdomen presented for emergent care. Of these 40 dogs, 15 had benign masses and 25 had

*This study was funded by Ethos Discovery.
malignant masses. Twenty-four of the malignant splenic masses were confirmed to be HSA and, therefore, accounted for the majority (60%) of pathologies. Of 9 dogs with hepatic nodules identified via ultrasound, surgical biopsy or resection of the liver nodules confirmed metastatic HSA lesions in only 3 dogs (33%). Immediate surgical outcomes were favorable, with 95% of dogs surviving to discharge. Collectively, although 60% of splenic masses were HSA, this percentage trends lower than what has been reported in previous retrospective studies (63.3%-70.4%)\(^5,6\) and may suggest a more favorable outcome in dogs with splenic tumor rupture that could guide owner’s decision-making during emergent situations.

**FIGURE 1** Ultrasound image of a splenic mass with a mixed echogenic pattern consistent with blended heterogeneous tumor and fluid-filled (blood) cavities in the splenic parenchyma

**FIGURE 2** Surgically resected spleen and associated mass effects involving both the head and tail of the spleen—histologically confirmed to be hemangiosarcoma

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**... TO YOUR PATIENTS**

Key pearls to put into practice:

1. Intraoperative and postoperative survival of dogs presented with splenic mass and associated hemoabdomen is high (≥95%) when appropriate and timely interventions are instituted.

2. Ultrasonographic identification of liver nodules in dogs presented for splenic mass and hemoabdomen should not be assumed to represent metastatic disease.

3. HSA should be considered the primary differential for splenic mass associated with hemoabdomen, but there is a significant percentage (≥40%) of dogs that may be cured if timely life-saving therapies (ie, surgical intervention with hemodynamic support) are instituted.

**References**


Effect of Dental Chews on Canine Plaque Microbiota

Heidi Lobprise, DVM, DAVDC
Main Street Veterinary Hospital & Dental Clinic
Flower Mound, Texas

In the literature

FROM THE PAGE …

Although bacteria are implicated in the initiation of periodontal disease in dogs, the specific mechanism is unknown. Many types of bacteria are found in the oral cavity, and changes in the microbial community can disturb the equilibrium of the oral ecosystem, allowing disease to begin or intensify. Better methods of identifying bacterial species, including classification of bacteria genera into those generally associated with health (ie, health-associated taxa) and those associated with disease (ie, disease-associated taxa), have improved the understanding of these alterations. This triple crossover study* evaluated the influence of an oral care chew on the composition of microbiota of the canine oral cavity.

Descaling, polishing, and brushing appeared to effectively change the microbiota profiles toward a healthy composition prior to the beginning of day 1 of the test phase. The most abundant phylum at the start of the pretest phase was disease-associated Firmicutes, whereas health-associated Bacteroides was the most abundant phylum at the beginning of the test phase. Proteobacteria was the most abundant phylum for both groups (chew and nonchew) at the end of the study.

Of those that received chews, 6 dogs with health-associated taxa and 3 dogs with disease-associated taxa had increased bacteria. Of those that did not receive chews, 1 dog with health-associated taxa and 8 dogs with disease-associated taxa had increased bacteria. This study may not have been long enough to generate significant differences between the groups.

… TO YOUR PATIENTS
Key pearls to put into practice:

1. Periodontal disease in dogs is greatly influenced by bacteria in the mouth but with minimal antibiotic response.

2. In uncomplicated cases, oral bacteria as a component of plaque and calculus can be effectively managed with complete dental cleaning (descaling and polishing) and effective home care.

3. Any level of home care (eg, chews that decrease plaque and tartar, chews that can impact the microbiota of the oral cavity) can play an important role in the complete dental care of a dog.

Supragingival plaque was collected from 12 beagles before the study (pretest phase), at which time a complete descale and polish was performed. During the 14-day pretest phase, the teeth were brushed daily with water. On day 1 of the test phase, another supragingival plaque sample was taken and another complete descale and polish was performed. Dogs were fed a commercially available wet and dry diet mix either alone or with an oral care chew. Plaque was sampled again after 28 days.

*This study was funded by Mars Petcare.
pH balance is vital to both the overall ear environment and how well it responds to topical applications. With pH•notix™, you can now balance pH and clean the ear — all without rinsing — to help manage the toughest ear challenges in dogs.
Up-to-date veterinary drug information, faster search, and powerful features like the first-of-its-kind drug interaction checker make Plumb’s an indispensable support tool in your daily practice.

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Radiographic Appearance of Benign Versus Malignant-Associated Bone Infarcts in Dogs

Stephen C. Jones, MVB, MS, DACVS-SA
The Ohio State University

In the literature

FROM THE PAGE …

A bone infarct is an area of osteonecrosis that develops following an ischemic event. Bone infarcts can be of benign or malignant origins and have been reported to occur secondary to previous surgery (eg, total hip replacement) or bone neoplasia (eg, osteosarcoma).1-7 The radiographic appearance of malignant-associated bone infarcts has been described but benign infarcts have not.

This retrospective study aimed to assess radiography in discerning benign versus malignant-associated bone infarcts. Two board-certified radiologists were blinded to case signalment and ultimate histologic diagnosis and asked to assess radiographs of bone infarctions, classifying them as likely benign, likely malignant associated, or undistinguishable in nature.

Of the 49 included cases, 33 had a histologic diagnosis of benign infarct and 16 had a malignant-associated infarct. Only 48% of the benign infarcts and 38% of the malignant-associated infarcts were correctly identified by both radiologists. Patterns of both the periosteal response and the medullary lysis were the only radiographic features significantly associated with the histologic diagnosis. Despite this finding, there was substantial crossover, with a high percentage of dogs in both histologic groups having an aggressive periosteal response and an aggressive medullary lysis pattern.

Overall, significant overlap was observed in the radiographic appearance of benign and malignant-associated infarcts, suggesting that radiographic assessment is not very useful in distinguishing the histologic nature of bone infarcts. These results underpin the need for additional diagnostics for bony lesions detected on radiology, even those with a radiographic pattern typical of an aggressive process.
References

Suggested Reading
Elura helps cats with CKD maintain or gain weight to keep them feline fabulous

It can be hard to watch cats with chronic kidney disease (CKD) waste away. Prescribe Elura at the first sign of weight loss in your feline CKD patients.

INDICATION
For the management of weight loss in cats with chronic kidney disease.

IMPORTANT SAFETY INFORMATION
For oral use in cats only. Do not use in cats that have a hypersensitivity to capromorelin, or in cats with hypersomatotropism (acromegaly). Elura may increase serum glucose for several hours after dosing; use in cats with current or historical diabetes mellitus has not been evaluated and may not be appropriate. Use with caution in cats that may have cardiac disease, severe dehydration, or hepatic dysfunction. Elura has not been evaluated in cats younger than 5 months of age, or in breeding, pregnant or lactating cats. The most common adverse reactions included vomiting, hypersalivation, inappetence, behavior change and lethargy. Please see accompanying brief summary for product safety information.

MORE THAN 8/10 CATS GAINED WEIGHT*1

UNIQUE MOA MIMICS THE NATURALLY OCCURRING HORMONE GHRELIN

SAFE TO USE DAILY AND APPROVED FOR LONG-TERM USE

ORAL SOLUTION WITH LOW DOSING VOLUME

*4/10 cats in the control group maintained or gained weight. A multi-center, placebo-controlled, randomized and masked field study including 176 cats with CKD and at least 5% unintended loss of body weight (as compared to the highest weight in the medical records for the 3 years preceding enrollment). Study period was 56 days (Day 0 to Day 55). Primary endpoint was percent change in weight from Day 0 to Day 55.

CKD, chronic kidney disease.


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PM-US-21-1162

See page 56 for product information summary.
Redonyl® Ultra products provide a convenient, easy to administer, concentrated source of palmitoylethanolamide (PEA) to support skin health in dogs and cats.

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For Technical Support Contact Dechra Veterinary Products at:

Improving Incidence of Upper Respiratory Infections in Shelter Kittens

Lisa L. Powell, DVM, DACVECC
BluePearl Veterinary Partners
Eden Prairie, Minnesota

Critical Consults
Pittsburgh, Pennsylvania

In the literature

FROM THE PAGE …

Airborne pathogens that cause respiratory infections can contribute to significant illness in kittens housed in animal shelters. These pathogens, including feline herpesvirus-1, feline calicivirus, Bordetella bronchiseptica, Chlamydia felis, and Mycoplasma spp, can persist on surfaces and lead to fomite transmission. Intensive disinfection can help decrease the persistence of these pathogens and other contagions in a shelter environment. Ultraviolet (UV) germicidal irradiation has been found to effectively disinfect surfaces, air, and water and to decrease the spread of respiratory infections in humans when added to heating, ventilation, and air-conditioning (HVAC) systems.1-5

This study compared the incidence of upper respiratory infections (URIs) in a kitten nursery setting before and after a UV germicidal irradiation system was installed in an HVAC system. Incidence of URIs (ie, URIs per 100 kittens housed) prior to installation of the UV irradiation system was compared with the incidence of URIs after the UV irradiation system was in place 2 years later. Records were reviewed for the number of kittens housed in the nursery, as well as the number of kittens diagnosed with URI based on clinical signs. Intensive disinfection and personal protective equipment (PPE) protocols for staff remained as standard operating procedures.

