

Efficacy of Denagard[®] formulations against ileitis

Issue

Enteric infections caused by *Lawsonia intracellularis* are widely recognized by swine veterinarians as a significant problem in pig production around the world.

What is the efficacy of Denagard premix, water soluble and injectable formulations against *Lawsonia intracellularis*?

Study 1

The effect of Denagard Premix as a treatment (150ppm, commencing 7 days post-challenge) or as a preventive (50ppm, commencing 2 days pre-challenge and continuing for 21 days until trial termination) were evaluated in a challenge study (McOrist et al. 1996).¹

All pigs receiving Denagard Premix at 50ppm pre-challenge and 150ppm post-challenge, remained clinically normal, were free from diarrhoea and had no PE lesions at post mortem.

Table 1: Necropsy results (ileum/caecum) of the prevention (50ppm) and treatment (150ppm) study - in-feed medication¹

	Gross findings (ileum/caecum)	Histological lesions ileum (average %)	Histological lesions caecum (average %)
Challenged, unmedicated	Mucosa hyperplasia and/or thickening	42%	46%
Challenged, Denagard 50ppm	–	0%	0%
Challenged, Denagard 100ppm	–	0%	0%

Findings 1

- Effective concentrations of tiamulin hydrogen fumarate are achieved in the ileal contents by in-feed medication
- Concentrations sufficient to inhibit the development of ileitis were achieved when Denagard was given in feed at 50ppm
- Concentrations sufficient to treat ileitis infections completely were achieved when Denagard was given in feed at 150ppm

Denagard is highly effective for the prevention and treatment of ileitis.



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Study 2

In a challenge study, water medication containing Denagard Solution at a treatment level of 60ppm was administered, for 5 consecutive days, and assessed for efficacy against *Lawsonia intracellularis* (Walter et al. 2001).²

The performance and clinical effect were monitored for 15 days (5 days during medication and 10 days post-medication).

Denagard effectively controlled the clinical, pathological and negative productivity effects of PPE infection in these pigs which were experiencing an outbreak of PPE infection.

Figure 1: Mean clinical scores of the treatment group vs. the unmedicated group - water medication study²

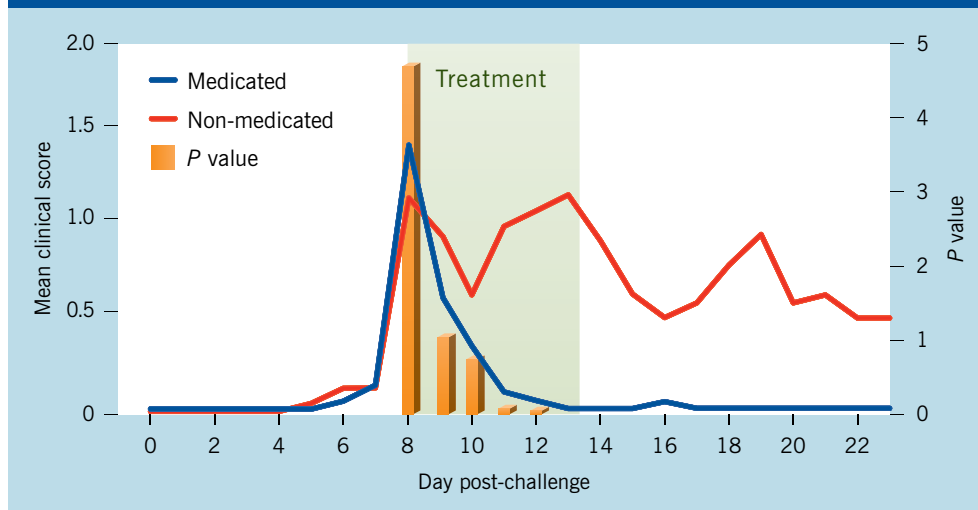
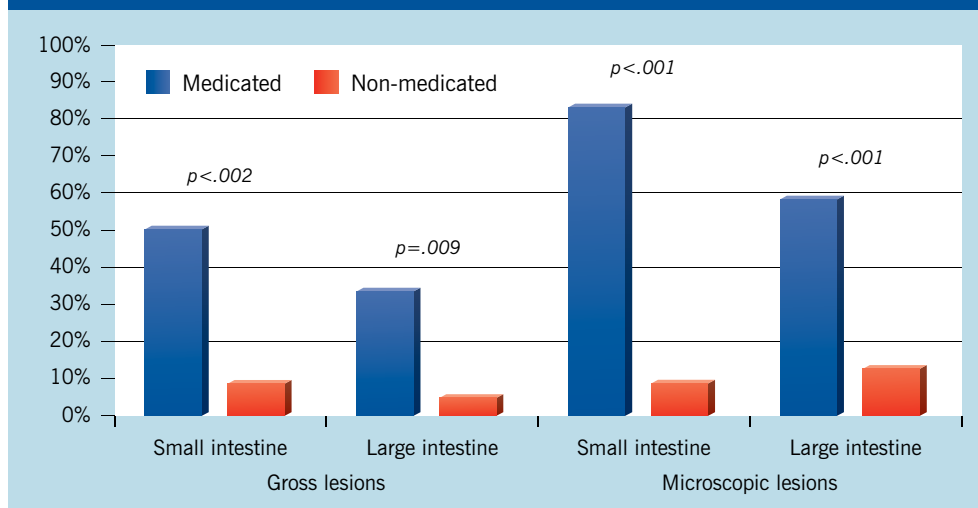


