Susceptibility of *B. hyodysenteriae* (*B. hyo*) to tiamulin, aivlosin and tylosin in Sweden

"Take home" messages

- In Sweden growth promoting antibacterials, including carbadox and olaquindox were banned in 1986 and swine dysentery is still a significant disease problem there.
- Resistance to tiamulin among *B. hyodysenteriae* (*B. hyo*) isolates has occasionally been reported, but develops only gradually, both in vivo and in vitro, as evidenced by practical experience around the world since the launch of Tiamutin in 1978.
- In Sweden tiamulin is an antibiotic of choice for swine dysentery since so far no strains of *B. hyo* have been proven to be resistant to it.
- Most field strains of *B. hyo* in Sweden are resistant to tylosin.
- A new tylosin derivative, aivlosin – (3 acetyl 4' isovaleryl tylosin) was registered in all EU countries by the European Medicines Evaluation Agency (EMEA) for use in Swine in May 2004.
- The 23SrRNA mutation causing macrolid resistance in *B. hyo* also affects the binding of aivlosin, which like tylosin is also a macrolid. It appears likely therefore that many strains of *B. hyo* which are resistant to tylosin could also be resistant to aivlosin.

Tiamulin has recently been shown in vitro to be 46.1x more potent than aivlosin against 20 Swedish field strains of B. hyo

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An informative paper on the above topic, inter alia, was published in the *Journal of Medical Microbiology* (2004) Vol. 53 p281 – 285 by Karlsson, M. et al.

In Sweden swine dysentery is a significant disease problem and, for example, during 2003 33% of the pig herds tested by Rasback et al. were positive for *B. hyo*. Further it reported that the infection rate has recently more than tripled from 1.3% of all Swedish pig herds in 1996, to 4.1% of all such herds in 2003.

As in many other countries tiamulin is an antibiotic of choice for effective swine dysentery control in Sweden since so far no strains of *B. hyo* have been proven to be resistant. Resistance to tiamulin among *B. hyo* isolates, both in vitro and in vivo develops gradually, (Karlsson, M. 2001 and 2002). However in a small number of countries (e.g. Germany, UK, Czech Republic and Hungary) there have been reports of isolates of *B. hyo* with decreased susceptibility to tiamulin.

Comparative antimicrobial sensitivity testing on 20 Swedish field isolates of *B. hyo* and one type strain B78 т (ATCC 27164) was carried out.

It was performed by broth dilution in brain heart infusion broth with 10% foetal calf serum. Antimicrobial agents were dried in serial two fold dilutions in tissue culture trays, in which a suspension of the bacteria was dispersed (0.5 ml per well) and incubated.

The minimum inhibitory concentration (MIC) was read as the lowest concentration of the antimicrobial agent which prevented visible growth.

The antimicrobials tested, along with tiamulin, were:

- Aivlosin – a chemically modified form of tylosin (3 acetyl 4' – isovaleryl tylosin) which is registered for the treatment of swine dysentery in the Czech Republic and was approved as a premix in EU during May 2004 for the treatment of swine.
- Doxycycline – not approved for swine dysentery in EU.
- Salinomycin – in EU approved in pigs only as a growth promoter and will be withdrawn from the market in approximately 18 months.
- Avilamycin – as Salinomycin, see above.
- Chloramphenicol – banned in many countries for food producing animals on account of potential toxicity to man of residues.

All the Swedish *B. hyo* isolates tested showed strong haemolysis and were indole positive.

The MIC results are tabulated below:

Table 1: Antimicrobial susceptibility for 20 Swedish field isolates of B. hyodysenteriae to tiamulin, aivlosin and tylosin

	MIC (mcg/ml)		
Isolate	**Tiamulin**	**Aivlosin**	**Tylosin**
S1	0.031	1	4
S2	0.125	1	4
S3	0.125	4	>128
S4	0.063	4	>128
S5	0.031	2	4
S6	0.125	2	8
S7	0.125	16	>128
S8	0.063	8	>128
S9	0.063	4	>128
S10	0.063	8	>128
S11	0.25	8	>128
S12	0.5	16	>128
S13	0.25	8	>128
S14	0.063	8	>128
S15	0.25	8	>128
S16	0.125	1	8
S17	0.063	1	4
S18	0.125	1	8
S19	0.031	2	4
S20	0.125	16	>128
Average MICs	**0.129**	**5.95**	**79**

It is of interest that, according to the authors:

- The MIC's for tylosin followed a similar pattern to those for aivlosin, thereby indicating that the 23SrRNA mutation causing macrolid resistance in *B. hyo* (Karlsson, M. et al. 1999) also affects the binding of aivlosin. This finding was expected since aivlosin is an antibiotic derived by modification of the tylosin molecule.

- Tiamulin was shown to be 46.1x more potent in vitro than aivlosin against 20 Swedish field strains of *Brachyspira hyodysenteriae*.

  (Tia. av. MIC = 0.129mcg/ml)
  (Aivlosin av. MIC = 5.95mcg/ml)

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Further information on the Tiamutin® (tiamulin) range of products is available from the Pig Products Manager at Novartis Animal Health operations in over 50 countries worldwide.