

# Denagard - the drug of choice against *Lawsonia intracellularis* (Ileitis)

## Issue

What is the comparative sensitivity of *Lawsonia intracellularis* to Denagard® and other antibiotics as determined by minimum inhibitory concentration (MIC) assessment?

## Study

New MIC data were generated by US researchers specialised in the use of tissue culture system (McCoy cell monolayer) for specific MIC determination<sup>1</sup>. A series of MIC tests evaluated the sensitivity of 10 *L.intracellularis* strains originating from the USA (6 strains) and Europe (4 strains). The MICs of different antimicrobials against *L.intracellularis* were determined using a tissue culture system. All antimicrobials were tested in a range of different concentrations (0.125 to 128 µg/ml), which makes a titration of low and high MICs possible. Intracellular and extracellular MIC assays for *L.intracellularis* were performed to mimic the real infectious situation in which the organism is exposed to antimicrobials before and after invasion into the intestinal cells. The MIC of each antimicrobial was identified as the lowest concentration that inhibited 99% of *L.intracellularis* growth, as compared to an antimicrobial-free control.

## Findings

**Table 1: Intracellular and extracellular MIC ranges for *L. intracellularis* strains from the United States and Europe<sup>1</sup>**

Antimicrobial agent	US <i>L.intracellularis</i> isolates (n=6)		European <i>L.intracellularis</i> isolates (n=4)	
	Intracellular MIC (µg/ml)	Extracellular MIC (µg/ml)	Intracellular MIC (µg/ml)	Extracellular MIC (µg/ml)
Chlortetracycline	4-64	32-64	0.25-16	16-64
Lincomycin	16->128	>128	8-64	32->128
Tylosin	0.25-32	1->128	0.5-2	2-16
Tiamulin	0.125-0.5	1-32	0.125	1-4

- Tiamulin was the most active antimicrobial inhibiting the intracellular activity of all *L.intracellularis* isolates at < 0.5 µg/ml

*L.intracellularis* strains demonstrated the highest degree of intracellular sensitivity to Denagard's active ingredient, tiamulin.

- The extracellular activity results indicate lower MIC ranges for tiamulin in comparison to the other antimicrobials

*L.intracellularis* strains demonstrated the highest degree of extracellular sensitivity to Denagard's active ingredient, tiamulin.

- The MIC results also demonstrate *L.intracellularis* strains show intermediate to low susceptibility and high variation in the sensitivity to drugs like tylosin, lincomycin and chlortetracycline

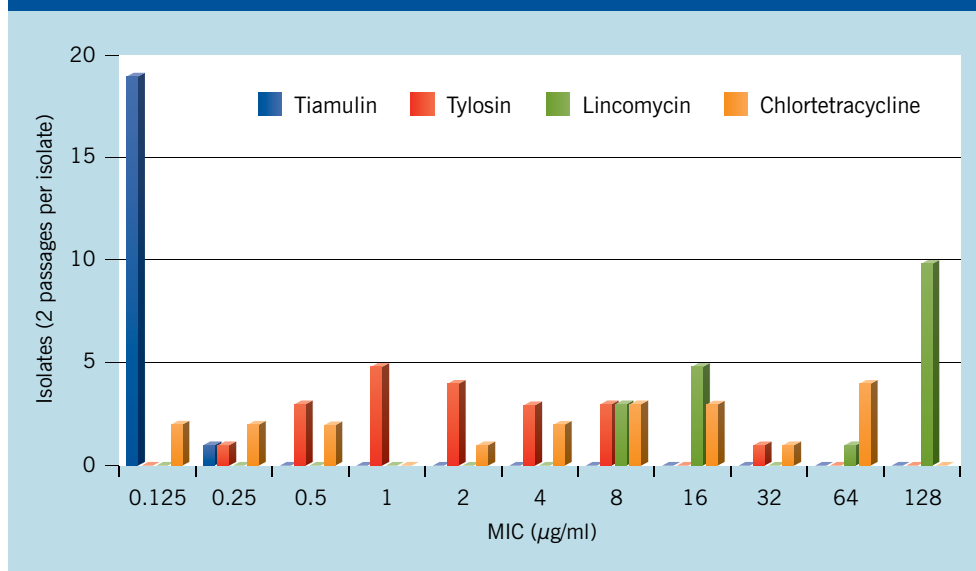
*L.intracellularis* strains demonstrate a low and non-uniform sensitivity to tylosin, lincomycin and chlortetracycline.



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Figure 1: Distribution of MIC of four antibiotics against *L.intracellularis* isolates from United States and Europe (10 isolates in total)<sup>1</sup>



- In vitro results show a different antimicrobial sensitivity pattern of the *L.intracellularis* strains. Intracellular and extracellular MICs for the European *L.intracellularis* strains tended to be lower than for the US isolates

The US strains of *L.intracellularis* appear to be less susceptible than the European strains to a range of antimicrobials.

## Conclusions

- Consistently low MICs and narrow MIC ranges for tiamulin prove the high susceptibility of *L.intracellularis* to tiamulin and the efficacy of Denagard against this pathogen
- Denagard's competitor antimicrobials possess higher MIC values and a far broader range of MIC variation indicating less susceptibility of *L.intracellularis* to these treatments
- Tiamulin (Denagard) is the most active antimicrobial for inhibiting the intracellular and extracellular activity of *L.intracellularis*
- The trial results provide a scientific basis for the clinical selection of tiamulin as the drug of choice for more definitive treatment and control regimes against *L.intracellularis* infection (ileitis)

### References:

1. S.Wattanaphansak, R.S.Singer, C.J.Gebhart (2009): In vitro antimicrobial activity against 10 North American and European *L.intracellularis* isolates. *Veterinary Microbiology*, 134, 305-310.

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