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Steven Claas
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Layout and CD-ROM
David Brown

Logo Design
Ruth Cronje, and Jan Swanson;
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Tulathromycin MIC interpretive criteria and *in vitro* susceptibility for swine respiratory pathogens

Jim Bradford DVM, Ellen S. Portis, Cindy J. Lindeman
Pfizer Animal Health

Tulathromycin is a novel triamilide antimicrobial that has been approved for use in the treatment and prevention of bovine respiratory disease (BRD) and the treatment of swine respiratory disease (SRD) in the European Union and the United States. In swine, tulathromycin is indicated for the treatment associated with *Actinobacillus pleuropneumoniae*, *Pasteurella multocida*, *Bordetella bronchiseptica* and *Haemophilus parasuis*.

A single dose of tulathromycin at 2.5 mg/kg BW delivers a full course of therapy. The drug is rapidly absorbed, extensively distributed, has an extended half-life and high availability (88%) making it an extremely effective single dose agent. Tulathromycin readily penetrates lung tissues, achieving high lung concentrations approximately 61-times greater than plasma. Tulathromycin accumulates in neutrophils and macrophages, so that high levels of drug are directly delivered to bacterial pathogens. In multi-location field studies, 266 pigs with naturally occurring SRD received a 2.5 mg/kg BW, single dose of tulathromycin. The treatment success rate was significantly greater ($P \leq 0.05$) in tulathromycin-treated animals compared to control. These studies have shown that tulathromycin administered as a single 2.5 mg/kg dose is effective in the treatment of SRD.

The Minimal Inhibitory Concentrations (MICs) of tulathromycin against SRD bacterial pathogens in the United States were evaluated using isolates collected during clinical development studies (1999 and 2001). MICs were also determined for tulathromycin against SRD bacterial pathogens received in 2004 as part of the Pfizer Animal Health BRD/SRD Susceptibility Monitoring Program.

Results from these studies yielded MIC_{90} values of 4.0 μg/mL for tulathromycin against porcine *P. multocida*, from the 1999-2001 isolates, and 1.0 μg/mL against the 2004 isolates. The effect of CO_2 incubation on media pH and its detrimental effect on the *in vitro* activity of macrolides are well known. The 1999-2001 clinical study *A. pleuropneumoniae* isolates were incubated in 5% CO_2 during MIC testing and had a tulathromycin MIC_{90} of 32 μg/mL. The 2004 monitoring *A. pleuropneumoniae* isolates were incubated in ambient air during MIC testing and had a tulathromycin MIC_{90} value of 8.0 μg/mL. CLSI now recommends all MIC testing of *A. pleuropneumoniae* be incubated in 5% CO_2.

Clinical and Laboratory Standards Institute (CLSI) approved a susceptible breakpoint of ≤16.0 μg/mL, intermediate breakpoint of 32 μg/mL, and a resistant breakpoint of ≥64.0 μg/mL for tulathromycin against the BRD label pathogens. (June 2006). Taking into consideration tulathromycin's *in vitro* activity, clinical pharmacology, and the high efficacy for treating naturally occurring swine respiratory infections, Pfizer Animal Health recommends use of the same breakpoints for the SRD pathogens *P. multocida*, and *Bordetella bronchiseptica*. Pfizer Animal Health is recommending a susceptible breakpoint of ≤32.0 μg/mL and resistant breakpoint of ≥64.0 μg/mL for *A. pleuropneumoniae*.

Tulathromycin is shown to be an effective SRD treatment as well as demonstrates good *in vitro* activity against the SRD label pathogens.