Divergent position on a CVMP opinion on an Article 34 referral of Directive 2001/82/EC

Baytril 2.5% injectable, Baytril 5% injectable and Baytril 10% injectable and their associated names (EMEA/V/A/091)

Only the 25 mg/ml strength is concerned

The aim of this referral was to consider the differences between the summaries of product characteristics of Baytril 2.5% injectable, Baytril 5% injectable and Baytril 10% injectable and their associated names as authorised in the Member States.

It is the opinion of the undersigned that the indication for treatment of skin and wound infections caused by *Staphylococcus aureus* in rabbits (food and pet rabbits) cannot be accepted.

On the benefit,

All clinical data referred to originates from the individual treatment of pets rabbits only,

Among 177 pets rabbits treated with enrofloxacin in the presented field study, *Staphylococcus aureus* was isolated in only four rabbits (4/177=2%) with skin infections and seven animals (7/177=4%) with dermatitis.

No data were provided to document the use in farm rabbits where epidemiological conditions are different and can largely impact the efficacy results. For example, food rabbits are handled less and less time is available for treatments compared to pet rabbits. Thus, food rabbits are far less likely to have regular local topical treatments for skin and wound infections, compared to pet rabbits, and far more likely to be given injectable treatments (*e.g.* enrofloxacin-containing products) for skin and wound infections.

On the risk,

Considering that no other veterinary products are indicated for this indication all over Europe, it is obvious that such a fluoroquinolone will be used as a first line product, which is in contradiction with the warnings of prudent use ("the fluoroquinolones should be reserved for the treatment of clinical conditions which have responded poorly, or are expected to respond poorly, to other classes of antimicrobials").

The minor size in EU terms of rabbit farming is not an argument when considering the risk for handlers, and a very recent study described the first case of zoonotic livestock-associated methicillin-resistant *Staph. aureus* LA-MRSA (ST398, spa types t034 and t5210) occurring in rabbits raised intensively for meat production and involving farm workers or their family members[1]. As with other animal species, veterinarians are also at a higher risk to acquire LA-MRSA from the food animal species

[1] Agnoletti et al. First reporting of methicillin-resistant *Staphylococcus aureus* (MRSA) ST398 in an industrial rabbit holding and in farm-related people. Vet Microbiol 2014;170:172-177

that they work with. In other species, increased use of fluoroquinolones is linked to higher rates of MRSA[2].

The withdrawal period of six days is far shorter than the one which will be used under the cascade, *i.e.* 28 days. Thus, it could follow that there will be increased use of the product in food rabbits. In this particular context, the shorter withdrawal period is not a "benefit" for people with direct contact with the rabbits such as workers at the slaughterhouse. Moreover, it follows that rabbits treated in the finishing stage carry a higher chance to reach the slaughter house with resistant bacteria, namely MRSA.

It is reminded that, in rabbit farming, different life stages of rabbits are present in relatively close contact to each other (for instance rabbit does may transmit resistance to the off-spring through close contacts) and in this type of population resistance is selected, developed and disseminated continuously over time. Plus, *Staphylococcus aureus* can easily be transmitted to farm workers/veterinarians and carried by farm workers/veterinarians to different life stages of rabbits.

The undersigned consider that the benefit/risk of such an indication is negative and considers that the recommendation of an indication for which there is no weight of evidence should not be used as a tool to prevent the off-label use of other products.

London, 9 April 2014

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[2] Charbonneau et al. Fluoroquinolone Use and Methicillin-Resistant *Staphylococcus aureus* Isolation Rates in Hospitalized Patients: A Quasi Experimental Study. Clinical Infectious Diseases 2006; 42:778–84.