TOP 5 POTENTIAL HEARTWORM TREATMENT CHALLENGES

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“Don’t worry; it’s not my blood.”—Jennifer B

“Did the poop look more like pudding or ice cream?”—Amanda S

“Can everyone check the bottom of their shoes to find the missing lump we need to send away?”—Helen H

“As long as Buster ate his vomit with the *Bordetella* spp vaccine in it, we shouldn’t need to revaccinate.”—Abby S

“Sniff, sniff, I smell maggots.”—Albert B

“Um, no, Mr. TSA Agent. I actually did not realize there were 3 to 4 used syringes and empty vaccine vials in the pocket of that coat. Oops!”—Alyssa W

If you had to choose one procedure to do over and over, what would it be?

“C-section. I love the excitement and having the whole team work together.”—Dan H

“Draining abscesses.”—Stacy H

“Ovariohysterectomy in street dogs.”—Malik R

“Cat neuter.”—Kim B

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Top 5 Complications During & After Heartworm Treatment
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MARY SARAH BERGH, DVM, MS, DACVS, DACVSMR, is an affiliate associate professor at Iowa State University and a small animal surgeon at Edinger Surgical Options in Madison, Wisconsin. Dr. Bergh completed an internship at University of Pennsylvania and a residency in small animal surgery at The Ohio State University. Her clinical and research interests include rehabilitation therapy, joint replacement, arthroscopy, treatments for cranial cruciate ligament disease, and sporting injuries.

TOP 5 PAGE 59

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PROCEDURES PRO PAGE 31

J. BRAD CASE, DVM, MS, DACVS (Soft Tissue), is an associate professor and small animal surgeon at University of Florida. He completed a rotating internship at Texas A&M University and a residency at Colorado State University. Dr. Case is a frequent speaker and laboratory instructor at the ACVS Surgery Summit and Veterinary Meeting & Expo. His primary research interest is minimally invasive soft tissue surgery, especially laparoscopy and thoracoscopy.

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CRAIG DATZ, DVM, MS, DABVP, DACVN, is an adjunct associate professor at University of Missouri and the director of scientific affairs at Royal Canin. Dr. Datz has spoken at a number of conferences and is a parasitology, immunology, and infectious disease consultant for Veterinary Information Network.

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W. ALEXANDER FOX-ALVAREZ, DVM, MS, is a small animal surgical resident and incoming assistant professor at University of Florida, where he also earned his DVM. Dr. Fox-Alexander completed a small animal emergency and zoo animal rotating internship at VCA Valley Animal Hospital and Emergency Center in Tucson, Arizona. His interests are minimally invasive surgery, surgical instrument design, and exotic animal surgery.

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PROCEDURES PRO PAGE 31

JENNIFER ANNE SIDLEY, DVM, DACVIM (Cardiology), is a practicing veterinary cardiologist with CVCA Cardiac Care for Pets in Alexandria, Virginia. She earned her DVM from University of Minnesota and completed a small animal rotating internship and cardiology residency at North Carolina State University.

TOP 5 PAGE 16

ALYSSA SULLIVANT, DVM, MS, DACVIM, is a faculty member in the small animal internal medicine department at Mississippi State University, where she earned her DVM and completed a specialty internship in internal medicine and oncology and a residency in small animal internal medicine. Her clinical interests include gastroenterology and oncology.

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LINDA TORESSON, DVM, is a PhD student in gastroenterology at University of Helsinki, Finland, and a senior consultant in gastroenterology at Evidensia Specialist Animal Hospital in Helsingborg, Sweden, where she previously served as the medical director. She is a Swedish specialist in diseases of dogs and cats and a Swedish specialist in small animal internal medicine. Dr. Toresson is a member of the Comparative Gastroenterology Society and the European Society of Comparative Gastroenterology.

DIET IN DISEASE PAGE 26
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TOP 5 COMPLICATIONS DURING & AFTER HEARTWORM TREATMENT

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► FIGURE Radiograph from a dog with severe heartworm disease illustrating severe pulmonary arterial dilation, right heart enlargement, diffuse bronchointerstitial infiltrate, and focal region of pulmonary consolidation from embolized heartworms
Treatment complications can make heartworm disease particularly challenging. Following are the most common complications the author has encountered from heartworm treatment, as well as strategies to minimize them.
TOP 5 COMPLICATIONS DURING & AFTER HEARTWORM TREATMENT

1. Pulmonary Emboli
2. Rapid Microfilarial Death
3. Incomplete Adulticide Efficacy
4. Injection Site Reactions
5. Caval Syndrome

Pulmonary Emboli

Embolized worms are one of the most dangerous risks following melarsomine therapy. As worms die, they decompose, leaving fragments that become lodged in the distal pulmonary artery and capillary beds and block blood flow (Figure 1). The higher the worm burden and heartworm classification, the higher the risk for life-threatening complications. Clinical signs are most common 10 to 21 days postinjection but can occur as early as 2 days postinjection or as late as 30 days postinjection.1 Sudden coughing, hemoptysis, dyspnea, lethargy, and anorexia are hallmark signs. Pale mucous membranes, pulmonary crackles, fever, leukocytosis, and thrombocytopenia are common. Strict cage confinement, oxygen (if needed), and tapering anti-inflammatory doses of prednisone (0.5 mg/kg q12h for 1 week, 0.5 mg/kg q24h for the second week, then 0.5 mg/kg q48h for 1-2 weeks) are recommended if signs develop.2

Before treatment, patients should be stabilized to maximize lung function and improve their ability to handle dying worms. Anti-inflammatory doses of prednisone 7 to 14 days before treatment should be given to patients with significant pulmonary infiltrate or respiratory signs (eg, coughing, tachypnea); right-sided heart failure should be treated and stabilized.

Exercise increases blood flow to damaged, blocked vessels and leads to worsening lung injury, increased pulmonary vascular resistance, pulmonary hypertension, and, potentially, right-sided heart failure. Therefore, strict exercise restriction is essential to minimize the severity of cardiopulmonary damage.3,4 Restriction should begin the day of diagnosis and extend throughout the entire treatment and recovery period, with the most extreme restriction lasting 4 to 6 weeks after each melarsomine injection.2 Restriction may vary depending on patient and owner needs but ideally involves cage confinement or restriction to a single room with just short leash walks to eliminate, particularly for more severe cases.
A split 3-dosage protocol can reduce the severity of complications from dying worms. The first injection kills approximately 50% of worms, then the lungs are able to recover for one month before the other half of the worms are killed. If the lungs have not fully healed at this point, the second and third injections can be delayed until signs have resolved.

2 Rapid Microfilarial Death

Rapid microfilarial death (Figure 2) can cause signs ranging from mild lethargy, ptalism, inappetence, and nausea to more severe hypotension, tachycardia, tachypnea, and collapse. If these signs develop, supportive care with IV fluids and soluble glucocorticoids (eg, dexamethasone sodium phosphate [0.25 mg/kg IV slowly over 2-4 minutes]) is indicated. Rapid microfilaricidal treatment with high-dose (ie, 50 μg/kg) ivermectin is no longer recommended by the American Heartworm Society; instead, a combination of doxycycline (10 mg/kg q12h for 4 weeks) with a monthly macrolide preventive is recommended to kill microfilariae at a slower rate with less potential for complications. Within 5 to 9 months, most dogs will become amicrofilaremic. Because milbemycin oxime kills microfilariae much more rapidly than do ivermectin, selamectin, and moxidectin, the latter 3 have a lower risk for microfilarial death complications and are preferred in dogs that are microfilaremic. In microfilaremic dogs, administration of glucocorticoids (eg, prednisolone [1 mg/kg PO], dexamethasone [0.25 mg/kg IV]) with or without antihistamines (eg, diphenhydramine [1 mg/kg IV or IM]) is recommended one hour before, and possibly again 6 hours after, administration of the first dose of preventive; patients should be monitored for potential adverse effects for the first 8 to 12 hours.

3 Incomplete Adulticide Efficacy

Closing the gap in treatment so that all stages present are susceptible can help prevent persistent heartworm infection post-adulticide therapy. Melarsomine kills adults and mature L5 larvae that are at least 4 months postinfection. Macrolide preventives reliably kill L3 and L4 larvae that are present up to 2 months postinfection; thus, there is a 2-month gap when immature L5 larvae are not sensitive to either preventive or melarsomine and can later develop into adult heartworms. Allowing 2 to 3 months to lapse after preventive treatment before administering melarsomine can help close this gap and allow all stages present to be sensitive to melarsomine and prevent treatment failure.

Melarsomine is not 100% effective, and not all worms are killed in every patient. The extended 3-dose treatment protocol has a higher efficacy than the 2-dose protocol. The American Heartworm Society recommends the 3-dose protocol for all dogs treated for heartworms, regardless of stage, because of its higher efficacy and lower risk for pulmonary complications. This may involve greater cost for the owner and a longer period of exercise restriction, but the potential benefit for the patient outweighs this added cost and inconvenience.
Improved sensitivity of tests over time has allowed clinicians to detect smaller worm numbers (as few as 1-3 female worms). Typically, the worm burden is still significantly reduced in persistently positive animals. The decision for retreatment should be made on a case-by-case basis, depending on patient age, activity level, worm burden, and history. A geriatric, low-energy dog would likely tolerate a few persistent worms better than would a young, active dog, and the latter would benefit more from retreatment.

Injection Site Reactions

Significant irritation can occur at the injection site, causing pain, swelling, tenderness, seroma formation, and reluctance to move. Care should be taken to follow the recommended technique and inject deep in the muscle belly to avoid superficial or subcutaneous injection and leakage. Administering butorphanol before the injection can help reduce discomfort, and the sedation may also help ensure proper technique. Hyperhydration, panting, vomiting, diarrhea, anorexia, and weakness have also been reported following injection.\(^6,8\)

Caval Syndrome

When large numbers of worms mature over a short period of time, the right heart chambers and vena cava can become engorged with worms (ie, caval syndrome), leading to severe right-sided heart dysfunction, pulmonary hypertension, intravascular hemolysis, hemoglobinuria, disseminated intravascular coagulation, shock, and multiple organ failure (Figures 3, previous page, and 4).

Prompt extraction of the worms to remove the obstruction is essential for survival and typically involves referral to a specialist with proper tools (eg, long alligator forceps, horsehair catheter, basket retrieval device).\(^9\) During extraction, care must be taken to avoid excessive intracardiac or vessel damage, as well as laceration to the worms themselves, which can cause sudden antigenic release from macerated heartworms and fragment emboli. Without prompt worm retrieval, most dogs live only a few days; with worm retrieval, survival rates up to 60% to 71% have been reported, although outcomes are likely highly dependent on the clinician’s expertise.\(^10\) Melarsomine therapy is usually needed to kill the remaining worms.

References

To many, the sight of an engorged tick in a pet’s fur is repulsive and a sure sign the pet needs immediate grooming. But Dr. Brian Herrin, veterinary parasitologist at Kansas State University, likes to remind his clients that ticks are far more than just a hygiene problem. Ticks pose a very real threat to pet health. Luckily, many tick-borne diseases can be diagnosed and treated effectively by veterinarians who stay informed and keep a game plan in mind.

DIFFERENT TICKS, DIFFERENT THREATS

Not all ticks pose the same threat. Different ticks transmit different microbes, and knowing which tick you are dealing with can help chart a path toward diagnosis. Many pet owners associate ticks foremost with Lyme disease, caused by the bacteria *Borrelia burgdorferi*, but the Lone Star tick species does not transmit *B. burgdorferi* strains1. Instead, the Lone Star tick can transmit the pathogens that cause other serious diseases like ehrlichiosis and Rocky Mountain spotted fever2. In humans, it has been linked with the red meat allergy known as alpha-gal syndrome3.

Herrin notes that some tickborne diseases, like ehrlichiosis, can cause clinical signs weeks before antibodies are detectable. In other cases, a positive antibody test may be the result of a past infection that does not require new treatment. A good patient record system will help with accurate diagnosis for each patient.

Other diseases, like Rocky Mountain spotted fever, are urgent in their need for antibiotic treatment. When you notice severe signs like skin sloughing and vasculitis that point toward Rocky Mountain spotted fever, Herrin strongly recommends that you “Treat first, and diagnose later.”

Most of all, says Herrin, veterinarians should be sure to have a game plan for scenarios like the ones above far ahead of time. Even better, he suggests advising clients that reducing pets’ exposure to ticks is key.

Learn more about the Lone Star tick and tick-borne diseases at the TickEncounter Resource Center website (tickencounter.org).

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**Canine Chronic Hepatitis**

Canine chronic hepatitis is a common inflammatory liver disease. Definitive diagnosis requires histopathology; hepatocellular apoptosis or necrosis, mononuclear or mixed inflammatory cell infiltrate, regeneration, and fibrosis are typically observed. Most cases are idiopathic and affect dogs that are middle-aged to senior; females appear to be predisposed. Clinical signs are generally nonspecific and may include waxing and waning GI signs, depression, lethargy, anorexia, weight loss, and polyuria and/or polydipsia. Jaundice, ascites, and hepatic encephalopathy may be present. Increased alanine aminotransferase is seen in >90% of cases; aspartate aminotransferase, alkaline phosphatase, and gamma-glutamyl transferase are generally elevated. Late findings include decreases in albumin, BUN, glucose, and coagulation factors and increases in bile acids, ammonia, and bilirubin. Liver size varies. Ultrasonography is preferred over radiography for imaging; however, a normal appearance using either modality does not exclude diagnosis.

Treatment is mostly supportive and directed at management of clinical signs. Recent data support steroid use for their anti-inflammatory, immune-modulating, and antifibrotic properties. An anti-inflammatory dose tapering to a low alternate-day dose is recommended, although ideal length of treatment is unknown. Most cases of canine chronic hepatitis are not caused by bacteria; thus, antibiotics are typically not warranted. Ursodeoxycholic acid is a choleretic with anti-inflammatory effects and is usually recommended. Antioxidants are likely indicated, given the oxidative damage that occurs with canine chronic hepatitis. Spironolactone is the preferred diuretic but may need to be used in conjunction with furosemide. The antifibrotic agent colchicine is not recommended. A commercial diet for liver disease or other high-quality diet is key; protein should not be restricted unless signs of hepatic encephalopathy are seen.—Bexfield N

**The EPIC Study**

A double-blind study was conducted to determine if pimobendan might delay the onset of congestive heart failure (CHF) or death in dogs with heart disease, specifically in dogs with cardiomegaly secondary to myxomatous mitral valve disease (MMVD) with no discernible evidence of congestive heart disease (ie, Stage B2). Pimobendan was shown to help decrease the likelihood of dogs reaching the primary endpoint (defined as time to onset of CHF, cardiac-related death, or euthanasia) by one-third, with CHF or death due to cardiac complications developing 15 months later in patients receiving pimobendan versus those receiving a placebo.

The clinical implications of this study are important, as dogs appear to benefit from starting therapy before development of clinical signs. Further investigation of patients that may have progressive MMVD, even in the absence of clinical signs, would be worthwhile. If these patients are shown to have cardiomegaly, initiating pimobendan therapy may prolong the period before clinical signs of heart failure develop and prolong the patient’s life.—Boswood A
Arterial Thromboembolism in Cats

Prevalence of arterial thromboembolism (ATE) in cats has reportedly ranged from 0.26% (general practice) to 0.7% (referral practice). ATE is most commonly associated with cardiomyopathy and has high morbidity and mortality rates. Clinical presentation typically involves loss of peripheral pulses in one or more limbs, tissue pallor, lower motor neuron signs, and cool extremities with neuromuscular pain. Although no prospective studies have reported the outcome of first episodes of acute clinical signs of ATE, several retrospective studies suggest euthanasia at presentation is common, and <50% survive to discharge. Hypothermia and 2 or more limbs affected are consistently associated with death or euthanasia before discharge. Cats in congestive heart failure may have shorter survival times following discharge. A retrospective study reported improved survival to 7 days following treatment with aspirin and/or clopidogrel. The author recommends immediate treatment with analgesia and antiplatelet agents. For cats presented with low temperatures and more than one affected limb, euthanasia is recommended.

ATE recurrence is common, but quality of life between episodes can be good. A study of clopidogrel versus aspirin in cats that survived for 3 months following an ATE episode reported that cats receiving clopidogrel (18.75 mg q24h) lived an average of 442 days before recurrence as compared with 192 days for cats receiving aspirin (18.75 mg q72h), which suggests that clopidogrel should be considered the standard of care for cats at high risk for ATE (ie, those with poor atrial function or left atrial enlargement).—Borgeat K

End-of-Life Discussions

Euthanasia, bereavement, and end-of-life discussions are unavoidable in routine veterinary practice. Veterinarians and their teams often struggle through situations that are made more difficult by lack of training. There are 5 common myths surrounding bereavement:

▶ The ability to deal with distressed owners is a fixed trait. This is not a fixed trait and can be learned.
▶ A veterinarian knows an owner’s grief support needs. This should never be presupposed.
▶ The best way to deal with grief is by talking it through. Some owners prefer nonparticipatory forms of grief support.
▶ Grief follows the traditional 5-stages model. Bereavement can be highly individual.
▶ Some pet owners do not grasp the severity of the situation. Denial is a psychologic defense mechanism noted in individuals who are overwhelmed by stress or grief.

Three communication tools can help bridge the communication gap:

▶ Empathizing with the owner’s emotions. This is different from distracting, offering solutions, or changing the subject.
▶ Collaborating with the owner in shared discussion that takes the owner’s concerns into account.
▶ Establishing the owner’s preferences in a personalized, rather than formulaic, way.

Effective, individualized communication is critical to smooth end-of-life discussions.—Hewson C
Weight Loss in Guinea Pigs

Because guinea pigs have a propensity to hide illness, most owners do not notice something is wrong until the disease is advanced and signs such as weight loss or anorexia are obvious. The focus of the evaluation for guinea pigs presented for weight loss should be food intake and fecal elimination. BCS and a dental examination are crucial, and husbandry and diet should also be evaluated. Because guinea pigs tend to hold food in their mouth, an empty mouth should prompt suspicion of anorexia. If anorexia is suspected, dehydration is likely, and fluids should be a part of therapy. Oxygen, rewarming, nutritional support, and pain medication may also be necessary. Pain should be suspected if the patient is lethargic or inappetent or if stool production is decreased.

Managing Resistant Ear Infections

Achieving the following goals will help eliminate resistant ear infections: removing exudate and debris in the ear canal, decreasing inflammation and further production of exudates, killing the organisms, normalizing ear canal epithelium and self-cleaning, and controlling the primary cause. Confirmation of multidrug resistance is typically made based on culture and susceptibility testing. In cases of mixed infection, the sample site chosen is important; the author samples from the most purulent areas, sometimes using a sterile red rubber catheter passed deep into the horizontal canal or middle ear to reach material deeper in the ear. Thorough cleaning is essential to medications reaching the organism and initiating epithelial healing. Thorough cleaning can best be achieved in clinic with the patient under sedation or anesthesia; owners can then be educated on how to maintain cleaning at home.

Topical glucocorticoids are most often used to control inflammation. Topical antiseptics kill organisms by methods other than antibiotics and can work synergistically with them. Acetylcysteine, chlorhexidine, and Tris-EDTA have been shown to be effective against Pseudomonas spp biofilms; these drugs may be the treatment of choice in infections that are resistant to all antibiotics. The author has had success using a sequential combination antiseptic protocol repeated every 3 to 5 days for 10 to 14 days. Synergistic agents (eg, polymyxin mixed with miconazole) can improve efficacy even against resistant organisms. Topical antibiotics (eg, enrofloxacin, marbofloxacin) are often used for resistant bacteria; newer generation human antibiotics (eg, vancomycin, imipenem) are considered rescue drugs.—Griffin C

NSAIDs or partial opioid agonists (eg, buprenorphine) can be used to control pain, and GI stimulants should also be considered. Use of sedation or anesthesia to facilitate a comprehensive dental examination, which should include skull radiographs, should only be considered once the patient is stable, at which point full body radiographs can also be taken. This can help identify many diseases for which the pet was not exhibiting specific signs. Blood work, including obtaining total thyroxine levels, is also important if a guinea pig loses weight, as hyperthyroidism appears to be common in female guinea pigs older than 3 years.—Hedley J
The Role of Nutrition in Managing Dogs with Epilepsy

What happens neurologically when idiopathic epilepsy manifests itself in a dog?

While seizures are the most common neurologic problem we deal with in veterinary medicine, it's surprising how little is actually understood about them as a phenomenon. Seizures occur when excitations — inappropriate discharges of neurons in the frontal matter of the brain — get out of control. The brain cannot suppress that activity and, with generalized seizures, we see the animal acutely lose consciousness and rhythmically convulse. When the seizure stops, the dog is disoriented until the brain resets.

Why do some idiopathic epileptics respond well to anti-seizure medications while others do not?

In cases of drug-resistant epilepsy or refractory epileptics, we suspect a combination of factors. Some may involve how medications are absorbed or metabolized in a patient. In addition, not all seizures arise from the same place in the brain, and not all seizure pathophysiology is the same. Individual genetics also play a role. Intrinsic differences can affect how animals respond to medical therapy.

Today, veterinarians have the option of feeding a therapeutic diet containing medium-chain triglyceride vegetable oil as an adjunct to medical therapy. How do medications and diet work differently in the epileptic patient?

In general, most antiepileptic drugs function by suppressing hyper-excitation in the brain. The goal is to decrease the clinical signs of seizure. Unfortunately, this can result in sedation and other adverse effects. By comparison, diets containing medium-chain triglycerides (MCTs) exert an antiepileptic effect by different mechanisms. Ketogenic diets, through effects on glucose metabolism and neurotransmitter production, may facilitate the body’s own ability to modulate seizure activity. Oxidative stress and inflammation are other factors in epilepsy that are affected by diet. MCTs and their metabolites also have direct antiepileptic properties through modulation of excitatory receptors in the brain. Consuming certain types of fats may have a direct effect on the brain, managing seizure activity in ways current antiepileptic drug therapies do not.

One note of caution: For patients on potassium bromide, veterinarians should pay close attention to dietary chloride levels. Switching an animal to a diet with a higher chloride level than its current diet may decrease bromide levels, which can cause dogs with idiopathic epilepsy to become unregulated.

