

## AAAP-AVMA Guidelines for Judicious Therapeutic Use of Antimicrobials in Poultry

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The Principles of Judicious Therapeutic Use of Antimicrobials of the American Veterinary Medicine Association (AVMA) are the framework for the Guidelines for Judicious Therapeutic Use of Antimicrobials in Poultry of the American Association of Avian Pathologists (AAAP). The purpose of this document is to provide information for field veterinarians on intervention strategies for common bacterial diseases of chickens and turkeys. This working document will be updated as needed by the American Association of Avian Pathologists Committee on Drugs and Therapeutics and the Committee on Food Safety.

The overarching goals of veterinary poultry practice are to address the health and wellness of poultry while protecting food safety and public health. When the decision is reached to use antimicrobials, veterinarians should strive to optimize therapeutic efficacy and minimize resistance to antimicrobials to protect public and animal health. Use of antimicrobials can be minimized through carefully planned and executed preventative practices, including vaccination programs, biosecurity, automated ventilation controls, and conventional poultry husbandry and management programs. These programs are the pillars of sound production practices, and antimicrobial therapy provides an important tool aiding veterinarians in maintaining animal health and welfare.

#### Disease Prevention and Diagnosis

To ensure proper use of antimicrobials in poultry, focus should be placed on disease prevention strategies. The poultry environment should be managed to reduce morbidity and mortality rates. The birds' environment should be optimized at all times. House environmental conditions should be altered frequently and as needed based on the appearance and activity of the birds. Noninfectious factors that predispose birds to disease include chilling, heat stress, inappropriate humidity, high ammonia concentrations, wet litter, high dust levels, very short down time between flocks and unpalatable or unsanitary feed or water. Ventilation must be managed to minimize the negative impact from ammonia, dust, excessive humidity, or combustion gases on primary defense mechanisms in the birds. Likewise, ventilation should be optimized for litter moisture control to reduce bacterial exposure and control ammonia concentrations. To assess the progression of disease within a flock, removal of morbid birds may be required. Diagnostic testing and troubleshooting procedures should be initiated to identify the primary microbial challenge and any predisposing conditions. Strict biosecurity should be maintained to prevent spread to other houses on the same farm, and immunization should be used when warranted.

#### Therapeutic Antimicrobials Available for Use in Poultry

The classes of antimicrobials (animal drugs given for the treatment, control, or prevention of confirmed bacterial disease and administered through feed, water, or injection) that are currently approved by the Food and Drug Administration<sup>1</sup> (FDA) for use in poultry are summarized in **Tables 1 and 2**.

#### Judicious Antimicrobial Use

Antimicrobials may be administered in feed only in accordance with label instructions. For administration via water or injection, extralabel use may be additionally permitted if the federally codified valid veterinarian-client-patient relationship is established (The Animal Medicinal Drug Use Clarification Act of 1994 – AMDUCA). Only after the valid veterinarian-client-patient relationship is established and flock and farm history and diagnostic procedures are performed is extralabel drug use permitted. The use of medically important antimicrobials (**Table 3**) in animals is intended for therapeutic purposes at therapeutic dosages and under the supervision of a veterinarian.

Products should be administered according to the manufacturer's labeled recommendations or based on the clinical experience of the attending veterinarian. When multiple barns are present on the farm with

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<sup>1</sup> [www.fda.gov/downloads/AnimalVeterinary/GuidanceComplianceEnforcement/GuidanceforIndustry/ucm052519.pdf](http://www.fda.gov/downloads/AnimalVeterinary/GuidanceComplianceEnforcement/GuidanceforIndustry/ucm052519.pdf)

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disease, birds within each barn should be evaluated for current disease status and risk of disease exposure. Only barns with clinically affected birds or those judged to be at definite risk should be treated. Morbidity and mortality rates should be evaluated closely to determine the treatment protocols. The least number of diseased and at-risk birds should be treated on a farm. Additionally, management, biosecurity, and vaccination programs should be reevaluated and corrective actions taken as necessary.

The following are general guidelines to aid veterinarians in making informed decisions regarding antimicrobial use:

