



ISSUES & ANSWERS

FROM THE DESK OF

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Is it ever safe to administer aminoglycosides?

Despite the intrinsic toxicity of aminoglycosides, several key management points can optimize their safe and effective use.



ISSUE

AMINOGLYCOSIDES HAVE EXCELLENT GRAM-NEGATIVE SPECTRUM

but poor activity against anaerobes and in abscesses.¹ The main limitations of aminoglycoside use are dose-dependent nephrotoxicity and ototoxicity, which are caused by the local generation of superoxide and other free radicals.²



ANSWERS

AMINOGLYCOSIDES ARE STILL INDICATED for human patients with acute pyelonephritis, intraabdominal infections, osteomyelitis, and pneumonias associated with cystic fibrosis.³

In dogs and cats, aminoglycosides are often the most cost-effective and convenient option for resistant isolates of *Escherichia coli*, *Pseudomonas* spp,⁴ and methicillin-resistant *Staphylococcus* spp.⁵ Despite the intrinsic toxicity of aminoglycosides, several key management points can optimize their safe and effective use.

GENERAL

Use once-a-day dosing

Aminoglycosides should be given once a day, which is more convenient than and (at least) as effective as administering 3 times a day.

- Once-a-day dosing may also be associated with less risk for nephrotoxicity.⁶
 - Lower trough urinary concentrations may result in less overall uptake into renal tubular cells.
- Gentamicin sulfate: 6-8 mg/kg IV, IM, or SC (less painful) once a day
- Amikacin: 10-15 mg/kg IV, IM, or SC (less painful) once a day
 - May show lower minimum inhibitory concentrations (MICs) than gentamicin does against some gram-negative and mycobacterial isolates^{7,8}

Monitor patient status

- Make sure the patient is hydrated.⁹
 - Consider concurrent IV or SC fluids.
- Monitor urine sediment.
 - Monitor for tubular damage via daily examination of fresh urine sediment for granular casts.⁹

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

Indications
SENTINEL[®] SPECTRUM[®] (milbemycin oxime/lufenuron/praziquantel) is indicated for the prevention of heartworm disease caused by *Dirofilaria immitis*; for the prevention and control of flea populations (*Ctenocephalides felis*); and for the treatment and control of adult roundworm (*Toxocara canis*, *Toxascaris leonina*), adult hookworm (*Ancylostoma caninum*), adult whipworm (*Trichuris vulpis*), and adult tapeworm (*Taenia pisiformis*, *Echinococcus multilocularis* and *Echinococcus granulosus*) infections in dogs and puppies two pounds of body weight or greater and six weeks of age and older.

Dosage and Administration
SENTINEL SPECTRUM should be administered orally, once every month, at the minimum dosage of 0.23 mg/lb (0.5 mg/kg) milbemycin oxime, 4.55 mg/lb (10 mg/kg) lufenuron, and 2.28 mg/lb (5 mg/kg) praziquantel. For heartworm prevention, give once monthly for at least 6 months after exposure to mosquitoes.

Dosage Schedule				
Body Weight	Milbemycin Oxime per chewable	Lufenuron per chewable	Praziquantel per chewable	Number of chewables
2 to 8 lbs.	2.3 mg	46 mg	22.8 mg	One
8.1 to 25 lbs.	5.75 mg	115 mg	57 mg	One
25.1 to 50 lbs.	11.5 mg	230 mg	114 mg	One
50.1 to 100 lbs.	23.0 mg	460 mg	228 mg	One
Over 100 lbs.	Administer the appropriate combination of chewables			

To ensure adequate absorption, always administer SENTINEL SPECTRUM to dogs immediately after or in conjunction with a normal meal.

SENTINEL SPECTRUM may be offered to the dog by hand or added to a small amount of dog food. The chewables 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 a few minutes after administration to ensure that no part of the dose is lost or rejected. If it is suspected that any of the dose has been lost, redosing is recommended.

Contraindications
There are no known contraindications to the use of SENTINEL SPECTRUM.

Warnings
Not for use in humans. Keep this and all drugs out of the reach of children.

Precautions
Treatment with fewer than 6 monthly doses after the last exposure to mosquitoes may not provide complete heartworm prevention. Prior to administration of SENTINEL SPECTRUM, dogs should be tested for existing heartworm infections. At the discretion of the veterinarian, infected dogs should be treated to remove adult heartworms. SENTINEL SPECTRUM is not effective against adult *D. immitis*. Mild, transient hypersensitivity reactions, such as labored breathing, vomiting, hypersalivation, and lethargy, have been noted in some dogs treated with milbemycin oxime carrying a high number of circulating microfilariae. These reactions are presumably caused by release of protein from dead or dying microfilariae.

Do not use in puppies less than six weeks of age.

Do not use in dogs or puppies less than two pounds of body weight.

The safety of SENTINEL SPECTRUM has not been evaluated in dogs used for breeding or in lactating females. Studies have been performed with milbemycin oxime and lufenuron alone.

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

To report suspected adverse drug events, contact Novartis Animal Health at 800-637-0281 or the FDA at 1-888-FDA-VEHS.

Manufactured for: Novartis Animal Health US, Inc.
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Minimize treatment duration

- Limit aminoglycoside therapy to 5 or fewer days¹⁰ when possible.

Avoid toxic drug interactions

Furosemide

- Systemic aminoglycosides should be avoided in patients being treated with furosemide, as the combination can increase nephrotoxicity and ototoxicity.¹¹

Cisplatin

- Aminoglycosides should be avoided in cancer patients being treated with cisplatin.¹²
—Cisplatin also can lead to dose-dependent nephrotoxicity and ototoxicity.

Consider other potential measures to prevent toxicity

- Silymarin (20 mg/kg PO once a day) and vitamin E (25 mg/kg PO once a day) can decrease aminoglycoside nephrotoxicity in dogs experimentally.¹³
—Needs to be assessed in clinical patients
- Melatonin, which has antioxidant properties, has been shown to decrease aminoglycoside nephrotoxicity in rodents.^{14,15}
—Has not been evaluated in dogs or cats

SPECIFICS

Use extra caution in patients with renal failure

- In patients with renal insufficiency, choose other agents when possible.
—Ask for susceptibilities to additional agents (eg, ticarcillin, cefotetan, aztreonam, meropenem).
- When aminoglycosides are necessary for patients with preexisting renal failure, extend the dosing interval¹⁶ (eg, to every other day).
—To minimize toxicity, aim for a serum trough level <2 µg/mL.¹⁷
- Always rehydrate the patient and use concurrent fluid therapy (IV or SC).

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