Freedom from seizures is not possible for every patient. How do you set treatment and seizure management goals for them — and realistic expectations for their owners?

The owner conversation is key. First, let owners know that seizures probably won’t be completely controlled with medications and/or diet, and then talk with them about what an acceptable level of control would be — both for the patient and for the family or the individual owner. If you reach that goal or surpass it, then you achieve an acceptable quality of life, with owners more accepting of the condition and more compliant about therapy.
Can Diet Really Make a Difference in Dogs with Epilepsy?

While prescription veterinary diets are well-recognized for their roles in helping nutritionally manage pets with certain conditions, such as allergies or endocrine disorders, the concept of nutrition as a tool in managing patients with neurologic conditions is a new one for many veterinarians. Understanding how providing an alternative source of energy for the brain can have a therapeutic effect may help veterinarians understand how diet can make a difference for dogs with idiopathic epilepsy.

Change the fuel, change the seizures
Antiepileptic drugs (AEDs) are the gold standard of treatment for canine epilepsy; however, a majority of dogs continue to have seizures in spite of medication. While addressing epilepsy with nutrition is a new concept in the veterinary world, traditional ketogenic diets (which are very high in fat and low in protein and carbohydrates) have been used for decades to help control epileptic seizures in children.

Brain glucose metabolism is disrupted in both people and dogs with epilepsy. One goal of a ketogenic diet is to provide an alternative energy source to the brain, thereby reducing the incidence and severity of epileptic seizures. Similar to fasting, the body fed a traditional ketogenic diet converts long-chain triglyceride fats into ketones (ketosis) as a normal physiological reaction when glucose is unavailable for energy production. However, due to differences in their metabolism, dogs do not readily become ketotic or demonstrate significant improvement in seizure control when fed traditional ketogenic diets. Furthermore, long-term feeding of high-fat, low-protein diets can present significant health concerns for dogs; too much fat may cause pancreatitis, and too little protein can cause loss in lean body mass. An alternative means of inducing ketosis is needed.

Inducing ketone production with a nontraditional ketogenic diet
While traditional ketogenic diets contain high levels of long-chain triglycerides (LCTs) as a source of energy, Purina® Pro Plan® Veterinary Diets NeuroCare contains medium-chain triglycerides (MCTs). Experts believe MCTs may offer anticonvulsant effects by inhibiting the excitatory neurotransmissions that occur during seizures. In addition, MCTs are also more readily digested and absorbed in the bloodstream of the dog — and more readily converted into ketones — than LCTs. When formulated with MCTs, the diet can also contain a lower level of total fat, thus averting the potential health risks associated with high-fat diets and maintaining a complete and balanced nutrient profile.

Experts believe MCTs may offer anticonvulsant effects by inhibiting the excitatory neurotransmissions that occur during seizures.

It’s clear that improved canine epilepsy management is needed. While AEDs remain an integral component of epilepsy management, a complete and balanced diet formulated with MCT vegetable oil can be a useful adjunct to traditional therapy.

References
As a neurologist working in a tertiary referral hospital, I see many cases of poorly managed epilepsy—dogs on multiple medications, all with side effects, that still lack adequate seizure control. I believe we need a more holistic approach that doesn’t rely on drugs alone.

We’re still learning about the role that a diet formulated with medium-chain triglyceride (MCT) vegetable oil can play in the nutritional management of dogs with epilepsy and how nutrients can affect the epileptic brain. It’s important to stipulate that dietary intervention is not designed to replace traditional antiepileptic drugs (AEDs); it’s an adjunct to therapy. Our ultimate goal with epileptic patients is satisfactory control of seizures, and nutrition provides a potential benefit.

Diet provides compliance-friendly approach
I currently recommend Purina® Pro Plan® Veterinary Diets NeuroCare formula for most of my epileptic patients. I explain to owners that they have to feed their pet anyway, so why not try a therapeutic approach that requires no extra work? Because NeuroCare is a complete and balanced diet, I also stress that it will do no harm to their otherwise healthy dogs.

All the clients I work with care deeply about improving their pets’ seizures, but some struggle to comply with treatment. For example, one of my clients has a 9-year-old Maltese that has had seizures for nearly six years. The seizures are fairly well-managed with zonisamide, but compliance is an ongoing problem because of the owner’s hectic work schedule. Since we added dietary intervention four months ago, the seizures due to compliance failure have completely stopped.

Setting expectations for success with dietary intervention
When working with epileptic patients, “success” is an individualized parameter. As veterinarians, we see everything from patients that have seizures less than once a year to patients that are on up to four AEDs and still not well-controlled. I think we’re not setting the diet up for success if we only recommend it to the hardest-to-control dogs (although it’s still worth trying in those cases). We need to learn how diet can help a wider range of patients with different levels of seizure severity over extended periods of time. I ask all of my owners to keep a log of seizure activity, including frequency, length of seizure, behavior prior to the seizure and recovery time. Based on this log, we can determine if we’re getting better control.

While dietary management may seem like an approach that is wholly different than managing with AEDs, the goals are one and the same: improved control of seizures. With minimal risk and much to gain, dietary intervention should be a welcome addition to any canine epileptic management strategy.

Key Takeaways

- Ketogenic diets, through effects on glucose metabolism and neurotransmitter production, may facilitate the body’s own ability to modulate seizure activity.
- Providing an alternative energy source for the brains of canine epileptic patients can help reduce the incidence and severity of epileptic seizures.
- Dietary intervention should be positioned as an adjunct form of therapy in the management of dogs with epilepsy, with the added benefits of being compliance-friendly and safe.

Dietary intervention for canine epilepsy patients offers a safe and convenient way to help patients that need improved seizure control.
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Nutritional Assessment in a Dog with Chronic Enteropathy

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Diet in Disease is a series developed by the WSAVA, the Academy of Veterinary Nutrition Technicians, and Clinician’s Brief.

Gregg K. Takashima, DVM
WSAVA Global Nutrition Committee Series Editor

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Academy of Veterinary Nutrition Technicians

THE CASE
A 4.5-year-old intact female shar-pei was presented for chronic recurrent diarrhea, which was either watery or mucoid, of more than a year’s duration. Vomiting and hyporexia developed the month before presentation and was associated with mild weight loss. The dog was the only pet in the household and was up-to-date on vaccinations and flea/tick preventives; heartworm prevention was unnecessary, as there is no heartworm disease in Sweden or northern Europe, where this dog lives.

Physical Examination
The patient had to be sedated for physical examination due to temperament. BCS was 4/9, with a muscle condition score showing mild muscle atrophy and a dull hair coat. Despite chronic diarrhea, no signs of dehydration were observed.
All other vital parameters were within normal limits. Rectal palpation was painful despite sedation.

**Dietary History**
Several therapeutic diets labeled *intestinal*, including a high-fiber diet, had been tried throughout the last year without clinical improvement. The protein sources of those diets included chicken, egg, and turkey, and the owners sometimes gave treats such as cold cuts and table scraps. Water intake remained the same throughout the year. Metronidazole had been prescribed on several occasions; diarrhea would cease with metronidazole but would recur each time after discontinuation of therapy.

**Diagnostic Results**
Diagnostics included screening for intestinal parasites, CBC, serum chemistry profile, urinalysis, and a GI panel, including trypsin-like immunoreactivity, cobalamin, and folate. No intestinal parasites were detected. Subnormal serum concentrations of folate, cobalamin, and cholesterol were detected (*Table*). CBC and serum chemistry profile were otherwise unremarkable.

Endoscopy of the stomach and small and large intestine were performed. Histopathology of biopsies of the small and large intestine revealed a moderate lymphocytic-plasmacytic enteritis, with a moderate degree of villous atrophy, and moderate lymphocytic-plasmacytic colitis.

**DIAGNOSIS:**
**CHRONIC ENTEROPATHY**

**Treatment & Follow-Up**
The dog’s diet was changed to a commercial lamb and rice novel single-source protein diet, and folate supplementation (5 mg PO q24h) was initiated. Treatment with prednisolone was initiated (initial dose, 1.5 mg/kg q24h) and slowly tapered over 6 months (maintenance dose, 0.2 mg/kg q48h). Several attempts to further taper the dose were made but would cause diarrhea to relapse. Four weekly cobalamin injections (800 µg) were administered according to Texas A&M University Gastrointestinal Laboratory recommendations (see *Suggested Reading*, page 35).

At follow-up 4 weeks after the last cobalamin injection, the dog’s stool had normalized, vomiting had stopped, and appetite returned. Serum cobalamin concentration, cholesterol, and folate had normalized (*Table*). Folate and cobalamin supplementation was stopped and prednisolone was further tapered to 0.5 mg/kg q48h.

At follow-up 3 months later, the dog had experienced 2 recurrences of diarrhea, and serum cobalamin concentrations had decreased to subnormal levels. A new parenteral cobalamin maintenance supplementation protocol was recommended; however, the owners were not interested in a new series of injections but were instead interested in oral cobalamin supplementation.

Oral cobalamin supplementation has been proven to be effective in humans with cobalamin deficiency, and recent studies have confirmed its efficacy in dogs and cats with chronic enteropathy and hypocobalaminemia. It offers an alternative to parenteral supplementation and may suit some owners better, as oral administration may be an easier and more cost-effective alternative to monthly injections, particularly for patients requiring long-term maintenance supplementation. Because oral supplementation in dogs with hypocobalaminemia had not been studied at the time of this case, the potential for failure of this therapy was carefully discussed with the owners before supplementation (1 mg PO q24h) was initiated.

At follow-up 2 months later, serum cobalamin concentration was higher than after the first series of injections and the dog was clinically stable. The dog has been on successful oral cobalamin maintenance therapy for 8 years.

---

**TABLE**

**SUBNORMAL SERUM CHEMISTRY RESULTS**

<table>
<thead>
<tr>
<th>Test</th>
<th>Reference Interval</th>
<th>Baseline After Baseline</th>
<th>9 Weeks After Baseline</th>
<th>5 Months After Baseline</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cobalamin</td>
<td>251-908 ng/L</td>
<td>231 ng/L</td>
<td>705 ng/L</td>
<td>250 ng/L</td>
</tr>
<tr>
<td>Folate</td>
<td>7.7-24.4 µg/L</td>
<td>3.5 µg/L</td>
<td>35 µg/L</td>
<td>25 µg/L</td>
</tr>
<tr>
<td>Cholesterol</td>
<td>158-282 mg/dL</td>
<td>124 mg/dL</td>
<td>189 mg/dL</td>
<td>N/A</td>
</tr>
</tbody>
</table>

Continues ➤
ASK YOURSELF …

**QUESTION 1**
Changing the diet to a novel protein is most likely to be successful in patients with chronic enteropathy if:
A. Albumin is below the normal reference interval
B. The dog is younger than 3 years
C. Large-bowel diarrhea is present
D. The dog weighs less than 22 lb

*Most accurate answer: B*

In a study, dogs with food-responsive chronic enteropathy were significantly younger, weighed more than 22 lb, and had a higher albumin than those with steroid-responsive chronic enteropathy. Differentiating food-responsive from steroid-responsive chronic enteropathy based on clinical signs was not possible.

**QUESTION 2**
Which of the following statements regarding cobalamin is true?
A. All cells in the body require cobalamin.
B. Cobalamin deficiency is a negative prognostic factor in canine chronic enteropathy.
C. Significant weight gain in cats with hypocobalaminemia after supplementation of cobalamin has been observed.
D. All of the above

*Most accurate answer: D*

Cobalamin is required as a cofactor for all DNA and protein synthesis; thus, all cells in the body require cobalamin. In 3 separate studies, cobalamin deficiency has been identified as a negative prognostic factor in dogs with chronic enteropathy, exocrine pancreatic insufficiency, and chronic diarrhea. In addition, cats with cobalamin deficiency experienced significant weight gain after cobalamin supplementation with no other changes in treatment.

**QUESTION 3**
What is the most likely mechanism behind the cobalamin deficiency in this patient?
A. Dietary insufficiency
B. Exocrine pancreatic insufficiency with decreased production of intrinsic factor
C. Chronic enteropathy affecting the cobalamin-intrinsic factor receptors in the ileum
D. Familial cobalamin malabsorption

*Most accurate answer: C*

Congenital cobalamin malabsorption in shar-peis has been described, and these dogs often have GI signs. However, shar-peis with familial cobalamin malabsorption usually have undetectable serum cobalamin at diagnosis.

**QUESTION 4**
In which breeds has congenital cobalamin malabsorption been reported?
A. German shepherd dog, shar-pei, and Staffordshire bull terrier
B. Beagle, giant schnauzer, shar-pei, border collie, and Australian shepherd dog
C. West Highland white terrier, Labrador retriever, Bichon Havanese, and shar-pei
D. Giant schnauzer, border collie, miniature schnauzer, Bedlington terrier, and Basenji

*Most accurate answer: B*

Congenital cobalamin malabsorption has been reported in beagles, giant schnauzers, shar-peis, border collies, and Australian shepherd dogs. German shepherd dogs and Staffordshire bull terriers have a predisposition for hypocobalaminemia, but congenital malabsorption in these breeds has not been proven.

**QUESTION 5**
A middle-aged intact female cocker spaniel with a history of lethargy and reduced appetite of 2 months’ duration has a subnormal serum cobalamin concentration. The dog has been fed a homemade diet due to hyporexia for 6 weeks. How should the cobalamin deficiency be interpreted?
A. Because no diarrhea is present, chronic enteropathy or exocrine pancreatic insufficiency is not the most likely cause of cobalamin deficiency; a dietary imbalance is more likely.
B. The dog could possibly be suffering from chronic enteropathy or exocrine pancreatic insufficiency, as neither condition needs to be associated with diarrhea.
C. Congenital cobalamin malabsorption is the most likely diagnosis.
D. A lipemic serum sample may have caused a false low serum cobalamin concentration.

*Most accurate answer: B*
A lack of diarrhea would not exclude a diagnosis of chronic enteropathy in this dog.6,8 In a study, only 33% of dogs with low serum cobalamin concentrations and chronic enteropathy had diarrhea.9 In another study, 5% of dogs with exocrine pancreatic insufficiency did not have diarrhea.13 Dietary insufficiency is less likely, as there have been no reports on naturally occurring cobalamin deficiency in dogs due to a poor diet. Breed and age further make congenital cobalamin deficiency less likely, and lipemia is not known to interfere with cobalamin analysis.23

References


References continue on page 35.
Important Safety Information for SENTINEL® SPECTRUM® (milbemycin oxime/lufenuron/praziquantel):

Dogs should be tested for heartworm infection prior to use. Mild hypersensitivity reactions have been noted in some dogs carrying a high number of circulating microfilariae. Treatment with fewer than 6 monthly doses after the last exposure to mosquitoes may not provide complete heartworm prevention. For complete product information, refer to the product insert. To obtain a product insert, contact Veterinary Technical Product Support at 1-800-338-3659, or visit us.virbac.com.

Corneal & Conjunctival Cytology

Leah Moody, BSc
Caroline Betbeze, DVM, MS, DACVO
Mississippi State University

An initial ocular examination with basic diagnostic testing (eg, direct and indirect ophthalmoscopy, fluorescein stain, Schirmer tear test, tonometry) is indicated for most patients presented with corneal and/or conjunctival diseases, which are common in domestic animals. Ulcerative keratitis (Figure 1) is particularly common and often resolves in 5 to 7 days with appropriate treatment.1 With complicated corneal ulcers and other progressive or persistent corneal diseases, investigation beyond basic diagnostics may be necessary.

Cytology can have a variety of applications, including:

- Immediate characterization of inflammatory or neoplastic cells or infectious organisms, including cases in which culture and susceptibility testing or PCR may be indicated
- Allowing for direction of empiric therapy while awaiting culture and susceptibility results
- Diagnosing many infectious and inflammatory diseases (eg, ulcerative or fungal keratitis, feline eosinophilic conjunctivitis or keratitis, bacterial conjunctivitis)
- Facilitating prompt and appropriate medical therapy
- Characterizing cells of a proliferative corneal or conjunctival mass
- In patients with corneal ulcers that are progressing in depth or do not respond to initial treatment within 5 to 7 days because a common cause of progression is infection3

Corneal cytology is contraindicated in patients that have severe ulcers with an exposed Descemet’s membrane (ie, descemetocele) or with corneal perforation. Because these patients require surgical treatment, cytology is unnecessary and could cause further injury to the eye.1,3 Conjunctival cytology is rarely contraindicated; however, it may not be of much diagnostic value in patients with conjunctival lesions without an ulcerated or easily exfoliated surface. Cases in which conjunctival cytology may not be diagnostic include conjunctival thickening or nodules (eg, nodular granulomatous episcleritis), certain infectious organisms (eg, mycobacterial, fungal), and some types of neoplasia (eg, squamous cell carcinoma).4

Figure 1. Mucopurulent ocular discharge, hyperemic conjunctiva, and elevation of the nictitating membrane in a dog. Signs of stromal ulcerative keratitis, including an obvious corneal defect and superficial corneal vascularization and cellular infiltration of the axial cornea, are present. Corneal and conjunctival cytology were performed.
In addition, conjunctival cytology, although not contraindicated, has minimal diagnostic utility in corneal ulceration.

Culture and susceptibility testing can be performed in combination with cytology if bacterial or fungal disease is suspected. If both procedures will be performed, culture samples should be taken before cytology collection.3,4

Corneal or conjunctival cytology can be used to identify the number, morphology, and staining characteristics of inflammatory cells and infectious organisms present in the disease. Neoplastic cells may also be identified in the sample.4 Normal corneal samples should include noncornified epithelial cells, few lymphocytes and neutrophils, and rare bacteria; moderate neutrophilic inflammation can be identified in keratitis cases, including ulcerative keratitis (Figure 2).5 Conjunctival samples are normally composed of squamous and columnar epithelial cells, goblet cells, melanin, and occasional bacteria; inflammatory cells can be visualized in conjunctivitis cases (Figure 3). Lymphocytes, neutrophils, monocytes, and plasma cells are rarely observed.

With bacterial disease, neutrophils predominate, may be degenerate or nondegenerate, and may contain intracellular bacteria. Even if bacteria are not visualized, presence of neutrophilic inflammation suggests infection of the cornea.1 Identification of fungal hyphae is suggestive of mycotic disease.3 Presence of eosinophils or mast cells is an abnormal finding in a corneal or conjunctival cytology sample and is suggestive of eosinophilic keratitis or allergic conjunctivitis, respectively.4,6

Successful treatment of corneal and conjunctival disease requires appropriate and immediate therapy, as vision loss can occur rapidly.3 Referral to an ophthalmologist should be considered for patients with complicated corneal ulcers and other progressive ocular diseases.
STEP-BY-STEP CORNEAL & CONJUNCTIVAL CYTOLOGY

WHAT YOU WILL NEED
- Topical anesthetic (eg, proparacaine, tetracaine)
- Glass slides
- Kimura spatula
- #15 scalpel blade (sterile)
- Microapplicator to collect cytology
- Romanowsky-type stain
- Microscope

STEP 1
Using a damp cotton ball or piece of ocular gauze, gently wipe away any ocular surface debris, mucus, or excess ointment. Traditional 4-by-4 gauze may be used to clear periocular debris but should never come in contact with the corneal or conjunctival surface.

STEP 2
Apply 1 to 2 drops of topical anesthetic to the eye, waiting approximately 30 seconds between each drop. Allow approximately 5 minutes for the topical anesthetic to achieve maximal effect; cytology supplies can be collected during this time.

Author Insight
Most patients require only topical anesthesia, and sedation is not usually necessary; however, fractious or excited patients may require chemical sedation to reduce the risk for injury during the procedure. If required, sedation may cause the globe to rotate ventrally, and small-toothed forceps (eg, Bishop-Harmon) will be needed to gently grasp the bulbar conjunctiva to position the globe for cytology collection.

STEP 3
Restrain or have an assistant properly restrain the patient by placing one hand on the back of the head and the other hand under the chin, being careful not to squeeze the muzzle too tightly.

Hold the eyelids open using the thumb and forefinger of the nondominant hand. Rest the dominant hand on the patient’s head. This position will ensure that, if the patient moves, the instruments move with the patient, which can decrease the chance of ocular injury. Be careful not to touch the eyelids with the instrument, as this may contaminate the sample.

Culture and susceptibility testing can be performed in combination with cytology if bacterial or fungal disease is suspected.
STEP 4

Using a microapplicator, Kimura spatula, or the blunt end of a sterile #15 scalpel blade, gently scrape the cornea or conjunctiva 5 to 7 times. The scraping movement can be up to 3 to 5 mm in length, depending on the size of the area of cellular infiltration. For the cornea, sampling the area surrounding the ulceration or any area that has a cellular appearance is recommended (A). For conjunctiva (palpebral or bulbar), any diseased tissue should suffice (B). An ideal sample is collected with minimal patient discomfort and provides an adequate monolayer of intact corneal or conjunctival epithelial cells.

Author Insight

The margin of the ulcerative defect, plaque, or raised inflammatory lesions will have the highest chance of containing causative organisms, inflammatory infiltrate, or diagnostic cells.

STEP 5

Transfer the sample from the collection instrument to a glass slide by gently tapping the instrument or rolling the brush on the slide, being careful not to smear or crush the cells. Preparing several slides from repeat sampling and multiple samples can increase the chances of collecting an adequate diagnostic sample, but the risks of collecting more than one sample must be evaluated based on the severity and depth of the lesion.
STEP 6

Stain the slides using a Romanowsky-type stain (eg, Diff-Quik) and Gram stain. Slides can also be submitted to a diagnostic laboratory that is familiar with veterinary ophthalmologic diseases. The authors suggest evaluating at least one slide in-house to quickly initiate proper patient therapy.

STEP 7

Evaluate a sample under oil immersion using a microscope, ensuring evaluation of multiple high-power fields.

References


Suggested Reading


Diet in Disease

CONTINUED FROM PAGE 29


Suggested Reading

Dosing Chart

<table>
<thead>
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<th>Weight Range (in lb)</th>
<th>Weight Range (in kg)</th>
<th>Number of Tablets to be Administered</th>
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<tr>
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<td>High</td>
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<tr>
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</table>

Warnings:

APOQUEL is not for use in dogs less than 12 months of age (see Animal Safety). APOQUEL is not for use in dogs with serious infections. APOQUEL may increase susceptibility to infection, including demodicosis and exacerbate neoplastic conditions (see Adverse Reactions and Animal Safety).

