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Dogs should be tested for heartworm 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.

See page 16 for full prescribing information.

* A. caninum.
** Prevents flea eggs from hatching; is not an adulticide.

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EDITORS IN CHIEF
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Clindamycin, a lincosamide antibiotic, is labeled for oral treatment of bacterial infections of the skin, soft tissue, periodontal tissue, and bone.

- **Dogs & cats:** Dental and soft tissue infections; skin infections (wounds and abscesses) caused by susceptible organisms
  - **Dogs:** 5.5–33 mg/kg PO q12h
  - **Cats:** 11–33 mg/kg PO q24h
- **Dogs only:** Osteomyelitis
  - 11–33 mg/kg PO q12h

In one study of canine posttraumatic osteomyelitis, 11 mg/kg q12h appeared more effective than a lower dose of 5.5 mg/kg q12h. In a more recent study, in vitro resistance was documented in 59% of organisms cultured from dogs with osteomyelitis (predominantly posttraumatic and staphylococcal).

Clindamycin is also used for treatment of toxoplasmosis in cats.

- 25 mg/kg PO q24h or divided q12h
- Except for ocular lesions, which typically require adjunct therapy, clinical signs resolve in most cats.

Inducible resistance to clindamycin may occur in methicillin-resistant staphylococci (even those reported sensitive in vitro) and is mediated by ribosomal modification.

- Cross-resistance can occur between macrolides and lincosamides.
  - When strains of methicillin-resistant staphylococci are reported resistant to erythromycin, inducible clindamycin resistance (not detectable by standard susceptibility methods) should be suspected.
  - In one study, 47% of MRSA and 74% of MRSP isolates from dogs and cats were reportedly resistant to clindamycin.
  - More testing showed that 58% of isolates initially reported as erythromycin-resistant but clindamycin-sensitive had inducible clindamycin resistance.
Mechanism & Spectrum of Action

As a lincosamide, clindamycin inhibits bacterial protein synthesis by binding to the 50S ribosomal subunit.
• Because they share the same mechanism of action, lincosamides and macrolides (eg, azithromycin) may interfere with each other’s antibacterial activity when used together.

Spectrum of action includes gram-positive organisms and anaerobes, as well as *Mycoplasma* spp and some protozoa.
• Susceptible organisms include
  — Gram-positive aerobes: *Streptococci*, coagulase-positive *staphylococci*
  — One study showed that some strains of *Bacteroides* spp (17% of veterinary isolates) and *Clostridium* spp (20%) may be resistant.7
  — Protozoa: *Toxoplasma* spp, *Neospora* spp

Pharmacokinetics

Oral absorption in dogs and cats is rapid.1
• FDA-approved veterinary use: PO formulation (ie, tablets, capsules, oral liquid)
• Extralabel use: Anecdotally, injectable formulation marketed for humans has been used in dogs and cats.
  — Generally used for patients that cannot be medicated orally or when GI disease may limit oral absorption
  — Parenteral dosing is similar to PO formulation because of high bioavailability by all routes studied.
    — Dogs: Bioavailability at least 87% after IM administration8,9 and 73% after PO administration10
    — Rapid IV injection of undiluted clindamycin has been associated with cardiac arrest and hypotension in humans, so dilution and slow IV administration is advised in animals.

Clindamycin undergoes hepatic metabolism and is excreted primarily in bile (less in urine).1
• Half-life after PO administration1
  — Dogs: 5 hours
  — Cats: 7.5 hours
• Prolonged half-life may be seen in patients with significant hepatic or renal dysfunction.

Because clindamycin undergoes hepatic metabolism and is primarily excreted in bile, prolonged half-life may be seen in patients with significant hepatic or renal dysfunction.
Clindamycin is well distributed into respiratory tissue, skin, other soft tissue, bone, and joints and can be found in pancreatic and prostatic secretions.

- Although high concentrations are not found in the cerebrospinal fluid of healthy cats, clindamycin does penetrate brain tissue\(^1\) and may more easily cross inflamed meninges.

### Adverse Reactions & Cautions

**Adverse effects in dogs and cats include vomiting, diarrhea, and inappetence.\(^1,8,12\)**

- In cats, capsules have been associated with esophageal strictures.\(^13\)
- Avoid dry-pilling\(^13\)
- Because clindamycin has neuromuscular-blocking properties, use with caution in the presence of anesthetics or other neuromuscular-blocking agents.\(^1\)
- Administer with caution in patients with very severe renal disease and/or hepatic disease accompanied by severe metabolic aberrations.\(^1\)

MELISSA CLARK, DVM, PhD, DACVCP, is a resident in small animal internal medicine at The Animal Medical Center in New York City. She earned her DVM from Washington State University and worked in small animal general practice before completing a residency in clinical pharmacology and earning her PhD in veterinary pharmacology at University of Illinois.

### REFERENCES


MRSA = methicillin-resistant Staphylococcus aureus, MRSP = methicillin-resistant Staphylococcus pseudintermedius

MORE on page 33
Methimazole is a popular antithyroid drug used for treating hyperthyroid cats in the U.S., particularly when radioiodine is not readily available or is cost prohibitive.

Overview

⚠ Methimazole is approved for use in animals (Felimazole; dechra-us.com) and humans.

⚠ Methimazole compounded with pluronic lecithin organogel (PLO) is one of few veterinary drugs with demonstrated efficacy when administered transdermally.
  —Concentration: 50 mg/mL
  —Starting dose: 2.5 mg/cat q12h

Toxicities

⚠ Dose-dependent
  • In 10%–20% of cats treated with oral methimazole, mild-to-moderate vomiting, diarrhea, and decreased appetite typically developed during the first 4 weeks of treatment.1,2
    —GI signs are significantly less common in cats receiving transdermal treatment than in those receiving oral methimazole.1
  • Cats often develop mild increases in BUN and creatinine with treatment to the euthyroid state.3
    —Low urine specific gravity and high serum thyroxine (T4) concentrations may increase risk for posttreatment development of azotemia,4 although cats with highly concentrated urine can still be at risk.5
    —Serum T4 concentrations should be targeted to the mid-normal range, as overtreatment to low serum T4 can worsen azotemia and lead to shortened survival times.6

⚠ Idiosyncratic
  • Acute, apparently nondose-dependent (ie, idiosyncratic) toxicities can develop at 1–4 weeks of treatment and typically include
    —Facial excoriation around the neck and pinnae, blood dyscrasias (eg, neutropenia, thrombocytopenia), and new hepatopathy
      —Leukopenia resulting from only lymphopenia does not indicate methimazole discontinuation.
  • Idiosyncratic hepatopathy is typically a mixed pattern (ie, with elevations in both hepatocellular and cholestatic enzymes) and may involve hyperbilirubinemia.
    —Liver enzyme activity should be compared with values obtained before treatment, as many hyperthyroid cats have elevated ALT and/or ALP at diagnosis.7
      ▫ These should resolve with treatment.
  • Cats may develop myasthenia gravis, characterized by neuromuscular weakness and positive acetylcholine receptor autoantibodies during the first few months of treatment8,9; however, this is rare.