Evaluation of incidence of infection revealed a significant decrease in URIs diagnosed in kittens after the UV germicidal irradiation system was in use. Incidence of URIs was 12.4 prior to and 1.6 after (2 years later) installation of the UV system—an 87.1% decrease in development of URIs.

… TO YOUR PATIENTS
Key pearls to put into practice:

1. In a shelter environment where URIs are common and easily transmitted, addition of a UV germicidal irradiation system could significantly decrease incidence of infections caused by common respiratory viruses.

2. Strict disinfection protocols and consideration for UV germicidal irradiation in shelter environments are also important.

3. UV irradiation in other veterinary environments (eg, general clinics, intensive care units, research facilities, rescue/large shelter organizations) could also be considered. It is unknown whether other types of viruses, bacteria, or fungal organisms may be susceptible to UV irradiation; thus, further studies are warranted.

References
**Credelio**

*(lotilaner)*

**Chewable Tablets**

**For oral use in dogs**

**Caution:**

Federal (USA) law restricts this drug to use by or on the order of a licensed veterinarian.

Before using Credelio, please consult the product insert, a summary of which follows:

**Indications:**

CREDIELI kills adult fleas and is indicated for the treatment and prevention of flea infestations (*Ctenocephalides felis*) and the treatment and control of tick infestations (*Amblyomma americanum* (lone star tick), *Dermacentor variabilis* (American dog tick), *Ixodes scapularis* (black-legged tick) and *Rhipicephalus sanguineus* (brown dog tick)) for one month in dogs and puppies 8 weeks of age and older, and weighing 4.4 pounds or greater.

**Dosage and Administration:**

CREDIELI is given orally once a month, at the minimum dosage of 9 mg/lb (20 mg/kg).

**Dosage Schedule:**

<table>
<thead>
<tr>
<th>Body Weight</th>
<th>Lotilaner Per Chewable Tablet (mg)</th>
<th>Chewable Tablets Administered</th>
</tr>
</thead>
<tbody>
<tr>
<td>4.4 to 6.0 lbs</td>
<td>56.25</td>
<td>One</td>
</tr>
<tr>
<td>6.1 to 12.0 lbs</td>
<td>112.5</td>
<td>One</td>
</tr>
<tr>
<td>12.1 to 25.0 lbs</td>
<td>225</td>
<td>One</td>
</tr>
<tr>
<td>25.1 to 50.0 lbs</td>
<td>450</td>
<td>One</td>
</tr>
<tr>
<td>50.1 to 100.0 lbs</td>
<td>900</td>
<td>One</td>
</tr>
</tbody>
</table>

**Dosage Schedule:**

Over 100.0 lbs   

Administer the appropriate combination of chewable tablets.

CREDELIO must be administered with food (see *Clinical Pharmacology*).

Treatment with CREDELIO can begin at any time of the year and can continue year-round without interruption.

See product insert for complete dosing and administration information.

**Contraindications:**

There are no known contraindications for the use of CREDELIO.

**Warnings:**

Not for human use. Keep this and all drugs out of the reach of children. Keep CREDELIO in a secure location out of reach of dogs, cats, and other animals to prevent accidental ingestion or overdose.

**Precautions:**

Lotilaner is a member of the isoxazoline class. This class has been associated with neurologic adverse reactions including tremors, ataxia, and seizures. Seizures have been reported in dogs receiving isoxazoline class drugs, even in dogs without a history of seizures. Use caution with dogs with a history of seizures or neurologic disorders. The safe use of CREDELIO in breeding, pregnant or lactating dogs has not been evaluated.

**Adverse Reactions:**

In a well-controlled U.S. field study, which included 284 dogs (198 dogs treated with CREDELIO and 86 dogs treated with an oral active control), there were no serious adverse reactions.

Over the 90-day study period, all observations of potential adverse reactions were recorded. Reactions that occurred at an incidence of 1% or greater are presented in the following table.

**Dogs with Adverse Reactions in the Field Study**

<table>
<thead>
<tr>
<th>Adverse Reaction (AR)</th>
<th>CREDELIO Group: Number (and Percent) of Dogs with the AR (n=198)</th>
<th>Active Control Group: Number (and Percent) of Dogs with the AR (n=86)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight Loss</td>
<td>3 (1.5%)</td>
<td>2 (2.3%)</td>
</tr>
<tr>
<td>Elevated Blood Urea Nitrogen (BUN)</td>
<td>2 (1.0%)*</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>Polyuria</td>
<td>2 (1.0%)*</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>2 (1.0%)</td>
<td>2 (2.3%)</td>
</tr>
</tbody>
</table>

*Two geriatric dogs developed mildly elevated BUN (34 to 54 mg/dL; reference range: 6 to 31 mg/dL) during the study. One of these dogs also developed polyuria and a mildly elevated potassium (6.5 mEq/L; reference range: 3.6 to 5.5 mEq/L) and phosphorous (6.4 mg/dL; reference range: 2.5 to 6.0 mg/dL). The other dog also developed a mildly elevated creatinine (1.7 to 2.0 mg/dL; reference range: 0.5 to 1.6 mg/dL) and weight loss.

In addition, one dog experienced intermittent head tremors within 1.5 hours of administration of vaccines, an ear cleaning performed by the owner, and its first dose of CREDELIO. The head tremors resolved within 24 hours without treatment. The owner elected to withdraw the dog from the study.

In an Australian field study, one dog with a history of seizures experienced seizure activity (tremors and glazed eyes) six days after receiving CREDIELIO. The dog recovered without treatment and completed the study. In the U.S. field study, two dogs with a history of seizures received CREDELIO and experienced no seizures throughout the study.

In three well-controlled European field studies and one U.S. laboratory study, seven dogs experienced episodes of vomiting and four dogs experienced episodes of diarrhea between 6 hours and 3 days after receiving CREDIELIO.

To report suspected adverse events, for technical assistance or to obtain a copy of the Safety Data Sheet (SDS), contact Elanco US Inc. at 1-888-545-5973. For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS or http://www.fda.gov/reportanimalae.

**Effectiveness:**

In well-controlled European laboratory studies, CREDELIO began to kill fleas four hours after administration or infestation, with greater than 99% of fleas killed within eight hours after administration or infestation for 35 days. In a well-controlled U.S. laboratory study, CREDELIO demonstrated 100% effectiveness against adult fleas 12 hours after administration or infestation for 35 days.

In a 90-day well-controlled U.S. field study conducted in households with existing flea infestations of varying severity, the effectiveness of CREDELIO against fleas on Days 30, 60 and 90 compared to baseline was 99.5%, 100% and 100%, respectively. Dogs with signs of flea allergy dermatitis showed improvement in erythema, papules, scaling, alopecia, dermatis/pseudodermatis and pruritus as a direct result of eliminating fleas.

In a well-controlled laboratory study, CREDELIO killed fleas before they could lay eggs, thus preventing subsequent flea infestations for 30 days after the start of treatment of existing flea infestations.

In well-controlled laboratory studies, CREDELIO demonstrated > 97% effectiveness against *Amblyomma americanum*, *Dermacentor variabilis*, *Ixodes scapularis* and *Rhipicephalus sanguineus* ticks 48 hours after administration or infestation for 30 days. In a well-controlled European laboratory study, CREDELIO started killing *Ixodes ricinus* ticks within four hours after administration.

**Storage Information:**

Store at 15-25°C (59 -77°F), excursions permitted between 5 to 40°C (41 to 104°F).

**How Supplied:**

CREDIELI is available in five chewable tablet sizes for use in dogs: 56.25, 112.5, 225, 450, and 900 mg lotilaner. Each chewable tablet size is available in color-coded packages of 56.25, 112.5, 225, 450, and 900 mg lotilaner.

Each chewable tablet size is available in color-coded packages of 1, 3 or 6 chewable tablets.