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 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.

Precautions:

APOQUEL is not for use in breeding dogs, or pregnant or lactating bitches. The use of APOQUEL has not been evaluated in combination with glucocorticoids, cyclosporine, or other systemic immunosuppressive agents.

Dogs receiving APOQUEL should be monitored for the development of infections, including demodicosis, and neoplasia.

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. During the 30-day study, there were no fatalities and no adverse reactions requiring hospital care. Adverse reactions reported (and percent of dogs affected) during Days 0-7 included diarrhea (2.3% APOQUEL, 0.8% placebo); vomiting (2.3% APOQUEL, 1.8% placebo); lethargy (1.8% APOQUEL, 1.4% placebo); anorexia (1.4% APOQUEL, 0% placebo); and polydipsia (1.4% APOQUEL, 0% placebo). In most of these cases, signs spontaneously resolved with continued dosing. Five APOQUEL group dogs were withdrawn from study because of: darkening areas of skin and fur (1 dog); diarrhea (1 dog); fever, lethargy and cystitis (1 dog); an inflamed footpad and vomiting (1 dog); and diarrhea, vomiting, and lethargy (1 dog). Dogs in the APOQUEL group had a slight decrease in mean white blood cell counts (neutrophil, eosinophil, and monocyte counts) that remained within the normal reference range. Mean lymphocyte count for dogs in the APOQUEL group increased at Day 7, but returned to pretreatment levels by study end without a break in APOQUEL administration. Serum cholesterol increased in 25% of APOQUEL group dogs, but mean cholesterol remained within the reference range.

Continuation Field Study

After completing APOQUEL field studies, 239 dogs enrolled in an unmasked (no placebo control), continuation therapy study receiving APOQUEL for an unrestricted period of time. Mean time on this study was 372 days (range 1 to 610 days). Of these 239 dogs, one dog developed demodicosis following 273 days of APOQUEL administration. One dog developed dermal pigmented viral plaques following 266 days of APOQUEL administration. One dog developed a moderately severe bronchopneumonia after 272 days of APOQUEL administration; this infection resolved with antimicrobial treatment and temporary discontinuation of APOQUEL. One dog was euthanized after developing abdominal ascites and pleural effusion of unknown etiology after 450 days of APOQUEL administration. Six dogs were euthanized because of suspected malignant neoplasms, including thoracic metastatic, abdominal metastatic, splenic, frontal sinus, and intracranial neoplasms, and transitional cell carcinoma after 17, 120, 175, 49, 141, and 286 days of APOQUEL administration, respectively. Two dogs each developed a Grade II mast cell tumor after 52 and 91 days of APOQUEL administration, respectively. One dog developed low grade B-cell lymphoma after 392 days of APOQUEL administration. Two dogs each developed an apocrine gland adenocarcinoma (one adrenal, one anal sac) after approximately 210 and 320 days of APOQUEL administration, respectively. One dog developed a low grade oral spindle cell sarcoma after 320 days of APOQUEL administration.

To report suspected adverse events, for technical assistance or to obtain a copy of the MSDS, contact Zoetis Inc. at 1-888-963-8471 or online at http://www.zoetis.com.

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.

Storage Conditions:

APOQUEL should be stored at controlled room temperature between 20° to 25°C (68° to 77°F) with excursions between 15° to 40°C (59° to 104°F).

How Supplied:

APOQUEL tablets contain 3.6 mg, 5.4 mg, or 16 mg of oclacitinib maleate per tablet. Each pinkish tablet is scored and 100 tablets per bottle. Each tablet is scored and marked with AQ and either an S, M, or L that correspond to the different tablet strengths on both sides.

NADA #141-345, Approved by FDA

Made in Italy

Distributed by: Zoetis Inc.
Kalorama, MI 49007
February 2013

428007800AJP
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. APOQUEL has not been tested in dogs receiving some medications including some commonly used to treat skin conditions such as corticosteroids and cyclosporine. 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.

For more information, please see Brief Summary of full Prescribing Information on adjacent page.


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See page 36 for product information summary.
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WMPB 2017: The Well-Managed Practice® Benchmarks Study can help your practice rise above the others.

Well-Managed Practice Benchmarks

HOW DO OTHER PRACTICES BECOME CHAMPIONS?
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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Frequency of Urinary Tract Infection in Dogs Treated with Oclacitinib

William Oldenhoff, DVM, DACVD
LeadER Animal Specialty Hospital
Cooper City, Florida

In the Literature

FROM THE PAGE …

Several drugs used to treat chronic skin diseases in dogs can predispose patients to UTI and bacteriuria. These sequelae have been established in dogs that receive glucocorticoids and cyclosporine,1-3 but it has not been established whether oclacitinib also predisposes dogs to UTI. Approximately 0.5% to 11.3% of allergic dogs treated with oclacitinib have had clinical signs described as cystitis; however, quantitative urine cultures were not performed.4-6 In addition, there were previously no studies that investigated the frequency of UTI or subclinical bacteriuria in dogs receiving oclacitinib in the absence of other predisposing urinary or metabolic concerns. The purpose of this study* was to evaluate the frequency of UTI and subclinical bacteriuria in dogs receiving oclacitinib.

Fifty-five dogs were included in the study. All were at least 24 months of age and had a history of allergic dermatitis and no apparent history of urinary tract disease or predisposition to UTI. Dogs with bacteriuria or positive urine culture and susceptibility results within the previous 24 months were excluded from the study. Steroids, antibiotics, cyclosporine, and lokivetmab were withdrawn for suitable periods before the study and were not allowed during the study. Forty-seven of the 55 dogs received oclacitinib for over 180 days and had follow-up urinalyses and quantitative urine cultures. The remaining dogs were withdrawn early due to need for systemic antimicrobials (n = 6), decreased efficacy of oclacitinib over time (n = 1), or urinary incontinence (n = 1); follow-up cultures were performed earlier in these dogs.

*This study was supported in part by a Zoetis Excellence in Dermatology Research Grant.
None of the study patients developed positive urine cultures during the study. A small number of dogs ($n = 7$) developed microscopic hematuria; however, in 6 of these dogs, this occurrence was suspected to be iatrogenic from cystocentesis. Granular casts, crystalluria, and pyuria were noted in 3 dogs, 9 dogs, and 1 dog, respectively. These developments were deemed not clinically significant because of lack of lower urinary tract signs and negative bacterial cultures.

**TO YOUR PATIENTS**

Key pearls to put into practice:

1. Oclacitinib was not associated with increased risk for UTI or subclinical bacteriuria. Routine urine cultures are not warranted if a dog is receiving only oclacitinib.

2. If a patient receiving oclacitinib has a prior history of UTI or suffers from a condition predisposing to UTI, routine urinalysis with culture is warranted.

3. No novel nonurinary adverse events were reported. Consistent with previous reports, GI events, which were noted in 7.3% of study patients, were the most common adverse event.

**References**


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**Vet Pro 3000 Veterinary Syringe Pump**

The Vet Pro 3000 is designed to give small quantities in precise time and volume.

**Features:**
- Automatic syringe detection: brand, volume, size
- Operated by battery or AC power
- Syringe range: 2ml to 50ml (any brand)

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*Smaller is better*

- Battery or AC use
- Weighs < 1.0lbs and is the size of a soda can
- Adjustable pressure settings
- All types of IV solutions
The challenge
Veterinarians recommend year-round flea and tick protection but...

Do pet owners follow the 12-month recommendation? No.

What do dog owners think?

<table>
<thead>
<tr>
<th>73% agree</th>
<th>62% remember</th>
</tr>
</thead>
<tbody>
<tr>
<td>of owners that their pets should have 12 months of flea and tick protection</td>
<td>of owners their veterinarian’s exact flea &amp; tick recommendation</td>
</tr>
</tbody>
</table>

As much as people love their pets, it can be hard to remember to give flea & tick treatment every month. BRAVECTO can help.

BRAVECTO Chew is well tolerated and palatable, 93% of dogs ate BRAVECTO Chew voluntarily. Available in topical applications for dogs and cats. The Twist’n’Use™ applicator makes administration easy.

Safety you can trust
FDA approved

The average dog owner doses their pet with approximately 4.6 monthly flea treatments in a year.

BRAVECTO kills fleas and prevents flea infestations for 12 weeks. BRAVECTO Chew kills ticks (black-legged tick, American dog tick, and brown dog tick) for 12 weeks and also kills lone star ticks for 12 weeks. BRAVECTO Topical Solution for Dogs kills ticks (black-legged tick) for 12 weeks and American dog ticks for 8 weeks.

IMPORTANT SAFETY INFORMATION: BRAVECTO has not been shown to be effective for 12-weeks’ duration in puppies or kittens less than 6 months of age. BRAVECTO Chew: The most common adverse reactions recorded in clinical trials were vomiting, decreased appetite, diarrhea, lethargy, polydipsia, and flatulence. BRAVECTO is not effective against lone star ticks beyond 8 weeks of dosing. BRAVECTO Topical Solution for Dogs: The most common adverse reactions recorded in clinical trials were vomiting, hair loss, diarrhea, lethargy, decreased appetite, and moist dermatitis/rash. BRAVECTO is not effective against lone star ticks beyond 8 weeks of dosing. For topical use only. Avoid oral ingestion. Seizures have been reported in dogs receiving fluralaner, even in dogs without a history of seizures.

BRAVECTO Topical Solution for Cats kills ticks (black-legged tick) for 12 weeks and American dog ticks for 8 weeks. BRAVECTO Topical Solution for Cats has not been established in breeding, pregnant and lactating cats. Use with caution in cats with a history of neurologic abnormalities. Neurologic abnormalities have been reported in cats receiving BRAVECTO, even in cats without a history of neurologic abnormalities.
Improve compliance
Recommend BRAVECTO®

Only BRAVECTO delivers up to 12 weeks* of flea and tick protection for dogs and cats with one convenient chew or topical dose.

Fewer doses per year help improve adherence — and reduce the chance of pet owners forgetting and missing a dose

- Fewer potential gaps in protection4,7
- More convenient for pet owners
- Available by prescription only

Easy to dose.

BRAVECTO Chew is well tolerated and palatable

93% of dogs ate BRAVECTO Chew voluntarily4,8

Available in topical applications for dogs and cats

The Twist’n’Use™ applicator makes administration easy

Ask your Merck Animal Health Rep about BRAVECTO or visit Bravectovets.com

BRAVECTO® (FLURALANER) CHEW OR TOPICAL SOLUTION

Safety you can trust
FDA approved
BRAVECTO
(Furalaner topical solution) for Dogs

BRIEF SUMMARY (For full prescribing information, see package insert)

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

Indications: Bravecto kills adult fleas and is indicated for the treatment and prevention of flea infestations (Ctenocephalides felis) and the treatment and control of tick infestations (Dodecascriptus (black-legged tick), Dermacentor variabilis (American dog tick), and Amblyomma americanum (American brown dog tick)) for 12 weeks in dogs and puppies 6 months of age and older, and weighing 4.4 pounds or greater.

Bravecto is also indicated for the treatment and control of A,blyomma anum (one star tick) infestations for 8 weeks in dogs and puppies 6 months of age and older, and weighing 4.4 pounds or greater.

Contraindications: There are no known contraindications for the use of the product.

WARNINGS: Not for human use. Keep this and all drugs out of the reach of children. Do not contact or allow children to contact the application site until dry. Keep the product in the original packaging until use in order to prevent children from getting direct access to the product. Do not eat, drink or smoke while handling the product. Wash hands thoroughly with soap and water immediately after use of the product.

Precautions: Bravecto has not been shown to be effective for 12-weeks duration in puppies less than 6 months of age. Bravecto is not effective against A,blyomma anum ticks beyond 8 weeks after dosing.

Adverse Reactions: In a well-controlled U.S. field study, which included 294 dogs (224 dogs were administered Bravecto every 12 weeks and 70 dogs were administered an oral active control every 4 weeks and were provided with a tick collar), there were no serious adverse reactions. All potential adverse reactions were recorded in dogs treated with Bravecto over a 128-day period and in dogs treated with the active control over an 84-day period. The most frequently reported adverse reaction in dogs in the Bravecto and active control groups was vomiting.

<table>
<thead>
<tr>
<th>Percentage of Dogs with Adverse Reactions in the Field Study</th>
<th>Adverse Reaction (AR)</th>
<th>Bravecto Group: Percentage of Dogs with the AR During the 182-Day Study (n=224 dogs)</th>
<th>Active Control Group: Percentage of Dogs with the AR During the 84-Day Study (n=70 dogs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vomiting</td>
<td>7.1%</td>
<td>14.3%</td>
<td></td>
</tr>
<tr>
<td>Decreased Appetite</td>
<td>6.7%</td>
<td>0.0%</td>
<td></td>
</tr>
<tr>
<td>Diarrhea</td>
<td>4.9</td>
<td>2.9</td>
<td></td>
</tr>
<tr>
<td>Lethargy</td>
<td>5.4</td>
<td>7.1</td>
<td></td>
</tr>
<tr>
<td>Polydipsia</td>
<td>1.8</td>
<td>4.3</td>
<td></td>
</tr>
<tr>
<td>Fatulence</td>
<td>1.3</td>
<td>0.0</td>
<td></td>
</tr>
</tbody>
</table>

In a well-controlled laboratory dose confirmation study, one dog developed edema and hyperemia of the upper lips within one hour of receiving Bravecto. The edema improved progressively through the day and had resolved without medical intervention by the next morning.

For technical assistance or to report a suspected adverse drug reaction, contact Merck Animal Health at 1-800-224-5318. Additional information can be found at www.bravecto.com. 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.

How Supplied: Bravecto is available in five strengths (112.5, 250, 500, 1000, and 1400 mg furalaner per chew). Each chew is packaged individually into aluminum foil blister packs sealed with a peelable paper backed foil lid stock. Product may be packaged in 1, 2, or 4 chews per package.

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NADA 141-459, Approved by FDA

BRAVECTO
(Furalaner topical solution) for Cats

BRIEF SUMMARY (For full prescribing information, see package insert)

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

Indications: Bravecto kills adult fleas and is indicated for the treatment and prevention of flea infestations (Ctenocephalides felis) and the treatment and control of louse infestations (Dodecascriptus (black-legged tick), Dermanvernix variabilis (American dog tick), and Amblyomma americanum (American brown dog tick)) for 12 weeks in cats and kittens 6 months of age and older, and weighing 2.6 pounds or greater.

Bravecto is also indicated for the treatment and control of Demodex canis infestations for 8 weeks in cats and kittens 6 months of age and older, and weighing 2.6 pounds or greater.

Contraindications: There are no known contraindications for the use of the product.

WARNINGS: Not for human use. Keep this and all drugs out of the reach of children. Do not contact or allow children to contact the application site until dry. Keep the product in the original packaging until use to prevent children from getting direct access to the product. Do not eat, drink or smoke while handling the product. Avoid contact with skin and eyes. If contact with eyes occurs, then flush eyes slowly and gently with water. Wash hands and contact skin thoroughly with soap and water immediately after use of the product.

Precautions: For topical use only. Avoid oral ingestion. Use with caution in cats with a history of neurologic abnormalities. Neurologic abnormalities have been reported in cats receiving Furalaner, even in cats without a history of neurologic abnormalities. Bravecto has not been shown to be effective for 12-weeks duration in kittens less than 6 months of age. Bravecto is not effective against Amblyomma anum ticks beyond 8 weeks after dosing.

Adverse Reactions: In a well-controlled U.S. field study, which included a total of 165 households (159 households were administered Bravecto with no prior history of seizures) and 321 treated dogs (221 with furalaner and 100 with a topical active control), there were no serious adverse reactions.

Percentage of Cats with Adverse Reactions (AR) in the Field Study

<table>
<thead>
<tr>
<th>Percentage of Cats with Adverse Reactions (AR) in the Field Study</th>
<th>Adverse Reaction (AR)</th>
<th>Bravecto Group: Percent of Cats with the AR During the 105-Day Study (n=224 cats)</th>
<th>Control Group: Percent of Cats with the AR During the 84-Day Study (n=87 cats)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vomiting</td>
<td>5.4%</td>
<td>1.1%</td>
<td></td>
</tr>
<tr>
<td>Diarrhea</td>
<td>4.9%</td>
<td>1.1%</td>
<td></td>
</tr>
<tr>
<td>Alopecia</td>
<td>4.9%</td>
<td>0.0%</td>
<td></td>
</tr>
<tr>
<td>Increased Appetite</td>
<td>3.1%</td>
<td>2.3%</td>
<td></td>
</tr>
<tr>
<td>Sclera/Uvea Lesions</td>
<td>3.1%</td>
<td>3.4%</td>
<td></td>
</tr>
</tbody>
</table>

In the field study, two cats treated with furalaner topical solution experienced ataxia. One cat became ataxic with a right tilt to the side after 36 days and improved within one week of starting antibiotics. The ataxia and right tilt recurred 82 days after administration of the first dose. The cat recovered with antibiotics and was retested with furalaner topical solution 92 days after administration of the first dose, with no further abnormalities during the study. A second cat became ataxic 15 days after receiving its first dose and recovered the next day. The cat was retested with furalaner topical solution 82 days after administration of the first dose, with no further abnormalities during the study.

In a European field study, two cats from the same household experienced tremors, lethargy, and anorexia within one day of administration. The signs resolved in both cats within 48-72 hours.

In a European field study, there were three reports of facial dermatitis in humans after close contact with the application site which occurred within 4 days of application.

For technical assistance or to report a suspected adverse drug reaction, or to obtain a copy of the Safety Data Sheet (SDS), contact Merck Animal Health at 1-800-224-5318. Additional information can be found at www.bravecto.com. 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.

How Supplied: Bravecto is available in three strengths for use in cats (112.5, 250, and 500 mg furalaner per tube). Each tube is packaged individually in a pouc. Product may be supplied in 1 or 2 tubes per carton.

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NADA 141-459, Approved by FDA

Flavored chews for dogs.

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155454 R1

NADA 141-426, Approved by FDA
Prognostic Markers in Feline Hepatic Lipidosis

Faith I. Buckley, DVM, DACVIM (SAIM)
Bulger Veterinary Hospital
North Andover, Massachusetts

In the Literature

FROM THE PAGE …

Hepatic lipidosis is a common liver disease in cats that is associated with high morbidity and mortality. Aggressive therapy to reverse the catabolic state and hepatic failure resulting from prolonged anorexia is required.1-3 Anorexia may be precipitated by comorbidities (eg, GI disease, pancreatitis, cholangiohepatitis) or may be primary (ie, decreased food intake in a healthy animal due to stress-related environmental events or food refusal).

In this study, clinical and laboratory parameters were evaluated in 71 cats diagnosed with hepatic lipidosis (based on liver cytology or histopathology) to identify those associated with mortality. Cats with hepatic lipidosis were older than those in the control group, and female cats were overrepresented.1-3 Primary idiopathic hepatic lipidosis resulting from stress-related anorexia accounted for 20% of cases, which emphasizes the importance of educating pet owners about prevention.

Severity of hepatobiliary enzyme elevation was not associated with survival, whereas markers of hepatic dysfunction (eg, hypoalbuminemia, hyperbilirubinemia, hypcholesterolemia, hyperammonemia) had greater impact on survival, regardless of whether they were observed at time of presentation or developed during hospitalization. Hypokalemia, hyponatremia, hypochloremia, and hypophosphatemia were associated with death, although these are correctable and may be indicative of unbalanced fluid therapy and/or overhydration.2

Recovery from hepatic lipidosis has been best predicted by a 50% progressive decrease in bilirubin concentration during the first 7 to 10 days of reinstitution of nutrition.2 Overall mortality in this study was 38%.

… TO YOUR PATIENTS

Key pearls to put into practice:

1. Aggressive therapy is often necessary to increase the chance of patient survival and complete recovery; early reintroduction of nutrition remains vital.
2. Close monitoring of electrolytes (ie, sodium, chloride, potassium, phosphorous) during hospitalization and aggressive correction of abnormalities are recommended to limit mortality.
3. The underlying cause of the anorexic event leading to hepatic lipidosis is not a prognostic factor.
4. Cats of all BCSs—not just obese cats—can develop hepatic lipidosis.

