FEDERATION OF VETERINARIANS OF EUROPE

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FVE position paper on coccidiostats or anticoccidials

'Coccidiostats to be under veterinary prescription'

ABSTRACT

Coccidiosis is a parasitic disease, which even in the presence of high sanitary standards and good management, can occur with a serious potential impact on animal welfare and possible high mortality rates. Effective coccidiostats are at the moment indispensable to protect the health and welfare of poultry and other species against coccidiosis.

The biggest problem associated with using coccidiostats is the development of resistance rendering the products ineffective. In European legislation, coccidiostats or anticoccidials are categorised both as feed additives and as Veterinary Medicinal Products. Strategies should be implemented to extend the useful life of coccidiostats, and more scientific research should be performed with the aim to minimize and finally phase out the use of coccidiostats. **FVE believes that all coccidiostats should be under veterinary prescription** following clinical examination and diagnosis; this would allow for **better surveillance** and the veterinarian to diagnose and choose the best strategy to **extend the useful life of coccidiostats**, such as through 'shuttle use' or 'rotational use' or the use of vaccines. Additionally it would allow more frequent **reporting of any adverse reactions seen, including lack of efficiency**, **ensure withdrawal periods are respected and could allow monitoring through ESVAC**.

Article 11 of Regulation (EC) No 1831/2003 on additives for use in animal nutrition laid down that the Commission shall submit to the European Parliament and the Council a report on the use of coccidiostats and histomonostats as feed additives with a view to a decision on the phasing out of the use of these substances as feed additives by 31 December 2012. This report was published in 2008. **FVE requests the European Commission to update its 2008 report on the use of coccidiostats and histomonostats as feed additives in view of the arguments presented in this paper and to explore ways to bring coccidiostats under veterinary prescription while safeguarding their availability.**

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Background:

Coccidiosis is a parasitic disease and without doubt the most important parasitic disease in poultry and of major importance in other species such as pigs, rabbits and cattle. Even in the presence of high sanitary standards and good management, coccidiosis occurs with a serious potential impact on animal health and welfare and possible high mortality rates.

Legislative framework

The legislative background for coccidiostats in the European Union (EU) considers them either as feed additives (category of coccidiostats and histomonostats) or Veterinary Medicinal Products (VMPs).

In the EU, feed additives are regulated under different legislation to VMPs. The legal basis for additives for use in animal nutrition is laid down in Regulation (EC) No. 1831/2003. Authorization and prerequisites for their use are defined for individual products (brand names) following review by the European Food Safety Authority (EFSA). Several coccidiostats of antibiotic origin to be used in chickens, turkeys and rabbits are included in the list of feed additives.

In order to use feed additives, there is currently no requirement for a clinical examination or diagnosis or veterinary prescription. Antibiotics used as feed additives are also not monitored by the European Surveillance system for Veterinary Antimicrobial Consumption (ESVAC) as are other antibiotics licensed as VMPs.

When changes to the existing legislative framework are under consideration, legislators should ensure that the transposition to a new system should be implemented in a way that will not lead to a reduction in the availability of these products. One has to be careful so as not to lose veterinary products as a consequence of the manufacturer being unable or unwilling to update an existing dossier or compile a new dossier as a result of insufficient data.

Coccidiostats:

Coccidiostats or anticoccidial drugs can act at specific times during the life cycle of the parasite, or exert their effects at several phases. Coccidiostats can act on extracellular stages (sporozoites and merozoites) to prevent penetration of cells or on the intracellular stages to stop or inhibit development, and a few anticoccidials affect the sporulation of oocysts after they are excreted.

There are two classes of coccidiostats:

(1) Coccidiostatics, which arrest or inhibit the growth of intracellular coccidian and give rise to latent infection after drug withdrawal and

(2) Coccidiocides, which kill most of the coccidial stages.

Some coccidiostatic drugs may be initially coccidiostatic but eventually coccidiocidal depending on factors such as the length of time on medication, dosage, and species of coccidia. All coccidiostats inhibit reproduction and do not fully eliminate the parasite from the intestine of the animal. Medication with coccidiostats in the feed remains the major way of preventing coccidiosis. Alternative preventive ways such as vaccination are also available for some species (Anadón and Martínez-Larrañaga, 2013).

Type of coccidiostats:

Coccidiostats can be grouped into two major classes, namely ***polyether ionophore antibiotics*** (i.e. monensin, lasalocid sodium, maduramicin, narasin, salinomycin, semduramicin) and the ***synthetic products not of an ionophoric nature*** (decoquinate, robenidine hydrochloride, amprolium, halofuginone, diclazuril, toltrazuril, nicarbazin and sulfonamides) as well as ***combinations*** of different classes (i.e. narasin and nicarbazin, sulfonamides with trimethoprim, ormetoprim or pyrimethamine). Polyether ionophores antibiotics, which are by far the most widely used coccidiostats, are currently not used in human medicine, but are being studied such as for possible future use as cancer therapy (Huczyński, 2015).

