FARAD Digest

Current update on drugs for game bird species

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The USDA considers game bird species to include grouse, guineafowl, partridges, pigeons (squabs), quail, pheasants, ducks, geese, and wild turkey. According to USDA regulations, although these game bird species may not be hunted in the wild for the purpose of being sold for human consumption, they may be sold for food when raised in captivity.[1]

In the United States, over 8 billion chickens and 220 million domestic turkeys are sold for human food consumption on an annual basis.[2] In comparison, 37 million quail, 4 million chukars, 10 million pheasants, and 1 million mallard ducks are reportedly sold for food.[1] Veterinarians who treat game birds need access to therapeutic drugs and need to be able to provide appropriate WDIs to ensure that drug residues will not enter the food chain. The purpose of this digest is to familiarize veterinarians with the few drugs that are approved for use in game birds and to provide information on the status of ELDU in these species.

Classification of Game Birds as Minor Food-Producing Species

Under the FDA's definition, birds, other than chickens or turkeys, are considered a minor species.[3] One of the major challenges for obtaining approval of veterinary products for use in minor species is the minimal economic return to the pharmaceutical sponsors because of the small market size. Currently, although there are more than 250 approved drugs for chickens and 45 approved drugs for turkeys, there are only 3 approved drugs for ducks, 5 for pheasants, 2 for chukars, 8 for quail, and 1 for pigeons (**Appendix**).

Guidelines for ELDU in Game Bird Species

The Animal Medicinal Drug Use Clarification Act states that if an appropriate labeled drug is not available, ELDU is permitted under specific guidelines.[4] The act, however, also expressly prohibits the extralabel use of an approved animal or human drug in or on animal feed.

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Abbreviations

WDI	Withdrawal interval
ELDU	Extralabel drug use
CPG	Compliance Policy Guidance
FARAD	Food Animal Residue Avoidance Databank
EWE	Extrapolated withdrawal-period estimator

In most commercial settings, it is not feasible to treat flocks on an individual basis. Therefore, treating a large population of game birds necessitates that medication be administered via food or water. Although medicated water may be allowed under AMDUCA, this can also be impractical if husbandry practices allow birds to preferentially drink pooled rainwater over medicated water. The FDA has recognized the difficulty of this situation for minor species such as game birds and farmed fish and has adopted a CPG for the extralabel use of medicated feeds.[5] According to the CPG, "extra-label use of medicated feed for treatment of minor species may be considered when the health of the animals is threatened and suffering or death would result from failure to treat the affected animals." Under veterinary guidance, a medicated feed for a major species can be prescribed for a minor species for up to 6 months. This CPG does not legalize ELDU of medicated feeds, but in circumstances of this nature, the FDA "will not ordinarily consider regulatory action against a veterinarian" provided specific regulations are followed.[5] These regulations include the use of a medicated feed that has already been approved in a major food species; appropriate labeling of feed; record-keeping requirements; confined population requirement; a valid veterinary-client-patient relationship; veterinary supervision; and determination of an appropriate, scientifically based WDI. A more detailed list of criteria and requirements can be found in the CPG Sec 615.115 or on the FARAD Web site.[6]

Species Considerations

Veterinarians considering ELDU must be aware of adverse effects of the drug and species hypersensitivities or contraindications. Species variations in avian physiology and metabolism can result in substantial variability in pharmacokinetics and toxicoses associated with various drugs. Although only a few studies have explored differences in the metabolism of avian species, a recent study[7] that investigated differences in hepatic cytochrome p450 metabolism in chickens, turkeys, pheasants, and quail found considerable vari-

ability in metabolism of midazolam, a known marker substrate for cytochrome p450 microsomal enzymes in mammals. It is important for practitioners to remember that although a medication may be safely used in one or both of the major food-producing avian species (ie, chickens and domestic turkeys), this does not mean that the same drug can be safely or effectively used in a minor food-producing avian species at similar dosages. For example, nitarsone, an arsenical compound used to treat histomoniasis, is approved for use in chickens and turkeys but is listed on the label as dangerous when administered to ducks and geese. Arsenical compounds can also cause hepatic lipidosis and death in waterfowl species when administered at the labeled dose for poultry.[8] Another example is the coccidiostat salinomycin, which has multiple formulations labeled for chickens and one for quail. In turkeys, salinomycin causes lethal muscle degeneration and necrosis.[9,a] Fenbendazole has been determined to be toxic in *Columbiformes* spp, such as pigeons, causing acute hemorrhagic enteritis.[10,11] These examples highlight the fact that there are substantial species differences between birds and between birds and nonavian species. Therefore, it is prudent to attempt initial treatment of a small population of animals before treating the entire flock if no species-specific data are available.