- The approved antimicrobial with the narrowest spectrum and the lowest level of human importance with a reasonable expectation of clinical efficacy at label doses should be the first choice. Antimicrobials with a broader spectrum or higher levels of human importance should be considered only when farm history, clinical judgment, or culture and sensitivity results indicate that the narrower spectrum and less important antimicrobials are unlikely to be efficacious.
- Use according to labeled instructions should be considered first, if farm history, results of in vitro antimicrobial susceptibility testing, and clinical judgment warrant.
- Extralabel drug use of antimicrobials administered via drinking water or injection may be considered if labeled use of antimicrobials in the same class have failed, if farm history or in vitro antimicrobial susceptibility testing dictates, or based on clinical experience of the attending veterinarian. Extralabel drug use must be within the context of a valid veterinarian-client-patient relationship (see the Principles of Judicious Therapeutic Use of Antimicrobials of the AVMA before initiating extralabel use).
- When farm history, results of in vitro antimicrobial susceptibility testing, or clinical judgment warrants the use of highly important antimicrobials, their use should be in accordance with labeled instructions before extralabel use is considered. Antimicrobial choice should be dictated by potency and site-of-infection drug concentrations derived from pharmacokinetic and pharmacodynamic data if available, with extended withdrawal periods as appropriate.
- Use of critically important antimicrobials should be considered as a last resort based on all appropriate information after antimicrobials classified as important or highly important have been carefully considered and all other intervention strategies have failed.
- With any therapeutic regimen of important or highly important antimicrobials, use of narrow-spectrum antimicrobials is recommended to avoid overuse of broad-spectrum antimicrobials.
- Bacteriostatic drugs should be considered cautiously when treating chronic infection due to decreased primary defense mechanisms in the birds. Overall effectiveness of bacteriostatic drugs in chronic infections may be decreased. Likewise, when immunosuppressive agents such as infectious bursal disease and chicken anemia virus are involved, bacteriostatic antimicrobials may not be clinically effective.

### **Antimicrobial Therapeutics Administered Via Water**

Antimicrobial therapy can be administered via drinking water. Addition of ammonia to raise the pH of water may increase the solubility of some antimicrobials, such as sulfonamides and penicillin. Addition of organic or inorganic acid to lower water pH may increase the solubility of some classes of antimicrobials (e.g., tetracyclines and erythromycin) when used via water application. In all cases, federal and state laws must be followed. For more information on compounding, visit the AVMA website ([www.avma.org](http://www.avma.org)). Any combination of antimicrobials would be subject to extralabel drug use rules as described in 21 CFR 530.13 (extralabel use from compounding of approved new animal and approved human drugs).

### **Feed-Grade Antimicrobial Therapeutics**

Poultry veterinarians have the option to administer in-feed medications. Combinations of FDA-approved in-feed medications that have obtained cross-clearance are limited. However, if in-feed antimicrobials are

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considered, the appropriate feed-grade antimicrobial must be used per the FDA-approved label indication. Extralabel drug use of in-feed antimicrobials is not permitted under any commercial conditions.

Veterinarians are limited in their use of therapeutic antimicrobials in-feed based on FDA regulations published in the Code of Federal Regulations (21 CFR) and veterinary feed directive drugs section of the Animal Drug Availability Act of 1996. On December 11, 2013, the FDA finalized Guidance for Industry #213, establishing procedures for phasing out growth promotion indications for antibiotics deemed medically important to humans in alignment with Guidance for Industry #209 and proposed changes to Veterinary Feed Directive (VFD) drug regulations. These guidance documents removed all growth promotion and feed efficiency indications from antibiotics of human importance, which are used in food animal production. The VFD regulation mandates the rules and responsibilities of licensed veterinarians in prescribing and administering medically important antimicrobials in feed. Guidance for Industry #209 establishes two principles: use of medically important antimicrobial drugs in food-producing animals should be limited to uses considered necessary for assuring animal health and use of medically important antimicrobial drugs in food-producing animals should include veterinary oversight or consultation. Veterinarians should be involved in decisions regarding antimicrobial use in food animals for the health of the animal as well as protecting the food supply. Use of all medicated feed articles and combinations in poultry must conform exactly to the FDA-approved label as extralabel drug use is not permitted. Veterinarians can refer to specific disease therapeutic strategies in this document to assess the potential benefit of approved feed-grade antimicrobials.

### Injectable Antimicrobial Therapeutics

Injectable antimicrobials are used predominately at 1 day of age or in ovo to control omphalitis in chicks and poults. In ovo administration to prevent infection when the yolk is withdrawn into the body cavity can be an important intervention strategy to control early bacterial contamination. However, appropriate sanitation and temperature controls must be maintained from breeder farm through the hatchery to minimize of the need for antimicrobials at 1 day of age and in ovo. Injection strategies should be used to support ongoing hatchery sanitation and proper egg collection techniques and not in lieu of these procedures. Routine, mass administration of prophylactic antibiotics to all birds hatched in a facility does not constitute judicious use. Rather, in ovo or day-of-age administration should be used on a case-by-case basis to control outbreaks of omphalitis while underlying causes are being investigated and corrected. Current antimicrobials cleared for use in 1-day-old chicks or poults are not approved for use in ovo, and therefore, extralabel drug use regulations must be followed. The use of cephalosporins at unapproved dosages, frequencies, durations or routes of administration is prohibited; therefore, in ovo use in chickens and turkeys is no longer permitted.