WORDS OF CAUTION | Risks | Adverse Events | Toxicities

Lauren A. Trepanier, DVM, PhD, DACVIM, DACVCP
University of Wisconsin–Madison
Management of Adverse Events

⚠️ For simple GI upset without biochemistry abnormalities, discontinue methimazole until signs resolve.
- Restart at a 50% dose reduction or switch to transdermal methimazole.¹

⚠️ Idiosyncratic toxicities fail to respond to dose reduction.
- Discontinue methimazole and schedule alternative treatment (eg, radiiodine, Hill’s Prescription Diet y/d Feline Thyroid Health [hillsvet.com], thyroidectomy).
  - For facial excoriation and if pruritus is severe, consider short-term antiinflammatory doses of prednisolone.
  - For blood dyscrasia, evaluate for fever or bruising.
    - Neutropenia and thrombocytopenia will typically resolve after drug discontinuation without additional intervention.¹⁰
    - In cases of severe neutropenia (ie, <1000–1500 µL), antibiotics (eg, amoxicillin–clavulanate) may be indicated.
    - Recheck CBC 1 week after discontinuation.
      - For hepatopathy, consider short-term treatment with glutathione precursor (eg, S-adenosylmethionine [SAMe])
      - Recheck liver enzyme activity 1–2 weeks after discontinuation.
      - For myasthenia gravis, consider pyridostigmine treatment.
      - Follow clinical response and acetylcholine receptor antibody titers after discontinuation.

⚠️ Rechecks at 2 and 4 weeks after treatment initiation should be sufficient to determine euthyroidism and presence of toxicity.
- Along with monitoring serum T₄ concentrations and general clinical status, cats should be monitored for
  - New azotemia via BUN, creatinine, and urine specific gravity
  - Idiosyncratic toxicity via CBC and liver enzyme activities
- Once euthyroid state reached, routinely (q3–6mo) check renal values, blood pressure, and serum T₄ concentrations.

Monitoring

⚠️ Clinical monitoring by owners is important, as toxicities can develop between routine re-checks.
**Fluoroquinolone-Resistant Escherichia coli**

**FLUOROQUINOLONE (FQ)-RESISTANT ESCHERICHIA COLI**

- FQ-resistant isolates are frequently multidrug resistant.
- Suggested alternative antimicrobials should be used only with favorable susceptibility test results.
- Therapeutic concentrations may not be achievable with intracellular or deep tissue infections or in the presence of biofilms.

**Dx = Diagnosis**

**Urinary tract infection**
- **Dx** Cystitis
- **Dx** Pyelonephritis
- **Dx** Prostatitis

**Dx = Diagnosis**

**Systemic infection**
- **Dx** Pneumonia
- **Dx** Septicemia

**Oral or parenteral**
- **Oral** Pradofloxacin PO
  - Extralabel in dogs
- **Oral** Amikacin IV, IM, SC
  - Unlikely to achieve therapeutic concentrations in sequestered or deep tissue infections
  - Because of nephrotoxicity, therapy limited to 5–7 days
  - High-protein diet can reduce risk for renal damage
- **Oral** Fosfomycin PO
  - Human drug
- **Oral** Meropenem IV, SC
  - Human drug
- **Oral** Cefoxitin or cefotetan IV, IM, SC
  - Human drug
- **Oral** Ampicillin–sulbactam IV
  - Human drug

**Dx = Diagnosis**

**Oral** Nitrofurantoin
- Human drug

**Oral** Pradofloxacin
- Extralabel in dogs

**Oral** Trimethoprim–sulfamethoxazole

**Oral** Chloramphenicol

**Oral** Fosfomycin
- Human drug

** Tx = Treatment**

**FQ = fluoroquinolone**
**Author Insight**

- Some FQ-resistant isolates are susceptible to third-generation FQ pradofloxacin.
- Most are susceptible to nitrofurantoin, amikacin, fosfomycin, and meropenem.

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**REFERENCE**


**SUGGESTED READING**


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The following capsules provide brief overviews of key therapeutics studies explored in leading scientific journals.

**Lipid Binding Proteins in Helminths**

Soluble lipid binding proteins (LBPs) in parasitic helminths are a global health problem in humans and animals. LBPs aid the helminth in obtaining nutrients (e.g., fatty acids, cholesterol) from the host and may alter the immune response of that host. Understanding host-parasite relationships mediated by LBP structures and their interactions with ligands and membranes is important. Targeting LBPs may contribute to the development of new therapies and disease prevention.


**Melamine Toxicity in the Spleen**

Acute toxicity of melamine, a synthetic chemical used in the production of certain plastics and other products, has generally been thought to be low. However, this study found that mice treated with melamine alone and in combination with cyanuric acid developed toxic changes (e.g., variable sizes, irregular shapes) to splenic lymphocytes, as well as large numbers of dead cells. These results contribute to the toxic profile of melamine.


**Tyrosine as a Training Aid**

Certain canine behaviors (e.g., easy distraction, low attention span) can resemble those of children with ADHD. Catecholamine levels (which might be correlated with ADHD) and training ease were examined in 3 dog breeds (i.e., German shepherd dogs, Labrador retrievers, toy poodles) given oral tyrosine, which can increase catecholamine levels in the brain. Peripheral catecholamine levels were seemingly unchanged after daily oral tyrosine administration; however, the number of successful reactions to commands and reaction times to unknown stimuli in the shepherd dogs and retrievers improved significantly, suggesting the potential importance of neuronal catecholamine for appropriate attention levels.


**Isoflurane–Fentanyl Effects on Lagomorph Anesthetic Mortality**

Rabbits have high anesthetic mortality rates, likely caused by cardiovascular depression associated with inhalant drug use. Six New Zealand White rabbits were anesthetized with isoflurane in oxygen, and fentanyl was administered IV to achieve 6 target plasma concentrations. Isoflurane minimum alveolar concentrations (MACs) and plasma fentanyl concentrations for each MAC were determined. Fentanyl reduced isoflurane MAC by approximately 60%, a level similar to those reported in dogs, rats, and goats. Fentanyl may be a useful anesthetic adjunct, but further investigation of cardiorespiratory effects of isoflurane–fentanyl combinations in rabbits is warranted.