Diagnosis

The clinical signs of coccidiosis may or may not be accompanied by large numbers of oocysts being shed in the faeces. Currently the most commonly used diagnostic methods are oocyst counts and lesion scoring of freshly dead carcasses. Some anti-coccidial sensitivity testing is available, but not often used. More rapid, low-cost and especially quantitative test should be developed.

Monitoring: The effectiveness of prescribed coccidiostats should be monitored on herd level, by continuous sampling and examination of lesions and/or oocysts.
A standard procedure/guidelines for such monitoring should be developed by e.g. EFSA, to enable national and regional monitoring.

Resistance

The biggest problem associated with the control of coccidiosis is the development of resistance by the coccidia to all medications available for use. A number of strategies have been developed to extend the useful life of coccidiostats, while still controlling coccidiosis; such as through ‘shuttle use’ or ‘rotational use’ or by using vaccines (Chapman *et al.*, 2010). Resistance is a great threat to the health and welfare of the animals and therefore should be prevented as much as possible.

Resistant bacteria to polyether ionophores can be seen in animals treated with this class of antibiotics but also in animals which have never been treated. However, there is little evidence that polyether ionophore resistance can be spread from one bacteria to another.

Cross-resistance to coccidiostats with the same mode of action from the same chemical class is common. The cross-resistance between polyether ionophores is also common, although strain differences in response to specific polyether ionophores have been demonstrated. In general, resistance to a monovalent polyether ionophore confer some cross-resistance to other monovalent polyether inophores (salinomycin, monensin, narasin, maduramicin, and semduramicin, but susceptibility to monovalent and divalent polyether ionophores (lasalocid) may be retained.

Drug interactions

Studies have reported drug interactions between macrolide antibiotics and/or pleuromutilin derivative (tiamulin) administered concurrently with several compounds including ionophoric antibiotics (monensin, salinomycin) which have metabolism partly or entirely dependent on the cytochrome P450 drug metabolising system of the liver. Moreover, toxic interactions between polyether ionophores (mainly monensin) and sulphonamides, erythromycin, oleandomycin and enrofloxacin have been observed. Due to the fact that polyether ionophores have a narrow margin of safety, they may result in severe adverse reactions, especially also in event of contamination through carry-over at the feed-mill level.

Residues and public health using coccidiostats

A critical factor in the medication of all food-producing animals is the mandatory withdrawal period, defined as the time after which the medicinal product was last administered and the point of slaughter of the animal for consumption or the taking of food products produced (e.g. eggs). Residue testing programs occasionally find residues of coccidiostats in food, which can cause food safety concerns. Anticoccidial residues are one of the most frequently found residues from veterinary drugs. For example in the European Commission Residue report (report published 2015, data 2013) non-compliant results were found for poultry of decoquinate (1.1%), lasalocid (0.4%), monensin (0.8%), narasin (0.5%), salinomycin (0.3%), and toltrazuril (2%) (EFSA, 2015). Feed cross-contamination is often a source of residue formation in edible tissues of non-target species and induces adverse health effects in these animals due to a specific sensitivity of mammalian species. Residue formation in edible tissues of non-target species may result in unexpected human exposure through the consumption of animal products.

Urgent need for improved veterinary supervision

The (prophylactic) use of coccidiostats or anticoccidial drugs remains for the time being necessary in modern animal husbandry in the EU.

However,

- Development of resistance is threatening the efficacy of these products
- The spectrum of activity of a coccidiostat must be taken into account when examining resistance. Additionally, some coccidiostats have antimicrobial activity.
- Coccidiostats can interact with other drugs and raise severe adverse reactions;
- Non adherence of the withdrawal time or feed-cross-contamination can lead to residues being found in food from animal origin, which can cause food safety concerns.

In the long term the aim should be to phase out the use of coccidiostats based on scientific research, and necessary changes in management

Based on all these reasons, **FVE recommends that coccidiostats should be under veterinary prescription,** as this would allow the farm veterinarian to choose the best strategy to, if possible, phase out the use of coccidiostats in the long run, and in the meantime extend the useful life of coccidiostats by minimising resistance, to feedback any adverse reactions seen including lack of efficacy and to ensure withdrawal periods are respected.

FVE advise the inclusion of coccidiostats in the ESVAC monitoring system and ensure that the transposition to the new system will be done in a way that will sustain the availability of those products.

References

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