Approved by FDA under NADA # 141-494

Manufactured for: Elanco US Inc
Greenfield, IN 46140 USA
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Rev. date 05/2020
INTERCEPTOR™ PLUS
(milbemycin oxime/praziquantel)

Caution
Federal (USA) law restricts this drug to use by or on the order of a licensed veterinarian. Before using INTERCEPTOR PLUS, please consult the product insert, a summary of which follows:

Indications
INTERCEPTOR PLUS is indicated for the prevention of heartworm disease caused by Dirofilaria immitis and for the treatment and control of adult roundworm (Toxocara canis, Toxascaris leonina), adult hookworm (Ankylostoma caninum), adult whipworm (Trichuris vulpis), and adult taenia (Taenia pisiformis, Echinococcus multilocularis, Echinococcus granulosus, and Dipylidium caninum) infections in dogs and puppies two pounds of body weight or greater and six weeks of age and older.

Dosage and Administration
INTERCEPTOR PLUS should be administered orally, once every month, at the minimum dosage of 0.23 mg/lb (0.5 mg/kg) milbemycin oxime, and 2.28 mg/lb (6 mg/kg) praziquantel. For heartworm prevention, give once monthly for at least 6 months after exposure to mosquitoes (see EFFECTIVENESS).

### Dosage Schedule

<table>
<thead>
<tr>
<th>Body Weight</th>
<th>Milbemycin Oxime per chewable</th>
<th>Praziquantel per chewable</th>
<th>Number of chewables</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 to 8 lbs.</td>
<td>2.3 mg</td>
<td>22.8 mg</td>
<td>One</td>
</tr>
<tr>
<td>8.1 to 25 lbs.</td>
<td>5.75 mg</td>
<td>57 mg</td>
<td>One</td>
</tr>
<tr>
<td>25.1 to 50 lbs.</td>
<td>11.5 mg</td>
<td>114 mg</td>
<td>One</td>
</tr>
<tr>
<td>50.1 to 100 lbs.</td>
<td>22 mg</td>
<td>226 mg</td>
<td>One</td>
</tr>
<tr>
<td>Over 100 lbs.</td>
<td>Administer the appropriate combination of chewables.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Adverse Reactions

The following adverse reactions have been reported in dogs after administration of milbemycin oxime or praziquantel: vomiting, diarrhea, depression/lethargy, ataxia, anorexia, convulsions, weakness, and salivation.

To report suspected adverse events, for technical assistance or to obtain a copy of the Safety Data Sheet (SDS), contact Elanco US, Inc. at 1-888-545-5973. For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS or http://www.fda.gov/reportanimalae.

Effectiveness

**Heartworm Prevention:**
In a well-controlled laboratory study, INTERCEPTOR PLUS was 100% effective against induced heartworm infections when administered once monthly for 6 consecutive months.

**Intestinal Nematodes and Cestodes Treatment and Control:**
Elimination of the adult stage of hookworm (Ankylostoma caninum), roundworm (Toxocara canis, Toxascaris leonina), whipworm (Trichuris vulpis), and taenia (Echinococcus multilocularis, Echinococcus granulosus, Taenia pisiformis and Dipylidium caninum) infections in dogs was demonstrated in well-controlled laboratory studies.

**Palatability**
In a field study of 115 dogs offered INTERCEPTOR PLUS, 108 dogs (94.0%) accepted the product when offered from the hand as if a treat, 1 dog (0.9%) accepted it from the bowl with food, 2 dogs (1.7%) accepted it when it was placed in the dog’s mouth, and 4 dogs (3.5%) refused it.

### Animal Safety

**INTERCEPTOR PLUS:**
Safety studies in pregnant dogs demonstrated that doses of 0.6X the maximum exposure dose of INTERCEPTOR PLUS, (1.5 mg/kg of milbemycin oxime), administered daily from mating through weaning, resulted in measurable concentrations of milbemycin oxime in milk. Puppies nursing these females demonstrated milbemycin oxime-related effects (depression, decreased activity, diarrhea, dehydration, nasal discharge). A subsequent study, which evaluated the daily administration of 0.6X the maximum exposure dose of INTERCEPTOR PLUS, from mating until one week before weaning, demonstrated no effects on the pregnant females or their litters. A study, in which pregnant females were dosed once, at 0.6X the maximum exposure dose of INTERCEPTOR PLUS before, on the day of, or shortly after whelping, resulted in no effects on the puppies.

Some nursing puppies, at 2, 4, and 6 weeks of age, administered oral doses of 9.6 mg/kg milbemycin oxime (3.8X the maximum exposure dose of INTERCEPTOR PLUS) exhibited tremors, vocalization, and ataxia. These effects were all transient and puppies returned to normal within 24 to 48 hours. No effects were observed in puppies administered 0.5 mg/kg milbemycin oxime (minimum label dose).

### Storage Information

Store at room temperature, between 59° and 77°F (15-25°C).

### How Supplied

INTERCEPTOR PLUS is available in four strengths, formulated according to the weight of the dog. Each strength is available in color-coded packages of six or twelve chewable tablets each. The tablets containing 2.3 mg milbemycin oxime/22.8 mg praziquantel or 5.75 mg milbemycin oxime/57 mg praziquantel are also available in color coded packages of one chewable tablet each.

**Manufactured for:** Elanco US Inc.; Greenfield, IN 46140, USA

**Approved by FDA under NADA # 141-338**

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**Revision date:** May 2020
2 OUT OF 5 WORMS RECOMMEND SIMPARICA TRIO®
(sarolaner, moxidectin, and pyrantel chewable tablets)

That’s because their one little chew misses two big parasites.

“My host was so generous, I stayed ‘til I was 2 feet long! Thanks Simparica Trio!”

- A. Tapeworm

Perfect spot for me and all the little Whippersnappers.
- A. Whipworm

We met the nicest gaggle of Whipworms.
- A. Whipworm

Plenty of room to spread out without a care in the world. Thanks Trio!
- A. Tapeworm

Interceptor Plus Indications
Interceptor Plus is indicated for the prevention of heartworm disease caused by Dirofilaria immitis and for the treatment and control of adult roundworm (Toxocara canis, Toxascaris leonina), adult hookworm (Ancylostoma caninum), adult whipworm (Trichuris vulpis), and adult tapeworm (Taenia pisiformis, Echinococcus multilocularis, Echinococcus granulosus, Dipylidium caninum) infections in dogs and puppies 6 weeks of age or older and 2 pounds of body weight or greater.

Interceptor Plus Important Safety Information
Treatment with fewer than 6 monthly doses after the last exposure to mosquitoes may not provide complete heartworm prevention. Prior to administration of Interceptor Plus, dogs should be tested for existing heartworm infections. The safety of Interceptor Plus has not been evaluated in dogs used for breeding or in lactating females. The following adverse reactions have been reported in dogs after administration of milbemycin oxime or praziquantel: vomiting, diarrhea, depression/lethargy, ataxia, anorexia, convulsions, weakness, and salivation. For full prescribing information see Interceptor Plus package insert.

Credelio Indications
Credelio kills adult fleas and is indicated for the treatment and prevention of flea infestations (Ctenocephalides felis) and the treatment and control of tick infestations [Amblyomma americanum (lone star tick), Dermacentor variabilis (American dog tick), Ixodes scapularis (black-legged tick) and Rhipicephalus sanguineus (brown dog tick)] for one month in dogs and puppies 8 weeks of age and older and weighing 4.4 pounds or greater.

Credelio Important Safety Information
Lotilaner is a member of the isoxazoline class. This class has been associated with neurologic adverse reactions including tremors, ataxia, and seizures. Seizures have been reported in dogs receiving this class of drugs, even in dogs without a history of seizures. Use with caution in dogs with a history of seizures or neurologic disorders. The safe use of Credelio in breeding, pregnant or lactating dogs has not been evaluated. The most frequently reported adverse reactions are weight loss, elevated blood urea nitrogen, polyuria, and diarrhea. For full prescribing information see Credelio package insert.
Say bye-bye to freeloaders with the powerful 360-degree protection of Interceptor® Plus (milbemycin oxime/praziquantel) and Credelio® (lotilaner) or Seresto.®

Interceptor Plus offers broad-spectrum worm protection beyond heartworm disease. It covers all 5 major worms, including the tapeworms and whipworms others skip.

With the tick and flea efficacy of Credelio or Seresto,® this is 360-degree parasite protection.

Be confident your patients are fully covered. Talk to your Elanco sales rep and prescribe 360-degree protection.

Interceptor Plus Indications
Interceptor Plus is indicated for the prevention of heartworm disease caused by Dirofilaria immitis and for the treatment and control of adult roundworm (Toxocara canis, Toxascaris leonina), adult hookworm (Ancylostoma caninum), adult whipworm (Trichuris vulpis), and adult tapeworm (Taenia pisiformis, Echinococcus multilocularis, Echinococcus granulosus and Dipylidium caninum) infections in dogs and puppies 6 weeks of age or older and 2 pounds of body weight or greater.