WHAT IS IT?
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• Treats/controls
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  – Adult roundworms: Toxascaris leonina, Toxocara canis
  – Adult tapeworms: Echinococcus multilocularis, Echinococcus granulosus, Taenia pisiformis

WHEN SHOULD I USE IT?
Monthly in dogs and puppies weighing at least 2 pounds and ≥ 6 weeks of age, year-round.

WHEN SHOULD I NOT USE IT?
• Dogs should be tested for existing heartworm infection prior to administration.
• Safety studies have not been conducted in pregnant or lactating dogs.
• Should not be administered to dogs or puppies weighing less than 2 pounds or less than 6 weeks of age.

WHERE CAN I GET IT?
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Parasitology

What Clients Need to Know

Dogs need protection from a range of parasites. SENTINEL® SPECTRUM® prevents flea infestation. In addition to the nuisance presented by fleas, disease risk is also a factor. SENTINEL SPECTRUM also prevents heartworm disease. When it comes to intestinal parasites, presence in a pet can be debilitating, and these parasites are easy for dogs to contract from the outdoor environment. SENTINEL SPECTRUM treats and controls hookworms, whipworms, roundworms, and tapeworms in a single monthly beef & bacon chewable that dogs actually like.

Dogs should be tested for heartworm 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. Please see full product label for more information.

The Rationale

- **Heartworm** disease can be devastating. CAPC and AAHA guidelines recommend prevention year-round.1,2
- **Tapeworms:** Studies have found that up to 60% of dogs can get tapeworms, yet tapeworms are commonly missed on fecal analysis.3
- **Fleas:** Lufenuron is the only systemic insect-growth regulator available, with a unique ability to inhibit the maturation process in fleas. *Ctenocephalides felis* remains on its host to feed, mate, and lay eggs. The drug is passed transovarially from the adult flea after feeding on host blood, and eggs fail to hatch. Immature fleas represent 95% of home infestation burdens.4
- **Intestinal Parasites:** Prevalence based on CAPC data is 1 out of every 49 dogs for hookworms, 1 out of every 49 dogs for roundworms, and 1 out of every 139 dogs for whipworms,5,6 which can survive in the soil for many years.5

Providing control for all these parasites in a single heartworm preventive keeps overall parasite control simple for the client, pet, and veterinarian.

References


See page 16 for complete prescribing information.

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HIV Antiviral Treatment Efficacy in FIV Patients

Six FIV-positive cats with clinical disease were treated with the antiretroviral compound (R)-9-(2-phosphonylmethoxypropyl)-2,6-diaminopurine [(R)-PMPDAP]. (R)-PMPDAP is an analog of tenofovir, a drug used to treat HIV in humans. An improvement in Karnofsky score, serum amyloid A, and gamma-globulin level, as well as a decreased FIV viral load, were noted in most cats, suggesting improved quality of life and well-being. Side effects were mild and reversible. Concurrent medications may have contributed to the observed improvements. The authors recommended further testing with more cats and the inclusion of control groups.


Susceptibility of Bacterial Isolates

In vitro studies were performed on 6 isolates each of Mycobacterium fortuitum and M smegmatis to determine how different drug combinations (commonly used individually to treat rapidly growing mycobacterial) interact against these bacteria. All of the M fortuitum isolates were sensitive to enrofloxacin, but only 4 were sensitive to doxycycline. Doxycycline, enrofloxacin, and trimethoprim–sulfanilamide were effective against all M smegmatis isolates. All 12 isolates were resistant to cefovecin, and one M smegmatis isolate was susceptible to clarithromycin. No synergistic or antagonistic effects were found.


Fentanyl & Buprenorphine: A Pharmacokinetic Comparison

Fentanyl, a mu-opioid agonist, and buprenorphine, a mu-opioid partial agonist, have similar physicochemical properties, both being highly protein-bound, lipophilic drugs. Despite these similarities, however, this study found that the pharmacokinetics differ. Distribution volume was larger, plasma clearance faster, and terminal half-life shorter for fentanyl as compared with buprenorphine. These differences may in part be attributed to plasma protein binding and its role in drug distribution.


Mometasone Furoate & Intradermal Test Reactions

This study aimed to determine the influence of mometasone furoate (MF), a topical glucocorticoid, on intradermal test (IDT) reactions. Results from 20 atopic dogs showed a significantly reduced global wheal score (GWS) after 14 days of MF treatment in inflamed ear canals; the GWSs were no longer significantly different 7 days after withdrawal of the medication. A withdrawal period of ≤7 days is sufficient before performing IDT in atopic dogs treated with MF for ≤14 days.

Study funded by a grant from Schering-Plough Animal Health


Fentanyl may be a useful anesthetic adjunct, but further investigation of cardiorespiratory effects of isoflurane–fentanyl combinations in rabbits is warranted.
ABVP Specialty & Recertification Examination Preparation
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Clinical Behavior: Getting Answers to Your Cases
Terry Marie Curtis, DVM, MS, DACVB

Feline Medicine: Finessing the Feline
Susan Little, DVM, DABVP (Feline Practice); Margie Scherk, DVM, DABVP (Feline Practice)

Oncology, Cytology & Hematology in Your Practice
C. Guillermo Couto, DVM, DACVIM (Internal Medicine and Oncology); Pablo Gómez Ochoa, DVM, PhD

Oral & Maxillofacial Surgery
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Mitral Valve Disease in a Dog

OSCAR, A 14-YEAR-OLD, CASTRATED DACHSHUND MIX, presented with a 1–2 day history of progressive cough, intermittent tachypnea with increased respiratory effort, and lethargy, and no interest in eating or drinking in the previous 12 hours. His 3-year history of heart murmur was characterized on imaging as myxomatous mitral valve (MV) disease with moderate left atrial enlargement; enalapril therapy was started at diagnosis. On examination, he was anxious and shaking. His heart and respiratory rates were 170 beats per minute and 60 breaths per minute, respectively. He was normothermic and normotensive. A grade IV/V systolic heart murmur was detected with a point of maximal intensity over the left apical region; heart rhythm was regular, and pulses were strong and synchronous. Lung sounds were increased, with no crackles or wheezes. Thoracic radiographs showing progressive left atrial and ventricular enlargements, mildly enlarged pulmonary veins, a moderate patchy unstructured interstitial pattern in the right caudal lung lobe, and a mild unstructured interstitial pattern in the left caudal lung lobe were consistent with pulmonary edema. Caudal mainstem bronchi were compressed on lateral projections secondary to the cardiomegaly and left atrial enlargement. Radiographic findings were compatible with left-sided congestive heart failure (CHF) secondary to MV disease.

Which of the following drugs would be appropriate in acute management of this patient?