References
# New York Vet Clinical Theaters

## November 8-9, 2018

### Thursday, November 8, 2018

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<th>Time</th>
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<th>Clinical Theaters 2</th>
<th>Clinical Theaters 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>9:00 AM - 9:50 AM</td>
<td>DENTAL EMERGENCIES &amp; COMPLICATIONS Mark Smith, VMD, DACVS, DAVDC</td>
<td>TRACHEAL WASHES: NO REFERRAL REQUIRED Julie Allen, BVMS, MS, MRCVS, DACVIM (SAIM)</td>
<td>CONTROLLED SUBSTANCE PRESCRIBING, REPORTING, RECORD KEEPING, &amp; DIVERSION PREVENTION: PART 1 Lisa Penny, RPh, FSVHP, FACVP</td>
</tr>
<tr>
<td>10:25 AM - 11:15 AM</td>
<td>IS FAMOTIDINE EVER INDICATED? AN UPDATE ON ACID SUPPRESSION Katie Tolbert, DVM, PhD, DACVIM</td>
<td>DON'T FORGET YOUR CANINE COGNITIVE DYSFUNCTION PATIENTS—PRACTICAL OPTIONS FOR MEDICAL CARE &amp; ENVIRONMENTAL ENRICHMENT Lisa Radosta, DVM, DACVB</td>
<td>CONTROLLED SUBSTANCE PRESCRIBING, REPORTING, RECORD KEEPING, &amp; DIVERSION PREVENTION: PART 2 Lisa Penny, RPh, FSVHP, FACVP</td>
</tr>
<tr>
<td>11:45 AM - 12:35 PM</td>
<td>HUNGRY FOR KNOWLEDGE ABOUT APPETITE STIMULANTS? Lauren Trepanier, DVM, PhD, DACVIM (SAIM)</td>
<td>YOU MUST ANESTHETIZE A PATIENT WITH KIDNEY DISEASE. NOW WHAT? Khursheed Mama, DVM, DACVAA</td>
<td>A PRACTICAL APPROACH TO BLINDNESS David Maggs, BVSc (Hons), DACVO</td>
</tr>
<tr>
<td>2:05 PM - 2:55 PM</td>
<td>WHAT'S THE NORM? DIAGNOSTIC BREED VARIANTS THAT ARE &quot;NORMAL&quot; Julie Allen, BVMS, MS, MRCVS, DACVIM (SAIM)</td>
<td>THE CLOUDY LENS: CATARACTS, NUCLEAR SCLEROSIS, OR MORE? David Maggs, BVSc (Hons), DACVO</td>
<td>DIAGNOSING AND MANAGING RESORPTIVE LESIONS IN DOGS &amp; CATS Mark Smith, VMD, DACVS, DAVDC</td>
</tr>
<tr>
<td>3:10 PM - 4:00 PM</td>
<td>PHOBIAS, PHARMACOLOGY, &amp; PSYCHOTHERAPY: CANINE ANXIETY SURVIVAL GUIDE Lisa Radosta, DVM, DACVB</td>
<td>FELINE PAIN UPDATE: OSTEOARTHRITIS &amp; BEYOND Susan Little, DVM, DABVP (Feline)</td>
<td>PROBIOTICS/PREBIOTICS/FEecal TRANSPLANTATION: DO THEY HAVE A PLACE IN SMALL ANIMAL MEDICINE? Katie Tolbert, DVM, PhD, DACVIM</td>
</tr>
<tr>
<td>4:15 PM - 5:05 PM</td>
<td>AN EPIC REVIEW OF INJECTABLE ANESTHESIA: TIPS, TRICKS, &amp; PROTOCOLS TO LIVE BY Khursheed Mama, DVM, DACVAA</td>
<td>OPENING PANDORA'S BOX: WHAT YOU NEED TO KNOW ABOUT PANDORA SYNDROME Elizabeth Colleran, DVM, MS, DABVP (Feline)</td>
<td>ARTHROCENTESIS FOR ANYONE: HOW TO DO IT, WHEN TO USE IT, &amp; HOW TO INTERPRET IT JULIE ALLEN, BVMS, MS, MRCVS, DACVIM (SAIM)</td>
</tr>
<tr>
<td>5:10 PM - 6:00 PM</td>
<td>EMERGING CANNABIS TOXICITY: CBD OIL, BAKED GOODS, MARIJUANA, &amp; MORE Marie Holowaychuk, DVM, DACVECC</td>
<td>CLINICAL &amp; SUBCLINICAL TICK-BORNE DISEASE: WHEN TO TREAT AND WHERE’S THE EVIDENCE? Mary Anna Labato, DVM, DACVIM (SAIM)</td>
<td>PROGRAM CURATED BY THE VETERINARY TEAM BEHIND CLINICIAN'S BRIEF</td>
</tr>
</tbody>
</table>

**Program Subject to Change**
**NEW YORK VET CLINICAL THEATERS**

**PROTOCOLS TO LIVE BY**
Katie Tolbert, DVM, PhD, DACVIM

**UPDATE ON ACID SUPPRESSION**
Is Famotidine Ever Indicated?

**VMD, DACVS, DAVDC**
Mark Smith

**COMPLICATIONS DENTAL EMERGENCIES &**

**DVM, DACVB**
DACVIM (SAIM)
Julie Allen, BVM&S, MS, MRCVS, BVM&S, MS, MRCVS, BVetMed (Hons), DECVIM-CA, DACVIM, MRCVS

**WHAT'S THE NORM? DIAGNOSTIC BREED APPETITE STIMULANTS?**
Marie Holowaychuk, DVM, DACVECC

**MARIJUANA, & MORE**

**EMERGING CANNABIS TOXICITY:**
Lisa Radosta, DVM, DACVB

**WHERE'S THE EVIDENCE? WHEN TO TREAT AND**

**OPENING PANDORA'S BOX: ENVIRONMENTAL ENRICHMENT**

**DACVIM (SAIM)**
Mary Anna Labato, DVM, DACVB

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Patellar Luxation & Cranial Cruciate Ligament Disease

Jason Bleedorn, DVM, DACVS
University of Wisconsin–Madison

In the Literature

FROM THE PAGE …

Cranial cruciate ligament (CCL) rupture occurs commonly in combination with medial patellar luxation (MPL) in dogs, with higher MPL grades increasing the risk for CCL rupture. Despite many surgical option combinations and studies describing these techniques, little (if any) objective clinical trial data comparing various surgical approaches exist.

This multi-institutional retrospective study compared clinical outcomes and complications following tibial tuberosity transposition-advancement (TTTA) against extracapsular stabilization and tibial tuberosity transposition (ECS+TTT) for correction of CCL rupture and/or MPL instability in dogs. A total of 72 stifles were evaluated in 66 dogs; over a 10-year period, 40 were stabilized using TTTA and 32 using ECS+TTT. Overall, complications occurred 2.7 times more often with ECS+TTT (46.9%) as compared with TTTA (17.5%). Major complications occurred only in the ECS+TTT group (5/32) and included premature implant failure, reluxation, and infection necessitating surgical revision or implant removal. Minor complications that occurred were predominantly wound-related. Dogs of greater weight were more likely to have TTTA performed over ECS+TTT; however, greater weights did not correspond with higher complication rates. Reluxation rate was

Surgical stabilization using TTTA may be a safer approach for correction of concomitant CCL rupture and MPL as compared with ECS+TTT.
similar in both groups (TTTA, 20%; ECS+TTT, 15.6%). The performance of a femoral sulcoplasty also reduced risk for a poor outcome.

The results of this study suggest that surgical stabilization using TTTA may be a safer approach for correction of concomitant CCL rupture and MPL as compared with ECS+TTT. The overall complication rates in both groups were higher than previously reported for each individual procedure alone; this higher rate could possibly be related to case contributions from many surgeons with varying experience levels. Despite the high rate of complications, the outcome was good to excellent in most cases.

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**TO YOUR PATIENTS**

Key pearls to put into practice:

1. Thorough examination for CCL instability in dogs with MPL is important.
2. Surgical stabilization of concurrent CCL and MPL may be associated with a higher complication rate than either procedure individually.
3. Surgeons already proficient in tibial tuberosity advancement (TTA) may consider a combination of this approach with tibial tuberosity transposition (TTT) to be a superior option for concurrent MPL/CCL rupture; however, this combination (ie, TTTA) should only be reserved for those surgeons who have mastered the TTA technique.

**Reference**

Biomarkers & Slow-Kill Protocol for Heartworm Disease

Amara Estrada, DVM, DACVIM (Cardiology)
University of Florida

In the Literature

FROM THE PAGE …

The therapeutic protocol for treatment of canine heartworm disease recommended by the American Heartworm Society consists of 3 intramuscular injections of melarsomine, with steroid and antithrombotic agents as needed. This regimen has long been the basis for heartworm adulticidal therapies and is safe and effective when used as directed; however, melarsomine periodically has limited availability and is unavailable in many countries. Thus, many slow-kill protocols have been circulated as possible alternatives when melarsomine is unattainable. Critics of these techniques have argued that dogs with high worm burdens would be at greater risk for complications (eg, pulmonary and systemic inflammation, pulmonary thromboembolic events, myocardial ischemia) related to their worm burden. In addition, it is assumed that dogs with a higher worm burden would be more resistant to effective long-term elimination of disease with a slow-kill protocol.

This study looked at a small population of shelter dogs with heartworm disease and assessed cardiac, hemostatic, and inflammatory biomarkers to try to correlate worm burden with changes in biomarkers during a course of a slow-kill protocol. The slow-kill protocol consisted of 4-week administration of doxycycline (10 mg/kg PO q24h) and 6-month administration of ivermectin (6-10 µg/kg PO every 15 days). All dogs survived and tested negative for microfilariae at the 6-month recheck; however, 4 of the 12 treated dogs that had higher worm burdens were still positive for heartworm antigen at the end of treatment, and 3 of the 4 remained positive at the end of the study. All biomarkers tested were initially higher (and pathologically abnormal) in dogs with higher worm burdens. Dogs with higher worm burdens and clinical signs had higher elevations in all biomarkers before therapy, and these elevations decreased during the course of therapy.

… TO YOUR PATIENTS

Key pearls to put into practice:

1. The slow-kill method does not appear to be an effective protocol for managing heartworm disease, particularly in dogs with higher worm burdens; current American Heartworm Society recommendations for adulticide therapy should continue to be followed.

2. Use of biomarkers as a tool to provide additional or supplementary prognostic information when other tools (eg, echocardiography) are not available may be helpful in identifying dogs with higher worm burdens. Clinical signs and radiographic or echocardiographic evaluation remain the gold standard for such investigation.

3. The slow-kill method appears to reduce biomarkers associated with cardiac, systemic, and pulmonary inflammation but not such that it would be recommended as initial therapy in an attempt to reduce possible complications from adulticide therapy.
Research Note: Urinary Effects of Allopurinol in Dogs with Leishmaniasis

Allopurinol is a parasitistatic drug used for long time periods (≥6 months) in the treatment of canine leishmaniasis. Reports indicate that prolonged allopurinol therapy is associated with xanthinuria and xanthine urolithiasis. The purpose of this retrospective study was to describe the most common urinary adverse effects associated with allopurinol use in the treatment of canine leishmaniasis. Medical records of 320 dogs diagnosed with leishmaniasis in endemic areas were reviewed. All dogs received anti-Leishmania spp treatment with meglumine antimoniate once or twice daily for 4 weeks and allopurinol twice daily. Median duration of treatment with allopurinol until diagnosis of xanthinuria, renal mineralization, and/or urolithiasis was one year (range, 3 weeks to 9 years). Forty-two dogs (13.1%) developed adverse urinary effects defined by presence of xanthinuria: 9 of the 42 dogs (21.4%) developed xanthinuria alone; 9 (21.4%) had xanthinuria with urolithiasis; 11 (26.2%) showed xanthinuria with renal mineralization; and 13 (31%) developed xanthinuria, renal mineralization, and urolithiasis. Clinical signs associated with the urinary tract (eg, urinary obstruction, dysuria) developed in 19 of the 42 dogs (45.2%). No other adverse effects associated with allopurinol were reported. The authors concluded that xanthine urolithiasis and renal mineralization can occur in dogs secondary to allopurinol therapy, warranting monitoring for development of urinary adverse effects from the beginning of treatment.

Source
Subcutaneous Administration of Synthetic B-Type Natriuretic Peptide in Dogs

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Buffalo Grove, Illinois

In the Literature

Several natriuretic peptides have been identified, and their use as adjunctive heart failure therapy is under investigation. B-type natriuretic peptide (BNP) has been studied most extensively in cats and dogs. It is normally released by atrial tissue; in heart disease, it is also released from ventricular tissue.¹ BNP binds to natriuretic peptide receptors, which results in activation of the secondary messenger molecule cGMP. Ultimately, BNP blocks the harmful effects of the renin-angiotensin-aldosterone system, inducing diuresis and natriuresis; these effects become blunted with advanced heart disease.² Administration of BNP in humans has been shown to be beneficial in acute congestive heart failure therapy.³

The primary goal of this study* was to evaluate the feasibility, tolerance, and safety of subcutaneous administration of synthetic canine BNP (syncBNP) in...
healthy dogs and dogs with mild heart disease. Pilot data were also collected for markers of biologic activity, particularly neurohormonal activity.

Six client-owned dogs were divided into 2 groups. The first group was given 2.5 µg/kg SC syncBNP followed by 5 µg/kg SC syncBNP 2 hours later. After no major adverse effects were observed, the second group was given 5 µg/kg SC syncBNP followed by 10 µg/kg SC syncBNP. Blood and urine samples were obtained from all dogs at baseline, 45, and 120 minutes after administration of the 5 µg/kg dose to evaluate for natriuresis, neurohormonal activity, and effects on renal function.

Overall, syncBNP was well tolerated in all patients. There was a significant increase in plasma cGMP concentration at both 45 and 120 minutes following subcutaneous administration of 5 µg/kg syncBNP, which suggests active binding of syncBNP to natriuretic peptide receptors. There was no significant change in any of the other blood and urine variables assessed, although there was a trend toward decreased plasma renin activity and increased fractional sodium excretion.

… TO YOUR PATIENTS

Key pearls to put into practice:

1. Natriuretic peptides are released in higher concentrations in patients with heart disease and are beneficial for antagonizing the harmful effects of renin-angiotensin-aldosterone system while promoting diuresis and natriuresis.

2. Effects of natriuretic peptides become blunted with chronicity and progression of heart disease.

3. Administration of syncBNP may be a promising therapy for congestive heart failure; it has been shown to be beneficial in humans with congestive heart failure and to be well tolerated in healthy dogs and dogs with mild heart disease.

References


Administration of syncBNP may be a promising therapy for congestive heart failure.
In animals with fever, the hypothalamic set point is elevated, typically by infection, inflammation, neoplasia, or drug administration. This retrospective study of 106 cats with persistent fever (≥102.6°F) evaluated common causes and effective treatment options for feline pyrexia.

Unlike previous studies that have shown immune-mediated disease to be a common cause of pyrexia in dogs, this study showed immune-mediated disease to be an uncommon cause in cats (5.7%); infectious disease was the most common cause (38.7%), followed by inflammatory conditions (17.9%) and neoplasia (12.3%). The most common infectious disease identified was feline infectious peritonitis (20.8%); others included cellulitis and/or otitis media, pyothorax, pyelonephritis and/or UTI, *Mycoplasma felis* infection, cholangiohepatitis, and abscess. The average length of hospitalization was 5 days. Survival outcome (67%) was comparable to that in a canine study (70%). These results emphasize the importance of infectious disease over immune-mediated disease as a cause of pyrexia in cats.
**Research Note: Babesiosis Vaccine Antigens**

Existing commercial vaccines against babesiosis contain soluble parasite antigens (SPAs) from in vitro culture supernatants of *Babesia canis*. This study identified and characterized the specific antigen in SPA serum that confers immunity in vaccinated dogs (ie, canine *Babesia* antigen [CBA]) and sequenced the gene that encodes it. The gene was then cloned and expressed in *Escherichia coli*. The recombinant CBA (rCBA) was found to protect against challenge infection in rCBA-vaccinated dogs. The rCBA antigen could replace existing SPA vaccines, thereby eliminating the need for dog blood and serum for production of vaccine.

**Source**

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**Research Note: Signalment & Heat Stress in Dogs**

Dogs rely on an increased respiratory rate to initiate the necessary cooling when overheated; as such, brachycephalic dogs are particularly susceptible to hyperthermia when heat stressed. This study demonstrated that brachycephalic dogs have a decreased capacity for thermoregulation but that BCS appears to be a more important factor than breed. When considering heat stress situations, including air travel, both factors should be taken into account.

**Source**

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**The rCBA antigen could replace existing SPA vaccines, thereby eliminating the need for dog blood and serum for production of vaccine.**
The initial recommended ProZinc dose is 0.1 – 0.3 IU insulin/pound of body weight dose from the vial. Using a U-40 insulin syringe, the injection should be administered subcutaneously on the back of the neck or on the side of the cat. Always provide the Cat Owner Information Sheet with each prescription. The initial recommended ProZinc dose is 0.1 – 0.3 IU insulin/pound of body weight (0.2 – 0.7 IU/kg) every 12 hours. The dose should be given concurrently with or right after a meal. The veterinarian should re-evaluate the cat at appropriate intervals and adjust the dose based on both clinical signs and glucose nadir until adequate glycemic control has been attained. In the effectiveness field study, glycemic control was considered adequate if the glucose nadir from a 9-hour blood glucose curve was between 80 and 150 mg/dL and clinical signs of hyperglycemia such as polyuria, polydipsia, and weight loss were improved. Further adjustments in the dosage may be necessary with changes in the cat’s diet, body weight, or concomitant medication, or if the cat develops concurrent infection, inflammation, neoplasia, or an additional endocrine or other medical disorder.

Contraindications: ProZinc insulin is contraindicated in cats sensitive to protamine zinc recombinant human insulin or any other ingredients in the ProZinc product. ProZinc insulin is contraindicated during episodes of hypoglycemia.

Warnings: User Safety: For use in cats only. Keep out of the reach of children. Avoid contact with eyes. In case of contact, immediately flush eyes with running water for at least 15 minutes. Accidental injection may cause hypoglycemia. In case of accidental injection, seek medical attention immediately. Exposure to product may induce a local or systemic allergic reaction in sensitized individuals.

Animal Safety: Owners should be advised to observe for signs of hypoglycemia (see Cat Owner Information Sheet). Use of this product, even at established doses, has been associated with hypoglycemia. An animal with signs of hypoglycemia should be treated immediately. Glucose should be given orally or intravenously as dictated by clinical signs. Insulin should be temporarily withheld and, if indicated, the dosage adjusted. Any change in insulin should be made cautiously and only under a veterinarian’s supervision. Changes in insulin strength, manufacturer, type, species (human, animal) or method of manufacture (rDNA versus animal-source insulin) may result in the need for a change in dosage. Appropriate diagnostic tests should be performed to rule out other endocrinopathies in diabetic cats that are difficult to regulate.

Precautions: Animals presenting with severe ketoadiposis, anorexia, lethargy, and/or vomiting should be stabilized with short-acting insulin and appropriate supportive therapy until their condition is stabilized. As with all insulin products, careful patient monitoring for hypoglycemia and hyperglycemia is essential to attain and maintain adequate glycemic control and to prevent associated complications. Overdosing can result in profound hypoglycemia and death. Progestogens, certain endocrinopathies and glucocorticoids can have an antagonistic effect on insulin activity, Progestogen and glucocorticoid use should be avoided.

Reproductive Safety: The safety and effectiveness of ProZinc insulin in breeding, pregnant, and lactating cats has not been evaluated. Use in Kittens: The safety and effectiveness of ProZinc insulin in kittens has not been evaluated. Adverse Reactions: Effectiveness Field Study In a 45-day effectiveness field study, 176 cats received ProZinc insulin. Hypoglycemia (defined as a blood glucose value of < 50 mg/dL) occurred in 71 of the cats at various times throughout the study. Clinical signs of hypoglycemia were generally mild in nature (described as lethargic, sluggish, weak, trembling, uncoordinated, groggy, glassy-eyed or dazed). In 17 cases, the veterinarian provided oral glucose supplementation for treatment. Most cases were not associated with clinical signs and received no treatment. One cat had a serious hypoglycemic event associated with stupor, lateral recumbency, hypothermia and seizures. All cases of hypoglycemia resolved with appropriate therapy and if needed, a dose reduction. Cats had injection site reactions which were described as either small, punctate, red lesions; lesions on neck; or palpable subcutaneous thickening. All injection site reactions resolved without cessation of therapy. Four cats developed diabetic neuropathy during the study as evidenced by plantigrade stance. Three cats entered the study with plantigrade stance, one of which resolved by Day 45. Four cats were diagnosed with diabetic ketoacidosis during the study. Two were euthanized due to poor response to treatment. Five other cats were euthanized during the study, one of which had hypoglycemia. Four cats had received ProZinc insulin for less than a week and were euthanized due to worsening concurrent medical conditions. The following additional clinical observations or diagnoses were reported in cats during the effectiveness field study: vomiting, lethargy, diarrhea, cystitis/hematuria, upper respiratory infection, dry coat, hair loss, ocular discharge, abnormal vocalization, bad stool, and rapid breathing. Extended Use Field Study Cats that completed the effectiveness study were enrolled into an extended use field study. In this study, 145 cats received ProZinc insulin for up to an additional 136 days. Adverse reactions were similar to those reported during the 45-day effectiveness study and are listed in order of decreasing frequency: vomiting, hypoglycemia, anorexia, poor appetite, diarrhea, lethargy, cystitis/hematuria, and weakness. Twenty cats had signs consistent with hypoglycemia described as: sluggish, lethargic, unsteady, wobbly, seizures, trembling, or dazed. Most of these were treated by the owner or veterinarian with oral glucose supplementation or food; others received intravenous glucose. One cat had a serious hypoglycemic event associated with seizures and blindness. The cat fully recovered after supportive therapy and finished the study. All cases of hypoglycemia resolved with appropriate therapy and if needed, a dose reduction.

Fourteen cats died or were euthanized during the extended use study. In two cases, continued use of insulin despite anorexia and signs of hypoglycemia contributed to the deaths. In one case, the owner decided not to continue therapy after a presumed episode of hypoglycemia. The rest were due to concurrent medical conditions or worsening of the diabetes mellitus. To report suspected adverse reactions, or to obtain a copy of the Material Safety Data Sheet (MSDS), call 1-866-638-2226. Information for Cat Owners: Please refer to the Cat Owner Information Sheet for more information about ProZinc insulin. ProZinc insulin, like other insulin products, is not free from adverse reactions. Owners should be advised of the potential for adverse reactions and be informed of the associated clinical signs. Potential adverse reactions include: hypoglycemia, insulin antagonism/resistance, rapid insulin metabolism, insulin-induced hypoglycemia (Gomogyi Effect), and local or systemic reactions. The most common adverse reaction observed is hypoglycemia. Signs may include: weakness, depression, behavioral changes, muscle twitching, and anxiety. In severe cases of hypoglycemia, severe tremors and coma can occur. Hypoglycemia can be fatal if an affected cat does not receive prompt treatment. Appropriate veterinary monitoring of blood glucose, adjustment of insulin dose and regimen as needed, and stabilization of diet and activity help minimize the risk of hypoglycemic episodes. The attending veterinarian should evaluate other adverse reactions on a case-by-case basis to determine if an adjustment in therapy is appropriate, or if alternative therapy should be considered.

