

NUMBER 6

IN VITRO STUDIES SHOW *M. HYOPNEUMONIAE* IS HIGHLY SUSCEPTIBLE TO VALNEMULIN (ECONOR®)

INTRODUCTION Several investigations conducted in Europe and Asia show that valnemulin, the active ingredient in Econor®, has exceptional *in vitro* activity against *Mycoplasma hyopneumoniae*, a common and costly cause of enzootic pneumonia in swine around the world.

These investigations further demonstrate that valnemulin is virtually the most active agent available against *M. hyopneumoniae* and that, even with repeated exposure to valnemulin, the development of *M. hyopneumoniae* resistance is minimal.

United Kingdom

Investigators determined minimum inhibitory concentrations (MICs) for valnemulin and several other antimicrobial agents against 10 strains of *M. hyopneumoniae* isolated from porcine lungs in the United Kingdom.¹ MICs were determined and represent the lowest concentration of antimicrobial needed to inhibit growth of *M. hyopneumoniae*.

In addition to valnemulin, antimicrobials tested in the study were tiamulin, oxytetracycline, tylosin and lincomycin.

Results

- > All strains of *M. hyopneumoniae* were susceptible to valnemulin.
- > The best MICs were obtained with valnemulin, followed by tiamulin, oxytetracycline, tylosin and lincomycin (Table 1).
- > Valnemulin was shown to be 16- to 129-fold more active than the other antimicrobials tested.

Researchers' observations: "In conclusion, Econor showed a range of activities against the bacterial pathogens in comparison with other antimicrobial agents, but was found to be the most active against *M. hyopneumoniae*..."

Denmark

In Denmark, researchers determined MIC values for valnemulin and tiamulin against 10 strains of *M. hyopneumoniae* obtained from various Danish herds with outbreaks of enzootic pneumonia.²

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Table 1
MIC₅₀s of antimicrobials to M. hyopneumoniae isolates from United Kingdom. Valnemulin provided the best results.

Antimicrobial	MIC ₅₀ (mcg/ml)
Valnemulin (Econor)	0.0024
Tiamulin	0.039
Oxytetracycline	0.078
Tylosin	0.16
Lincomycin	0.31

KEY POINTS

- > Strains of *M. hyopneumoniae* from several countries around the world are highly susceptible to valnemulin, the active ingredient in Econor®.
- > Valnemulin combined with chlortetracycline has a synergistic effect against a broad range of respiratory pathogens that affect swine.
- > Repeated exposure to valnemulin did not result in significant *M. hyopneumoniae* resistance.

Results

- > All *M. hyopneumoniae* strains were highly susceptible to valnemulin (Table 2).
- > MIC values for valnemulin were 10 to 40 times less than those for tiamulin, both at initial and final readings.

Researchers' observations: *M. hyopneumoniae* is highly susceptible to valnemulin, and makes Econor an interesting compound for treating enzootic pneumonia in infected herds.

Table 2

MIC (mcg/ml) results from Denmark show that *M. hyopneumoniae* was more sensitive to valnemulin than tiamulin.

Antimicrobial	<i>M. hyopneumoniae</i>
Valnemulin (Econor)	0.0025
Tiamulin	0.05 – 0.1

Germany

Using *M. hyopneumoniae* isolates obtained from infected German pig herds in different locations around the country, investigators tested the sensitivity of 10 *M. hyopneumoniae* isolates to valnemulin, tiamulin and enrofloxacin.³

Results

- > All *M. hyopneumoniae* strains were found to be highly sensitive to valnemulin.
- > Of the three antimicrobials tested, valnemulin was the most active against *M. hyopneumoniae* strains in the study.
- > Most strains of *M. hyopneumoniae* were sensitive to enrofloxacin but, for some strains, the MIC for valnemulin was at least five times lower.

Researchers' observations: "The results confirm that recent field isolates are extremely sensitive to Econor... [This antimicrobial] could be a potent agent in the treatment of enzootic pneumonia and other mycoplasma infections of swine."

Korea

Researchers determined MICs for valnemulin and several other antimicrobials against 10 strains of *M. hyopneumoniae* isolated in Korea.⁴ The other antimicrobials tested were chlortetracycline, lincomycin, tylosin and penicillin.