Based on the information provided, how would you grade the following drugs and why?

Turn the page and compare your results

CHF = congestive heart failure, MV = mitral valve
Did you answer?
The following represents the best responses based on drug metabolism, pharmacokinetics, species, diagnostic differentials, clinical and laboratory data, and other pertinent findings.

**Acepromazine**

Acepromazine is a strong sedative with potent vasodilatory properties. Low-dose acepromazine may be added to the treatment protocol for a very anxious patient that cannot be managed with more cardiofriendly choices (eg, opioids). However, caution should be used in any dog with low blood pressure. The author's preferred sedation in an anxious dog with CHF is butorphanol, because its dose–response effect is more predictable than that of acepromazine.

**Atenolol**

Atenolol is a selective β₁-adrenergic blocker. Although this dog’s heart rate is fast and sympathetic nervous system activated, heart rate suppression with a β-blocker should be avoided because of possible worsening of heart failure caused by atenolol’s actions of lowering heart rate and decreasing contractility. Because this patient’s heart rate is not pathologically fast and is appropriate for his level of nervousness and cardiac insufficiency, it should be lowered by administering antianxiety drugs and successfully managing the pulmonary edema.

**Butorphanol**

Low-dose injectable butorphanol, a sedative and good antitussive, is safe to administer to an anxious dog with respiratory distress. A breathless sensation, unfamiliar environments, and patient–owner separation can accelerate the fight-or-flight response and lead to further decompensation.

**Enalapril**

Before this presentation, this dog had been receiving the ACE inhibitor enalapril for its proposed cardioprotective effects. Enalapril should be continued in this dog. However, in acute management of a dog with CHF, an ACE inhibitor could be withheld transiently until the dog is stable, eating, and drinking well, at which time the author generally reinstitutes and increases the enalapril dose to q12h.¹⁻⁴ The primary benefit of ACE inhibitors (eg, enalapril, benazepril) is thought to be renin-angiotensin-aldosterone system (RAAS) inhibition, leading to a survival benefit in dogs with CHF. ACE inhibitors are only modest systemic vasodilators and thus may not provide adequate
afterload reduction in the acute management phase of CHF; they can also reduce renal perfusion pressure and decrease glomerular filtration rate, resulting in azotemia.

**Furosemide**

Injectable furosemide is the most effective immediate treatment for this dog’s cardiogenic pulmonary edema. The IV route is ideal because of its rapid-onset action and bioavailability. However, if IV administration is too stressful for a patient, the IM or SC routes would be acceptable alternatives. After the patient is more stable and breathing more comfortably, the transition to oral furosemide can be made.

**IV lactated Ringer’s solution**

Although this dog had not eaten or drunk for 24 hours before presentation, IV fluids (eg, lactated Ringer’s solution) are contraindicated because of the sodium load. This dog should be able to withstand transient lapse of fluid and food intake while heart failure medications improve his condition. However, it is important to keep oral water available at all times during hospitalization.

**Nitroglycerin**

Nitroglycerin is a topical venodilator that reduces preload by dilating the splanchnic vasculature. Nitroglycerin augments preload reduction but is not generally used as a sole vasodilator, as the effects are fairly weak. Nitroglycerin is generally used only in acute management of heart failure because of the potential for the patient to develop tolerance if used continuously.

**Pimobendan**

In the U.S., pimobendan is available in large chewable tablets, which may be difficult for a dog with respiratory compromise to swallow. However, as soon as the dog is breathing more comfortably, oral pimobendan is indicated for emergency management. The peak effect of pimobendan, an inodilator, is within 1 hour of administration. Pimobendan is indicated in all cases of CHF secondary to MV disease.

ACE = angiotensin-converting enzyme, CHF = congestive heart failure, MV = mitral valve, RAAS = renin-angiotensin-aldosterone system
Lateral and DV views showing mild CHF in a dachshund with mitral valve disease.

**Spironolactone** | CORRECT RESPONSE

Spironolactone is a potassium-sparing diuretic that blocks the aldosterone receptor at the renal distal tubule. The primary hypothetical benefits of spironolactone are its aldosterone-inhibition effects, leading to a potential survival benefit in dogs with MV disease and CHF. Because spironolactone is not a potent diuretic and does not have rapid-onset action, it would not be an appropriate choice for acute management of a dog with CHF. Spironolactone should be introduced after the patient has been stabilized with other heart failure medications.

**Theophylline** | CORRECT RESPONSE

Theophylline, like aminophylline, is a methylxanthine bronchodilator that is most helpful for small airway bronchodilation in dogs with chronic bronchial disease. Addition of a bronchodilator should only be considered if concurrent airway disease is highly suspected. Possible side effects of this class of drugs include tachycardia, diarrhea, and anxiety, all of which are particularly undesirable in patients with heart disease.

CHF = congestive heart failure, MV = mitral valve

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**REFERENCES**


**MORE on page 33**
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See product information summary on page 16.

* A. caninum
** Prevents flea eggs from hatching; is not an adulticide.

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Feline asthma is an allergic airway inflammatory disease triggered by aeroallergens, resulting in type 1 (IgE-mediated) hypersensitivity reaction and dominated by type 2 T-helper cells.\(^1\,2\) It affects about 1%-5% of the feline population, with a median age of 4-5 years; Siamese and Havana brown cats are overrepresented.\(^2\,3\)

**Hallmark features** - Naturally occurring asthma
- Eosinophilic airway inflammation
- Mucus hypersecretion
- Bronchoconstriction
- Hyperresponsiveness (in response to both allergenic and nonallergenic stimuli)
- Airway remodeling\(^2,4,5\)

**Inflammation in airways** - Can lead to irreversible airway-remodeling damage\(^2,4\)
- Controlling inflammation is, therefore, the primary goal of therapy.
- Despite similarities between human and feline asthma, much about the inflammatory processes that occur in feline asthma remains to be ascertained.\(^6\)

**Primary treatment options** - Primary therapeutic approaches include
- Glucocorticoid [steroidal] therapy: systemic and inhalant
- Bronchodilator [asthmatic crisis] therapy
- Supplemental/concomitant therapy

**Glucocorticoid (Corticosteroid) Therapy**
Glucocorticoids, although nonspecific in their actions, are the mainstays of treatment for feline asthma. Glucocorticoids have potent antiinflammatory effects and are used to suppress airway inflammation and thus slow down or minimize irreversible airway-remodeling damage. Detailed explanation of the pharmacology, mechanisms of action, and resistance of glucocorticoids in the inflammatory process are beyond the scope of this article but can be found in the literature.\(^7,8\)

**General note** - Two distinct protocols: systemic (oral, injectable) and aerosol inhalant (metered dose inhaler [MDI])
If the patient does not have good response to oral corticosteroids, it may be unlikely that response to inhaled corticosteroids would be better.