Injectable antimicrobials are occasionally used in an extralabel manner, except for the cephalosporin class, for acute disease outbreaks in valuable and long-lived poultry. Fowl cholera and erysipelas can be treated in this manner. Antimicrobials used in this manner include long-acting oxytetracycline, florfenicol, and penicillin. With any such extralabel administration, extralabel drug use regulations must be followed.

### Further Reading

For further details on treatment of specific disease in poultry, please refer to references below.

- Boulianne M, Brash ML, Charlton, BR, et al, eds. *Avian disease manual*. 7th ed. Jacksonville, Fla: American Association of Avian Pathologists, 2013.
- Swayne DE, Glisson JR, McDougald LR, et al, eds. *Diseases of poultry*. 13th ed. Hoboken, NJ: Wiley-Blackwell, 2013.

For a complete and current list of all the products affected by Guidance for Industry No. 213 and VFD drug regulations, refer to the FDA Center for Veterinary Medicine's (CVM) website [www.fda.gov/AnimalVeterinary/SafetyHealth/AntimicrobialResistance/JudiciousUseofAntimicrobials/default.htm](http://www.fda.gov/AnimalVeterinary/SafetyHealth/AntimicrobialResistance/JudiciousUseofAntimicrobials/default.htm)

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or [www.fda.gov/downloads/AnimalVeterinary/SafetyHealth/AntimicrobialResistance/JudiciousUseofAntimicrobials/UCM378330.pdf](http://www.fda.gov/downloads/AnimalVeterinary/SafetyHealth/AntimicrobialResistance/JudiciousUseofAntimicrobials/UCM378330.pdf)). This is a public document. The VFD drug regulations ([www.gpo.gov/fdsys/pkg/FR-2013-12-12/pdf/2013-29696.pdf](http://www.gpo.gov/fdsys/pkg/FR-2013-12-12/pdf/2013-29696.pdf)) and Guidance for Industry No. 213 ([www.fda.gov/downloads/AnimalVeterinary/GuidanceComplianceEnforcement/GuidanceforIndustry/UCM299624.pdf](http://www.fda.gov/downloads/AnimalVeterinary/GuidanceComplianceEnforcement/GuidanceforIndustry/UCM299624.pdf)) were published in the *Federal Register* on December 12, 2013. The original listing of medical important antimicrobials can be found in Appendix A of Guidance for Industry No. 152 ([www.fda.gov/downloads/AnimalVeterinary/GuidanceComplianceEnforcement/GuidanceforIndustry/UCM052519.pdf](http://www.fda.gov/downloads/AnimalVeterinary/GuidanceComplianceEnforcement/GuidanceforIndustry/UCM052519.pdf)).

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Table 1—Classes of antimicrobials approved for use in poultry.

<b>Class</b>	<b>Drug or combination</b>	<b>FDA Ranking</b>
Aminoglycosides	Streptomycin	Highly Important
	Gentamicin	Highly Important
	Neomycin	Highly Important
Aminocyclitols	Spectinomycin	Highly Important
Cephalosporins	Ceftiofur	Critically Important
Decapeptides	Bacitracin	Not important
Macrolides	Erythromycin	Critically Important
	Tylosin	Critically Important
Penicillins	Potassium penicillin G	Highly Important
Sulfonamides	Sulfadimethoxine	
	Sulfaquinoxaline	
	Sulfamethazine	
	Sulfamerazine, sulfamethazine, and sulfaquinoxaline	
Tetracyclines	Chlortetracycline	Highly Important
	Oxytetracycline	Highly Important
	Tetracycline hydrochloride	Highly Important
	Sulfadimethoxine-ormetoprim	Critically Important

Table 2—Classification of poultry antimicrobials approved for use in poultry, by human medical importance (FDA CVM Guidance for Industry No. 152).

<b>Critically important</b>	<b>Highly important</b>
3 <sup>rd</sup> Generation Cephalosporins (Ceftiofur)	Penicillin
Macrolides (Tylosin, Erythromycin)	Streptogramins (Virginiamycin)
Sulfadimethoxine-ormetoprim	Tetracyclines (Tetracycline, Chlortetracycline, Oxytetracycline)
	Lincosamides (Lincomycin)
	Aminoglycosides (Neomycin, Gentamicin, Streptomycin)
	Aminocyclitols (Spectinomycin)

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Table 3—Medically important antimicrobials based on FDA CVM Guidance for Industry No. 152 and also delineated by the medical importance classification of antimicrobial products in regard to their human medical importance.