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The American Veterinary Dental College greatly appreciates iM3 for their support for the practical portion of the 2021 AVDC certifying examination and their dedication to the advancement of veterinary oral and dental health.
Top 5 Fine-Needle Biopsy Sample Collection & Handling Errors

Isabelle Soga, DVM candidate
Lisa M. Pohlm, DVM, MS, DACVP
Kansas State University

Fine-needle biopsy is an effective diagnostic tool that allows for the retrieval of samples without anesthesia (and often without analgesia), thereby significantly reducing cost and avoiding potential adverse effects associated with more invasive procedures. In-clinic cytology examination or submission to a reference laboratory with a rapid turnaround time can provide cursory information. In cases in which a definitive diagnosis is not achieved, cytology can typically help direct additional testing. One study found 89% sensitivity and 100% specificity for cyto-

logic detection of neoplasia in cutaneous and sub-

cutaneous lesions.1 Sample quality is a key factor in ensuring diagnostic yield, and proper technique in sample collection and handling can help avoid nondiagnostic samples.2

Following are, in the authors’ opinion, the 5 most common fine-needle biopsy collection and handling errors that result in nondiagnostic samples, along with corrective actions.

1 Improper Collection Technique

The 2 fine-needle biopsy collection techniques are aspiration and nonaspiration. The nonaspiration technique (also called nonaspiration...
The capillary, stab, or woodpecker technique is the preferred method of collection because it reduces the amount of blood contamination and can produce samples of excellent diagnostic quality.\(^3,4\)

Common errors with the nonaspiration technique include lack of redirection, which can result in a nonrepresentative sample, and timid collection, which can result in a poorly cellular sample. Occasionally (ie, when lesions are poorly exfoliative), the nonaspiration technique does not yield an adequately cellular sample for cytologic interpretation. Therefore, an additional (less common in the authors’ opinion) error is not recognizing when use of the nonaspiration technique alone does not suffice and, consequently, when additional sampling via the aspiration technique is required.

The nonaspiration technique can be performed using a needle only (Figure 1, previous page) or a needle attached to an air-filled syringe (Figure 2).\(^3\) For cutaneous and subcutaneous masses or peripheral lymph nodes, the tissue to be sampled should be stabilized with the clinician’s free hand, and the needle should be inserted into the tissue and redirected (ie, moved back and forth) several times without exiting the tissue.\(^5\) The sample can then be expelled onto a slide via an air-filled syringe. The goal is to gather a representative population of cells.\(^3,5\)

Errors with the aspiration technique are common and include prolonged aspiration or repeated pulses of negative pressure, both of which can result in significant blood contamination and an overly diluted sample;\(^3,5\) failure to release negative pressure and stop aspiration before the needle is removed from the tissue, which can result in the sample entering the barrel of the syringe and an inability to easily retrieve it; and timid collection, which can result in a poorly cellular sample.\(^3\)

For the aspiration technique, the needle should be attached to an empty syringe and inserted into the mass. Negative pressure should then be applied by withdrawing the plunger once (Figure 3) and redirecting the needle while negative pressure is maintained and without the needle exiting the mass. Before the needle is removed, the negative pressure should be released, as maintaining pressure while the needle exits the mass can result in the...
sample entering the barrel of the syringe. After the needle is removed from the mass, it must be removed from the syringe. Air is added to the syringe, then the needle is reattached so the sample can then be expelled on a clean glass slide.  

Highly exfoliative and vascular tissues (eg, lymph nodes, round and epithelial cell neoplasms) are typically successfully sampled using the nonaspiration technique; thus, the nonaspiration technique should be attempted first. The aspiration technique should only be used if cells are not exfoliating with the nonaspiration technique. In the authors’ opinion, spindle cell lesions are more likely to be poorly exfoliative with the nonaspiration technique and may require the aspiration technique to obtain an adequate sample.

2 Incorrect Needle and/or Syringe Size

In general, 22- to 25-gauge needles can be used for fine-needle biopsy collection, but needle size should be determined based on firmness of the tissue to be aspirated. Softer tissue requires a needle gauge on the higher side of the range (eg, 23-25-gauge). Using needles that are <25-gauge increases the risk for breakage and distortion of cells. Firmer tissue requires a larger needle size; hence, a 22-gauge needle is ideal. Needles >22-gauge often result in tissue cores, preventing creation of a proper monolayer for analysis. Larger needles also increase the risk for blood contamination.

For the nonaspiration technique, the size of the syringe is not critical, as it is simply used to rapidly expel the sample on the slide after collection. However, for the aspiration technique, the size of the syringe (much like needle size) should be selected based on tissue consistency. A smaller syringe size (3-mL) is sufficient for softer tissue (eg, lymph nodes) because minimal negative pressure is needed for sample collection. Firmer tissue requires increased negative pressure to obtain a sufficient number of cells.

If there is uncertainty, a 12-mL syringe with a 23-gauge needle is generally safe.

3 Localization Error

Successful sample collection depends on the accuracy of the needle-tip delivery. Common localization errors include a geographic miss (ie, the needle misses the lesion entirely and instead samples a nonrepresentative area [eg, subcutaneous or perinodal fat]); shallow passes of the collection needle (ie, the needle hits the lesion, but just barely), which can result in a poorly cellular sample; and inadequate or insufficient needle redirection—the likelihood of a nondiagnostic sample increases with <4 redirections.

4 Inappropriate Slide-Preparation Technique

The slide-over-slide (also called squash prep) method is the preferred smear preparation for fine-needle biopsy samples. The goal is to achieve a thin film of cells spread out in a single layer (ie, the monolayer) without damaging the cells. Contrary to its name, this procedure requires minimal to no pressure, as overly aggressive pressing of the slides can result in cell rupture (Figure 4). The

![FIGURE 4](nondiagnostic sample from a fine-needle biopsy of a lymph node. Almost all cells on the smear are ruptured. One nucleated cell (a neutrophil; circle) is intact. Nuclei with no associated cytoplasm (ie, naked nuclei; solid arrows) can be seen. Streaming nuclear material (dashed arrows) and scattered RBCs (curved arrows) can be seen. Large, clear spaces (asterisks) represent lipid (likely subcutaneous or perinodal fat in this case), which is a common finding on cytology samples. Modified Wright’s stain, 600× magnification)
sample should first be expelled onto a clean glass slide toward one end, leaving room for the sample to be spread; this is referred to as the sample slide. A spreader slide is then gently placed either parallel to or perpendicular on top of the sample slide with no downward digital pressure, allowing just the weight of the slide to “squash” the preparation. The top slide should be pulled horizontally to glide over the bottom slide until the 2 slides are separate. A common error is to pull the 2 slides vertically apart; the resulting suction can rupture the cells.3

Slides that are being used for cytologic preparation (including sample and spreader slides) should never be heat- or formalin-fixed. After the squash preparation is made, the smears should be air-dried via rapid waving of the slides or by placing the slides in front of a fan.3,5 After air-drying, the slides can either be shipped unstained to a reference laboratory for assessment by a clinical pathologist or stained for in-clinic viewing.

5 Inappropriate Shipping Procedure
Properly protecting slides during transport/shipping is a major concern.3,8 Cardboard and soft-plastic casings require additional protection (eg, bubble wrap), as slides are easily broken (Figure 5).3 Containers made of hard plastic or polystyrene foam are ideal (Figure 6). Unstained slides should be packaged separately from formalin-containing samples. Even if the slides are individually wrapped, the formalin fumes can penetrate packaging and deleteriously affect the cytology preparations, resulting in a nondiagnostic sample.3,5

Relevant history and clinical findings are essential to provide context for clinical pathologists. Therefore, it is important to include location and macroscopic description of the lesion, method of sample collection, clearly labeled slides, time of collection, and concise clinical history (including signalment) with every shipped sample.6 Submitting several slides (rather than one) increases the likelihood of a productive report.
Conclusion
Collection and preparation of quality fine-needle biopsy samples is a skill that is honed through experience and refinement of technique. Collection method and needle and syringe size should be determined based on tissue characteristics. In the authors’ opinion, the nonaspiration technique should be attempted first because it is the preferred method to obtain a sample of excellent diagnostic quality.3,4 If the nonaspiration technique fails to exfoliate cells, the aspiration technique may be successful, but it is also more likely to be contaminated with peripheral blood. Squash preparations should be prepared with a view to minimize cell damage and maximize production of a monolayer of well-spread, intact cells. Labeled, air-dried smears can then be stained for in-clinic viewing or packed appropriately and shipped (along with relevant history and lesion description) to a reference laboratory for evaluation by a clinical pathologist.

References
Canine Transitional Cell Carcinoma: What’s New?

Detection: Commercially Available Molecular Test
The most common cancer of the canine urinary tract is transitional cell carcinoma (TCC), also known as urothelial carcinoma (UC). It is estimated to represent 1% to 2% of all canine cancers, with increasing prevalence seen at university teaching hospitals. Risk factors for TCC/UC include obesity, female sex, and exposure to specific environmental agents such as herbicide-treated lawns. An elevated incidence has been observed in a number of dog breeds, including Scottish terriers, Shetland sheepdogs, West Highland white terriers, wire fox terriers, and beagles.

