



Treatment of *Actinobacillus pleuropneumoniae* (APP) infection

“Take home” messages

- APP occurs either as a single infection or as a complicating factor in respiratory infections associated with PRRS, PCV-2 and other viruses.
- APP infection is a highly contagious, often fatal infection when it occurs alone.
- Feed and water consumption during an APP outbreak can be reduced by 85%.
- A recent in vitro study has demonstrated high sensitivity of APP strains to tiamulin, with an MIC range of 2-4mcg/ml and an MIC₉₀ of 4mcg/ml.
- Previous experimental field studies indicate high clinical efficacy of Tiamutin Injection in a dose level of 15.0 mg thf/kg bwt I/M.
- Tiamutin Injection at 15mg thf/kg bwt as a single I/M injection achieves lung levels of 8mcg/g between 2-8 hours post injection and Tiamutin Water Soluble at 120ppm thf for several consecutive days achieves levels in pneumonic lungs of 5-15.5mcg/g.
- Tiamutin Water Soluble at 120 ppm thf for several consecutive days was reported to successfully treat APP infection by preventing mortality and by reducing production loss and lung lesions.
- The optimal use of Tiamutin preparations to combat acute APP infections is:
 - *in the early treatment phase use Tiamutin[®] Injection for 2-3 consecutive days*
 - *in the later treatment phase, when regular water consumption patterns have returned, use Tiamutin[®] Water Soluble for up to 5 days (120-180 ppm thf).*

tiamutin[®]
the original – tried, tested, trusted

UNRELATED TO HUMAN USE ANTIBIOTICS • NOT USED IN HUMAN MEDICINE





Introduction

Actinobacillus pleuropneumonia is a highly contagious often fatal respiratory disease of weaned, growing and finishing pigs in which infection of the lungs with *Actinobacillus pleuropneumoniae* (APP) causes fibrinous pleurisy, pneumonia and a depressed growth rate in chronically affected pigs.

As a single entity infection it is now less common than formerly but APP is also frequently present in viral respiratory conditions caused by PRRS and PCV-2 viruses. APP produces fimbria, capsules and secretes toxins. Twelve major serotypes of Biotype 1 and at least three of Biotype 2 exist.

Clinically the infection exists in acute and sub-acute forms. The acute form occurs in a non-immune herd or in individuals which have not received protective vaccination. 15-30% of pigs may suffer depression, anorexia, high temperature 42.8°C (109°F) or laboured breathing.

Cyanosis, subnormal rectal temperature and death may follow within 6-12 hours of the onset of clinical signs. Some pigs may be found dead and mortality may reach 30% - 50% in cases of non-treatment. Conversely, in the sub-acute form, groups of pigs show anorexia, are pyrexemic and exhibit respiratory distress, coughing and reduced rates of weight gain. Mortality is variable.

Treatment must be started early and injectable antibiotic treatment is the method of choice, at least until the sickly pigs are drinking adequate quantities of water.



Rationale for Tiamulin[®] as a treatment for APP infection

1) In vitro sensitivity studies

Recent studies by Fodor, L. and others (2004) and Jablonski and others (2004) have confirmed the superior in vitro sensitivity of APP to tiamulin compared to antibiotics, such as tylosin, lincomycin and CTC (see Tables 1&2).

Table 1: Range of MIC's, MIC₅₀ and MIC₉₀ for 10 strains of APP (µg/ml) – Fodor et al. (2004)

Antibiotic	MIC range	MIC ₅₀	MIC ₉₀
tiamulin	2-4	2.0	4.0
Tylosin	4-32	16	32
lincomycin	1-16	8	16
CTC	1-32	8	32

Jablonski and others reported on the pooled results of submissions to diagnostic laboratories in USA at Iowa State University, South Dakota State University and the University of Minnesota for the years 1998-2001 (see Table 2).

Table 2: % of isolates of APP found sensitive to tiamulin, tylosin, lincomycin and CTC – Jablonski et al. (2004)

Antibiotic	
tiamulin	84.6%
Tylosin	1.8%
lincomycin	4.4%
CTC	57.4%

For the interpretation of tiamulin-specific MIC data the suggested breakpoint scheme of Casals et al. (1990) can be used (see Table 3).

Table 3: Breakpoints of tiamulin for APP suggested by Casals (1990)

Fully sensitive	Moderately sensitive	Resistant
< 8.0 µg/ml	< 9-16 µg/ml	>16.0 µg/ml

2) In vivo tissue concentration data

a) Injection

McKellar and others (2004) reported on the concentration of tiamulin in target tissues, such as the lung, achieved with a single intramuscular injection of 15 mg tiamulin hydrogen fumarate per kg bwt. He reported that constant tiamulin concentrations in lung tissue of 8mcg/g were achieved between 2 and 8 hours post-injection and lungs levels were still greater than 3 mcg/g at 32 hours post-injection.

b) Water Soluble

Taylor (2004) reported that in pigs artificially infected with APP (isolate 6664, serotype 3) the concentration of tiamulin achieved in pneumonic lung with a level of 120 ppm tiamulin hf, applied in drinking water for several consecutive days, was 5-15.5 mcg/g.

3) In vivo artificial infection study and its successful treatment with Tiamutin® Water Soluble and field injection study with Tiamutin® Injection

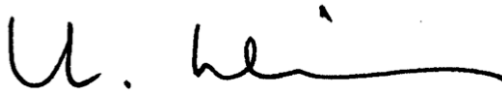
Taylor, D.J. (2004) reported on a small scale controlled experimental infection study with *APP* carried out at the University of Glasgow Veterinary School, U.K.

The study demonstrated that Tiamutin water medication:

- eliminated mortality and reduced clinical signs and *APP*-specific lung lesions
- improved the growth rate and substantially increased water and feed intake in the *APP* infected pigs.

Edwards and Pott (1992) tested the efficacy of Tiamutin injection (dose 15.0 mg thf /kg bwt I/M for 2 consecutive days) in a herd affected by an *APP* infection. The health status of the pigs improved significantly in the character of respiration (coughing, $p < 0.001$), body condition ($p < 0.001$) and clinical appearance ($p < 0.05$).

It can be concluded that Tiamutin® Injection at 15mg/kg bwt I/M for 2-3 consecutive days and water medication with Tiamutin® at 120 ppm thf for several consecutive days can successfully treat APP infection, by preventing mortality and reducing production losses and lung lesions.



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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.

References

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