**Avoid glucocorticoid therapy if possible** → In cats with concurrent diabetes mellitus, heart disease, or chronic FHV-1 infection

- Other contraindications: pancreatitis, GI ulceration (except ulcers secondary to IBD), concurrent administration of NSAIDs

- Individual cats can vary greatly in their response to the therapeutic and adverse effects of glucocorticoids.
  —There may be qualitative differences between the effects of different glucocorticoids in the same cat.

### Systemic Glucocorticoids

Cats generally tolerate systemic glucocorticoids well and tend to develop fewer adverse effects than do dogs. Nevertheless, long-term, high-dose therapy can lead to cushingoid effects.

Other adverse effects include PU/PD, polyphagia, alopecia, skin atrophy, poor wound healing, bruising, increased susceptibility to infections, weight gain with or without concurrent muscle mass loss, and obesity.

Caution: Steroid-induced diabetes mellitus may occur, and cats with underlying heart disease may develop heart failure (see also Inhalant Glucocorticoids).

**Prednisolone & Prednisone**

**Formulation** → Oral, parenteral

**Dose** → Oral prednisolone/prednisone: 1–2 mg/kg PO q24h or 0.5–1 mg/kg PO q12h for 10–14 days, then taper over next 2–3 months until <0.5 mg/kg q48h (if possible) or taper to lowest effective dose

**Emergency dose** → Injectable prednisolone sodium succinate: 15–30 mg/kg IV; repeat q4–6h as needed.

**Key Points**

- Cats do not convert prednisone (a prodrug) to prednisolone (the active compound) very efficiently, although the reason (enzyme, process) remains unknown.
unknown; therefore, oral prednisolone is preferred over oral prednisone in cats when possible.
—If oral prednisone must be used, consider increasing the dose.19-21
• Of note, prednisolone tablets are not FDA approved for use in cats.
• When cats with asthma or chronic bronchitis are treated with high-dose oral glucocorticoids, clinical signs may resolve despite persistent lower airway inflammation.
—Exercise caution in equating absence of clinical signs with absence of airway inflammation.
—In cats with subclinical airway inflammation, premature tapering of glucocorticoids based on absence of clinical signs may be detrimental.
—Current recommendations to taper therapy based on resolution of clinical signs should be reevaluated.14

Dexamethasone

Formulation → Oral, parenteral

Dose → Oral dexamethasone: 0.1–0.2 mg/kg PO q24h for 10–14 days, then taper over the next 2–3 months until <0.05–0.1 mg/kg q48–72h (if possible)22

Emergency dose → Injectable dexamethasone, dexamethasone sodium phosphate: 0.5–1 mg/kg SC, IV, IM23
• Can be used in conjunction with β2-agonist for status asthmaticus (acute asthma attack)

Key Points
• Dexamethasone 2 mg/mL injectable is FDA approved for use in cats, while dexamethasone SP 4 mg/mL injectable and dexamethasone tablets are not.
• Dexamethasone sodium phosphate usually formulated at concentration of 4 mg/mL (equivalent dexamethasone, 3 mg/mL)
• It has been suggested that dexamethasone exhibits greater diabetogenic effects than equipotent doses of prednisolone.11

Methylprednisolone

Formulation → Oral, parenteral

Dose → Oral methylprednisolone: 0.8–2.2 mg/kg PO q24h or 0.4–1.1 mg/kg PO q12h for 10–14 days, then taper over next 2–3 months until <0.3 mg/kg q48h (if possible) or to lowest effective dose23

Repository dose → Injectable methylprednisolone acetate: 1–5 mg/kg up to 20 mg/cat IM q4–8wk22-24
• May last as long as 2–6 months

Emergency dose → Injectable methylprednisolone sodium succinate: 4–6 mg/kg IV slowly over 2 minutes q2–3h as needed23
Key Points
• Methylprednisolone acetate has reportedly led to CHF in cats.9
  — May predispose cats to CHF through extracellular hyperglycemia10 but requires further evaluation
• Iatrogenic hyperadrenocorticism has been reported in a cat following short therapeutic course of methylprednisolone acetate (20 mg SC weekly for 4 weeks).25
• Some cats with preexisting FHV-1 infection may become symptomatic when treated with methylprednisolone acetate.26
• Methylprednisolone tablets are FDA approved for use in cats, while methylprednisolone acetate is FDA approved for IM (but not SC) injection.

Inhalant Glucocorticoids
Inhalant glucocorticoids have demonstrated efficacy in reducing airway inflammation in asthmatic cats and may be an alternative to systemic therapy.27 Inhalants appear to result in fewer endocrinologic and immunologic side effects as compared with oral or injectable steroids. Although inhaled glucocorticoids may be an appealing alternative, their expense could be a deterrent.8

Inhalants are administered by an MDI attached to a spacer device and facemask; see the literature for product information and use.27,28

Clinically effective absorption can be delayed, with optimal clinical effects not realized for days, possibly up to 1–2 weeks.

In moderately affected cats, concurrent administration of prednisolone at 0.5–1 mg/kg PO q12h tapered over 2–3 weeks can allow time for maximum inhalant effect.29,30

Caution: Aerosol inhalant steroids are not recommended for emergency management of status asthmaticus because of delayed effect. Instead, a fast-acting β2-receptor agonist is recommended [see Bronchodilators].29,30

Fluticasone Propionate

Formulation → Aerosol inhalant (MDI)

Dose → Available in 3 strengths: 44 or 50, 110 or 125, and 220 or 250 μg MDI q12–36h as needed23 [see Key Points]

Key Points
• Most commonly used aerosol inhalant corticosteroid
• Shows minimal hypothalamic-pituitary-adrenocortical axis (HPAA) suppression in cats.31
• Available in three strengths per actuation, with the labeling varying by country: 44 or 50 μg, 110 or 125 μg, and 220 or 250 μg23
  — In the U.S., MDIs are labeled by amount of drug delivered at the mouthpiece;

CHF = congestive heart failure, FHV-1 = feline herpesvirus type 1, HPAA = hypothalamic-pituitary-adrenocortical axis, MDI = metered dose inhaler
Bronchoconstriction is one of the hallmark features of feline asthma. Elsewhere, they can be labeled by amount of drug delivered from the valve, which accounts for apparent dose differences.32

• A recent study has shown that fluticasone propionate doses of 44, 110, and 220 μg q12h are equally efficacious in suppressing eosinophilic airway inflammation in experimental models of feline asthma.31
  — In contrast, anecdotal responses indicate that 44 µg fluticasone is not always effective clinically, but 110 µg q12h is effective in managing most cats with mild-to-moderate disease; cats with more serious disease require 220 µg q12h.
  — It has been suggested that once-daily dosing is occasionally effective.32

Flunisolide

*Formulation* → Aerosol inhalant (MDI)

*Dose* → 250 μg MDI q12h33

Key Points

• Because flunisolide suppresses the HPAA, it is not a first-choice inhalant steroid.
  — However, it may have an index superior to systemically administered corticosteroids.
• Flunisolide can be tried if other steroids are not available or effective.

