

# FACTSHEET

## The use of 3<sup>rd</sup> and 4<sup>th</sup> generation cephalosporins and fluoroquinolones in Food-Producing Animals

### Introduction

Compared to human medicine, veterinarians have a much more limited arsenal of antibiotics for their use. All the new classes introduced to human medicine in the last 20 or more years are not registered anywhere in the world for veterinary uses, therefore not allowed and not available for use in farm animals. The last modern class of antibiotics introduced to veterinary medicine were the Fluoroquinolones almost 30 years ago. In view of the importance of the Fluoroquinolones and Cephalosporines in human medicine, stakeholders in many regions have instituted special measures for a responsible veterinary use. Consequently, both classes are used very judiciously e.g. in the US, Canada, Europe, Japan representing 1-5% of all antibiotic uses only. Both classes are used to treat severe cases of diseased animals, and are often the only available therapeutic options that works. Because of that they are also considered to be of critically importance for animal health. Like humans animals get sick with bacterial infectious diseases and have the right to be treated properly. In this regard and the fact that therapy limiting resistance is occurring in animals these CIAs play a crucial role in veterinary medicine and the vets need these options. Measures should not lead to situations where sick animals cannot be treated resulting in severe Animal Welfare issues.

### Cephalosporins

**Cephalosporins are generally categorized by “Generations” based on their spectrum of activity. 1st Generation cephalosporins** (including cephalothin, cephalexin, cefazolin, cephapirin) have activity predominantly against Gram positive bacteria. **2nd Generation** (including cefuroxime, cefaclor, cefoxitin) have an increased spectrum that includes the fastidious Gram negative bacteria such as *Haemophilus influenzae*, **3rd Generation** (including cefuroxime, ceftriaxone, ceftiofur) have increased Gram negative activity but with some loss in activity against Gram positive bacteria while the **4th Generation** (cefepime, cefquinome) **cephalosporins** have equivalent activity against both Gram positive and Gram negative bacteria, including, in some cases, *Pseudomonas spp.*

#### Diseases and species treated

- Respiratory disease in cattle caused by a range of bacteria including *Mannheimia haemolytica*, *Pasteurella multocida* and *Histophilus somni* (e.g. ceftiofur, cefquinome).
- Respiratory disease in pigs caused by a range of bacteria including *Actinobacillus pleuropneumoniae*, *Pasteurella multocida* and *Streptococcus suis*. (e.g. ceftiofur, cefquinome).
- Mastitis in cows caused by *Staphylococcus aureus*, *Streptococcus agalactiae*, *S. uberis* and *S. dysgalactiae*, *Escherichia coli* (e.g. cefoperazone, cephapirin, cefazolin, cefquinome).
- Acute interdigital necrobacillosis caused by *Fusobacterium necrophorum* and *Bacteroides spp.* (e.g. ceftiofur, cefquinome).
- Metritis in cows; mastitis-metritis-agalactia syndrome in sows
- Bacterial infections in horses including *Streptococcus spp.*, *Staphylococcus spp.* (e.g. ceftiofur).
- Early mortality of young chickens and turkey poult by individual injection (e.g. ceftiofur).
- Pasteurellosis in sheep and goats.

#### Individual or group treatment

Treatment with cephalosporins is limited to individual animals, either parenterally, orally or locally (mastitis). The 3<sup>rd</sup> and 4<sup>th</sup> generation cephalosporins are only available on prescription by the veterinarian and only for therapeutic purposes. Cephalosporins have never been licensed as growth promoters.

#### Importance to veterinary medicine

- Cephalosporins, particularly the more potent 3rd and 4th generation compounds, form a critically important therapeutic option available to the veterinarian for the treatment of both companion animals and food species for conditions including the diseases listed.
- Alternatives are limited in efficacy through either narrow spectrum or presence of antimicrobial resistance.
- They are the only intramammary product with an approval for treatment of Gram-Negative Mastitis as well as the systemic use of these agents (along with FQs) for the treatment of severe, systemic *E. coli* mastitis.
- The last therapeutic option for the treatment of multi-drug resistant strains of the pathogens responsible for bovine respiratory disease. Dramatic increases in morbidity and mortality are observed in groups of animals where the MDR strains are present.

## Fluoroquinolones

Fluoroquinolones are active against a wide range of Gram-negative and Gram-positive bacteria and *Mycoplasma* species. Several fluoroquinolones are registered for and used in veterinary medicine: danofloxacin, difloxacin, enrofloxacin, marbofloxacin, norfloxacin (in less regulated markets) for use in food animals. It should be noted that ibafloxacin, pradofloxacin, orbifloxacin and ofloxacin are only for use in companion animals. Fluoroquinolones are only available on prescription by the veterinarian and only for therapeutic purposes. Fluoroquinolones have never been used or licensed as growth promoters. Route of administration are oral (but not in feed) or parenteral. Livestock animals are usually treated individually. Poultry is treated orally via drinking water as this is the only possible medication in case of a disease outbreak in poultry flocks.

This paper relates to the three fluoroquinolones actually on the market for food animals (dano-, enro-, and marbofloxacin) which have been specifically and comprehensively developed and registered for use in farm animals, almost globally.

### Major diseases treated by fluoroquinolones

- Respiratory disease in cattle caused by *Mannheimia haemolytica*, *Pasteurella multocida*, *Histophilus somni* and *Mycoplasma bovis*.
- *E. coli* infections in cattle such as colidiarrhea, colisepticaemia and colimastitis.
- Respiratory disease in swine (*Actinobacillus pleuropneumoniae*, *P. multocida*, *Mycoplasma hyopneumoniae*, *Bordetella bronchiseptica*).
- *E. coli* infections in swine (digestive tract, MMA).
- *E. coli* infections in chickens and turkeys; fowl cholera particularly in turkeys.
- *Ornithobacterium rhinotracheale* infections and dual infections with *E. coli* in turkeys.
- Mycoplasma infections in poultry (predominantly *Mycoplasma gallisepticum*) and dual infections with *M. gallisepticum* and *E. coli* (Chronic Respiratory Disease).

### Importance to veterinary medicine

- The most effective treatment for colibacillosis in poultry. No meaningful alternative registered.
- Fluoroquinolones are often a life-saving injectable treatment for severe *E. coli* mastitis. One of the few injectables together with 3<sup>rd</sup> Gen. Cephalosporins in *E. coli* and Gram-Negative Mastitis treatments.
- Fluoroquinolones are one of the few options to treat Pseudomonas infections in animals.
- Fluoroquinolones are effective against Mycoplasma in mixed infections in BRD and SRD, while most of the new macrolides are ineffective (in about 92% of the BRD/SRD Mycoplasma was diagnosed in outbreaks in 3 countries in EU).
- Morbidity and mortality in food and companion animals will increase due to the special utility of the fluoroquinolones.
- In absence of Fluoroquinolones and/or Cephalosporines, there will be an unavoidable shift to other “older” classes leading to an increase in resistance and in the long-term seriously reduced treatment options.

This factsheet was produced by experts working together in HealthforAnimals, the global animal medicines association. [www.healthforanimals.org](http://www.healthforanimals.org)