Effectiveness: A total of 187 client-owned cats were enrolled in a 45-day field study, with 176 receiving ProZinc insulin. One hundred and fifty-one cats were included in the effectiveness analysis. The patients included various purebreds and mixed breed cats ranging in age from 3 to 19 years and in weight from 4.6 to 20.8 pounds. Of the cats included in the effectiveness analysis, 101 were castrated males, 49 were spayed females, and 1 was an intact female. Cats were started on ProZinc insulin at a dose of 0.1-0.3 IU/kg (0.2-0.7 IU/kg) twice daily. Cats were evaluated at 7, 14, 30, and 45 days after initiation of therapy and the dose was adjusted based on clinical signs and results of 9-hour blood glucose curves on Days 7, 14, and 30. Effectiveness was based on successful control of diabetes which was defined as improvement in at least one blood glucose variable (glucose curve mean, nadir, or fructosamine) and at least one clinical sign (polyuria, polydipsia, or body weight). Based on this definition, 115 of 151 cases (76.2%) were considered successful. Blood glucose curve means decreased from 415.3 mg/dL on Day 0 to 203.2 mg/dL by Day 45 and the mean blood glucose nadir decreased from 407.9 mg/dL on Day 0 to 142.4 mg/dL on Day 45. Mean fructosamine values decreased from 505.9 μmol/L on Day 0 to 380.7 μmol/L on Day 45. Cats that completed the effectiveness study were enrolled in an extended use field study. The mean fructosamine value was 342.0 μmol/L after a total of 181 days of ProZinc therapy. How Supplied: ProZinc insulin is supplied as a sterile injectable suspension in 10 mL multidose vials. Each mL of ProZinc product contains 40 IU recombinant human insulin. Storage Conditions: Store in an upright position under refrigeration at 36-46°F (2-8°C). Do not freeze. Protect from light. Manufactured for: Boehringer Ingelheim Vetmedica, Inc. St. Joseph, MO 64506 U.S.A. Manufactured by: AAIPharma Services Corp., Charleston, SC 29405 ProZinc® is a registered trademark of Boehringer Ingelheim Vetmedica, Inc. © 2010 Boehringer Ingelheim Vetmedica, Inc. All Rights Reserved. 449901-01-1002 Revised 02/2010 Code 449911
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Important Safety Information: For use in cats only. Animals presenting with severe ketoacidosis, anorexia, lethargy, and/or vomiting should be stabilized with short-acting insulin and appropriate supportive therapy until their condition is stabilized. As with all insulin products, careful patient monitoring for hypoglycemia and hyperglycemia is essential to attain and maintain adequate glycemic control and to prevent associated complications. Overdosage can result in profound hypoglycemia and death. Progestogen and glucocorticoid use should be avoided. PROZINC insulin is contraindicated in cats during episodes of hypoglycemia and in cats sensitive to protamine zinc recombinant human insulin or any other ingredients in the PROZINC product.

Indication: CYTOPOINT® aids in the reduction of clinical signs associated with atopic dermatitis in dogs.

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Muscles and tendons are essential parts of the musculoskeletal system that allow standing, ambulating, and flexion and extension of joints. Injuries can be caused by external trauma (eg, vehicular accident), internal trauma from fracture fragments, or, most commonly, repetitive fatigue and/or application of supraphysiologic forces.

A good working knowledge of musculoskeletal anatomy is important to understand the clinical impact of injuries to the muscle–tendon unit (ie, strains). Strains are common in small animals and should be included in the differential list for any type of lameness or decrease in working or sporting performance. Clinicians should always take a complete history, perform a thorough examination, and obtain radiographs of the affected region to evaluate bony structures. Ultrasonography, CT, and MRI offer more complete evaluation of the muscle–tendon unit and can aid in diagnosis and guide treatment.

**TOP 5 MUSCLE & TENDON INJURIES IN LAME PATIENTS**

1. Biceps Tenosynovitis
2. Achilles Tendon Strain
3. Iliopsoas Muscle Strain
4. Contracture of the Infraspinatus Muscle
5. Luxation of the Superficial Digital Flexor Tendon

**FIGURE 1** Arthroscopic image of the shoulder joint of a dog with biceps tenosynovitis. The biceps tendon (B) originates on the supraglenoid tuberosity of the scapula (A) and traverses distally through the bicipital groove of the humerus (closed arrowheads). Synovitis and increased vascularity of the tendon sheath are present (open arrowheads).
Following are the author’s most common muscle and tendon injuries to consider in the lame patient.

**1 Biceps Tenosynovitis**

Biceps tenosynovitis is a common cause of forelimb lameness that most frequently affects medium- and large-breed dogs secondary to repetitive fatigue. It is characterized by inflammation of the biceps brachii tendon and the synovial sheath that envelops it in the shoulder joint (*Figure 1*, previous page). Clinical presentation often consists of a chronic progressive forelimb lameness that is worsened by exercise. The severity of lameness can vary from mild to nonweight-bearing, and atrophy of the supraspinatus and infraspinatus muscles is often present (*Figure 2*). Pain may be elicited during the biceps test, in which pressure is applied on the biceps tendon in the intertubercular groove when the shoulder is flexed and the elbow extended (*Figure 3*). Additional diagnostics (eg, ultrasonography, MRI, arthroscopy) are often needed to confirm diagnosis. Medical management (eg, rest, NSAIDs, physiotherapy) often results in resolution of mild lesions. Some dogs may require biceps tendon release or tenodesis to resolve pain and lameness.

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*FIGURE 2* Left shoulder of a dog with severe muscle atrophy of the supraspinatus (S) and infraspinatus (I) muscles. The outline of the scapula and the prominent spine of the scapula (arrowheads) are visible.

*FIGURE 3* Pain caused by biceps tenosynovitis may be elicited with the biceps test (*A*). During this maneuver, the shoulder is flexed, the elbow is extended, and pressure is applied on the biceps tendon in the intertubercular groove. This region is located on the medial aspect of the proximal humerus (*B*; star).
Achilles Tendon Strain

The Achilles tendon consists of 3 tendons: the superficial digital flexor tendon, the gastrocnemius tendon, and the combined tendon of the gracilis, semitendinosus, and biceps femoris muscles. Injury can occur secondary to acute trauma (ie, laceration, avulsion) or secondary to chronic degeneration, and clinical presentation depends on the severity of the injury and the tendons that have been injured.4,5 Mild strains may result only in lameness, pain, and swelling. If all 3 tendons have been severely compromised, the patient will walk with a complete plantigrade stance (Figure 4A); if only the gastrocnemius tendon has been injured, the patient will walk with a partial plantigrade stance (ie, increased flexion of the tarsus) with a noticeable flexion of the digits due to increased tension on the superficial digital flexor tendon (Figure 4B).4-6 Mild strains can be treated with medical management (eg, rest, NSAIDs, physiotherapy, orthotics); however, if a gait abnormality is present, surgical repair of the muscle–tendon unit is recommended.4-6

Iliopsoas Muscle Strain

The iliopsoas muscle consists of the iliacus and psoas major muscle groups, which originate along the lumbar spine and ilium and insert on the lesser trochanter of the femur. Its main function is to flex and externally rotate the hip. Injury can occur secondary to an acute excessive force or repetitive use and/or trauma, resulting in a mild-to-severe pelvic limb lameness.7-10 Pain often can be elicited on examination by extension and internal rotation of the hip joint, abduction of the femur, and direct palpation of the muscle–tendon junction near the lesser trochanter.7-10 Because the femoral nerve runs through the iliopsoas muscle, some dogs that strain this muscle may also develop a peripheral neuropathy from compression of the nerve.8,9 Standard radiography can identify mineralization in the tendon, whereas ultrasonography, CT, and MRI are helpful for identifying early and subtle lesions and can help direct therapy (Figures 5 and 6, next page).8-10 Mild-to-moderate acute lesions can often be treated with medical management.
(eg, rest, NSAIDs, physiotherapy, platelet-rich plasma injections). If the lesion is severe and results in fibrosis or contracture of the muscle, a partial tenectomy may be indicated.

### Contracture of the Infraspinatus Muscle

Contracture of the infraspinatus muscle is most commonly seen in medium- and large-breed hunting dogs. Patients frequently have an initial forelimb lameness associated with an acute strain that resolves over several weeks. A characteristic forelimb gait abnormality then develops as the muscle irreversibly contracts. Because the infraspinatus muscle runs from the infraspinous fossa to the lateral aspect of the greater tubercle of the humerus, contracture results in the inability to extend the shoulder completely, and the limb is externally rotated and held in an abducted position. When walking, the limb is circumducted with the elbow partially flexed. This unique gait abnormality is easily observed when the patient walks up or down stairs. Surgical treatment is required and consists of a partial tenectomy of the infraspinatus muscle, which results in immediate improvement in gait abnormality and provides an excellent prognosis.

### Luxation of the Superficial Digital Flexor Tendon

The superficial digital flexor tendon extends distal to the calcaneus, gliding...
over a bursa and the calcaneal tuber as it is supported by retinaculum on either side. Traumatic injury resulting in rupture of the retinaculum and medial or lateral displacement of the tendon has been reported in dogs and a cat.15,16 In Shetland sheepdogs, a hereditary basis has been established, and luxation is almost always lateral and caused by varying degrees of flattening of the lateral aspect of the calcaneal tuber.17 Depending on the inciting cause, clinical signs can include acute or chronic intermittent pelvic limb lameness and swelling around the calcaneal tuber.15,17

In some cases, the tendon can be luxated and reduced manually, with the tarsus held in extension.15,16 Medical management is ineffective for this condition.15,17 Prognosis is good to excellent following surgical treatment directed at repairing the torn retinaculum, imbrication of redundant retinaculum, and, in some cases, deepening the groove between the medial and lateral processes of the calcaneal tuber.15-17

References
Interceptor Plus is a soft, flavored chewable tablet that contains milbemycin oxime to protect dogs against several common intestinal parasites and heartworm disease. The addition of praziquantel boosts coverage even more to include four species of tapeworms for broad-spectrum parasite control.

Prevents heartworm disease and treats and controls adult hookworm (A. caninum), roundworm, whipworm and tapeworm (T. pisiformis, E. multilocularis, E. granulosus and D. caninum) infections in dogs.

Safe for use in dogs and puppies 6 weeks of age and older and 2 lbs of weight or greater.

**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, weight loss, convulsions, weakness, and salivation. For product label, including complete safety information, see page 63.
Isoxazolines kill fleas and are indicated for the treatment and prevention of flea infestations, as well as the treatment and control of various tick infestations.\(^1\text{-}^6\)

**OVERVIEW**
- The isoxazoline drug class was launched in the United States in 2014 with afoxolaner, followed shortly by oral fluralaner, sarolaner, topical fluralaner, and lotilaner.

**MECHANISM OF ACTION**
- Isoxazolines are absorbed systemically; fleas and ticks must bite the animal to be killed.
  - Isoxazolines work by selective inhibition of GABA- and glutamate-gated chloride channels, leading to hyper-excitation and death of the flea or tick.\(^7\text{-}^{10}\)
  - Because GABA channels in mammals have much a lower sensitivity to isoxazolines and mammals lack anion-inhibitory glutamate channels, there is low toxicity potential.\(^8\)
- For fleas, the onset of action for all products is reported to be 2 to 4 hours, with nearly 100% of fleas killed within 8 hours\(^1\text{-}^6\); for ticks, the onset of action for >90% tick control is 4 to 8 hours, although study protocols often assess tick control at 48 hours after administration.\(^1\text{-}^6\)

**CLINICAL APPLICATION**
- Several studies have shown that isoxazolines can reduce the risk for tick-borne disease transmission.
  - Afoxolaner and sarolaner each prevented *Borrelia burgdorferi* infection (ie, Lyme disease) in controlled laboratory studies.\(^11\text{-}^{12}\)
  - In other laboratory studies, afoxolaner, fluralaner, and lotilaner each prevented transmission of *Babesia canis*.\(^13\text{-}^{16}\)
  - *Ixodes holocyclus*, the Australian paralysis tick, was controlled by afoxolaner, fluralaner, and sarolaner.\(^17\text{-}^{18}\)
  - In a comparative laboratory study, transmission of *Ehrlichia canis* was prevented by permethrin–imidacloprid and prevented in some but not all dogs by either afoxolaner or fluralaner.\(^19\)

**ADMINISTRATION & DOSING**
- Fluralaner and lotilaner chewables should be administered with food, whereas afoxolaner and sarolaner may be given with or without food.\(^1\text{-}^3\text{-}^6\)

Disclosure: Dr. Datz is also affiliated with Royal Canin.
Labeled ages, body weights, and dosing intervals vary (see Isoxazolines at a Glance).

- Collies with the multidrug sensitivity gene (MDR1 gene, also known as ABCB1 gene) mutation (ivermectin-sensitive) were treated with up to 10 times the label dose of afoxolaner or 3 times the label dose of fluralaner with no adverse effects noted.20,21

- Fluralaner has been shown to be well tolerated with concurrent use of milbemycin–praziquantel and deltamethrin collars in dogs and emodepsid–praziquantel in cats.22-24

- Extra-label use of isoxazolines for other ectoparasites has been reported.
  - In one study of generalized demodicosis in 8 adult dogs, a single dose of fluralaner resulted in elimination of *Demodex canis* mites and resolution of dermatologic signs.25
  - Afoxolaner, sarolaner, and lotilaner at label doses were also shown to be effective in dogs with generalized demodicosis.26-29

- In dogs with *Sarcoptes scabiei var canis*, 2 doses of afoxolaner (on days 0 and 28) or sarolaner (on days 0 and 30) or a single dose of fluralaner eliminated mites and resulted in skin improvement within 4 weeks.30-33

- Dogs with ear mites (*Otodectes cynotis*) have been successfully treated with afoxolaner, fluralaner, and sarolaner; topical fluralaner is effective in cats with ear mites.28,34,35

## SAFETY & ADVERSE EFFECTS

- Vomiting, diarrhea, lethargy, and decreased appetite were occasionally observed in safety studies in puppies 8 to 9 weeks old (in both treated and control groups) at 1 time, 3 times, and 5 times the maximum oral label dose and in field studies.1-4,6,9,36-38

- Neurologic signs (eg, tremors, seizures) were noted in approximately 29% of young puppies treated with sarolaner at 1 to 5 times the label dose.3

- Fluralaner topical solution was similarly studied in dogs and cats; other than cosmetic changes at the application sites, no treatment-related adverse effects were observed.4,5

- In the feline field study, neurologic signs were seen with topical fluralaner in 2 of 224 cats5; this drug should be used with caution in cats with a history of neurologic disease.5

- Safety in breeding, pregnant, or lactating dogs has not been evaluated for afoxolaner, sarolaner, or lotilaner.1,3,6

- Oral fluralaner was studied at up to 3 times the maximum label dose at 8-week intervals in male and female beagles through breeding, pregnancy, and lactation.
  - No treatment-related effects were observed in the adult dogs or on reproductive performance.
  - In litters from 2 of 10 dams, abnormalities (eg, limb deformity, cleft palate) were noted in some puppies on gross examination.2

- In uncontrolled, open-label field studies, all drugs were effective in reducing or resolving signs of flea allergy dermatitis in dogs.39-43

## TABLE

### ISOXAZOLINES AT A GLANCE1-5

<table>
<thead>
<tr>
<th>Drug</th>
<th>Species</th>
<th>Product</th>
<th>Minimum Age</th>
<th>Minimum Body Weight</th>
<th>Dosing Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Afoxolaner</td>
<td>Dog</td>
<td>Chew</td>
<td>8 weeks</td>
<td>4 lb (1.8 kg)</td>
<td>1 month</td>
</tr>
<tr>
<td>Fluralaner</td>
<td>Dog</td>
<td>Chew</td>
<td>6 months</td>
<td>4.4 lb (2 kg)</td>
<td>12 weeks*</td>
</tr>
<tr>
<td>Sarolaner</td>
<td>Dog</td>
<td>Chew</td>
<td>6 months</td>
<td>2.8 lb (1.3 kg)</td>
<td>1 month</td>
</tr>
<tr>
<td>Lotilaner</td>
<td>Dog</td>
<td>Chew</td>
<td>8 weeks</td>
<td>4.4 lb (2 kg)</td>
<td>1 month</td>
</tr>
<tr>
<td>Fluralaner</td>
<td>Dog</td>
<td>Topical solution</td>
<td>6 months</td>
<td>4.4 lb (2 kg)</td>
<td>12 weeks*</td>
</tr>
<tr>
<td>Fluralaner</td>
<td>Cat</td>
<td>Topical solution</td>
<td>6 months</td>
<td>2.6 lb (1.2 kg)</td>
<td>12 weeks*</td>
</tr>
</tbody>
</table>

* The dosing interval is every 8 weeks for *Amblyomma americanum* (lone star) ticks.2,6

- In dogs with *Sarcoptes scabiei var canis*, 2 doses of afoxolaner (on days 0 and 28) or sarolaner (on days 0 and 30) or a single dose of fluralaner eliminated mites and resulted in skin improvement within 4 weeks.30-33

- Dogs with ear mites (*Otodectes cynotis*) have been successfully treated with afoxolaner, fluralaner, and sarolaner; topical fluralaner is effective in cats with ear mites.28,34,35
5. Pichikanthan R, Hodge A, Brueellie N, Davis K, Maeder S. Comparative speed of kill of sarolaner (Simparica) and afoxolaner (cXGard) against induced infestations of Ixodes holocyclus on dogs. Parasit Vectors. 2017;10:970.
4. Fisara P, Webber M. A randomized controlled trial of the efficacy of orally administered fluralaner (Bravecto) against induced Ixodes holocyclus (Australia paralysis tick) infestations on dogs. Parasit Vectors. 2015;8:257.
WSAVA Unveils New Website
The World Small Animal Veterinary Association (WSAVA; wsva.org) has unveiled a new website, which aims to enhance and mobilize its global veterinary community and to provide an online hub for the latest veterinary resources, knowledge, and news from the WSAVA and its member associations. It will feature an increasing volume of content in Spanish, Russian, and simplified Chinese, in addition to English. Optimized for viewing on all internet-connected devices, the website includes a range of new features, including recordings of lectures at previous World Congresses and an interactive map for members to learn about WSAVA activity or CE in their region. The website's Global Village feature will go live later in 2018 and will enable WSAVA member veterinarians to participate in discussion boards, view CE lectures, access quizzes, vote on WSAVA business, and connect with fellow WSAVA members around the world.—Press Release 2/2018

The Pet Effect Releases New Data
Zoetis (zoetis.com) has released 2 videos as part of The Pet Effect (thepeteffect.org), an educational campaign to raise awareness of the positive health benefits of pet ownership and how veterinary professionals are key contributors to public health. The videos demonstrate the physical and emotional impacts that service dogs and adopted shelter pets can have on humans.

For more information about The Pet Effect and to view the new videos, visit thepeteffect.org.—Press Release 3/2018

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

Description: Vetmedin® (pimobendan) is supplied as oblong half-scored chewable tablets containing 1.25, 2.5, or 5 mg pimobendan per tablet. Pimobendan: a benzimidazole-pyridazinone derivative, is a non-cardiac, non-glycoside inotropic drug with vasodilator properties. Pimobendan exerts a stimulatory myocardial effect by a dual mechanism of action consisting of an increase in calcium sensitivity of cardiac myoflaments and inhibition of phosphodiesterase (Type III). Pimobendan exerts vasodilating activity by inhibiting phosphodiesterase activity. The chemical name of pimobendan is 4,5-dihydro-6-[2-(4-methoxyphenyl)-1H-benzimidazole-5-yl]-5-methyl-3(2H)-pyridazinone.

Indications: Vetmedin (pimobendan) is indicated for the management of the signs of mild, moderate, or severe (modified NYHA Class III, or IV) congestive heart failure in dogs due to aortic stenotic valve insufficiency (AVS) or dilated cardiomyopathy (DCM). Vetmedin is indicated for use concurrent therapy for congestive heart failure (e.g., furosemide, etc.) as appropriate on a case-by-case basis.

A dog with modified New York Heart Association (NYHA) Class II heart failure has fatigue, shortness of breath, coughing, etc. apparent when ordinary exercise is exceeded.

A dog with modified NYHA Class III heart failure is comfortable at rest, but exercise capacity is minimal.

A dog with modified NYHA Class IV heart failure has no capacity for exercise and disabling clinical signs are present even at rest.

Contraindications: Vetmedin should not be given in cases of hypotrophic cardiomyopathy, aortic stenosis, or any other clinical condition where an augmentation of cardiac output is inappropriate for functional or anatomical reasons.

Warnings: Only for use in dogs with clinical evidence of heart failure. All 3 and 5 times the recommended dosage, administered over a 6-month period of time, pimobendan caused an exaggerated hemodynamic response in the normal dog heart, which was associated with cardiac pathology.

Human 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.

Precautions: The safety of Vetmedin has not been established in dogs with asymptomatic heart disease or in heart failure caused by other than AVS or DCM. The safe use of Vetmedin has not been evaluated in dogs younger than 6 months of age, dogs with congenital heart defects, dogs with diabetes mellitus or other serious metabolic diseases, dogs used for breeding, or pregnant or lactating bitches.

Adverse Reactions: Clinical findings/new adverse reactions were recorded in a 56-day field study of dogs with congestive heart failure (CHF) due to AVS (256 dogs) or DCM (99 dogs). Dogs were treated with either Vetmedin (175 dogs) or the active control enalapril maleate (180 dogs). Dogs in both treatment groups received additional background cardiac therapy. The Vetmedin group had the following prevalence (percent of dogs with at least one occurrence) of common adverse reactions/new clinical findings (not present in a dog prior to beginning study treatments): poor appetite (38%), lethargy (33%), diarrhea (26%), dryness (26%), azotemia (14%), weakness and ataxia (13%), pleural effusion (10%), syncope (9%), cough (7%), sudden death (6%), reptates (6%), and heart murmur (5%). Prevalence was similar in the active control group. The prevalence of renal failure was higher in the active control group (4%) compared to the Vetmedin group (1%).

Adverse reactions/new clinical findings were seen in both treatment groups and were potentially related to CHF, the therapy of CHF, or both. The following adverse reactions/new clinical findings are listed according to body system and are not in order of prevalence: CHF death, sudden death, choroiditis, tremor, left atrial/atrium, arrhythmias overall, tachycardia, syncope, weak pulse, irregular pulse, increased pulmonary edema, dryness, increased respiratory rate, coughing, gagging, pleural effusion, ascites, hepatic congestion, decreased appetite, vomiting, diarrhea, melena, weight loss, lethargy, depression, weakness, collapse, shaking, trembling, alopecia, seizures, restlessness, agitation, pruritus, increased water consumption, increased urination, urinary accidents, azotemia, dehydration, abnormal serum electrolyte, protein, and glucose values, mild increases in serum hepatic enzyme levels, and mildly decreased plateau counts.