Beclomethasone Dipropionate

*Formulation* → Aerosol inhalant (MDI)

*Dose* → 80–160 μg MDI q12–24h32,34

Key Points

• Beclomethasone dipropionate is a first-choice inhalant steroid used to treat human asthmatics but has not been well studied in cats.
• Veterinarians can try it if other steroids are not available or effective.
• It may have more systemic side effects (eg, HPAA suppression) than does fluticasone.

Bronchodilator (Asthmatic Crisis) Therapy

Bronchoconstriction is one of the hallmark features of feline asthma, and severe bronchoconstriction can lead to a life-threatening asthmatic crisis. Therefore, short-acting bronchodilators are important therapeutic drugs, particularly for treating cats in asthmatic crisis.

*Usually not indicated for long-term use* → Avoid using as monotherapy, as bronchodilators fail to control airway inflammation that exacerbates airway hyperresponsiveness.2

*If corticosteroid therapy alone fails to control clinical signs* → Use bronchodilators symptomatically in combination with corticosteroid therapy.
**β₂-Receptor Agonists**

Short-acting β₂-receptor agonists are the drugs of choice for treating status asthmaticus and can be used as an early at-home intervention for asthmatic crisis.

β₂-receptor agonists should be used only with careful clinical monitoring in cats with preexisting cardiac disease, hyperthyroidism, hypertension, or history of seizures.

**Terbutaline**

*Formulation* → Oral, parenteral (short-acting)

**Emergency dose** → 0.01 mg/kg SC, IM, IV

- If beneficial, breathing rate will decrease by ~50% within 10–30 minutes.
- Can be readministered 30 minutes later at the same dose if minimal effect has been noted.
- A heart rate approaching 240 bpm indicates that the drug has been absorbed.¹⁷,²³,³²

**Long-term oral dose** → 0.625–1.25 mg/cat PO q8–12h or 0.1–0.2 mg/kg PO q8–12h¹⁷,³²,³⁵

**Key Points**

- Terbutaline is the treatment of choice for acute respiratory difficulty when inhaled albuterol therapy is not possible.
- Most adverse effects are dose-related and associated with sympathetic stimulation, including
  - Increased heart rate, tremors, CNS excitement (nervousness), dizziness
  - Effects are generally transient and mild and do not require discontinuation of therapy.²³
- Transient hypokalemia has been reported in humans.²³

**Albuterol Sulfate (USAN) & Salbutamol Sulfate (INN)**

*Note* → Albuterol and salbutamol are the same drug. Albuterol (90 μg/actuation) is the name used in the U.S. as assigned by the U.S. Adopted Names (USAN), and salbutamol (100 μg/actuation) is the name used in the rest of the world as assigned by the World Health Organization (WHO [International Proprietary Name, or INN]).

*Formulation* → Aerosol inhalant (MDI; short-acting)

**Emergency dose** → 90 μg (albuterol) or 100 μg (salbutamol) per actuation, ×2 actuations MDI q30min as needed for up to 4–6h²³

**Key Points**

- Two enantiomers of albuterol (salbutamol) exist.
R-albuterol (R-salbutamol) is the pharmacologically active form. S-albuterol (S-salbutamol) is the inactive form and can cause paradoxical inflammation and bronchoconstriction. Avoid long-term use of albuterol (salbutamol); standard formulations are racemic mixtures. The R-enantiomer formulation is available but very expensive. Albuterol (salbutamol) may be considered for intermittent, short-term asthma intervention, but its long-term use for feline asthma management may be detrimental. Clinical effects in humans usually occur within 15 minutes and can last 3–4h. Anecdotally, effects are similar in cats.

Salmeterol Xinafoate

**Formulation** → Aerosol inhalant (long-acting)

**Dose** → 25 μg for long-term/maintenance use

**Key Points**

- Salmeterol may be given before bedtime to provide bronchodilation throughout the night or given twice daily in more severe cases in which a β2-receptor agonist is beneficial.
- A large U.S. human trial showed statistically and clinically significant increase in asthma-related deaths in subjects receiving salmeterol.39
- **Warning**
  - Per FDA black label warning for human use, this drug should be used only when nothing else works to control asthma symptoms; its use for the treatment of asthma without a concomitant long-term asthma control medication (eg, inhaled corticosteroid) is contraindicated.
- Salmeterol–chlorofluorocarbon (CFC) inhalant has been discontinued in the U.S. since 2002 but is still available in the UK.

Fluticasone Propionate–Salmeterol Xinafoate Combination

**Formulation** → Aerosol inhalant (MDI)

**Dose** → 250 μg fluticasone, 25 μg salmeterol MDI q12–48h

**Key Points**

- Combination inhaler products should only be used to treat asthma not controlled by other long-term asthma-control medication (eg, inhaled corticosteroids).

Methylxanthines

Methylxanthines promote airway smooth muscle relaxation and bronchodilation via phosphodiesterase inhibition and adenosine receptor antagonism and are generally less-effective bronchodilators than are the β2-receptor agonists.
Theophylline

*Formulation* → Oral

*Dose* → 4 mg/kg PO q8–12h\(^{17,43}\)
- 20–25 mg/kg PO q24h for extended-release products\(^ {44}\)

**Key Points**
- Extended-release products are no longer available in the U.S.\(^ {44}\)
- Generic extended-release theophylline offered from various manufacturers should be avoided because pharmacokinetics vary and are unpredictable.\(^ {32}\)
- Clinicians should consider several known drug interactions.\(^ {23}\)
- Because of its low therapeutic index and pharmacokinetic characteristics, dosage should be based on lean body mass.\(^ {17,32,43}\)
- Because of adverse effects, use theophylline and other methylxanthines cautiously.
  —CNS stimulation/excitement, insomnia, GI disturbances (eg, vomiting, diarrheal), nausea, polyphagia, PU/PD
  —Seizures or cardiac dysrhythmias may occur in severe intoxications.\(^ {23}\)
- Therapeutic drug monitoring is advised.\(^ {23}\)

Aminophylline

*Formulation* → Oral

*Dose* → 5–6 mg/kg PO q12h\(^ {32,43}\)

**Key Points**
- Aminophylline should rarely be used for treatment of asthma, as other safer, more efficacious bronchodilators are available.\(^ {32}\)
- Side effects are similar to those listed for theophylline.

