Many of the drugs used in exotic pets have never been pharmacologically evaluated in the species of interest, and doses are extrapolated from sometimes non-related animal species. In addition, many of the drugs have no safety data in anything other than common domestic species. A drug may cause no problems in certain species, but lead to death in other closely related species. Widespread death of Old World vultures after ingestion of cattle carcasses treated with diclofenac is an example of this phenomenon, as no apparent toxicity is seen in certain other vulture species when treated directly with various NSAIDs. The purpose of this review is to provide a brief overview of drugs that are contraindicated in certain pet exotic species, but could be administered in other species without complications. Specific toxins (i.e. lead), drugs that have known complications in all species (i.e. renal toxicity of aminoglycosides), and drugs that are contraindicated for regulatory reasons will not be discussed, as this is outside the scope of this review.

**Reptiles**

**Ivermectin** is a macrocyclic lactone that affects the gamma-aminobutyric acid (GABA) synapse to stimulate excessive release of GABA (inhibitory neurotransmitter in nematodes). In many species of animals, it does not cross the blood brain barrier; however, in certain species, neurologic signs can occur following ivermectin administration, even at recommended doses. Ivermectin toxicity in chelonian species was first described in 1983 by Teare, et al. Five red-footed tortoises (*Geochelone carbonaria*) received a single IM injection of ivermectin (0.4 mg/kg), and developed paresis or flaccid paralysis. Additional studies in the red-footed tortoise showed that paresis will occur with dosages as low as 0.05 mg/kg. These authors found at several other species of chelonians were considered to be susceptible to ivermectin toxicosis at dosages of 0.1 mg/kg or less. The leopard tortoise (*Geochelone pardalis*) appeared to be the most susceptible of the species tested, and they consistently developed paresis with a dosage of as low as 0.025 mg/kg, and death with dosages as low as 0.3 mg/kg. Based on this and other published data, the use of ivermectin in any chelonian species is not recommended. Treatment of ivermectin toxicity is largely supportive, and respiratory support must be maintained for at least the duration of action of ivermectin at the neurotransmitter site (7 days). After this initial report in chelonians, reports of toxicity in other reptile species have been documented including certain crocodilian species, indigo snakes, and skinks.

Toxicity associated with **benzimidazole anthelmintics** has been reported in avian, reptile, elasmobranch and mammalian species, humans included. These drugs bind to tubulin, which interferes with mitosis. Their binding affinity is greater to parasitic tubulin, which interferes with the parasite cytoskeleton. However, vertebrate tubulin can also be affected, especially rapidly
dividing cells, including bone marrow and the cells lining the intestinal tract. Extensive hepatic metabolism (by cytochrome P450 and others) occurs following oral administration. This pancytopenia can lead to severe immunosuppression and subsequent bacterial and/or fungal infections, which may be fatal in a number of species.

A study was performed in six Hermann’s tortoises (*Testudo hermanni*) to evaluate hematologic parameters after administration of a standard fenbendazole treatment (two 5-day courses of fenbendazole 2 weeks apart at a dosage of 50 mg/kg). The tortoises remained clinically healthy during the 125-day study; however, there were significant biochemical changes that were considered to be in response to fenbendazole administration, including an extended heteropenia with transient hypoglycemia, hyperuricemia, hyperphosphatemia, and equivocal hyperproteinemia/hyperglobulinemia. Based on this study and several anecdotal reports of toxicity in many reptile species (snakes, chelonians, lizards), clinicians should carefully consider the risk of mortality of an individual from a nematode infection compared with the risk of septicemia following damage to hematopoietic and gastrointestinal systems by fenbendazole therapy. Certain practitioners prefer oxfendazole because it doesn’t require any prior bioconversion, verses fenbendazole, which relies on hepatic metabolism (S. Divers, personal communication). This makes oxfendazole more efficient following a single dose, and redosing (and subsequent toxicity) is often not necessary. Oxfendazole is licensed for use in domestic equids, suids, and ruminants.