<b>Critically Important</b>	<b>Highly Important</b>	<b>Important</b>
Third-generation cephalosporins	Natural penicillins	First-generation cephalosporins
Flouroquinolones	Penase-resistant penicillins	Second-generation cephalosporins
Macrolides	Antipseudomonal penicillins	Cephameycins
Trimethoprim-sulfamethoxazole	Aminopenicillins	Monobactams
	Fourth-generation cephalosporins	Quinolones
	Carbapenems	
	Aminoglycosides	
	Clindamycin	
	Tetracyclines	
	Glycopeptides	
	Streptogramins	
	Oxazolidones	
	Pyrazinamide	
	Isoniazid	
	Rifamycins	
	Chloramphenicol	
	Metronidazole	
	Polymyxin B	

The intent of the categorizations is to restrict the use of medically important antimicrobials in animals to particular indications—particularly use in animals intended for food—while ensuring that sufficient therapeutic alternatives remain available to treat sick animals.

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Table 4. Administered in-feed (VFD) FDA approved medications for poultry. ^ = Not currently marketed. G = Includes label claim for improved weight, gain and feed conversion. ® All trademarks or trade names are property of their respective owners. \*CAUTION: Federal law restricts medicated feed containing this veterinary feed directive (VFD) drug to use by or on the order of a licensed veterinarian. Extralabel Drug Use (EDLU) is not permitted. Species can vary, observe label indications.

VFD Medications*	Chickens	Turkeys	Non-VFD Medications	Chickens	Turkeys
Aureomycin® (Chlortetracycline)	X	X	Albac® (Bacitracin Zinc) <sup>G</sup>	X	X
ChlorMax® (Chlortetracycline)	X	X	Amprol® (Amprolium)	X	X
Inteprity™ (Avilamycin)	X		Avatec® (Lasalocid)	X	X
Lincomix® (Lincomycin)	X		Aviax® (Semduramicin)	X	
Neo-Oxy® (Neomycin + Oxytetracycline)	X	X	Bio-Cox® (Salinomycin)	X	
Neo-Terramycin® (Neomycin + Oxytetracycline)	X	X	BMD® (Bacitracin Methylene Disalicylate) <sup>G</sup>	X	X
Pennchlor®(Chlortetracycline)	X	X	Clinacox® (Diclazuril) <sup>A</sup>	X	X
Pennox® (Oxytetracycline)	X	X	Coban® (Monensin)	X	X
RofenAid® (Sulfadimethoxine + Ormetoprim)	X	X	Coyden® (Clopidol) <sup>A</sup>	X	X
Stafac® (Virginiamycin)	X		Deccox® (Decoquinatate)	X	
Terramycin® (Oxytetracycline)	X	X	Flavomycin® (Bambermycin) <sup>G</sup>	X	X
			Hygromix® (Hygromycin B) <sup>A</sup>	X	
			Maxiban® (Narasin + Nicarbazin)	X	
			Monteban® (Narasin)	X	
			Nicarb® (Nicarbazin)	X	
			Robenz® (Robenidine HCl)	X	
			Sacox® (Salinomycin)	X	
			Safe-Guard® (Fenbendazole)		X
			Stenorol® (Halofuginone) <sup>A</sup>	X	X
			Topmax™ (Ractopamine) <sup>A</sup>		X
			Zoamix® (Zoalene)	X	X

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Table 5. Administered in-water (Prescription) FDA approved medications for poultry. ® All trademarks or trade names are property of their respective owners. \*CAUTION: Federal (USA) law restricts this drug to use by or on the order of a licensed veterinarian. Species can vary, observe label indications.

Prescription Medications*	Chickens	Turkeys	Non Script Medications	Chickens	Turkeys
Aureomycin® Soluble (Chlortetracycline)	X	X	Amprol (Amprolium)	X	X
Di-Methox® (Sulfadimethoxine)	X	X	BMD® Soluble (Bacitracin Methylene-Disalicylate)	X	X
Gallimycin® PFC (Erythromycin)	X	X	Safe-Guard® AquaSol (Fenbendazole)	X	
Lincomycin Hydrochloride Soluble (Lincomycin HCl)	X				
Neo-Sol® (Neomycin)		X			
NeoMed® (Neomycin)		X			
Oxytet® Soluble (Oxytetracycline)	X	X			
PenAqua Sol-G® (Penicillin G Potassium)		X			
Pennchlor 64® (Chlortetracycline)	X	X			
Pennox 343® (Oxytetracycline)	X	X			
PoultrySulfa® (Sulfamerazine, Sulfamethazine, Sulfaquinoxaline)	X	X			
R-Pen® (Penicillin G Potassium)		X			
TetraMed® 324 HCA (Tetracycline)	X	X			
Tetroxy® HCA Soluble (Oxytetracycline)	X	X			
Tet-Sol™ 324 Soluble (Tetracycline)	X	X			
Tylan® Soluble (Tylosin Tartrate)	X	X			
Tylovet® Soluble (Tylosin Tartrate)	X	X			