Oxygen

When a cat is in respiratory distress, it is appropriate to provide an oxygen-rich environment. However, oxygen supplementation by mask should not be forced if the cat experiences untoward stress. A mild sedative may aid in decreasing anxiety associated with hypoxia.

Patient handling should also be minimized to avoid worsening respiratory distress.\(^ {32}\)

**Methods of supplemental oxygen delivery** → flow-by, face mask, Elizabethan collar canopy, nasal catheter, oxygen chamber

**Doses**\(^ {45}\)
- Flow-by: flow rate 6–8 L/min to achieve ~25%–45% FiO\(_2\)

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Aminophylline should rarely be used for treatment of asthma, as other safer, more efficacious bronchodilators are available.\(^ {32}\)
**Supplemental/Concomitant Therapy (continued)**

- Face mask: flow rate 6–8 L/min to achieve ~35%–55% FiO₂
- Elizabethan collar canopy: flow rate of 2–5 L/min to achieve ~30%–40% FiO₂
- Nasal catheter: flow rate of 100–150 mL/min to achieve ~30%–50% FiO₂
- Oxygen chamber with controlled O₂, humidity, and temperature

**Antibiotics (Mycoplasma felis)**

*Mycoplasma felis* is a primary pathogen that can mimic or aggravate asthma. The following empirical doses are based on treating upper respiratory *M felis* infections.

**Dose** → Medications with efficacy against *M felis*
- Doxycycline: 5 mg/kg PO q12h or 10 mg/kg PO q24h for 2–4 weeks
- Marbofloxacin: 2.75–5.5 mg/kg PO q24h for 2–4 weeks
- Pradofloxacin: 7.5 mg/kg PO q24h for 7 days
- Azithromycin: 5–10 mg/kg PO q24h for 2 weeks

**Key Points**
- *Mycoplasma* spp are the smallest known prokaryotes, lack a cell wall, and require sterols for growth.
  - They are considered to be normal commensal organisms associated with the mucous membranes of the upper respiratory system in cats.
- *M felis* has been suggested to cause lower respiratory tract and pleural cavity disease, acting as a primary pathogen and possibly exacerbating clinical signs in cats with asthma.
- Tetracycline, fluoroquinolone, and macrolide antimicrobials are most frequently used treatments for respiratory *Mycoplasma* spp infection in cats.

**Immunomodulators (Cyclosporine)**

In asthmatic patients, immunomodulatory therapy (specifically, cyclosporine) refers to the use of treatment designed to normalize inappropriate responses of the immune system.

**Initial cyclosporine dose** → 5–7 mg/kg PO q24h

- Doses are empirical and based on those recommended for treating allergic dermatitis in cats.
- Therapeutic drug monitoring, blood trough level in 72 hours: 300–600 ng/mL
  - Most human medical centers perform cyclosporine assays that can be applied to veterinary patients, providing a faster turnaround time than with veterinary laboratories.

**Key Points**
- Cyclosporine can be considered for treating feline asthma in patients with concurrent diseases (eg, diabetes mellitus, severe heart disease) that may contraindicate glucocorticoid therapy.
- Cyclosporine treatment does not appear to inhibit early-phase asthmatic
response or mast cell degranulation following antigen challenge in sensitized cats.54
—However, it reduced airway eosinophilia, airway responsiveness, and histologic changes/airway remodeling in an experimental model of feline asthma.55
• Cyclosporine is FDA approved for use in cats with atopic dermatitis but not those with asthma.
• Further studies are needed to validate its use for treating feline asthma.

Omega-3 Polyunsaturated Fatty Acids
• Omega-3 polyunsaturated fatty acids (PUFAs) with antioxidant/luteolin provide antiinflammatory effects by inhibiting key inflammatory signaling pathways.
• They may have some beneficial effects in reducing airway hyperresponsiveness.2,56

Inhaled Budesonide
• Inhaled budesonide at 400 μg/cat MDI q12h has been shown to be well tolerated in asthmatic cats, with improvement in clinical signs.
—However, it may suppress the HPAA in some cats.57

Inhaled Lidocaine
• Chronic nebulized lidocaine 2% with no preservatives and administered at 2 mg/kg q8h appears to be well tolerated in cats, causing no signs of toxicity.58
• Lidocaine decreases hyperresponsiveness and improves airway flow, but it does not reduce airway eosinophilia.
—It is not a suitable monotherapy but may serve as an adjunct to other treatments.2,58

Allergen-Specific Immunotherapy
• Has potential to be curative treatment by inducing immunologic tolerance to allergens
• Has met with some success in treating human asthmatics2,59
• Abbreviated protocol referred to as rush immunotherapy (RIT) has been shown to successfully reduce airway eosinophilia in experimental feline asthma.2,60
• Limitations of therapy rest with methods of determining exact (or closely matched) allergens required for inducing immunologic cure.2,61
—Sensitivity and specificity of intradermal skin testing and serum allergen testing have so far produced unreliable asthma allergen-specific IgE.2,62

FiO2 = fraction of inspired oxygen, HPAA = hypothalamic–pituitary–adrenal axis, IgE = immunoglobulin E, MDI = metered dose inhaler
Stem Cell Therapy

- May decrease long-term lung remodeling\(^2,63\)
- Tyrosine kinase inhibitor (TKI): masitinib at 50 mg PO q24h\(^64\)
  - Stem cell factor is associated with proliferation and activation of mast cells and eosinophils; blockage of this factor is possible with TKIs\(^2,65\)
  - Side effects (eg, severe proteinuria, neutropenia, GI disturbances) may limit the use of TKIs as treatment for feline asthma\(^2,56,66\)

Ipratropium (Anticholinergic)

- Ipratropium bromide with or without albuterol (inhaled aerosol) is not routinely used in cats at this time, but better potency of this combination may warrant further studies and its possible use in cats in asthmatic crisis\(^38,67,68\)
- Emergency dose of 20 μg/90 μg MDI (ipratropium bromide–albuterol) has been documented\(^38,68\)

Precautionary Warning

Avoid/Ineffective Therapies

Several drug classes have been investigated for treating feline asthma because of their benefits in treating human asthma. However, their efficacy in treating feline asthma has been disappointing and, therefore, these drugs are not recommended at this time.