Following the 56-day masked field study, 137 dogs in the Vetmedin group were allowed to continue on Vetmedin in an open-label extended-use study without restrictions on concurrent therapy. The adverse reactions/new clinical findings in the extended-use study were consistent with those reported in the 56-day study, with the following exception: One dog in the extended-use study developed acute cholestatic liver failure after 140 days on Vetmedin and furosemide.

In foreign post-approval drug experience reporting, the following additional suspected adverse reactions were reported in dogs treated with a capsule formulation of pimobendan: hemolysis, petechiae, anemia, hyperactivity, excited behavior, erythema, rash, drooling, constipation, and diabetes mellitus.

Effectiveness: In a double-masked, multi-site, 56-day field study, 355 dogs with modified NYHA Class III, or IV CHF due to AVS or DCM were randomly assigned to either the active control (enalapril maleate or the Vetmedin (pimobendan) treatment group. Of the 355 dogs, 52% were male and 48% were female; 72% were diagnosed with AVS and 28% were diagnosed with DCM; 34% had Class II, 47% had Class III, and 19% had Class IV CHF. Dogs ranged in age and weight from 1 to 17 years and 3.3 to 191 lb. respectively. The most common breeds were mixed breed, Dachshund, Pinscher, Cocker Spaniel, Miniature/Toy Poodle, Maltese, Chihuahua, Miniature Schnauzer, Dachshund, and Cavalier King Charles Spaniel. The 180 dogs (130 AVVI, 50 DCM) in the active control group received enalapril maleate (0.5 mg/kg once or twice daily), and all but 2 received furosemide. Per protocol, all dogs with DCM in the active control group received digoxin. The 175 dogs (126 AVVI, 49 DCM) in the Vetmedin group received pimobendan (0.5 mg/kg divided into 2 portions that were not necessarily equal, and the portion were administrated approximately 12 hours apart), and all but 4 received furosemide. Digoxin was optional for treating supraventricular tachyarrhythmia in either treatment group, as was the addition of a β-adrenergic blocker if digoxin was ineffective in controlling heart rate. After initial treatment at the clinic on Day 1, dog owners were to administer the assigned product and concurrent medications for up to 56±4 days.

The determination of effectiveness (treatment success) for each case was based on improvement in at least 2 of the 5 following primary variables: modified NYHA classification, pulmonary edema score by a masked veterinary radiologist, and the investigator’s overall clinical effectiveness score (based on physical examination, electrocardiography, and clinical pathology). Altitude, pleural effusion, coughing, activity level, furosemide dosage change, cardiac size, body weight, survival, and other observations were secondary contributions informing subjective to product effectiveness and safety. Based on protocol compliance and individual case integrity, 265 cases (134 Vetmedin, 131 active control) were evaluated for treatment success on Day 29. At the end of the 56-day study, dogs in the Vetmedin group were enrolled in an unmasked field study to monitor safety under extended use, without restrictions on concurrent medications.

Vetmedin was used safely in dogs concurrently receiving furosemide, digoxin, enalapril, amiodarone, spirinolactone, nitroglycerin, hydroxizine, diltiazem, antiparasitic products (including heartworm prevention), antibiotics extended use, without restrictions on concurrent medications.

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Manufactured for:
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St. Joseph, MO 64506 U.S.A.
I have clients who notice a great response with VETMEDIN. Their animal feels perkier at home, they’re brighter, their heart failure is well-controlled, they really feel like themselves. Or they feel like a puppy again, a lot of people say. Which I think is what we all want for our pet.

—Dr Danielle Laughlin
Cardiologist
Blue Pearl Specialty + Emergency Pet Hospital
Sandy Springs, GA

See more stories at DecadeOfVetmedin.com.
Dasuquin Advanced for Cats Launched
Nutramax Laboratories (nutramaxlabs.com) has announced the launch of Dasuquin Advanced for Cats soft chews (dasuquinadvanced.com), its latest formulation in joint health supplements. Dasuquin Advanced for Cats soft chews contain FCHG49 glucosamine, TRH122 sodium chondroitin sulfate, and NMX1000 avocado/soybean unsaponifiables. This formulation also contains Boswellia serrata extract, green tea extract, omega-3 fatty acids, and β-glucans for additional support. —Press Release 2/2018

Hill’s Addresses Obesity with Healthy Weight Challenge
Hill’s Pet Nutrition (hillspet.com) has launched a program to help veterinary clinics and pet owners tackle obesity in dogs. The Healthy Weight Challenge uses Vetrax (vetrax.com) wearable technology to give clinics and pet owners the opportunity to track achievements for set activity goals and weight loss milestones in overweight dogs over a 12-week challenge period. The Vetrax sensor, worn on a dog’s collar, enables clinicians and pet owners to monitor aspects of the animal’s behavior. Data gained from the sensor are analyzed by Vetrax and can be accessed via a mobile app. For every pound that each participating dog loses, Hill’s will donate a week’s worth of food to a shelter pet. For more information or to participate in the Healthy Weight Challenge, visit hillssmartcare.com/challenge. —Press Release 3/2018

Study Reveals Concerns About the Future of the Veterinary Profession
Merck Animal Health (merck-animal-health.com) has announced the results of a large, controlled study designed to definitively quantify the prevalence of mental illness and stress in the veterinary profession and compare the findings with previous studies and the general US population. Conducted in collaboration with the AVMA (avma.org), the study found that only 27% would endorse the profession to a friend or family member, and veterinarians 45 years and younger are more likely to experience serious psychologic distress; depression (94%), burnout (88%), and anxiety (83%) are the most frequently reported conditions. High student debt was the top concern voiced, with 67% rating it a critical issue. Just over half (53%) of respondents reported that the second most serious issue is stress level. Poor mental health is closely associated with the stresses of professional life (eg, excessive work hours, poor work–life balance, student debt). Awareness about resources for mental health and well-being is low; the study reports that only half of veterinarians with serious psychologic distress are seeking help, creating a big mental health treatment gap. Read the full study report at bit.ly/2FWiIpo. —Press Release 2/2018

Merial Expands Canine Vaccine Portfolio
Merial (merial.com; now a part of Boehringer Ingelheim) has expanded its canine vaccine portfolio with the launch of RECOMBITEK Oral Bordetella, an oral vaccine shown to be effective against canine infectious tracheobronchitis caused by Bordetella bronchiseptica, one of the primary pathogens responsible for canine infectious respiratory disease complex. RECOMBITEK Oral Bordetella is administered in the buccal cavity; clinical studies suggest that, as a mucosal vaccine, it offers dogs a robust immune response after a single dose. —Press Release 2/2018

VitusVet Partners with The Pet Vet
VitusVet (vitussvet.com), a pay-for-performance digital communication solution for veterinary practices, has announced its partnership with The Pet Vet Hospital (thepetvet.com), a veterinary clinic co-located in select Petco (petco.com) stores. The partnership aims to improve sharing of pet medical information among veterinarians operating within Petco stores and the pet owners they serve; VitusVet’s electronic medical records platform for pets is now available to those who take their pet to The Pet Vet clinics at Petco stores in Addison, Texas, and Highland Village, Texas. Future location opportunities are being explored. —Press Release 2/2018

SEND INFORMATION FOR PRACTICE HOTLINE TO editor@cliniciansbrief.com
Flea and tick protection that goes on and on and on...all month long

Introducing Simparica

Monthly chewables for dogs that offer persistent protection from fleas and ticks.

Simparica acts fast—it starts killing fleas within 3 hours and ticks within 8 hours\(^1\)—and keeps going strong for 35 days\(^2\) without losing effectiveness at the end of the month.

IMPORTANT SAFETY INFORMATION: Simparica is for use only in dogs, 6 months of age and older. Simparica may cause abnormal neurologic signs such as tremors, decreased conscious proprioception, ataxia, decreased or absent menace, and/or seizures. Simparica has not been evaluated in dogs that are pregnant, breeding or lactating. Simparica has been safely used in dogs treated with commonly prescribed vaccines, parasiticides and other medications. The most frequently reported adverse reactions were vomiting and diarrhea. See full Prescribing Information on the facing page and at www.zoetisUS.com/SimparicaPI.

IMPORTANT SAFETY INFORMATION: See page 72 for product information summary.


Fetch more information about Simparica from Zoetis Customer Service at 1-888-ZOETIS-1 or 1-888-963-8471.
FOR ORAL USE IN DOGS ONLY

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

Description: SIMPARICA is a flavored, chewable tablet for administration to dogs over 6 months of age according to their weight. Each tablet is formulated to provide a minimum sarolaner dosage of 0.91 mg/lb (2 mg/kg) body weight.

Sarolaner is a member of the isoxazoline class of parasiticides and the chemical name is 1-(5'-((5S)-5-(3,5-Dichloro-4-fluorophenyl)-5-(trifluoromethyl)-4,5-dihydroisoxazol-3-yl)-3'-H-spiro(azetidine-3,1'-(2)benzofuran)-1-yl)-2-(methylsulfonyl)ethanone. SIMPARICA contains the 5-enantionomer of sarolaner.

Additionally, one female dog aged 8.6 years exhibited lethargy, ataxia while posturing to eliminate, elevated third eyelids, and inappetence one day after receiving SIMPARICA concurrently with a heartworm preventive (i.e., ivermectin/pyrantel pamoate). The signs resolved one day later. After the day 14 visit, the owner elected to withdraw the dog from the study.

For a copy of the Safety Data Sheet (SDS) or to report adverse reactions call Zoetis Inc. at 1-888-963-8471. Additional information can be found at www.SIMPARICA.com. For additional information about adverse drug experience reporting for animals, contact FDA at 1-888-FDA-VETS or http://www.fda.gov/AnimalVeterinary/SafetyHealth.

Clinical Pharmacology: Sarolaner is rapidly and well absorbed following oral administration of SIMPARICA. In a study of 12 Beagle dogs the mean maximum plasma concentration (Cmax) was 1100 ng/mL and the mean time to maximum concentration (Tmax) occurred at 3 hours following a single oral dose of 2 mg/kg to fasted animals.

Fleas and ticks: SIMPARICA 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), Amblyomma maculatum (Gulf Coast tick), Dermacentor variabilis (American dog tick), Ixodes scapularis (black-legged tick), and Rhipicephalus sanguineus (brown dog tick)) for one month in dogs 6 months of age or older and weighing 2.8 pounds or greater.

DOSAGE AND ADMINISTRATION:

SIMPARICA is a flavored, chewable tablet for administration to dogs over 6 months of age according to their weight. Each tablet is formulated to provide a minimum sarolaner dosage of 0.91 mg/lb (2 mg/kg) body weight. SIMPARICA contains the 5-enantionomer of sarolaner.

The chemical structure of the 5-enantionomer of sarolaner is:

Indications: SIMPARICA 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), Amblyomma maculatum (Gulf Coast tick), Dermacentor variabilis (American dog tick), Ixodes scapularis (black-legged tick), and Rhipicephalus sanguineus (brown dog tick)) for one month in dogs 6 months of age or older and weighing 2.8 pounds or greater.

DOSAGE AND ADMINISTRATION:

SIMPARICA is given orally once a month at the recommended minimum dosage of 0.91 mg/lb (2 mg/kg).

Dosage Schedule:

<table>
<thead>
<tr>
<th>Body Weight</th>
<th>SAROLANER per Tablet (mg)</th>
<th>Number of Tablets Administered</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.8 to 5.5 lbs</td>
<td>5</td>
<td>One</td>
</tr>
<tr>
<td>5.6 to 11.0 lbs</td>
<td>10</td>
<td>One</td>
</tr>
<tr>
<td>11.1 to 22.0 lbs</td>
<td>20</td>
<td>One</td>
</tr>
<tr>
<td>22.1 to 44.0 lbs</td>
<td>40</td>
<td>One</td>
</tr>
<tr>
<td>44.1 to 88.0 lbs</td>
<td>80</td>
<td>One</td>
</tr>
<tr>
<td>88.1 to 132.0 lbs</td>
<td>120</td>
<td>One</td>
</tr>
<tr>
<td>&gt;132.1 lbs</td>
<td>Administer the appropriate combination of tablets</td>
<td></td>
</tr>
</tbody>
</table>

SIMPARICA can be offered by hand, in the food, or administered like other tablet medications. Care should be taken that the dog consumes the complete dose, and treated animals should be observed for a few minutes to ensure that part of the dose is not lost or refused. If a dose is missed, administer SIMPARICA and resume a monthly dosing schedule.

SIMPARICA should be administered at monthly intervals.

Flea Treatment and Prevention:

Treatment with SIMPARICA may begin at any time of the year. In areas where fleas are common year-round, monthly treatment with SIMPARICA can continue the entire year without interruption.

To minimize the likelihood of re-infestation, it is important to treat all dogs and cats within a household with an approved flea control product.

Tick Treatment and Control:

Treatment with SIMPARICA can begin at any time of the year (see Effectiveness).

Contraindications:

There are no known contraindications for the use of SIMPARICA.

Warnings:

Not for use in humans. Keep this and all drugs out of reach of children and pets. For use in dogs only. Do not use SIMPARICA in cats.

SIMPARICA should not be used in dogs less than 6 months of age (see Animal Safety).

Precautions:

SIMPARICA may cause abnormal neurologic signs such as tremors, decreased conscious proprioception, ataxia, decreased or absent menace, and/or seizures (see Animal Safety).

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

Adverse Reactions:

SIMPARICA was administered in a well-controlled US field study, which included a total of 479 dogs (315 dogs treated with SIMPARICA and 164 dogs treated with active control once monthly for three treatments).

Over the 90-day study period, all observations of potential adverse reactions were recorded.

<table>
<thead>
<tr>
<th>Table 1. Dogs with adverse reactions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adverse reaction</td>
</tr>
<tr>
<td>Vomiting</td>
</tr>
<tr>
<td>Diarrhea</td>
</tr>
<tr>
<td>Lethargy</td>
</tr>
<tr>
<td>Inappetence</td>
</tr>
</tbody>
</table>

In a separate exploratory pharmacokinetic study, one female dog dosed at 12 mg/kg (3X the maximum intended clinical dose of 4 mg/kg, steady-state plasma concentrations were reached after the 6th dose. Following treatment at IX, 3X, and 5X the maximum intended clinical dose of 4 mg/kg, sarolaner systemic exposure was dose proportional over the range IX to 5X.

Mode of Action:

The active substance of SIMPARICA, sarolaner, is an acaricide and insecticide belonging to the isoxazoline group. Sarolaner inhibits the function of the neurotransmitter gamma aminobutyric acid (GABA) receptor and glutamate receptor, and works at the neuromuscular junction in insects. This results in uncontrolled neuromuscular activity leading to death in insects or arachnids.

Effectiveness:

In a well-controlled laboratory study, SIMPARICA began to kill fleas 3 hours after initial administration and reduced the number of live fleas by ≥96.2% within 8 hours after flea infestation through Day 35.

In a separate well-controlled laboratory study, SIMPARICA demonstrated 100% effectiveness against adult fleas within 24 hours following treatment and maintained 100% effectiveness against weekly re-infestations for 35 days.

In a study to explore flea egg production and viability, SIMPARICA killed fleas before they could lay eggs for 35 days. In a study to simulate a flea-infested home environment, with flea infestations established prior to the start of treatment and re-infestations on Days 7, 37 and 67, SIMPARICA administered monthly for three months demonstrated ≥99.6% reduction in adult fleas within 14 days after treatment and reached 100% on Day 60.

In all 4 laboratory studies, SIMPARICA demonstrated ≥99% effectiveness against an initial infestation of Amblyomma americanum, Amblyomma maculatum, Dermacentor variabilis, Ixodes scapularis, and Rhipicephalus sanguineus 48 hours post-administration and maintained >96% effectiveness 48 hours post-re-infestation for 30 days.

In a well-controlled 90-day US field study conducted in households with existing flea infestations of varying severity, the effectiveness of SIMPARICA against fleas on Day 30, 60 and 90 visits compared to baseline was 99.4%, 99.8%, and 100%, respectively.

In a well-controlled laboratory study, SIMPARICA demonstrated >95.6% reduction in infestations established prior to the start of treatment and re-infestations on Days 7, 37 and 67. SIMPARICA administered monthly for three months demonstrated >99.6% reduction in adult fleas within 14 days after treatment and reached 100% on Day 60.

In a separate well-controlled laboratory study, SIMPARICA demonstrated >99% effectiveness against a parasiticide that kills adult fleas within 24 hours following treatment and maintained 100% effectiveness against weekly re-infestations for 35 days.

Animal Safety:

In a margin of safety study, SIMPARICA was administered orally to 8-week-old Beagle puppies at doses of 0, 1X, 3X, and 5X the maximum recommended dose (4 mg/kg) at 28-day intervals for 10 doses (8 dogs per group). The control group received placebo tablets. No neurologic signs were observed in the IX group. In the 3X group, one male dog exhibited tremors and ataxia post-dose on Day 0; one female dog exhibited tremors on Days 1, 2, and 5, and one female dog exhibited tremors on Day 1. In the 5X group, one female dog had a seizure on Day 61 (5 days after third dose); one female dog had tremors post-dose on Day 0 and abnormal head coordination after dosing on Day 140; and one female dog exhibited seizures associated with the second and fourth doses and tremors associated with the second and third doses. All dogs recovered without treatment. Except for the observation of abnormal head coordination in one dog in the 5X group two hours after dosing on Day 140 (dose). There were no treatment-related neurological signs observed once the dogs reached the age of 6 months.

In a separate exploratory pharmacokinetic study, one female dog dosed at 12 mg/kg (3X the maximum recommended dose) exhibited lethargy, anorexia, and multiple neurological signs including ataxia, tremors, disorientation, hypersalivation, diminished proprioception, and absent menace, approximately 2 days after a third monthly dose. The dog was not treated, and was ultimately euthanized. The first two doses resulted in plasma concentrations that were comparable with those of the other dogs in the treatment group. Starting at 7 hours after the third dose, there was a rapid 2.5 fold increase in plasma concentrations within 41 hours, resulting in a Cmax more than 7-fold higher than the mean Cmax at the maximum recommended use dose.

Storage Information:

Store at or below 30°C (86°F) with excursions permitted up to 40°C (104°F).

How Supplied:

SIMPARICA (sarolaner) Chewables are available in six flavored tablet sizes: 5, 10, 20, 40, 80, and 120 mg. Each tablet size is available in color-coded packages of one, three, or six tablets.

NADA #141-452, Approved by FDA
The spleen has a diverse set of functions, including hematopoiesis, RBC filtration and storage, and immune surveillance. Despite its many functions, removal of the spleen is commonly performed in dogs and cats with rarely observed long-term adverse sequelae. Splenectomy is indicated in cases of splenic neoplasia, trauma, torsion, and infiltrative disease and, occasionally, as treatment for immune-mediated disorders. It is also commonly performed on an emergency basis for hemoabdomen of splenic origin.

Spleen Anatomy
Clinicians should have an understanding of the splenic and regional vascular anatomy before performing splenectomy. The spleen is located on the left side of the body. The head of the spleen is the craniodorsal-most portion and is attached to the greater curvature of the stomach via the gastroplenic ligament, in which the short gastric arteries and veins are located. The tail of the spleen is the larger, caudal, more mobile portion that sweeps across the ventral midline, with a loose terminal attachment to the greater omentum.

The main blood supply to the spleen comes from the splenic branch of the celiac artery. This splenic artery runs along the left limb of the pancreas, giving off pancreatic branches before spreading into the vessels supplying the splenic parenchyma. It is important to avoid ligating the splenic vessels proximal to these pancreatic branches to avoid damaging pancreatic blood supply.

The head of the spleen is supplied by the short gastric arteries, which arise from the dorsal branch of the splenic artery and anastomose with the branches of the left gastric artery. The majority of the spleen is supplied by the ventral branch of the splenic artery and its numerous intermediate branches into the hilus. The ventral splenic artery continues as the left gastroepiploic artery.
supplying the greater curvature and fundic portion of the stomach. Ideally, this continuation should be preserved; however, it was shown that sacrifice of the left gastroepiploic vessel did not compromise gastric blood flow or the integrity of the gastric wall in healthy dogs. At the terminal portion of the tail of the spleen, the vessels continue as branches to the omentum.

**Surgical Approach**
The least complicated anatomic approach to splenectomy that ensures no inadvertent ligation of the pancreatic or left gastroepiploic vessels is the hilar ligation technique. With this technique, the vessels are ligated as they terminate into the spleen. The speed of this technique varies depending on the manner of ligation used, with the use of a vessel-sealing device being the fastest, followed by a staple or clip device, and lastly suture ligation. Some devices can seal vessels up to 7 mm in diameter, whereas hemostatic clips are appropriate for vessels up to 3 mm in diameter. With the appropriate size and material, hand ligation with suture can be used in any size vessel for splenectomy. The following describes the hilar approach to splenectomy.

Of note, one study evaluating the relationship between gastric dilatation volvulus and previous splenectomy found dogs with a previous splenectomy to be 5.3 times more likely to develop gastric dilatation volvulus than were dogs without splenectomy. Other studies have reported development of gastric dilatation volvulus in atypical breeds (eg, bichon frise, beagle) after splenectomy, which suggests splenectomy may be a potential predisposing factor. Thus, some surgeons may recommend prophylactic gastropexy be performed in dogs undergoing splenectomy.

**FIGURE** Splenic and regional vascular anatomy showing the splenic artery (A), gastroepiploic artery (B), short gastric arteries (C), and omental arteries (D)

**With the appropriate size and material, hand ligation with suture can be used in any size vessel for splenectomy.**
STEP-BY-STEP SPLENECTOMY: HILAR LIGATION TECHNIQUE

STEP 1
Position the patient in dorsal recumbency (A), and prepare the abdomen with a standard aseptic technique. Drape the patient from xiphoid to pubis (B). In male dogs, maintain the penis out of the sterile field.