Meat WDIs

Few studies have been performed to document how physiologic, metabolic, and excretory differences vary between the major and minor food-producing avian species. When data are lacking in minor avian species, residue and pharmacokinetic data from major avian species are sometimes used to estimate potential residues and WDIs for minor avian species. Extrapolating these data should be done with great caution and in some cases may not be appropriate. FARAD has developed an EWE algorithm[12] that has been used to estimate conservative WDIs in instances where minor food animal species are exposed to drugs in an extralabel manner. The WDI estimates are best performed with complete pharmacokinetic data sets, but such data sets are often difficult to obtain for game birds. However, in situations where pharmacokinetic information for a labeled drug is limited, the EWE algorithm uses half-life multipliers to determine a very conservative WDI. It should be noted, however, that many of these WDI estimates are in accordance with the CPG for the extralabel use of medicated feeds.[5]

Egg WDIs

Drug residues in eggs depend on many factors including blood and tissue half-lives of the drug, character of the drug (eg, protein binding), and species and environmental factor variability in egg development. Egg WDIs are notoriously difficult to establish because of the prolonged process of egg development and the complicated pharmacodynamics of drug uptake and residues within the developing egg.[13] There are few studies available on residues in major avian species, and no definitive studies were found evaluating residues in game bird eggs.

Prohibited Drugs

The FDA has prohibited specific drugs from use in food animals because of human safety concerns associated with the drugs[14] There are also drugs that are prohibited from being used in an extralabel manner including, but not limited to, chloramphenicol, dimetridazole, ipronidazole, other nitroimidazoles, nitrofurans, fluoroquinolones, glycopeptides (eg, vancomycin), adamantine, and neuraminidase inhibitor drugs. Some of these drugs are prohibited from use in all food-producing animals, whereas others are prohibited from extralabel use only.

Enrofloxacin and sarofloxacin are specific examples of drugs prohibited for use in avian species. These fluoroquinolones were labeled for use in chickens and turkeys to treat bacterial infections, including *Pasteurella* spp and *Escherichia coli*. These drugs were also reportedly used as a prophylactic treatment for gastroenteritis in poultry[15] In 2005, the avian approval for enrofloxacin was withdrawn by the FDA because of human health concerns. Research in Europe and the United States suggests that the continued use of fluoroquinolones was causing an increase in the development of fluoroquinolone-resistant *Campylobacter* spp in poultry.[16] These resistant organisms could then be transferred to humans, resulting in fluoroquinolone-resistant human *Campylobacter* infections.[17]

As of June 20, 2006, the FDA has expressly prohibited the use of certain antiviral drugs in poultry. The drugs specified are adamantanes (amantadine and rimantadine) and neuraminidase inhibitors (oseltamivir and zanamivir). These medications are used to treat and prevent influenza viral infections in humans, and use of such drugs in avian species (eg, for H5N1 avian influenza) could encourage the evolution of drug-resistant viruses. Currently, chickens, turkeys, and ducks are the only birds specified by the measure, but other species may be added in the future. Ducks and other waterfowl are of particular concern because of their role as vectors for influenza viruses.[18] Although not expressly prohibited in other avian species, the use of these drugs in any avian population would be questionable given that the same concern for viral resistance could apply.

For further questions regarding potential drug residues for a specific proposed treatment plan in game birds, please contact FARAD at 1-888-US-FARAD or at www.farad.org. FARAD will attempt to provide drug residue information according to available data whenever possible.

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Appendix

Food and Drug Administration–approved drugs for game birds.

Species	NADA or ANADA	Drug	Trade name	Label meat WDT	Additional notes
Ducks	048-761	Chlortetracycline (calcium)	Aureomycin 100 Granular	N/V	Do not feed to ducks producing eggs for human consumption
	046-699	Chlortetracycline HCl	CTC 10, 50, 65, 70, 100	0 days	Do not feed to ducks producing eggs for human consumption
	040-209	Sulfadimethoxine/ ormetoprim	Rofenaid 40	5 days	Do not feed to ducks producing eggs for human consumption
Pheasants	012-350	Amprolium	Amprol 25% Type A medicated article for poultry	0 days	
	046-592	Bacitracin methylenedisalicylic acid	BMD 10, 25, 30, 40, 50, 60, 75	0 days	
	046-920	Bacitracin zinc	Baciferm 10, 25, 40, 50	0 days	
	098-452	Bacitracin zinc	Albac 50	0 days	
	200-223	Bacitracin zinc	Albac 10, 25, 40, 50	0 days	
Chukars	096-298	Lasalocid (sodium)	Bovatec 68, 91, L 20	N/V	
	040-209	Sulfadimethoxine/ ormetoprim	Rofenaid 40	N/V	
Quail	046-592	Bacitracin methylenedisalicylic acid	BMD 10, 25, 30, 40, 50, 60, 75	0 days	
	065-470	Bacitracin methylenedisalicylic acid	BMD Soluble	N/V	
	046-920	Bacitracin zinc	Baciferm 10, 25, 40, 50	0 days	
	200-223	Bacitracin zinc	Albac 10, 25, 40, 50	0 days	
	098-452	Bacitracin zinc	Albac 50	0 days	
	038-878	Monensin (sodium)	Coban 60	0 days	
	130-736	Monensin (sodium)	Coban 45	0 days	
	128-686	Salinomycin	Bio-Cox	0 days	
	200-075	Salinomycin sodium	Sacox: Type A medicated article	N/V	
Pigeons	139-879	Carnidazole	Carnidazole; Spartrix	N/V	Do not use in pigeons intended for human food

NADA = New animal drug application. ANADA = Abbreviated new animal drug application (200-XXX are generic formulations). Meat WDT = Meat withdrawal time. N/V = No value listed in Code of Federal Regulations for this drug, indicating that appropriate withdrawal time has not been determined for this drug label.