- Cetirizine [antihistamine]\(^69\)
- Cyproheptadine [antiserotonergic and antihistamine]\(^15,69\)
- Zafirlukast [antileukotriene]\(^15\)

MDI = metered dose inhaler, TKI = tyrosine kinase inhibitor

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39. SMART Study Group. The Salmeterol Multicenter Asthma Research Trial: A comparison of usual pharmacotherapy for asthma or usual pharmacotherapy


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From the publisher of Clinician's Brief and Veterinary Team Brief.
To study antibiotic potential of isoquinolines (natural substances), isoquinoline-238 (IQ-238), a synthetic analog of the novel-type N,C-coupled naphthylisoquinoline alkaloid ancisheynine, was tested via genome-wide gene expression data, metabolic network modeling, Voronoi tessellation-based data analysis, cytotoxicity measurements, chemical properties calculations, and principal component analysis. Results showed strong antibiotic potential for staphylococci and low cytotoxicity against murine and human cells. Changes in enzyme activity caused by IQ-238 are predominantly located in carbohydrate metabolism. Spontaneous resistance was not observed, nor were resistant mutations at lower concentrations.


IQ = isoquinoline

Drug–drug interactions, especially those involving anticancer drugs (which have narrow therapeutic indices), can increase patient morbidity and mortality risks. These interactions can be caused by pharmaceutical interactions, altered drug metabolism, inhibited renal excretion, and displacement of protein-bound drugs. Inhibition of P-glycoprotein–mediated drug transport has recently been identified as another cause; these transporters are important in limiting drug distribution to sensitive tissues (eg, the brain) in biliary drug excretion—an elimination pathway for many anticancer drugs. Drug–drug interactions of anticancer drugs can be avoided by selecting alternate drugs or adjusting the dose of interacting drugs.


Drug–drug interactions, especially those involving anticancer drugs, can increase patient morbidity and mortality risks.
9. Pharmacokinetics of clindamycin HCl administered intravenously, intramuscularly and subcutaneously to dogs. 

10. Clindamycin bioavailability and pharmacokinetics following oral administration of clindamycin hydrochloride capsules in dogs. 

11. Tissue concentrations of clindamycin after multiple oral doses in normal cats. 

12. Effect of clindamycin on clinical, hematological, and biochemical parameters in clinically healthy cats. 


SUGGESTED READING


WORDS OF CAUTION


SUGGESTED READING

Dogs were treated with either Vetmedin (175 dogs) or the failure (CHF) due to AVVI (256 dogs) or DCM (99 dogs).

Lactating bitches.

Established in dogs with asymptomatic heart disease or signs caused by etiologies other than AVVI or DCM.

Indications:

Vetmedin (pimobendan) is indicated for use in dogs as a treatment for congestive heart failure (e.g., AVVI, DCM, myocardial infarction) in dogs due to atrioventricular valvular insufficiency (AVVI) or dilated cardiomyopathy (DCM).

Human Warnings:

Cardiac drug for oral use in dogs only.

 Chewable Tablets

Caution:

Unintentional or accidental poisoning, even at rest.

Human Warnings:

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- UTI and isolation of methicillin-resistant Staphylococcus spp
- Bartonella spp
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- Drug snapshot
- Drugs used to treat canine atopic dermatitis
**THERAPEUTIC DIET | NEW**

**Metabolic Diets Expanded:** New canine and feline metabolic diets [Hill’s Pet Nutrition] combine the nutritional needs of weight management with the specific needs of joint and urinary health. Prescription Diet Metabolic + Mobility Canine combines weight management with the joint-friendly nutrition found in Prescription Diet j/d Canine Mobility. The new Prescription Diet Metabolic + Urinary Feline is formulated to promote a healthy body condition score combined with the nutrition needed to maintain a healthy urinary tract, as found in Prescription Diet c/d Multicare Feline Urinary Tract Health.

*Source*  

**DRUG | STATUS UPDATE**

**L-Asparaginase May Return to Market:** Development of the chemotherapeutic agent L-asparaginase by Assisi Research Laboratories has been authorized by the FDA. After removal of the previous agent (Elspar, Lunbeck) from the market in December 2012, veterinarians had to rely on compounded formulations for patient treatments. On February 17, 2015, the FDA granted Assisi Research Laboratories Minor Use Minor Species [MUMS] designation. This status allows the company to begin developing the product for treatment of canine multicentric lymphoma; however, the drug cannot be marketed until it receives FDA or conditional approval.

*Sources*  
1. Assisi Research Laboratories (2015). Minor use minor species designation for L-asparaginase (FDA; February 17, 2015); Oak Park, IL.  

**BIOLOGIC | NEW**

**Feline Fibrosarcoma Treatment:** The USDA has granted conditional licensing of Feline Interleukin-2 Immunomodulator [Merial] as a biologic treatment option for feline fibrosarcoma.

*Sources*  
1. Merial, Press Release, March 10, 2015; Greensboro, NC.  
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IMPORTANT SAFETY INFORMATION: VETMEDIN should not be given in case of hypertrophic cardiomyopathy, aortic stenosis, or any other clinical condition where an augmentation of cardiac output is inappropriate for functional or anatomical reasons. The safety of VETMEDIN has not been established in dogs with asymptomatic heart disease or in heart failure caused by etiologies other than atrioventricular valvular insufficiency or dilated cardiomyopathy. Use only in dogs with clinical evidence of heart failure. The most common side effects reported in field studies were poor appetite, lethargy, diarrhea, dyspnea, azotemia, weakness, and ataxia. If side effects should occur, pet owners should contact their veterinarian. Please refer to the package insert for complete product information or visit www.vetmedin.com.

VETMEDIN is a well-established treatment for CHF caused by atrioventricular valvular insufficiency and dilated cardiomyopathy.¹ ² Now, no matter the size of the dog, our new dosing options can help you give owners convenient, cost-effective choices that help encourage compliance.

ACT NOW. Use VETMEDIN at the first clinical signs of CHF in dogs of any size or shape.

VETMEDIN is now available in four sizes: 1.25 mg, 2.5 mg, 5 mg, and 10 mg.

<table>
<thead>
<tr>
<th>Dog</th>
<th>Weight</th>
<th>Dosing Example</th>
</tr>
</thead>
<tbody>
<tr>
<td>Simon</td>
<td>12 lb</td>
<td>Two 10 mg in morning and one 10 mg in evening*</td>
</tr>
<tr>
<td>Clyde</td>
<td>55 lb</td>
<td>10 mg in morning and half a 10 mg in evening*</td>
</tr>
<tr>
<td>Lucky</td>
<td>22 lb</td>
<td>2.5 mg (2x day) OR half a 5 mg (2x day)*</td>
</tr>
<tr>
<td>Busby</td>
<td>12 lb</td>
<td>1.25 mg (2x day) OR half a 2.5 mg (2x day)*</td>
</tr>
</tbody>
</table>

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*All doses are provided as tablets.


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See product information summary on page 34.