WHAT YOU WILL NEED
- Standard general surgery pack including needle holders, thumb forceps, Metzenbaum scissors, suture scissors, and hemostatic forceps (8-12 inches)
- Balfour retractor
- Abdominal laparotomy sponges
- Suction device and Poole suction tip
- Electrosurgery handpiece (helpful, but not required)
- Suture for ligation (generally 2-0 to 3-0 size, depending on patient and pedicle size)
- +/- Hemostatic clip or staple applicator (optional alternative or supplement to sutures)
- +/- Vessel sealing device (optional alternative or supplement to sutures)

Some surgeons may recommend prophylactic gastropexy be performed in dogs undergoing splenectomy.

GASTROPEXY
Find a step-by-step guide to open and laparoscopic-assisted incisional gastropexy at cliniciansbrief.com/article/open-laparoscopic-assisted-incisional-gastropexy
STEP 2

Make a ventral midline abdominal incision from the xiphoid to 2 to 3 cm caudal to the umbilicus (A). The incision can be extended caudally if the size of the mass requires. Using electrosurgical instruments or ligation, remove the falciform fat en bloc to improve exposure (B). In rare cases, extension from midline into a paracostal incision may be indicated for removal of larger splenic masses.

STEP 3

Perform a methodical exploration of the abdomen. If hemoabdomen is present, use suction to remove the hemorrhage and improve visualization. Carefully inspect the liver and the remaining abdominal viscera to monitor for presence of gross metastasis. A liver biopsy is indicated in cases of suspected malignancy regardless of gross appearance (see Liver Biopsy). Gently manipulate the spleen out of the body and onto moistened laparotomy sponges. A diseased spleen is often friable and should be carefully handled to prevent rupture. If the omentum is adhered to a splenic mass, divide the adhesions using electrosurgical devices or ligation. Digital dissection is not recommended, as rupture of the splenic mass may occur.

LIVER BIOPSY

**STEP 4**

The hilar vessels can be visualized as they enter the splenic parenchyma (A). Using hemostatic forceps, bluntly isolate the vessels (B). Using 3-0 absorbable suture, circumferentially double ligate the hilar pedicles (C and D). Before transecting the vessel, place hemostatic forceps on the pedicle close to the spleen (E); this will help prevent splenic bleeding. Repeat this step for all vessels along the splenic hilus until the spleen is removed (F).
**STEP 5**

After removing the spleen, biopsy any other grossly abnormal tissue. Check the splenic pedicles and biopsy sites for appropriate hemostasis, then gently lavage with warm sterile saline and evacuate the fluid. Perform routine abdominal closure.

Submit the spleen and tissue for histopathologic evaluation.

---

**Postoperative Care & Monitoring**

IV fluids should be continued postoperatively and matched to meet the patient’s needs. Ongoing monitoring should include serial packed cell volume checks, continuous ECG for assessment of changes in heart rate and rhythm, twice-daily urine output assessment, body weight monitoring, and serial venous blood gas and lactate monitoring. IV opioid analgesics should be administered for at least 48 hours before weaning or switching to oral analgesic medications. Perioperative antibiotics should not be required for longer than 24 hours unless splenectomy was performed for splenic abscess, in which case antibiotics should be chosen based on results of culture and susceptibility testing and administered for 10 to 14 days.

---

**Author Insights**

As an alternative to suture ligation, splenic hilar vessels can be ligated using a vessel-stapling apparatus or a vessel-sealing device.\(^4\)

To speed up splenectomy, a surgical assistant can work on isolating the splenic hilar vessels using hemostatic forceps while the surgeon ligates and divides the isolated vessels.

One veterinary study demonstrated no difference in clinical outcome between splenectomy performed using a vessel-sealing device versus a stapler; however, the sealing device yielded significantly shorter procedure times.\(^5\)

Another study found the bursting strength of the sealing device to be greater than 300 mm Hg (ie, \(\approx\)3 times systolic pressure).\(^6\)

---

**TRIFEXIS\textsuperscript{*} (spinosad + milbemycin oxime)**

**Chewable Tablets**

Each Chewable Tablet contains spinosad and milbemycin oxime. For the treatment of heartworm disease, please consult the product insert, a summary of which follows:

**Indications:**

TRIFEXIS is indicated for the prevention of heartworm disease (Dirofilaria immitis).

**Dosage and Administration:**

TRIFEXIS is given orally once a month as a single dose. TRIFEXIS should be administered on the same day each month. TRIFEXIS is not effective against adult heartworms. TRIFEXIS is not effective against adult heartworms. Heartworm prevention should be given to unprotected dogs at least 2 months after exposure to mosquitoes (see EFFECTIVENESS).

**Contraindications:**

There are no contraindications to the use of TRIFEXIS.

**Warnings:**

- Nonhuman use. Keep this and all drugs out of the reach of children.
- Serious adverse reactions have been reported following incorrect administration of spinosad with adult anthelmintics.
- TRIFEXIS may cause adverse reactions in individual dogs.
- The number of circulating microfilariae may decrease following treatment with TRIFEXIS. This effect is not indicated for microfilaria clearance.
- Malaria, hypereosinophilia, neutropenia as an isolated finding, vomiting, salivation and diarrhea, and pyrexia when administered with heartworm preventative may cause a high number of circulating microfilariae. These reactions are presumably caused by the use of a system to control dogs.
- Use with caution in breeding females. The safety of TRIFEXIS in breeding males has not been evaluated.
- Use with caution in dogs with pre-existing epilepsy (ADVERSE REACTIONS).
- Puppies less than 8 weeks of age may experience a higher rate of vomiting.

**Adverse Reactions**

A well-controlled US field study, which included a total of 155 dogs treated with TRIFEXIS, demonstrated an overall incidence of adverse reactions that were consistent with those expected to occur naturally (\(\approx\)3 times systolic pressure).

**Average Monthly Rate (%) of Dogs With Adverse Reactions**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>TRIFEXIS Chewable Tablets*</th>
<th>Active Control Tablets*</th>
</tr>
</thead>
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<tr>
<td>Vomiting</td>
<td>8.33</td>
<td>9.50</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>2.50</td>
<td>3.22</td>
</tr>
<tr>
<td>Anorexia</td>
<td>1.67</td>
<td>1.67</td>
</tr>
<tr>
<td>Pyrexia</td>
<td>1.67</td>
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<tr>
<td>Dermatitis</td>
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<tr>
<td>Dysuria</td>
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<td>1.95</td>
</tr>
<tr>
<td>Increased appetite</td>
<td>1.27</td>
<td>1.95</td>
</tr>
</tbody>
</table>

**Postoperative Care & Monitoring**

**Heartworm Prevention:**

- In a well-controlled laboratory study, TRIFEXIS was 100% effective against induced heartworm infections when administered for 6 consecutive monthly doses. Two consecutive monthly doses did not provide 100% effectiveness against heartworm infection in another well-controlled laboratory study; a single dose of TRIFEXIS was 100% effective against induced heartworm infections.

**Efficacy:**

- In a well-controlled US field study conducted with TRIFEXIS, dogs were positive for heartworm infection as determined by heartworm antigen testing performed on the second, third, fourth, and final doses.

**Adverse Reactions:**

- Heartworm infection as determined by heartworm antigen testing performed on the second, third, fourth, and final doses.

**Conclusion:**

- TRIFEXIS is indicated for the prevention of heartworm disease in dogs at risk for heartworm infection.

**Side Effects:**

- Vomiting, diarrhea, anorexia, dermatitis, pruritus, dermatitis, and pyrexia were observed in heartworm-free dogs treated with TRIFEXIS.

**Further Information:**

- For technical assistance or to report suspected adverse drug events, contact Boehringer Ingelheim at 1-888-246-3471 or Boehringer Ingelheim Animal Health 1-866-255-6962.

**Package Insert:**

For technical assistance or to report suspected adverse drug events, contact Boehringer Ingelheim at 1-888-246-3471 or Boehringer Ingelheim Animal Health 1-866-255-6962.

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See page 90 for references.
**Indications**

Trifexis is indicated for the prevention of heartworm disease (*Dirofilaria immitis*). Trifexis kills fleas and is indicated for the prevention and treatment of flea infestations (*Ctenocephalides felis*), and the treatment and control of adult hookworm (*Ancylostoma caninum*), adult roundworm (*Toxocara canis* and *Toxascaris leonina*) and adult whipworm (*Trichuris vulpis*) infections in dogs and puppies 8 weeks of age or older and 5 pounds of body weight or greater.

**Important safety information**

Serious adverse reactions have been reported following concomitant extra-label use of ivermectin with spinosad alone, one of the components of Trifexis. Treatment with fewer than three monthly doses after the last exposure to mosquitoes may not provide complete heartworm prevention. Prior to administration of Trifexis, dogs should be tested for existing heartworm infection. Use with caution in breeding females. The safe use of Trifexis in breeding males has not been evaluated. Use with caution in dogs with pre-existing epilepsy. The most common adverse reactions reported are vomiting, lethargy, pruritus, anorexia and diarrhea. To ensure heartworm prevention, dogs should be observed for one hour after administration. If vomiting occurs within one hour, redose. Puppies less than 14 weeks of age may experience a higher rate of vomiting. For product information, including complete safety information, see page 78.
“The work was very rewarding and very appreciated. The Mission Rabies project has made a tremendous impact on the reduction of rabies in Malawi. I am thankful to have been a volunteer. I would recommend this project to anyone interested in a global, humanitarian, animal welfare project.”

-Karen Taylor-Sorenson, DVM

For more information about the Mission Rabies projects, visit: missionrabies.com
The spleen is a complex organ composed of 2 distinct parenchymal areas (red pulp and white pulp), each with important hematologic and immunologic functions. The red pulp filters blood and removes senescent or damaged blood cells, aids in the metabolism and subsequent recycling of iron, and serves as a site for hematopoiesis, producing leukocytes, platelets, and RBCs when demand is increased. Regions of white pulp consist of lymphoid tissue that produces and stores immune cells (eg, lymphocytes, macrophages), which provide immune surveillance of blood for “foreign” material (eg, cells harboring infectious organisms, antibody-coated cells that are targeted for destruction and removal from circulation). The spleen also acts as a reservoir of blood, storing up to 20% of the total RBC mass and up to 30% of the platelet mass in the body. The spleen releases RBCs and platelets readily to meet physiologic demand.

Splenic disorders are common in middle-aged and older dogs, with clinical signs ranging from vague signs of illness to life-threatening hemoabdomen. In these disorders, splenomegaly is often present, regardless of disease severity. Splenomegaly is typically caused by discrete nodule(s) or diffuse enlargement. Although splenomegaly can be present in the absence of clinical signs, patients with chronic splenic disease may exhibit lethargy, inappetence, vomiting, abdominal enlargement, and

**Top 5 Causes of Splenomegaly in Dogs**

Todd Archer, DVM, MS, DACVIM
Alyssa Sullivant, DVM, MS, DACVIM
Mississippi State University

1. Hemangiosarcoma
2. Extramedullary Hematopoiesis
3. Multicentric Lymphoma
4. Nodular Hyperplasia/Hematoma
5. Congestion
weight loss. Patients presented with hemoabdomen are often collapsed and in hypovolemic shock. Arrhythmias are common with splenic diseases, especially hemangiosarcoma. Splenomegaly may be detected on abdominal palpation or through imaging modalities such as radiography, ultrasonography, or advanced imaging. Imaging is useful for differentiating a splenic mass from diffuse splenomegaly and is important in narrowing the possible causes of splenomegaly.

The “two-thirds/two-thirds” and “fifty/fifty” rules are often cited regarding the incidence of splenic malignancy. In a study of 325 dogs, 66% of dogs with splenomegaly were diagnosed with splenic malignancy, and 65% of those malignancies were hemangiosarcoma. An earlier study of 1480 dogs found that approximately 50% of splenic samples represented malignancy, with hemangiosarcoma accounting for approximately 50% of malignancies. However, in a study of 105 dogs with nonruptured splenic masses, 70.5% had benign splenic lesions and 29.5% had malignant neoplasia, with hemangiosarcoma accounting for 58% of malignancies. Although splenic neoplasia is a common cause of splenomegaly, it is impossible to differentiate between malignant and benign lesions grossly. A definitive diagnosis should be obtained before considering euthanasia. Fine-needle aspiration of the spleen is safe, and cytologic diagnoses correspond to histologic diagnoses in at least 50% of cases. Submission of the entire spleen for histopathology is recommended to increase the likelihood of distinguishing between benign and malignant processes, particularly between hemangiosarcoma and hematoma.

Following are the authors’ top 5 causes of splenomegaly seen most often in veterinary practice.

1 **Hemangiosarcoma**

Hemangiosarcoma is the most common malignant disease of the spleen, representing one-half to two-thirds of all malignant splenic tumors. It is more prevalent in older medium- and large-breed dogs (eg, German shepherd dogs, golden retrievers, Labrador retrievers, standard poodles). Hemangiosarcoma arises from the vascular endothelium and often develops into a large cavity mass in the spleen (Figure 1). Approximately 25% of dogs with splenic hemangiosarcoma may have concurrent hemangiosarcoma affecting the right side of the heart. Clinical signs are typically related to anemia, which may be mild to severe and life-threatening, and include pale mucous membranes, tachycardia, lethargy, and abdominal distention. Intra- and extrasplenic hemorrhage may occur and can cause marked hemoabdomen and acute anemia with subsequent hypovolemia and collapse. Although hematomas and, less commonly, other benign splenic lesions may cause hemoabdomen, hemangiosarcomas are more likely to cause hemoabdomen. Blood study findings can include schistocytosis, thrombocytopenia, and, possibly, disseminated intravascular coagulation.

Initial testing and staging should include CBC, serum chemistry profile, coagulation testing (prothrombin time and partial thromboplastin time), 3-view thoracic radiography, abdominal ultrasonography, and cardiac ultrasonography. Splenic aspirates may disclose malignant cells or evidence of nonspecific hemorrhage only, and a definitive diagnosis requires histopathology. Dogs with Stage I hemangiosarcoma have a solitary primary tumor less than 5 cm in diameter, and dogs with Stage II have a primary tumor that is ruptured, is greater

![FIGURE 1 Hemangiosarcomas are the most common splenic malignancy in dogs.](https://example.com/filename.png) Lesions are often cavitary, and hemoabdomen is common.
than 5 cm in diameter, or has lymph node involvement. Stage III dogs have splenic rupture or lymph node involvement and evidence of distant metastasis. Survival times do not differ markedly between stages. Splenectomy alone yields a median survival time of 86 days, whereas dogs receiving adjunctive doxorubicin-based chemotherapy have a longer median survival time of 172 days if no evidence of gross disease is present after surgery.

### Extramedullary Hematopoiesis

Extramedullary hematopoiesis (EMH; ie, hematopoiesis occurring outside the bone marrow) causes diffuse uniform symmetric enlargement of the spleen (because of “work hypertrophy”) with increased activity of the mononuclear phagocytic system and increased blood cell production. Hypoxia is the main stimulus for splenic EMH in an adult animal and can be seen with any disease that undermines the ability of the bone marrow to function properly. Because EMH is a benign condition that occurs in response to an underlying hematologic abnormality, diagnostic efforts are directed at the disease process driving the EMH. Mild EMH occurs with many splenic and nonsplenic disorders and can be seen with both immune-mediated hemolytic anemia and immune-mediated thrombocytopenia, as the spleen is a major site of removal and destruction of antibody-coated cells and a site for extramedullary production of blood cells. EMH can also be associated with a variety of splenic neoplasms. In patients with EMH, ultrasonography typically shows focal or diffuse, heterogeneous nodules or masses within the spleen.

Fine-needle aspiration of lesions yields a predomiance of small lymphocytes. Myeloid and erythroid precursors may be seen, particularly in anemic patients (Figure 2). A concurrent CBC analysis is recommended to determine which hematologic abnormality is responsible for splenic EMH. Frequently, increased numbers of immature cells (eg, nucleated RBCs) may be seen in the circulation due to splenic EMH.
**Multicentric Lymphoma**

Lymphoma is a systemic disorder of uncontrolled proliferation of neoplastic lymphoid cells. Multicentric lymphoma is the most common form of lymphoma in dogs, and the liver and/or spleen are frequently involved (Stage IV).\textsuperscript{12} Infiltration of neoplastic lymphoid cells often causes a diffuse enlargement of the spleen that results in a characteristic “honeycomb” or “moth-eaten” appearance on ultrasonography (\textit{Figure 3}, previous page),\textsuperscript{13} which has a sensitivity of 100\%, specificity of 23.3\%, positive predictive value of 64.7\%, negative predictive value of 100\%, and accuracy of 68.1\% for diagnosis of splenic lymphoma.\textsuperscript{13}

In one study, fine-needle splenic aspirate findings confirmed lymphoma in all multicentric lymphoma patients with a moth-eaten appearance of the spleen.\textsuperscript{13} Further differentiating lymphoma type (B-cell vs T-cell) using flow cytometry helps with prognosis. Treatment with chemotherapy is considered standard of care and is associated with 80\% to 90\% remission rates with median survival times of 10 to 12 months, depending on the chemotherapy protocol used.\textsuperscript{12}

**Nodular Hyperplasia/Hematoma**

Nodular hyperplasia and hematoma are thought to be a continuum of the same process, which starts as nodular hyperplasia and possibly results in formation of a hematoma.\textsuperscript{10} Hyperplastic nodules are benign masses that typically cause discrete abnormal areas in the spleen. During ultrasonography, hyperplastic nodules appear as focal or diffuse discrete hyperechoic, hypoechoic, or isoechoic masses—which may or may not cause shadowing—in the spleen. They may cause an irregular splenic border, but rarely do hyperplastic nodules distort, or bulge, the splenic capsule. These nodules cannot be distinguished from neoplasia by ultrasonography alone.\textsuperscript{13,14} They consist of a benign accumulation of cells normally found in the spleen, including lymphoid, hematopoietic, and plasmacytic cellular infiltrates, and develop in response to antigenic stimulation from a variety of inflammatory or neoplastic conditions.\textsuperscript{11}
One study suggested that a hematoma may develop when blood flow (out of the spleen) is disrupted by hyperplastic nodules.3

Hematomas consist of hemorrhage and organized fibrin and are the most common benign splenic lesion (Figure 4).2,3 Although uncommon, some hyperplastic nodules, especially large hyperplastic nodules, may distort or bulge the splenic capsule. Hemoabdomen may also occur, but the incidence is markedly lower than in hemangiosarcoma.2 Surgical excision is indicated for hematomas and hyperplastic nodules large enough to cause splenomegaly, with excision being curative. Because hematomas may develop in neoplastic tissue, submission of the entire spleen for histopathology is crucial to minimize the risk for misclassifying a malignant neoplasm as a hematoma.16

5 Congestion

Splenic congestion has numerous causes, including sedation, anesthesia, thrombosis, right-sided congestive heart failure, splenic torsion, and portal hypertension. Splenic congestion may cause severe splenomegaly and clinical signs, as the spleen is capable of pooling up to 30% of blood volume.10 Smooth muscle relaxation may be responsible for drug-induced splenic congestion, which is transient and may be limited to certain drugs (eg, phenothiazine sedatives, ultrashort-acting barbiturates).17 Administration of acepromazine, thiopental, or propofol produces marked splenomegaly.18 Severe hepatic disease may lead to portal hypertension and subsequent splenomegaly. Increased systemic hydrostatic pressure from right-sided congestive heart failure or increased splenic vein hydrostatic pressure because of thrombosis may cause splenic congestion.

Treatment of the underlying disease in these conditions may relieve or reduce splenomegaly. In cases of splenic torsion (Figures 5 and 6), splenectomy is the recommended treatment, with approximately 90% of dogs surviving to discharge.19

References

Over recent decades, the incidence of tick-borne diseases has been steadily increasing as many species of ticks expand their range into new areas and increase their abundance in areas where they are already present.

A clinician’s ability to make an accurate differential diagnosis for a patient showing clinical signs is greatly enhanced through knowledge of the tick species found where patients may be exposed and the diseases they transmit.

The following images feature ticks commonly identified on humans and companion animals in the northeastern United States, though their range may extend throughout much of North America. Attached ticks may be in varying degrees of engorgement when found infesting a host; these images represent the active host-seeking stage and may also help identify a tick attached to a host for less than 24 hours. The ticks were photographed on the author’s hand to show scale; a close-up view is included to show details useful for identification.

**FIGURE** Male (A) and nymphal (B) deer ticks (*Ixodes dammini*), also known as black-legged ticks or the northern clade of *Ixodes scapularis*.

These ticks are distinguished by their oval shape and dark black legs and mouthparts. The female tick has a small black dorsal shield and a red body, whereas the male tick has a black dorsal shield covering its entire body.

Deer ticks are typically found in the northeastern United States from Virginia north into Canada, as well as in Wisconsin and Minnesota, though their range is rapidly expanding. They serve as the vectors for Lyme disease (*Borrelia burgdorferi*), anaplasmosis (*Anaplasma phagocytophilum*), babesiosis (*Babesia microti*), *Borrelia miyamotoi*, ehrlichiosis (*Ehrlichia muris*), and deer tick virus encephalitis (a subtype of Powassan virus).

All active stages, except for the adult male, feed on a variety of animals.
IMPORTANT SAFETY INFORMATION: NexGard® (afoxolaner) is for use in dogs only. The most frequently reported adverse reactions included pruritus, vomiting, dry/flaky skin, diarrhea, lethargy, 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. For more information, see full prescribing information or visit www.NexGardForDogs.com.

NexGard is a Merial product. Merial is now part of Boehringer Ingelheim.

Preferred by dogs¹ and dog owners² – NexGard® (afoxolaner) makes it easy to protect your canine patients against fleas and four of the most common species of ticks in North America.

¹Data on file at Merial. 
²Data on file at Merial. Based on veterinary dispensed dose data.

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NexGard® (afoxolaner) is available in four sizes of beef-flavored, soft chewables for oral administration to dogs and puppies of body weight 4 pounds or greater, weighing 4 pounds of body weight or greater, for one month.

CAUTION:

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

Description:

NexGard is available in four sizes of beef-flavored soft chewables 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) to dogs of body weight 1.1 lbs and greater. Each chewable is formulated to provide a minimum afoxolaner dosage of 1.14 mg/lb (2.5 mg/kg) to dogs of body weight 4 pounds or greater, weighing 4 pounds of body weight or greater, for one month.

