Dose optimization of tiamulin (Denagard®) for the metaphylaxis and treatment of *Mycoplasma gallisepticum* infections in chickens

KLEIN, Ulrich¹, BURCH, David²

¹Elanco Animal Health, Schwarzwaldallee 215, CH-4058 Basel, Switzerland. ²Octagon Services Ltd, Friary Round House, Old Windsor, Berkshire, SL42NR, United Kingdom

**INTRODUCTION**

Dose optimization or prediction (1, 2) is becoming an important aspect of pharmacokinetic (PK) and pharmacodynamic (PD) integration for an antimicrobial product to help achieve successful therapy. However, much of the work and standards have been carried out using bactericidal products such as the fluoroquinolones and aminoglycosides and therefore has some limitations when it comes to antibiotics primarily with a bacteriostatic mode of action. Tiamulin (Denagard® - Elanco), a pleuromutilin antibiotic is very active in vitro against *Mycoplasma gallisepticum* (MG) but can be considered primarily a bacteriostatic drug. It is the purpose of this paper to explore the limitations of this PK/PD approach in contrast to clinical evaluation.

**MATERIALS AND METHODS**

**Pharmacodynamics:**

The PK of tiamulin in chickens at the recommended dose of 25mg/kg bwt is concentration max (Cmax) 1.86µg/ml, time max (Tmax) 2.80h and area under the concentration (Css) 0.31µg/ml and estimated clearance is 2.98(L/h/kg).

Plasma protein binding (PPB) the AUC becomes 7.55µg.h/ml, steady state (Dose rate) is becoming an important aspect of Dose optimization or prediction (1, 2) is becoming an important aspect of Pharmacokinetics and Pharmacodynamics for an antimicrobial product to help achieve successful therapy. However, much of the work and standards have been carried out using bactericidal products such as the fluoroquinolones and aminoglycosides and therefore has some limitations when it comes to antibiotics primarily with a bacteriostatic mode of action. Tiamulin (Denagard® - Elanco), a pleuromutilin antibiotic is very active in vitro against *Mycoplasma gallisepticum* (MG) but can be considered primarily a bacteriostatic drug. It is the purpose of this paper to explore the limitations of this PK/PD approach in contrast to clinical evaluation.

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Pharmacokinetics:

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**RESULTS AND DISCUSSIONS**

Clinical assessment:

In an early dose-titration study (6) oral dosing of tiamulin was used for the early treatment (metaphylaxis/control) of an artificial infection with MG injected into the left air sac of 3 week old chicks. Chicks were treated for 3 days and then monitored for a further 5 days before necropsy. Efficacy (cure rate %) was judged by the absence of air sac lesions and the failure to re-isolate MG from the air sacs (see Figure 2).

A tiamulin dose of 10mg/kg bwt and above gave a 90-100% eliminatory effect. The tiamulin MIC of the strain of MG used in the study was 0.0039µg/ml.

**REFERENCES**


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