**Avian**

The use of steroids in any avian species is controversial, and many anecdotal reports exist of severe adverse effects including immunosuppression, delayed wound healing, hepatic disease, and gastrointestinal ulceration. Unfortunately, clinical efficacy, pharmacokinetic, and safety studies are lacking. The author rarely uses systemic steroids in birds, and the most frequent steroid application is transient use of topical ophthalmic steroids for certain ocular inflammatory diseases. Because of the risk of steroid use in birds, clinicians should adequately inform owners of the risks of steroid use and have ruled out all other possible treatment options. Some clinicians have proposed concurrent use of prophylactic antibiotics and/or antifungal medications.

**Intraconazole** is a triazole, which inhibits cytochrome P450-dependent ergosterol synthesis and other oxidative enzymes. These ultimately lead to fungal cell disruption and death. This drug has been used in a wide variety of avian species, with good clinical success. Use of compounded oral formulations of itraconazole have led to treatment failure in several species, which is likely due to the lack of cyclodextrin in the compounded drug, when compared with the commercially available formulation (Sporonox ®). Use of itraconazole in African Grey parrots has been associated with anorexia, lethargy and death in some cases. The recommended dosage for this species is half or less (2.5mg/kg PO q24 hours) that of other avian species. Despite this reduced dose, the author has seen numerous cases of African grey parrots that experienced acute onset of lethargy, regurgitation, and anorexia following itraconazole therapy. Voriconazole, a newer azole drug, is the considered by many as the treatment of choice for avian fungal infections, and it has been used with minimal side effects in African grey parrots.
**Small mammals**

**Fipronil** (Frontline®) is a topical ectoparasitic drug approved for use in dogs and cats. There are multiple anecdotal reports of toxicity in rabbits, even when administered topically in small doses. To the author’s knowledge, no toxicity studies (LD50, or other) have been published on this drug in rabbits, so the overwhelming recommendation is to avoid its use entirely in this species. Clinical signs of intoxication usually appear within 24 hours of application, and include non-specific signs of lethargy and anorexia. These often progress quickly to seizures and death. Prognosis for recovery is poor once clinical signs are noted. Treatment includes bathing (if the drug was recently applied), and oral activated charcoal.

Certain **antibiotics** are contraindicated with oral administration to hind-gut fermenters, including rabbits and herbivorous rodents (guinea pigs, chinchillas, degus). These drugs lead to disruption of the normal intestinal flora and subsequent dysbiosis. Proliferation of clostridial or coliform bacteria occurs, and their toxins lead to diarrhea within 24-48 hours in most animals. Drugs with narrow-spectrums, such as beta-lactams, macrolides, and lincosamides are most commonly implicated. Antibiotic-associated enteritis or enterotoxaemia can occur from any antibiotic, but it is uncommon in the sulfa and fluoroquinolone classes. Interestingly, most rabbits can tolerate parenteral use of procaine, benzocaine, or dual-penicillin with minimal gastrointestinal side effects.

A recent study has evaluated the parenteral use of ceftiofur crystalline free acid (CCFA) in rabbits, and found CCFA (40 mg/kg) could be administered subcutaneously every 24 to 72 hours to New Zealand White rabbits to treat infections with ceftiofur-susceptible bacteria, and had minimal side effects. Treatment for dysbiosis is often restricted to supportive care (fluids, syringe feeding, etc). Some clinicians have advocated the use of drugs which bind to clostridial toxins (i.e. Cholestyramine), but no studies have evaluated the pharmacology or effectiveness in rabbits to date. Others advocate the use of Lactobacillus products (i.e Bene Bac), which have questionable efficacy as most orally administered organisms are killed by stomach acid, and this bacterium is not a normal intestinal inhabitant of rabbits.

**Benzimidazole toxicosis** in rabbits often present with nonspecific signs including inappetance, lethargy, and ataxia. Erythroid and myeloid cell production may both be affected, leading to pancytopenia. The pathophysiology is described in the reptile section of this document. This can also lead to severe immunosuppression and subsequent bacterial and/or fungal infections, which may be fatal. A recent retrospective article examined 13 cases of benzimidazole toxicosis in rabbits, all presented with non-specific clinical signs. Ten out of 13 cases received higher than recommended doses or prolonged duration of treatment with either albendazole, fenbendazole, or oxibendazole. Only one of the cases survived, making the prognosis for this toxicity poor in rabbits. The author always recommends checking at least a PCV (ideally a full CBC) 1-2 weeks after starting fenbendazole therapy (administration only for 30 days), and if any abnormal clinical signs

**References:**