TCC/UC is often identified following observation of lower urinary tract signs (eg, stranguria, pollakiuria, hematuria). These signs may also result from other more common bladder health issues such as UTI, polyps, prostatitis, and bladder stones.

Because bladder infections are a common reason for dogs to be presented with lower urinary tract signs, first-line management often involves antibiotic and/or anti-inflammatory medications, with recurrence of signs eventually creating concern for TCC/UC.

Histopathology is the gold standard for detection of TCC/UC, but this approach requires invasive and costly procedures. The use of traditional, noninvasive options relies on cytologic identification of abnormal epithelial cells in urine specimens, which may be misleading and contribute to delayed detection. Once TCC/UC is diagnosed, management options vary and can include cyclooxygenase inhibitors, cytotoxic chemotherapy, radiation therapy, and surgery. Prognosis is generally guarded.

Molecular studies of canine TCC/UC have identified the presence of a single base mutation in the canine BRAF gene, which has been detected in ≈85% of cases studied. The remarkably high prevalence of this mutation in patients with TCC/UC as compared with patients with other cancers has facilitated development of a commercially available molecular test with high sensitivity and specificity using a noninvasive (free-catch) urine sample. Further, using a technical approach that is not impacted by the presence of blood, protein, and bacteria in the urine enhances the utility of this approach to aid detection of TCC/UC for dogs with overt clinical signs. Earlier detection may increase the time for appropriate intervention, thus enhancing opportunities to potentially improve outcomes. Moreover, detection of low-level mutation, associated with preclinical cases of TCC/UC, provides opportunities for veterinarians to consider the most appropriate management, which could improve quality and duration of life of these patients.

KEY POINTS
- A molecular approach is available to noninvasively aid in detecting patients suspected of having TCC/UC and breeds predisposed to TCC/UC, allowing the approach to management to be determined earlier.
- Dog breed and environmental elements are predisposing factors for TCC/UC.
- Biological phytochemical compounds that may support approaches to traditional multimodal management have been identified.
- A bioavailable sulforaphane production supplement (Avmaquin™) has been shown to increase sulforaphane in the bloodstream of dogs.
In addition to earlier detection, it is critical to focus on measures that optimize canine urinary tract health, such as avoiding environmental risk factors, maintaining a healthy weight, and ensuring a healthy diet, including cruciferous vegetable supplementation. Studies of dietary supplements aimed at supporting management of human cancers, bladder included, suggest that sulforaphane, found in raw cruciferous vegetables, may provide added benefits to humans, with potential translation to canine patients.18-24

What Is Sulforaphane?
Cruciferous vegetables, most notably broccoli, contain crucial isothiocyanates, which produce a key compound: sulforaphane (SFN).25 It releases into the body upon breaking down from its precursor, the phytonutrient glucoraphanin. Although glucoraphanin occurs in all parts of the broccoli plant, it is concentrated in the seeds and sprouts. The introduction of the plant enzyme, myrosinase, from intracellular vesicles catalyzes the hydrolysis of glucoraphanin into SFN. This breakdown process initiates through damage to the plant (eg, chewing, chopping, cutting).

Mechanisms of Action
The primary mechanism through which SFN supports cellular health is by direct antioxidant effects or by indirectly inducing phase 2 detoxifying enzymes by upregulating the nuclear factor erythroid 2-related factor 2 (Nrf2) pathway, thereby reducing oxidative stress. Nrf2 has been shown to support cells and tissue from various insults by increasing the expression of a number of these phase 2 enzyme genes.28 Phase 2 detoxification enzymes (eg, NQO1, glutathione reductase, glutathione-S-transferases) play an important role in detoxifying potential mutagenic toxicants. Under physiologic conditions, Nrf2 is primarily localized in a complex with Kelch-like ECH-associated protein 1 (Keap1). Keap1 is inactivated upon exposure to oxidative stress, which dislodges Nrf2 and allows Nrf2 to transfer into the nucleus to activate phase 2 enzyme genes. SFN is one of the most potent phytochemicals that can activate the Nrf2 pathway.26

Sulforaphane Research
SFN has been the subject of extensive research identifying major supportive pathways of cellular activity, leading to the initiation of numerous studies indicating its role in aiding cellular health in humans. SFN research in veterinary medicine is emerging, with further research warranted to identify clinical applications. When administered to healthy dogs in a study, a broccoli sprout supplement containing glucoraphanin and active myrosinase (the precursors to SFN) showed absorption in plasma and urine that remained detectable at 24 and 48 hours, respectively, postconsumption. Researchers also noted a decrease in activity of histone deacetylase, a chromatin-modifying enzyme that has been shown to have increased activity with certain mutagenic cells in the body, at 24 hours postadministration. A study of SFN supplementation in dogs with compromised lymphatic health was associated with significant changes in lymph node proteome. The proteins impacted by SFN involved immune health and oxidative stress responses. A study using canine cell lines demonstrated diminished cell invasion in the cells treated with SFN. Studies of the pharmacodynamic and pharmacokinetic properties of an oral glucoraphanin and myrosinase supplement supporting sulforaphane production were performed in beagle dogs. Blood samples of 4 dogs administered a tablet containing a proprietary blend of glucoraphanin and active myrosinase (Avmaquin™) orally once a day for a 3-day period revealed induced phase 2 enzyme gene expression at all time points after administration and increases in plasma SFN levels. Furthermore, administration of glucoraphanin in a fasted state has been shown to significantly increase SFN plasma levels as compared with administration with food. Results from this study showed higher total peak plasma SFN than a recently published study.

Supplemental Options
Consumption of specific levels of SFN from routinely harvested broccoli or sprouts alone can be difficult to achieve due to variations in environment, plant genotype, and harvesting methods. In addition, because heat can damage SFN hydrolysis, variation in cooking methods can lead to inconsistencies in amounts. Sprouts can contain ≥100 times more phytonutrients than mature plants, but broccoli is particularly sensitive to metals in contaminated soil, which can affect plant development.

Glucoraphanin, the precursor of SFN, is a comparatively stable molecule that can be converted to SFN by exposure to myrosinase, making it a good candidate for dietary supplementation. Although glucoraphanin occurs in all parts of broccoli plants, it is most abundant in the sprouts and seeds. Seed extraction of glucoraphanin and myrosinase ensure a stabilized, consistent source of SFN as compared with cruciferous vegetable supplementation.

Future Directions
With a commercially available detection method for dogs with TCC/UC issues, veterinarians may be able to intervene more appropriately and target management of patients. SFN has been extensively studied for its mechanisms of action and shown to be of benefit in various human studies. As SFN research continues to emerge in veterinary medicine, additional studies are warranted to assess potential benefits of SFN for clinical applications.
Dear AHS,

Three weeks ago, I gave the first of three melarsomine injections to a 2-year-old, 118-pound, intact female Mastiff undergoing heartworm treatment. However, in the past 24 hours, she has developed significant swelling around the injection site. We’re a little concerned about giving the next two injections. What do you recommend? -Dr. W.

**The Short Answer**

Proceed with the next two injections, but be sure to divide the dose, avoid the previous injection site and take steps to minimize injection stress and trauma.

**A**

The inflammatory reaction you describe is most likely due to a large volume of melarsomine being injected into the epaxial muscle and getting into the fascial planes; however, I would rule out an injection abscess by checking for a fluid pocket with ultrasound or aspiration. Inflammation like this can take weeks to appear and resolve. Using warm compresses will help resolve the swelling and discomfort and enable you to move forward with the remaining two injections.

Both medication volume and patient movement can be significant factors in injection-site complications with melarsomine treatment. In the future, consider these steps:

- **Give several smaller injections.** The AHS recommends injecting no more than 2 ml of melarsomine per injection site. In a patient like this Mastiff, you would administer three injections of 1.75 ml each, avoiding the previous injection site.

- **Pick the proper needle.** A 1 ½-inch, 22-gauge needle is appropriate for larger dogs, while a 23-gauge needle would be advisable for a smaller dog. To minimize injection pain, always use a new needle—and don’t use the same needle for injection that you used to draw up the medication.

