

Aivlosin® – excellent activity against *Ornithobacterium rhinotracheale* (ORT)

Introduction

Aivlosin®, although a relatively new macrolide antibiotic, is currently successfully used in many countries of the world for the treatment and control of the major mycoplasmal infections such as chronic respiratory disease (CRD) and infectious synovitis in poultry.

Aivlosin® is up to 8 times more active *in-vitro* than tylosin against *Mycoplasma gallisepticum* & *M. synoviae*, is 3 times better absorbed, and also concentrates in target tissues. It is thus a powerful treatment for mycoplasmosis at a quarter the dose of tylosin. Furthermore Aivlosin® is effective against Mycoplasma strains resistant to tylosin and other macrolides.

Aivlosin® also shows strong activity against, *Clostridium perfringens*, the causal organism of Necrotic Enteritis in poultry. Now, in two new trials, it has shown extremely promising *in vitro* activity against *Ornithobacterium rhinotracheale* (ORT), an organism that is an important cause of respiratory disease in poultry.

O. rhinotracheale infections

Ornithobacterium rhinotracheale (ORT) may be called an emerging disease in that the bacterium responsible was only named in 1994. In recent years there has been increasing awareness of the significance of ORT as a worldwide cause of disease and economic loss in poultry. There are however varying levels of awareness of the disease in different parts of the world due to difficulty of diagnosis and confusion with other respiratory diseases.

The prevalence of ORT in meat type poultry in Europe is very high. Surveys performed in Germany revealed that all broiler breeder flocks during their life experienced an infection. Furthermore in Belgian broilers, ORT infection isolated between weeks three and six of rearing from 80% of the monitored flocks. Particularly virulent strains of the disease have been reported in South Africa and parts of South America (De Herdt *et al*, 2001).

ORT is a cause of both primary and secondary respiratory disease in chickens and turkeys. Infection in broilers may be seen as early as 3 weeks of age and results in reduced growth, respiratory signs and increased mortality but is more commonly seen in laying birds and breeders, causing reduced egg production and egg size.

In turkeys respiratory signs including sinusitis are common with increased mortality especially in older birds and also following turkey rhinotracheitis (TRT) virus infections. The common post-mortem findings include

pneumonia, air-sacculitis, a fibrino-purulent exudate with pericarditis and peritonitis.

Spread is by horizontal transmission, although its rapid appearance around the world over the past decade may suggest vertical transmission (van Empel and Hafez, 1999). Diagnosis can be difficult, as it relies on a combination of clinical signs, post-mortem pathology, isolation of the bacterium and confirmatory ELISA serology. Additionally, the bacteria can be difficult to grow, and require microaerophilic conditions and inclusion of gentamicin or polymyxin to prevent overgrowth with less fastidious bacteria such as *E. coli* or proteus spp.

Although sensitivity patterns differ slightly from region to region, recent publications show few of the antibiotic drugs currently used are consistently effective against circulating ORT isolates. Extensive resistance in over 50% of 45 isolates has been reported in Belgium (Devriese *et al.*, 2001) for ampicillin, doxycycline, lincomycin, tylosin, tilmicosin and borderline resistance to enrofloxacin has appeared.

Recent Aivlosin[®] microbiological study results

Study 1

Initial MIC work on Aivlosin[®] in South Africa reported by Ludwig *et al.* (2001 – data on file) showed that Aivlosin[®] was more active than tilmicosin (Pulmotil[®] – Elanco), against ORT. Tilmicosin is a relatively new antibiotic, so has been used less to control ORT.

Table 1. Comparative activity of Aivlosin[®] against ORT MICs (µg/ml) – (Ludwig *et al.*, 2001-data on file)

Isolate	Aivlosin [®]	Tilmicosin
1	0.5	4.0
2	0.5	4.0
3	0.5	4.0
4	0.5	8.0

Burch, (2002) reports maximum lung and airsac tilmicosin concentrations of 2.3 and 3.3 µg/ml respectively. On this evidence the South African data reported above indicates likely resistance.

Study 2

Further work was commissioned in Hungary, following the publication by Varga *et al.* (2001), where they described the activity of various antimicrobials on 12 ORT isolates. Varga (2002) –data on file, used 10 of these isolates to test Aivlosin[®] and compare it with tilmicosin. The latter

study produced MIC and MBC (minimum bacteriacidal concentration) values.

Table 2. Comparative activity of Aivlosin[®] against ORT MICs (µg/ml) – (Varga *et al*, 2001; Varga, 2002 –data on file)

Varga <i>et al.</i> , 2001	MIC50	MIC90	Range	MBC
Amoxicillin	0.12	≥ 64	≤ 0.06- ≥64	-
Enrofloxacin	4.0	8.0	≤ 0.06-8.0	-
Lincomycin	1.0	32	1.0-32	-
Oxytetracycline	4.0	4.0	2.0-8.0	-
Tylosin	0.12	4.0	≤ 0.06-8.0	-
Tilmicosin	0.12	0.25	≤ 0.06-1.0	-
Varga, 2002				
Tilmicosin	0.12	0.5	≤ 0.06-1.0	0.25 – 4.0
Aivlosin[®]	0.12	0.12	≤ .06- 0.12	0.12 – 0.25

Aivlosin[®] showed an exceptional activity against Hungarian isolates of ORT, which showed marked resistance development to enrofloxacin, amoxicillin and oxytetracycline and some resistance development to lincomycin and tylosin based on MIC 90.

In the work by Varga, 2002 (Table 2), the range of MBC values was 0.12 to 0.25 µg/ml. This value is close to the MIC90 and indicates possible bactericidal activity at the normal recommended dose rate used for mycoplasma treatment, of 125-250 ppm in drinking water.

It is anticipated that Aivlosin[®] will prove as highly effective in treating this organism as it is against *M. gallisepticum* & *M. synoviae*. Based on the comparative MIC data for ORT and mycoplasma, the dose rate currently recommended for mycoplasma treatment (125-250 ppm in drinking water) is expected to be effective against ORT.

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Eco Animal Health, August 2003

References

Burch, D.G.S. (2002) Antimicrobial sensitivity data for the major poultry bacterial pathogens. On <http://www.octagon-services.co.uk/index.htm>

Devriese, L.A. *et al.* (2001) Antibiotic sensitivity in *Ornithobacterium rhinotracheale* strains from Belgian broiler chickens. Avian Pathology, 30, 197-200.

De Herdt, P. *et al.*, (2001) The relevance and efficacy of *Ornithobacterium rhinotracheale* control in chickens. World Poultry, 17, 32-33.

Ludwig *et al.*, (2001) data on file.

van Empel, P.C.M. and Hafez, H.M. (1999) *Ornithobacterium rhinotracheale*: a review. Avian Pathology, 28, 217-227.

Varga, J. *et al.*, (2001) Characterisation of some *Ornithobacterium rhinotracheale* strains and examination of their transmission via eggs. Acta Veterinaria Hungarica, 49, 125-130.

Varga. J. (2002) data on file.

Aivlosin[®] is a patented molecule. The use of Aivlosin[®] as a treatment or prevention for ORT is covered under UK Patent Application No: 0315629.6