Korean investigators also determined MICs for a combination of valnemulin and chlortetracycline against *M. hyopneumoniae* and four other respiratory pathogens of swine responsible for porcine respiratory disease complex: *Actinobacillus pleuropneumoniae*, *Pasteurella multocida*, *Haemophilus parasuis* and *Streptococcus suis*.

Results

- > *M. hyopneumoniae* strains were most susceptible to valnemulin.
- > A combination of valnemulin and chlortetracycline was even more effective against *M. hyopneumoniae*, resulting in MICs from 4 to 8 times lower than those for valnemulin or chlortetracycline alone.
- > Together, valnemulin and chlortetracycline demonstrated synergistic activity against a broad spectrum of respiratory pathogens.

Researchers' observations: "The results suggest that the combined use of valnemulin and chlortetracycline may be useful in the treatment of respiratory disease in swine."

Thailand

Thai researchers determined MICs for valnemulin and several other antimicrobials against 27 field isolates of *M. hyopneumoniae*.⁵ The other antimicrobials tested included tiamulin, tilmicosin, chlortetracycline, lincomycin, josamycin, spectinomycin and oxytetracycline.

“Valnemulin was far more active against *M. hyopneumoniae*”

Results

- > All isolates of *M. hyopneumoniae* were extremely sensitive to valnemulin and tiamulin, but were more sensitive to valnemulin.
- > Valnemulin was 16 times more active than lincomycin and josamycin and 65 times more effective than oxytetracycline.
- > Susceptibility of *M. hyopneumoniae* to tilimicosin, oxytetracycline and chlortetracycline was only moderate.

Researchers' observations: "Valnemulin showed very high activity against all *M. hyopneumoniae* isolates."

TESTING FOR RESISTANCE

The development of resistance to antimicrobials is always an important concern for pork producers battling enzootic pneumonia. Consequently, British researchers have conducted *in vitro* testing and determined MIC values to see if *M. hyopneumoniae* is likely to develop resistance to valnemulin after repeated exposure to the antimicrobial.⁶

For the study, they used two strains of *M. hyopneumoniae*, which were exposed 10 times to valnemulin, tiamulin, tylosin and oxytetracycline. One isolate was a "J" strain obtained from a collection

of type cultures and the other was a recent field isolate known as MEVT G23.

Results

- > Valnemulin was far more active against *M. hyopneumoniae* than either tiamulin, tylosin or oxytetracycline (Table 3).
- > The development of resistance to valnemulin was minimal in both strains of *M. hyopneumoniae* after 10 passages.
- > With one of the isolates used, there was no increase in resistance to tiamulin and with the other isolate, there was a slight increase.
- > In both *M. hyopneumoniae* strains, there was a marked development of resistance after eight exposures to tylosin and a moderate development of resistance after 10 exposures to oxytetracycline.

Researchers' observations: "These results show that Econor is considerably more active against *M. hyopneumoniae in vitro* than either tiamulin, tylosin or oxytetracycline and that it does not induce significant resistance to itself in *M. hyopneumoniae* strains *in vitro*. These combined properties indicate that Econor has potential advantages over all of the other compounds examined in the current study."

	"J" Strain			Field Strain (MEVT G23)		
	Pre-Passage	Post-Passage	Factor Resistance Increase	Pre-Passage	Post-Passage	Factor Resistance Increase
Econor	0.0025	0.005	2	0.001	0.0025	2.5
Tiamulin	0.1	0.25	2.5	0.05	0.05	0
Tylosin	0.25	>500	>2000	0.125	62.5	500
Oxytetracycline	0.25	1.0	4	0.25	1.0	4

Table 3

In vitro development of resistance in two strains of *M. hyopneumoniae* (MIC mcg/ml)

***moniae* than either tiamulin, tylosin or oxytetracycline."**

SUMMARY

In vitro studies show valnemulin to be highly active against *M. hyopneumoniae*. The results have been reproduced by several different investigators using strains from different countries. Valnemulin offers pork producers an effective agent for controlling *M. hyopneumoniae*-induced enzootic pneumonia.

When combined with chlortetracycline, valnemulin is active against a broad spectrum of respiratory pathogens, indicating this combination could be very helpful in herds with porcine respiratory disease complex. Valnemulin has another apparent important advantage: Even after repeated exposure to the antimicrobial, *M. hyopneumoniae* strains did not develop significant resistance.

For more information on this study, please contact your local Novartis Animal Health representative or Dr. Ulrich Klein at ulrich.klein@ah.novartis.com

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