- **Hold Techniques to Consider:**
  - Keep the patient calm and comfortable. I recently received my first COVID-19 immunization, and the nurse administering the vaccine had to remind me twice to “Relax!” While I can’t caution my canine patients about tensing up, I can apply “fear-free” techniques to minimize their stress and injection-site pain.
    - **Pick a comfortable position.** Some dogs are calmer in lateral recumbency, while others fight to stay standing. With big dogs, I keep a bent knee under the belly and use one hand to stabilize the rump; this supports them while keeping them from sitting. I also discuss the patient’s temperament with the owner beforehand, since some dogs dislike being held.
    - **Consider premedication.** We have a variety of medications to consider, including methocarbamol, melatonin, gabapentin, trazodone and tramadol. For patients that need additional sedation, a dexdomitor/telazol/torbugesic combination can be administered. NSAIDs should be avoided, as patients undergoing heartworm treatment are often on prednisone. But plan ahead, since most medications must be given minutes to hours before the injection.
    - **Deploy distraction techniques.** Having an assistant on hand to give ear scratches, speak soothing words or give the dog a treat can help keep the dog calm.
    - **Take it slow.** After prepping the injection site, insert the needle gently at a slight angle, targeting the belly of the epaxial musculature, and release the melarsomine slowly. If the dog starts to squirm during the injection, stop, then start again when the dog is still. After the needle is withdrawn, apply gentle but firm pressure to the injection site for 60 seconds.
Zsa Zsa, an 18-month-old, 8-lb (3.6-kg) spayed domestic longhair cat, was presented for a 2-week history of left pelvic limb lameness and decreased activity levels. She was an indoor-only cat and was current on annual vaccinations, and her owners reported no known trauma.

**Physical Examination**
On physical examination, Zsa Zsa was bright, alert, and responsive. Vital parameters were within normal limits, except for an elevated heart rate (260 bpm). Oral examination revealed persistent deciduous teeth with eruption of the permanent teeth, gingivitis, and calculus (Figure 1, next page). Thoracic auscultation was unremarkable. Orthopedic examination revealed moderate left pelvic limb lameness. Pain and swelling were identified on palpation of the left stifle joint. Her BCS (5/9) and muscle condition score (3/3) were normal. The remainder of the clinical examination was unremarkable.

**Diagnosis**
Differential diagnoses for the patient’s stifle swelling, lameness, and pain included patellar luxation, atraumatic stress fracture of the patella, long bone fracture, soft-tissue or musculoskeletal injury (eg, cranial cruciate ligament injury), viral polyarthritis, and slipped capital femoral epiphysis. Inflammatory and neoplastic processes were considered less likely due to the patient’s age and absence of other clinical abnormalities. Patellar insufficiency fracture (ie, stress fracture) remained a likely differential due to the presence of persistent deciduous teeth and the possibility of osteogenic disease. Hypothyroidism was considered less likely due to the patient’s normal conformation and weight, as well as the absence of lethargy and anorexia.

The patient received buprenorphine (15 µg/kg IV) for analgesia, followed by an induction with alfaxalone (0.5 mg/kg IV) and general anesthesia with isoflurane to facilitate dental and orthopedic radiography. Dental radiographs revealed persistent deciduous teeth and impacted permanent teeth. Lateral and craniocaudal pelvic limb radiographs revealed a displaced left patellar fracture and a nondisplaced right patellar fracture (Figure 2, next page).
Persistent deciduous premolars in the right maxilla (A), left maxilla (B), right mandible (C), and left mandible (D). Coeruption of the deciduous and permanent maxillary canines, as well as marked gingivitis and calculus, particularly of the maxillary teeth, can be seen.

Coeruption of the deciduous and permanent maxillary canines, as well as marked gingivitis and calculus, particularly of the maxillary teeth, can be seen. - FIGURE 1

Lateral radiographs of the left (A) and right (B) stifles show a complete, displaced left patellar fracture and a nondisplaced right patellar fracture, respectively. - FIGURE 2
DIAGNOSIS: FELINE KNEES & TEETH SYNDROME

Treatment & Management
Zsa Zsa was discharged on an NSAID (robenacoxib, 2 mg/kg PO for a total of 3 days) for pain management. Exercise restriction over the next several weeks was advised. She was returned to the clinic several days later for dental cleaning and nerve blocks, after which all persistent deciduous teeth and impacted permanent teeth were extracted. Buprenorphine (15 ug/kg IV) was administered, followed by an induction with alfaxalone (0.5 mg/kg IV). General anesthesia was maintained with

A

B

C

D

► FIGURE 3 Radiographs of the patellar fractures taken 2 years (A, left stifle; B, right stifle) and 8 years (C, left stifle; D, right stifle) after initial presentation. Progressive fragmentation and osteophytosis of the left patella and displacement of the right patellar fragments can be seen.
isoflurane. Postoperative dental radiographs confirmed that no retained teeth or roots remained.

The patient was managed postoperatively with buprenorphine (15 µg/kg IV every 8-12 hours), and a transdermal fentanyl patch (12.5 µg/hour) was placed on the left lateral thorax. She began to eat within a few hours after recovery; left pelvic limb lameness persisted. Gabapentin (50 mg PO every 12 hours) was prescribed for multimodal analgesia.

**Prognosis & Outcome**

At the 3-week postoperative recheck, Zsa Zsa demonstrated decreased left pelvic limb lameness and reduced associated stifle swelling. Oral examination revealed appropriate healing of the gingiva. Continued exercise restriction over the following 6 weeks, with gradual return to previous activity, was recommended. At the 3-month recheck, she was ambulating normally and exhibited no residual lameness or stifle swelling. Repeat pelvic limb radiographs revealed unchanged bilateral patellar fractures. No additional therapy was recommended for the patellar fractures due to concerns of surgical failure.

**Discussion**

Feline knees and teeth syndrome is an association of nontraumatic patellar fractures and persistent deciduous teeth. This pathologic syndrome may include persistence of deciduous teeth, unerupted permanent teeth, and insufficiency fractures of the patella.1,2 Other fractures, including in the long bones and pelvis, and spinal abnormalities have also been reported.3,4 Pathologic fractures of the tibia and fibula can occur up to 10 years after diagnosis.2

Feline knees and teeth syndrome was first identified in the United States, but affected cats have since been identified in South America and the United Kingdom.2,5 This syndrome was believed to be a manifestation of osteogenesis imperfecta, but another mechanism is currently supported,6,7 as patellar fractures showing radiographic evidence of sclerosis and generalized osteosclerosis have been seen in both humans and cats.8 In humans, osteomyelitis of the jaw associated with osteopetrosis and dental pathology has been reported.8-10 In addition, fractures of the patella and other bones have been associated with generalized osteopetrosis.8,10 Patellar sclerosis has similarly been observed in some cats with knees and teeth syndrome.2,4,11

Feline knees and teeth syndrome is typically recognized in young cats, with male cats more frequently affected than female cats.2,12 The mean age of onset of pelvic limb lameness or radiographic diagnosis is 28 months (range, 4 months-8 years).9 Physical examination findings typically reveal persistent deciduous teeth, pelvic limb lameness, and swelling of the distal quadriceps muscle; concurrent paronychia has also been reported.2,4 Intraoral and

**TREATMENT AT A GLANCE**

- A thorough orthopedic examination should be performed on all cats with persistent deciduous teeth.
- Careful extraction of retained deciduous teeth or impacted adult teeth is critical.
- Staged dental extractions may be warranted to avoid iatrogenic mandibular fracture.
- Conservative management with exercise restriction and pain management is generally advised.
- Surgical management of patellar fractures is typically discouraged due to the high rate of surgical failure.
- Fractures of the acetabulum, tibia, and other bones can occur; serial radiography should be pursued depending on the progression of clinical signs.
- Some cats may heal and adapt to fractures, whereas others may continue to have an altered, plantigrade gait.

Serial radiographs of the pelvic limbs were taken periodically to monitor progression of the patellar fractures. Comparative orthopedic radiographs ([Figure 3](#), previous page) 2 and 8 years after initial presentation revealed persistence of patellar fractures, with fragmentation, progressive sclerosis, and osteophytosis of the left patella.
whole-body orthopedic radiography, with particular attention given to the pelvic limbs, should be performed for evaluation. In some cases, lameness and quadriceps swelling precede visible radiographic fractures.2,4

Failure of deciduous tooth exfoliation in cats is rare and most often the result of an altered eruption path of the permanent tooth (see Take-Home Messages). Persistence of deciduous cheek teeth was reported in 40 of 60 cats with patellar fractures in one case series.2 Another series of 191 cats with various fractures reported that 48% had dental anomalies possibly related to knees and teeth syndrome.4 Extraction of both the persistent deciduous teeth and the impacted adult teeth is key, as proliferative osteomyelitis, dentigerous cysts, and jaw deformation may develop when these teeth are left in situ (see Treatment at a Glance).2,11,13,14 A careful, meticulous technique is required to avoid mandibular fracture due to the space occupancy of the impacted teeth in the mandible/mandibular canal.2

Although surgical reduction of patellar fractures may seem like a good option, surgical failure was reported in 86% of cats with feline knees and teeth syndrome.15 Therefore, nonsurgical, conservative approaches should be considered.15 Fractures in these patients may heal or the patient may adapt to the fractures and function normally even without surgical management; other cats may develop a plantigrade gait.3 A study of cats with knees and teeth syndrome that developed humeral fractures lacked sufficient data to determine the long-term prognosis for surgical repair, suggesting that many of these fractures may heal with medical management alone.3