Dosing Schedule:

<table>
<thead>
<tr>
<th>Body Weight</th>
<th>Minimum Afoxolaner Dosage Per Chewable (mg)</th>
<th>Afoxolaner Administered</th>
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<tbody>
<tr>
<td>10.1 to 24.0 lbs.</td>
<td>28.3 One</td>
<td>11.3 mg</td>
</tr>
<tr>
<td>24.1 to 33 lbs.</td>
<td>68 One</td>
<td>13.6 mg</td>
</tr>
<tr>
<td>Over 33 lbs.</td>
<td>136 One</td>
<td>27.2 mg</td>
</tr>
</tbody>
</table>

NexGard can be administered with or without food. Care should be taken that the dog consumes the complete dose, and treated animals should be observed for a few minutes to ensure that part of the dose is not lost or refasted. It is suspected that any of the dose has been lost if vomiting occurs within two hours of administration, notice with another full dose. If a dose is missed, administer the next dose on the next monthly day.

Mode of Action:

Afoxolaner is a member of the isoxazoline family, shown to bind at a binding site to inhibit insect and acarine ligand-gated chloride channels, in particular those present on the nervous system, neuronal and gamma-aminobutyric acid (GABA). Presynaptically, afoxolaner reduces transmitter release in an uncompetitive manner onto the cerebellum and other brain regions of the nervous system. The selective toxicity of afoxolaner depends on the affinity of the insect and acarines for AChBP receptors versus mammalian GABA receptors.

Effectiveness:

In a well-controlled laboratory study, NexGard began to kill fleas four hours after initial administration and demonstrated 99% effectiveness at eight hours. In a separate well-controlled laboratory study, NexGard demonstrated 100% effectiveness against adult Ixodes scapularis post-infection by 25 days, and 99% effectiveness at 12 days post-infection against Dermacentor variabilis post-infection by 53 days. In a field study, NexGard was effective against both the treated and control groups that were infested with fleas on day 0.1 gastro-jejunal-flea eggs on day 3 and 24-hour post-treatment (D. 11 eggs and 1 egg in the NexGard treated dogs, and 46 eggs and 18 eggs in the control dogs, or 12 and 24 hours, respectively). At subsequent evaluations post-infection, fleas from dogs in the NexGard dogs were essentially unable to produce any eggs (0-1 egg) while fleas from dogs in the control group continued to produce eggs (11-14 eggs).

In a 30 day US field study conducted in households with existing flea infestations of varying severity, the effectiveness of NexGard against fleas on day 30 on 60%, 30%, 17%, and 4%, respectively. Collectively, the data from the three studies conducted in laboratory and field demonstrate that NexGard’s flea efficacy before they can lay eggs, thus preventing subsequent infestation after the start of treatment of existing flea infestations.

Adverse Reactions:

For well-controlled US field study, which included a total of 333 households and 615 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 were vomiting and soft defecations, and short episodes of transient serum enzyme increases (see Table 1). The most frequently reported adverse reactions were vomiting. The occurrence of vomiting was generally self-limiting and of short duration and did not lead to decreases with subsequent dosings in both groups. Five trueto nine dogs experienced anorexia during the study, and two of these dogs experienced anorexia with the first dose but not subsequent dosages.

Table 1. Dogs With Adverse Reactions.

<table>
<thead>
<tr>
<th>Treatment Group</th>
<th>Number of Dogs</th>
<th>Number of Dogs with Adverse Reaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>NexGard</td>
<td>333</td>
<td>146</td>
</tr>
<tr>
<td>Control</td>
<td>332</td>
<td>132</td>
</tr>
</tbody>
</table>

Number of days in the administration group with the identified abnormality. Number of dogs in the control group with the identified abnormality.

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 the same day after receiving the second dose of NexGard. This dog experienced a first seizure 1 week after receiving the third dose. The day remained vomiting and completed the study. This dog remained vomiting and completed the study. A third dog with a history of seizures received NexGard and experienced no seizures throughout the study.

In a well-controlled laboratory study, NexGard demonstrated >97% effectiveness against Dermacentor variabilis, Ixodes scapularis, and Lone Star tick (Amblyomma americanum) and Brown dog tick (Rhipicephalus sanguineus) infestations in dogs and puppies 8 weeks of age and older, weighing 4 pounds of body weight or greater, for one month.

Dosage and Administration:

NexGard is given orally, one time, at the minimum afoxolaner dosage of 1.14 mg/lb (2.5 mg/kg) in the dog by ligation of the splenic and short gastric arteries. Vet Surg. 1989;18(2):110-113.


15. Lee A. Personal communication. Mississippi State University College of Veterinary Medicine Radiology Department.


**HEARTGARD® Plus (ivermectin/pyrantel)**

**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 ascarids (Toxascaris canis, Toxascaris leonina) and hookworms (Ancylostoma caninum, Uncinaria stenocephala, Ancylostoma braziliense). Monthly treatment with HEARTGARD Plus also provides effective treatment and control of ascarids (Toxascaris canis, Toxascaris leonina) and hookworms (Ancylostoma caninum, Uncinaria stenocephala, Ancylostoma braziliense).

**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 ascarids (Toxascaris canis, Toxascaris leonina) and hookworms (Ancylostoma caninum, Uncinaria stenocephala, Ancylostoma braziliense).

**DOSEAGE:** HEARTGARD® Plus (ivermectin/pyrantel) should be administered orally at monthly intervals at the recommended minimum dose level of 6 mg of ivermectin per kg (2.72 mg/lb) of body weight. The recommended dosing schedule for prevention of canine heartworm disease and for the treatment and control of ascarids and hookworms is as follows:

<table>
<thead>
<tr>
<th>Dog Weight</th>
<th>Chewables Per Month</th>
<th>Ivermectin Content</th>
<th>Pyrantel Content</th>
<th>Color Coding On Foil Backing and Carton</th>
</tr>
</thead>
<tbody>
<tr>
<td>Up to 10 lb</td>
<td>1</td>
<td>68 mcg</td>
<td>57 mcg</td>
<td>Blue</td>
</tr>
<tr>
<td>11 to 20 lb</td>
<td>1</td>
<td>136 mcg</td>
<td>114 mcg</td>
<td>Green</td>
</tr>
<tr>
<td>21 to 50 lb</td>
<td>1</td>
<td>272 mcg</td>
<td>227 mcg</td>
<td>Brown</td>
</tr>
</tbody>
</table>

**HEARTGARD® Plus is recommended for dogs 6 weeks of age and older.**

**ADMINISTRATION:** Remove only one chewable at a time from the foil-backed blister card. Return the card with the remaining chewables to its box to protect the product from light. Because most dogs get HEARTGARD Plus pastable, the product can be offered to the dog by hand. Alternatively, it may be added intact to a small amount of dog food. The chewable should be administered in a manner that encourages the dog to chew, rather than to swallow without chewing. Chewables may be broken into pieces and fed to dogs that normally swallow treats whole.

Care should be taken that the dog consumes the complete dose, and treated animals should be observed for a few minutes after administration to ensure that the entire dose of the chewable is not lost or rejected. If it is suspected that any of the dose has been lost, redosing is recommended.

**HEARTGARD® Plus should be given at monthly intervals during the period of the year when mosquitoes (bites), 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 on 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 retesting of the recommended dosing regimen will maximize the opportunity for the development of adult heartworms.

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

**EFFICACY:** HEARTGARD Plus Chewables, given 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 ascarids (T. canis, T. leonina) and hookworms (A. caninum, U. stenocephala, A. braziliense).

**ACCEPTABILITY:** In acceptability and field trials, HEARTGARD Plus was shown to be an acceptable oral dosage form 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 adult D. immitis. Infected dogs must be treated to remove adult heartworms and microfilariae before initiating a program with HEARTGARD Plus. When replacing another heartworm preventive product in a heartworm disease preventive program, the first dose of HEARTGARD Plus should be given within a month (30 days) after the dog's last exposure to mosquitoes.

**SHEEP/GOAT HEARTGARD Plus® is not effective for microfilaria clearance. A mild hypersensitivity-type reaction, presumably due to death of microfilariae and particularly interesting transient diarrhea, has been observed in clinical trials with ivermectin alone after treatment of some dogs that have circulating microfilariae.**

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

**ADVERSE REACTIONS:** In clinical field trials with HEARTGARD Plus, vomiting or diarrhea within 24 hours of dosing was rarely observed (1.1% of administered doses). The following adverse reactions have been reported following the use of HEARTGARD: Depression/lethargy, vomiting, anorexia, diarrhea, myclitis, ataxia, staggering, convulsions and hypoglycemia.

**SAFETY:** HEARTGARD Plus has been shown to be equivalent to HEARTGARD, with respect to the bioavailability of ivermectin. The dose regimens of HEARTGARD Plus and HEARTGARD are the same with regard to ivermectin (6 mcg/kg). Studies with invertebrates 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. Elevated doses, sensitive dogs showed adverse reactions which included myclitis, depression, ataxia, tremors, drooling, panting, recumbency, excitement, stupor, coma and death. HEARTGARD® Plus demonstrated signs of toxicity at 10 times the recommended dose (60 mcg/kg) in sensitive Collies. Results of these trials and bioequivalency studies, support the safety of HEARTGARD® Plus 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 multi-clinical trials, many commonly used flea collars, dips, shampoos, anthelminics, antibiotics, vaccines and other products have been administered with HEARTGARD Plus in a heartworm disease prevention program.**

In one trial, where some puppies 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 DOSEAGE section) for dogs of different weights. Each strength comes in convenient cartons of 6 and 12 chewables.

For customer service, please contact Merial at 1-888-637-4251.

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QUIZ CORNER

1. **TOP 5 PAGE 16**
   Which of the following would not be a consequence of caval syndrome in a heartworm-infected dog?
   A. Pulmonary hypotension
   B. Right-sided heart dysfunction
   C. Intravascular hemolysis
   D. Hemoglobinuria

2. **PROCEDURES PRO PAGE 31**
   Uncomplicated ulcerative keratitis typically resolves in ________ days with appropriate treatment.
   A. 1 to 2
   B. 3 to 5
   C. 5 to 7
   D. 8 to 10

3. **TOP 5 PAGE 59**
   When examining a patient for biceps tenosynovitis, pain may be elicited from an affected patient by applying pressure on the biceps tendon in the intertubercular groove when the shoulder is ________ and the elbow is ________.
   A. Flexed, flexed
   B. Flexed, extended
   C. Extended, flexed
   D. Extended, extended

4. **THERAPEUTICS SNAPSHOT PAGE 65**
   What is the mode of action of the isoxazoline class of parasiticides?
   A. Antagonize nicotinic acetylcholine receptors
   B. Alter nerve membrane permeabilities to sodium and potassium ions
   C. Inhibit GABA- and glutamate-gated chloride channels
   D. Inhibit acetylcholinesterase

5. **PROCEDURES PRO PAGE 73**
   The majority of the spleen blood supply comes from the:
   A. Short gastric arteries
   B. Ventral branch of the splenic artery
   C. Dorsal branch of the splenic artery
   D. Left gastric artery

6. **TOP 5 PAGE 81**
   Which of the following is not a function of the spleen red pulp?
   A. Removal of senescent or damaged blood cells
   B. Storage of immune cells
   C. Metabolism and recycling of iron
   D. Hematopoiesis

**WE ASKED …**
Which parasite have you never seen during microscopic evaluation?

**YOU ANSWERED …**
A. *Cheyletiella spp* (either *Cyasguri* or *C. Blakei*) .......... 14%
B. *Capillaria plica* .............................................. 28%
C. *Demodex gatoi* .............................................. 10%
D. *Dirofilaria immitis* microfilariae .............. 6%
E. More than one of the above .............. 42%

**THIS MONTH’S QUESTION …**
If you could add any diagnostic modality to your practice, what would it be?
A. Endoscopy
B. Ultrasonography
C. Telemedicine services
D. Dental x-ray unit

Go to cliniciansbrief.com to weigh in.
Nutrition clinically shown to stabilize markers of kidney function in cats with early chronic kidney disease (CKD)

Provides 13% more high quality, highly digestible protein for cats*

Nutrition clinically shown to help sustain a healthy body condition

*vs. Prescription Diet® k/d®

NEW PRESCRIPTION DIET®

k/d® Early Support

Introducing the food specifically designed for patients with Stage 1 CKD. Combined with an earlier diagnosis using the IDEXX SDMA™ test, you can change the lives of cats sooner than ever.

ACT EARLY — talk to your Hill’s Representative about k/d® Early Support today.
TRUST.

PREVENTS HEARTWORM DISEASE
TREATS AND CONTROLS 3 SPECIES OF HOOKWORMS
TREATS AND CONTROLS 2 SPECIES OF ROUNDWORMS
OWNERS PREFER IT1 AND DOGS LOVE IT2

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 visit www.HEARTGARD.com. See page 91 for product information summary.
Not AllTicks
Are Created Equal

Know the Difference. Know the Risks.

Although there are between 800-900 species of ticks globally, only a portion of them have the ability to transmit diseases to dogs. But that doesn’t mean this small group doesn’t pose major threats to your patients. In fact, a single tick can expose a dog to multiple disease agents, and some can even cause paralysis due to the absorption of toxins released by the tick during the feeding process.1,2

Additionally, ticks have the ability to transmit a variety of bacterial, viral and protozal diseases. Afflictions such as bite wounds, secondary bacteria infections and blood loss can pose significant medical issues during a tick infestation, even if the dog has no other diseases.

The chart below makes it easy to identify the four most common species of ticks in the U.S. by looking at two key factors: the mouthparts and the scutum.

<table>
<thead>
<tr>
<th>Simple Tick Identification</th>
<th>Long mouthparts</th>
<th>Short mouthparts</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ornate scutum</td>
<td>Lone star tick</td>
<td>American dog tick</td>
</tr>
<tr>
<td></td>
<td><em>Amblyomma americanum</em></td>
<td><em>Dermacentor variabilis</em></td>
</tr>
<tr>
<td>Inornate scutum</td>
<td>Deer tick or black-legged tick</td>
<td>Brown dog tick</td>
</tr>
<tr>
<td></td>
<td><em>Ixodes scapularis</em></td>
<td><em>Rhipicephalus sanguineus</em></td>
</tr>
</tbody>
</table>

**Indications**

Credelio kills adult fleas and is indicated for the treatment 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.

**Important Safety Information**

The safe use of Credelio in breeding, pregnant or lactating dogs has not been evaluated. Use with caution in dogs with a history of seizures. The most frequently reported adverse reactions are weight loss, elevated blood urea nitrogen, excessive urination, and diarrhea. See back cover for full safety information.
Assess the Risk

Tick populations across the U.S.

Geographically, Regionally and Environmentally

Geographic and climatic conditions can result in dramatic variations in tick species. 1 Ticks thrive in areas with high relative humidity, which is conducive to their development, activity and survival. Additionally, areas with dense vegetation provide ideal microclimates. 1

To assist in the proper identification of dangerous ticks, the table below highlights the four tick species Credelio protects against, including their appearance, when they are most active and the diseases they can spread.

<table>
<thead>
<tr>
<th>Common Name</th>
<th>Scientific Name</th>
<th>Larvae:</th>
<th>Nymphs:</th>
<th>Adults:</th>
<th>Seasonality</th>
<th>Diseases Transmitted</th>
</tr>
</thead>
<tbody>
<tr>
<td>American dog tick</td>
<td>Dermacentor variabilis</td>
<td>Some seek hosts in late summer but others overwinter and become active in February</td>
<td>Spring and early summer</td>
<td>April through August</td>
<td>Late spring to early fall in temperate zones, year-round in warmer areas</td>
<td>Rocky Mountain spotted fever (Rickettsia rickettsii), Babesiosis (Babesia canis, Hepatozoonosis (Hepatozoon canis)</td>
</tr>
<tr>
<td>Brown dog tick</td>
<td>Rhipicephalus sanguineus</td>
<td>Late spring to early fall in temperate zones, year-round in warmer areas</td>
<td></td>
<td></td>
<td></td>
<td>Rocky Mountain spotted fever (Rickettsia rickettsii), Babesiosis (Babesia canis, Ehrlichiosis (Ehrlichia ewingii, Ehrlichia chaffeensis), other spotted fevers (Rickettsia amblyommii), Ehrlichiosis (Ehrlichia canis)</td>
</tr>
<tr>
<td>Deer tick or black-legged tick</td>
<td>Ixodes scapularis</td>
<td>August and September</td>
<td>May to July (north) and January to September (south)</td>
<td>October to December or March to May</td>
<td>Larvae: August and September, Nymphs: May to July (north) and January to September (south), Adults: October to December or March to May</td>
<td>Lyme disease (Borrelia burgdorferi), Anaplasmosis (Anaplasma phagocytophilum)</td>
</tr>
<tr>
<td>Lone star tick</td>
<td>Amblyomma americanum</td>
<td>Late summer to fall</td>
<td>March to September</td>
<td>Late February to early June</td>
<td></td>
<td>Ehrlichiosis (Ehrlichia ewingii, Ehrlichia chaffeensis), other spotted fevers (Rickettsia amblyommii)</td>
</tr>
</tbody>
</table>

Assess the Risk

Geographically, Regionally and Environmentally

Geographic and climatic conditions can result in dramatic variations in tick species. Ticks thrive in areas with high relative humidity, which is conducive to their development, activity and survival. Additionally, areas with dense vegetation provide ideal microclimates.

To assist in the proper identification of dangerous ticks, the table below highlights the four tick species Credelio protects against, including their appearance, when they are most active and the diseases they can spread.

### Tick Field Guide

<table>
<thead>
<tr>
<th>Common Name</th>
<th>Scientific Name</th>
<th>Adult Female</th>
<th>Adult Male</th>
<th>Seasonality</th>
<th>Diseases Transmitted</th>
</tr>
</thead>
<tbody>
<tr>
<td>American dog tick</td>
<td>Dermacentor variabilis</td>
<td>![Image]</td>
<td>![Image]</td>
<td>Larvae: Some seek hosts in late summer but others overwinter and become active in February. Nymphs: spring and early summer. Adults: April through August.</td>
<td>Rocky Mountain spotted fever (Rickettsia rickettsii), ehrlichiosis (Ehrlichia canis).</td>
</tr>
<tr>
<td>Brown dog tick</td>
<td>Rhipicephalus sanguineus</td>
<td>![Image]</td>
<td>![Image]</td>
<td>Late spring to early fall in temperate zones, year-round in warmer areas.</td>
<td>Rocky Mountain spotted fever (Rickettsia rickettsii), babesiosis (Babesia canis vogeli), ehrlichiosis (Ehrlichia canis), hepatozoonosis (Hepatozoon canis).</td>
</tr>
<tr>
<td>Deer tick or black-legged tick</td>
<td>Ixodes scapularis</td>
<td>![Image]</td>
<td>![Image]</td>
<td>Larvae: August and September. Nymphs: May to July (north) and January to September (south). Adults: October to December or March to May.</td>
<td>Lyme disease (Borrelia burgdorferi), Anaplasmosis (Anaplasma phagocytophilum).</td>
</tr>
<tr>
<td>Lone star tick</td>
<td>Amblyomma americanum</td>
<td>![Image]</td>
<td>![Image]</td>
<td>Larvae: Late summer to fall. Nymphs: March to September. Adults: Late February to early June.</td>
<td>Ehrlichiosis (Ehrlichia ewingii, Ehrlichia chaffeensis), other spotted fevers (Rickettsia amblyomnii).</td>
</tr>
</tbody>
</table>

References:
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 CREDELIO. 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 CREDELIO.

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/AnimalVeterinary/SafetyHealth.

Clinical Pharmacology:

Following oral administration of 43 mg/kg (approximately 1X the maximum labeled dose), peak lotilaner concentrations were achieved between 6 hours and 3 days in dogs 2 months of age and between 1 and 7 days in dogs 10 months of age. Dogs 2 months of age had a shorter elimination half-life (average of 9.8 days) than at 10 months of age (average of 39.4 days). Due to reduced drug bioavailability in the fasted state, CREDELIO must be administered with a meal or within 30 minutes after feeding.

Mode of Action:

Lotilaner is an ectoparasiticide belonging to the isoxazoline group. Lotilaner inhibits insect and acarine gamma-aminobutyric acid (GABA)-gated chloride channels. This inhibition blocks the transfer of chloride ions across cell membranes, which results in uncontrolled neuromuscular activity leading to death of insects and acarines. The selective toxicity of lotilaner between insects and acarines and mammals may be inferred by the differential sensitivity of the insects and acarines' GABA receptors versus mammalian GABA receptors.

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, dermatitis/pyoderma and pruritus as a direct result of eliminating fleas.

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.

Palatability: In the U.S. field study, which included 567 doses administered to 198 dogs, 80.4% of dogs voluntarily consumed CREDELIO when offered by hand or in an empty bowl, an additional 13.6% consumed CREDELIO when offered with food, and 6.0% required placement of the chewable tablet in the back of the dog’s mouth.

Animal Safety:

In a margin of safety study, CREDELIO was administered orally to 24 8-week-old Beagle puppies at doses of 43 mg/kg, 129 mg/kg, and 215 mg/kg (approximately 1, 3, and 5X the maximum labeled dose, respectively) every 28 days for eight consecutive doses. The 8 dogs in the control group (OX) were untreated. There were no clinically-relevant, treatment-related effects on clinical observations, physical and neurological examinations, body weights, food consumption, electrocardiograms, clinical pathology (hematology, clinical chemistry, coagulation profiles and urinalysis), gross pathology, histopathology, or organ weights. Blood concentrations of lotilaner confirmed systemic exposure of all treated dogs, although the exposure was less than dose proportional at 5X.

In a well-controlled field study, CREDELIO was used concurrently with other medications, such as vaccines, anthelmintics, antibiotics, steroids, NSAIDS, anesthetics, and antihistamines. No adverse reactions were observed from the concomitant use of CREDELIO with other medications.

Storage Information:

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

How Supplied:

CREDELIO 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 1 or 6 chewable tablets.

NADA #141-494, Approved by the FDA

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Credelio.com

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