Figure 2: Gross and microscopic ileitis related lesions for the treatment group vs unmedicated group - water medication study²



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Gross lesions (un-medicated)	- Small intestine: 12 animals	= 50%
	- Large intestine: 8 animals	= 33%
Gross lesions (Denagard)	- Small intestine: 2 animals	= 8%
	- Large intestine: 1 animal	= 4%
Micro lesions (un-medicated)	- Small intestine: 20 animals	= 83%
	- Large intestine: 14 animals	= 58%
Micro lesions (Denagard)	- Small intestine: 2 animals	= 8%
	- Large intestine: 2 animals	= 8%

Findings 2

- The ability of cellular penetration, accumulation and inhibition of ingested organisms is demonstrated for tiamulin (Nielsen 2002).³ The results in this study verify the uptake of tiamulin by leukocytes, the production of intracellular concentrations several times higher than the extracellular concentration and pronounced intracellular activity against pathogens located within the cells
- The substantial therapeutic effect of Denagard water medication at 60 ppm (8mg THF / kg bw) is based on the THF gut pharmacokinetics and its high concentration in the colon and ileum

Water medication with Denagard water soluble formulations can be considered a highly effective tool for ileitis treatment.

Efficacy for *Lawsonia intracellularis* (ileitis) eradication

Lawsonia intracellularis can be eradicated without total depopulation based on Denagard strategic medication programmes (Flo 2000, Nielsen 2004, Ellegaard 2008).^{4,5,6}

Farms can be kept free of *L.intracellularis* if biosecurity measures are maintained at a very high level and monitoring investigations (clinical, bacteriology, serology) can confirm *L.intracellularis* disease-free status several years after the eradication programme.

Results of eradication programmes confirm the exceptional potency / efficacy of Denagard against ileitis in cases of strategic application combined with partial depopulation.

The above trial results, and Denagard's proven effectiveness in medication based eradication programmes, establish that Denagard is the drug of choice for more definitive treatment and control regimes against *Lawsonia intracellularis*.

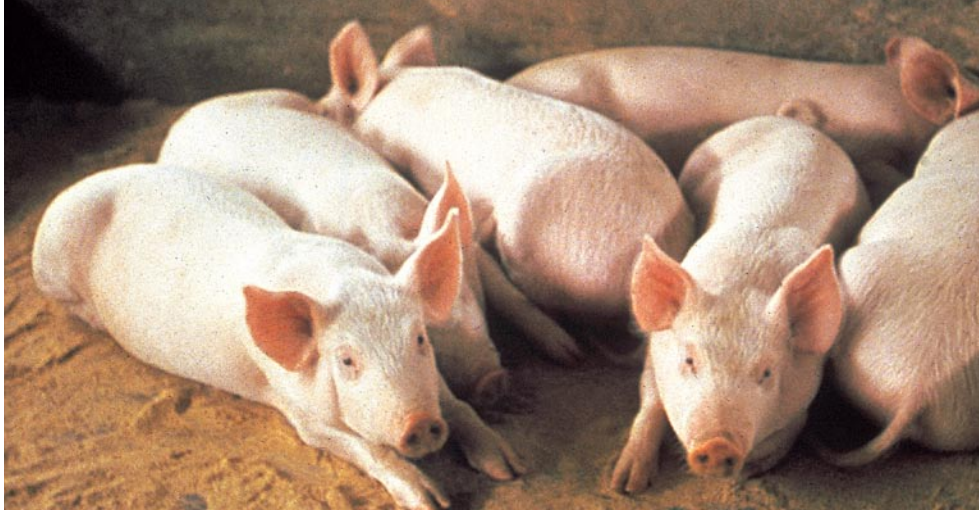
Other aspects

- Tiamulin (Denagard) was the first antimicrobial shown to be effective against *Lawsonia intracellularis* in challenge study models (1996)
- Tiamulin (Denagard) is the only antimicrobial shown to be effective for the eradication of *Lawsonia intracellularis*
- Tiamulin (Denagard) concentrates inside the enterocytes and provides high efficacy inside those cells



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Conclusions

- **The effectiveness of Denagard's active ingredient (THF) is proven after administration via feed and water when clinical disease of ileitis is evident**
- **Denagard in-feed and water medication provides high THF concentrations in the ileum and colon**
- **Reduction in lesion development, clinical disease, faecal shedding and productivity losses associated with PPE prove the consistent efficacy of Denagard against ileitis**
- **Denagard can successfully eliminate *Lawsonia intracellularis* from pig farms when coupled with hygiene and management control measures**
- **Tiamulin, the active ingredient of Denagard, is the most active antimicrobial inhibiting intracellular and extracellular activity of *Lawsonia intracellularis***
- **These data are the scientific basis for selection of Denagard as the product of choice for more definitive treatment regimes against ileitis**

References:

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Novartis Animal Health Inc., PO Box CH-4002, Basel, Switzerland.
Tel: +41 61 697 57 35 Fax: +41 61 697 67 88 www.denagard.com



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