Most cats that sustain pathologic fractures of the patellae related to knees and teeth syndrome adapt with good return to function. Cats with persistent deciduous cheek teeth should be closely monitored because development of pathologic insufficiency fractures of the patellae and other bones may be anticipated.2

**TAKE-HOME MESSAGES**

- Feline knees and teeth syndrome should be considered in cats that have spontaneous onset of pelvic limb lameness.
- Cats with persistent deciduous cheek teeth should be closely monitored, as pathologic (especially patellar) fractures can occur.
- Cats with juvenile dental anomalies should be further evaluated with dental radiography.
- Extraction of any persistent deciduous teeth and unerupted adult teeth is recommended to prevent osteomyelitis, pain, and jaw deformation.
- Acute lameness associated with nontraumatic patellar fracture often occurs at ≈2 years of age in cats with feline knees and teeth syndrome.
- Pelvic limb lameness and distal quadriceps swelling may precede patellar fractures.
- Radiography of both pelvic limbs should be performed, even if lameness is only noted on one side.
- Surgical reduction of patellar fractures is not recommended due to the high rate of failure.
- Persistent lameness and an altered gait are possible long-term consequences of feline knees and teeth syndrome.
- Fractures of bones other than the patellae may occur and should be monitored.

Pathologic fractures of the tibia and fibula can occur up to 10 years after diagnosis.2

See page 80 for references.
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Groomer: Owner
Coat: Model's Own
Collar: Seresto®

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PM-US-20-2035
Neutrophilia

Marie Chartier, DVM, DACVIM
BluePearl Pet Hospital
Charlestown, Massachusetts

Following are differential diagnoses for patients presented with an elevated neutrophil count.

- Increased production associated with bone marrow response to inflammation
  - Infection (eg, bacterial, viral, fungal, protozoal) of any organ system
  - Sterile inflammation (eg, immune-mediated disease, neoplasia, tissue trauma or necrosis)
- Increased production associated with bone marrow response to peripheral cytopenias (eg, hemolytic anemia, hemorrhagic anemia, thrombocytopenia)
- Glucocorticoid-associated
  - Stress (physical)
  - Glucocorticoid administration
  - Hyperadrenocorticism
- Granulocytic leukemia
- Specific infections causing severe leukemoid response
  - Hepatozoonosis (Hepatozoon canis)
  - Babesiosis (Babesia canis)
- Leukocyte adhesion deficiencies in dogs (eg, Irish setter), usually associated with hypersegmented neutrophils

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Adverse Reactions

Orthopaedic Surgery: In a controlled field study evaluating orthopaedic postoperative pain and inflammation, 238 dogs (ages 10.5 years to 16 years) were evaluated for safety when given PREVICOX Chewable Tablets at a dose of 2.27 mg/kg (5.0 mg/kg orally every 24 hours) for 30 days. The following adverse reactions were observed. Dogs may have experienced more than one of the observed adverse reactions during the study.

Adverse Reactions in U.S. Field Studies

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>PREVICOX (n=129)</th>
<th>Active Control (n=127)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>14</td>
<td>4</td>
</tr>
<tr>
<td>Vomiting</td>
<td>7</td>
<td>3</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>13</td>
<td>8</td>
</tr>
<tr>
<td>Appetite Decreased</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Pyrexia</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Seizures</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Anemia</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Depression</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Death</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

PREVICOX (firocoxib) Chewable Tablets were safely used during field studies concurrently with other therapies, including vaccines, dental hygiene, and dietary management.

Soft-Tissue Surgery: In controlled field studies evaluating soft tissue postoperative pain and inflammation, 258 dogs (ages 10.5 years to 16 years) were evaluated for safety when given PREVICOX Chewable Tablets at a dose of 2.27 mg/kg (5.0 mg/kg orally every 24 hours) for 30 days. The following adverse reactions were observed. Dogs may have experienced more than one of the observed reactions during the study.

Adverse Reactions in the Soft-Tissue Surgery Postoperative Pain Field Study

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>Firocoxib (n=139)</th>
<th>Control Group* (n=131)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apparent Loss</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>10</td>
<td>8</td>
</tr>
<tr>
<td>Abnormal Surgery Site</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Respiratory Arrest</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Urinary Tract Infection</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>1</td>
<td>0</td>
</tr>
</tbody>
</table>

*Sham-dosed (pilled)

Orthopedic Surgery: In a controlled field study evaluating orthopaedic postoperative pain and inflammation, 238 dogs of various breeds, ranging in age from 1.0 to 11.5 years in the PREVICOX-treated groups and 0.7 to 11.7 years in the control group were evaluated for safety. Of the 256 dogs, 118 were given PREVICOX Chewable Tablets at a dose of 2.27 mg/kg (5.0 mg/kg orally every 24 hours) for 30 days. The following adverse reactions were observed. Dogs may have experienced more than one of the observed reactions during the study.

Adverse Reactions in the Orthopaedic Surgery Postoperative Pain Field Study

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>Firocoxib (n=118)</th>
<th>Control Group* (n=118)</th>
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</thead>
<tbody>
<tr>
<td>Apparent Loss</td>
<td>20</td>
<td>19</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>21</td>
<td>15</td>
</tr>
<tr>
<td>Appetite Decreased</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Pyrexia</td>
<td>12</td>
<td>10</td>
</tr>
<tr>
<td>Acute Renal Failure</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Urinary Tract Infection</td>
<td>2</td>
<td>2</td>
</tr>
</tbody>
</table>

*Sham-dosed (pilled)

One case may be represented in more than one category.

**One dog had hemagglutinin-gammariters.
Incision Swelling, Redness 9 5
Inappetence/ Decreased Appetite 1 2

Indications: PREVICOX Oral Suspension is indicated for the control of pain and inflammation associated with osteoarthritis in dogs.

Contraindications: Dogs with known hypersensitivity to meloxicam should not receive METACAM Oral Suspension. Do not use METACAM Oral Suspension in cats. Acute renal failure and death have been associated with the use of meloxicam in cats.

Warnings: Not for use in humans. Keep this and all medications out of reach of children. Consult a physician in case of accidental ingestion by humans. For oral use only.

As with any NSAIad all dogs should undergo a thorough history and physical examination before the initiation of NSAID therapy. Appropriate laboratory testing to establish hematological and serum biochemical baseline data is recommended prior to, and periodically during use of any NSAIad in dogs.

Adverse Reactions: Field safety was evaluated in 306 dogs. Based on the results of two studies, GI abnormalities (vomiting, soft stools, diarrhea, and inappetence) were the most common adverse reactions associated with the administration of meloxicam. The following adverse events are based on post-approval adverse drug experience reporting. Not all adverse reactions are reported to FDA/CVM. It is not always possible to reliably estimate the adverse event frequency or establish a causal relationship to product exposure using these data. The following adverse events are listed in decreasing order of frequency by body system.

Gastrointestinal: vomiting, anorexia, diarrhea, melena, gastrointestinal ulceration
Urinary: azotemia, elevated creatinine, renal failure
Neurological/Behavioral: lethargy, depression
Hepatic: elevated liver enzymes
Dermatologic: pruritus

Death has been reported as an outcome of the adverse events listed above. Acute renal failure and death have been associated with the use of meloxicam in cats.

Information for Dog Owners: METACAM, like other drugs of its class, is not free from adverse reactions.

Owners should be advised of the potential for adverse reactions and be informed of the clinical signs associated with meloxicam-induced adverse reactions. These signs include vomiting, diarrhea, decreased appetite, dark or tarry stools, increased water consumption, increased urination, pale gums due to anemia, yellowing of gums, skin or white of the eye due to jaundice, lethargy, incoordination, seizures, or behavioral changes. Serious adverse reactions associated with this drug class can occur without warning and in rare situations result in death (see Adverse Reactions). Owners should be advised to discontinue METACAM and contact their veterinarian immediately if signs of intolerance are observed.

The vast majority of patients with drug related adverse reactions have recovered when the signs are recognized, the drug is withdrawn, and veterinary care, if appropriate, is initiated. Owners should be advised of the importance of periodic follow up for all dogs during administration of any NSAIad.

Effectiveness: The effectiveness of meloxicam was demonstrated in two field studies involving a total of 277 dogs representing various breeds, between six months and sixteen years of age, all diagnosed with osteoarthritis. Efficacy was evaluated twice: 24 hours after the initial dosing (day 14) and 4 days later. All dogs received 0.2 mg/kg meloxicam on day 1.

On day 2, all dogs were maintained on 0.1 mg/kg oral meloxicam from days 2 through 14. Sixty percent of the dogs showed clinical improvement after 14 days of meloxicam treatment for all parameters. In the second field study (n=48), dogs receiving meloxicam showed a clinical improvement after 14 days of therapy for all parameters; however, statistical significance was determined only for the overall investigator evaluation and owner evaluation on day 14.

Reference: 1. FIO for NADA 141-213 METACAM (meloxicam oral suspension).

Approved by FDA under NADA # 141-213

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60143-05/601568-05 8699869/60698535

5 mg/mL Solution for Injection
Non-steroidal anti-inflammatory drug for use in dogs and cats only

Caution: Federal law restricts this drug to use by or on the order of a licensed veterinarian.

Description: Meloxicam is a non-steroidal anti-inflammatory drug (NSAIad) of the oxicam class. Each milliliter of this sterile product for injection contains meloxicam 5.0 mg, alcohol 15%, glycerol 10%, polysorbate 188 5%, sodium chloride 0.6%, glycerine 0.5% and meglumine 0.3%, in water for injection, pH adjusted with sodium hydroxide and hydrochloric acid.

Indications: METACAM Injection is indicated in dogs for the control of pain and inflammation associated with osteoarthritis.

Contraindications: Dogs with known hypersensitivity to meloxicam should not receive METACAM Injection. Warnings: Not for use in humans. Keep this and all medications out of reach of children. Consult a physician in case of accidental ingestion by humans. For IV or SQ injectable use in dogs. All dogs should undergo a thorough history and physical examination before administering any NSAIad. Appropriate laboratory testing to establish hematological and serum biochemical baseline data is recommended prior to, and periodically during use of any NSAIad in dogs.

Owner should be advised to observe their dogs for signs of potential drug toxicity.

Precautions: The safe use of METACAM Injection in dogs younger than 6 months of age, dogs used for breeding, or in pregnant or lactating bitches has not been evaluated. Meloxicam is not recommended for use in dogs with bleeding disorders, as it has not been established in dogs with these disorders. As a class, cyclooxygenase inhibitory NSAIads may be associated with gastrointestinal, renal and hepatic toxicity. Sensitivity to drug-associated adverse events varies with the individual patient. Dogs that have experienced adverse reactions to one NSAIad may experience adverse reactions from another NSAIad. Patients at greatest risk for renal toxicity are those that are dehydrated, on concomitant diuretic therapy, or those with existing renal, cardiovascular, and hepatic dysfunction. Concurrent administration of potentially nephrotoxic drugs should be carefully approached. NSAIDs may inhibit the prostaglandins that maintain normal hematopoietic function. Such anti-prostaglandin effects may result in clinically significant disease in patients with underlying or pre-existing disease that has not been previously diagnosed. Since NSAIads possess the potential to induce gastrointestinal ulcerations and/or perforations, concomitant use with other anti-inflammatory drugs, such as NSAIads or corticosteroids, should be avoided. If additional pain medication is needed after administration of the total daily dose of METACAM Oral Suspension, a non-NSAIad or non-corticosteroid class analgesic should be considered. Concomitant use with another NSAIad is not recommended. Consider appropriate washout times when switching from corticosteroid use or from one NSAIad to another in dogs. Use of concurrently protein-bound drugs may inhibit metabolism of METACAM Injection has not been evaluated. Drug compatibility should be monitored in patients requiring adjunctive therapy. The effect of cyclooxygenase inhibition and the potential for thromboxane production or a hypercoagulable state has not been studied.

Adverse Reactions: Dogs: A field study involving 224 dogs was conducted. Based on the results of this study, GI abnormalities (vomiting, soft stools, diarrhea, and inappetence) were the most common adverse reactions associated with the administration of meloxicam.

The following adverse reactions are based on post-approval adverse drug event reporting. The categories are listed in decreasing order of frequency by body system:

Gastrointestinal: vomiting, diarrhea, melena, gastrointestinal ulceration
Urinary: azotemia, elevated creatinine, renal failure
Neurological/Behavioral: lethargy, depression
Hepatic: elevated liver enzymes
Dermatologic: pruritus

Death has been reported as an outcome of the adverse events listed above. Acute renal failure and death have been associated with the use of meloxicam in cats.

Information for Dog Owners: Meloxicam, like other NSAIads, is not free from adverse reactions. Owners should be advised of the potential for adverse reactions and be informed of the clinical signs associated with meloxicam-induced adverse reactions. Adverse reactions may include vomiting, diarrhea, decreased appetite, dark or tarry stools, increased water consumption, increased urination, pale gums due to anemia, yellowing of gums, skin or white of the eye due to jaundice, lethargy, incoordination, seizure, or behavioral changes. Serious adverse reactions associated with this drug class can occur without warning and in rare situations result in death (see Adverse Reactions). Owners should be advised to discontinue METACAM and contact their veterinarian immediately if signs of intolerance are observed.

The vast majority of patients with drug related adverse reactions have recovered when the signs are recognized, the drug is withdrawn, and veterinary care, if appropriate, is initiated. Owners should be advised of the importance of periodic follow up for all dogs during administration of any NSAIad.

Effectiveness: The effectiveness of meloxicam was demonstrated in two field studies involving a total of 277 dogs representing various breeds, between six months and sixteen years of age, all diagnosed with osteoarthritis. Efficacy was evaluated twice: 24 hours after the initial dosing (day 14) and 4 days later. All dogs received 0.2 mg/kg meloxicam on day 1.

On day 2, all dogs were maintained on 0.1 mg/kg oral meloxicam from days 2 through 14. Sixty percent of the dogs showed clinical improvement after 14 days of meloxicam treatment for all parameters. In the second field study (n=48), dogs receiving meloxicam showed a clinical improvement after 14 days of therapy for all parameters; however, statistical significance was determined only for the overall investigator evaluation and owner evaluation on day 14.

Reference: 1. FIO for NADA 141-213 METACAM (meloxicam oral suspension).

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**QUIZ CORNER**

**QUIZ YOURSELF on this issue’s features**

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1. **TOP 5 PAGE 14**
Global effects of pentoxifylline include ________________________________.
A. Promotion of RBC deformability and microvascular constriction
B. Increased neutrophil degranulation and leukocyte adhesion
C. Improved circulation and decreased inflammation
D. Inhibition of fibroblasts

2. **DIAGNOSTIC TREE PAGE 22**
During elimination diet trial for suspected food allergy, signs of pruritus should be decreased to what percentage to support a diagnosis of food allergy?
A. 20%
B. 30%
C. 40%
D. 50%

3. **PROCEDURES PRO PAGE 25**
Which of the following euthanasia techniques results in the longest time to death?
A. Intraperitoneal
B. Intracardiac
C. Intrarenal
D. Intrahepatic

4. **TOP 5 PAGE 65**
Which of the following should not be included when shipping/transporting fine-needle biopsy sample slides?
A. Hard plastic box to contain slides
B. Relevant history and clinical findings
C. Method of sample collection
D. Additional formalin-containing samples

5. **CASE IN POINT PAGE 73**
Which of the following statements regarding feline knees and teeth syndrome is false?
A. It occurs more commonly in male cats than in female cats.
B. It typically affects middle-aged cats.
C. Persistent deciduous teeth are commonly noted.
D. Pathologic fractures of the tibia and fibula can occur up to 10 years after diagnosis.

**Answer Key:**
SUPPORTING MOBILITY IS A JOINT EFFORT

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JOINT HEALTH SUPPLEMENT

#1 joint health brand recommended by veterinarians.*

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Patented ASU and ALA combination helps inhibit mediators that break down joint cartilage in dogs.

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Also available in a formula with partially hydrolyzed egg shell membrane.
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While others talk about pain management, our pain portfolio is proven in more than 20 favorable studies. When you prescribe METACAM® (meloxicam) or PREVICOX® (firocoxib) for your post-operative (PREVICOX only) and canine osteoarthritis patients, the research stands with you, so that you can get your patients back to living the life they love.

IMPORTANT SAFETY INFORMATION: METACAM® (meloxicam oral suspension) and PREVICOX® (firocoxib) Chewable Tablets are for use in dogs only. METACAM® (meloxicam) Solution for Injection is approved for use in dogs or cats (not indicated for osteoarthritis in cats). Repeated use of meloxicam in cats has been associated with acute renal failure and death. Do not administer additional injectable or oral meloxicam to cats. As a class, cyclooxygenase inhibitory NSAIDs like METACAM® and PREVICOX® may be associated with gastrointestinal, kidney, or liver side effects. Dogs should be evaluated for pre-existing conditions and currently prescribed medications prior to treatment with METACAM® or PREVICOX®, then monitored regularly while on therapy. Concurrent use with another NSAID, corticosteroid, or nephrotoxic medication should be avoided or monitored closely. Please refer to the package insert or product website for complete product information.

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See pages 82 & 83 for product information summary.