Pharmacokinetics of eprinomectin in lactating ewes following administration of a subcutaneous formulation of eprinomectin

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Objectives

Eprecis® 2% (Ceva Santé Animale) is a subcutaneous formulation of eprinomectin that has been recently registered in cattle at a dose rate of 0.2 mg/kg without milk withdrawal period. In order to precise the optimal dose rate of this new formulation in sheep, we performed a pharmacokinetic study in lactating ewes at 0.2 and 0.4 mg/kg. Additionally, we determined the milk residue profile associated with the optimal dose rate.

Materials and methods

Sixteen healthy lactating Lacaune ewes (mean age = 6.1 years, mean BW = 70.4 kg) were randomly allocated to two treatment groups. Half of the ewes received Eprecis® 2% subcutaneously at 0.2 mg/kg while the other half was administrated 0.4 mg/kg. Milk and blood were sampled at defined intervals after treatments for 7 days. Plasma and milk samples were assayed for eprinomectin B1a using LC/MS–MS methods. Pharmacokinetic parameters were determined and compared to the minimal effective concentration required for optimal antiparasitic activity against endoparasites (1 to 2 µg/L, Lifschitz, 2004).[1]

Results

Eprinomectin plasmatic concentrations following subcutaneous administration of Eprecis® 2% at either 0.2 mg/kg or 0.4 mg/kg were above the efficacy threshold (>2 µg/L) at all time during the study (figure 1). Consequently, it can be anticipated that the optimal dose rate for Eprecis® 2% in sheep is 0.2 mg/kg. At this dose rate, 96% of the milk samples did not have detectable eprinomectin residues and the 4% of eprinomectin positive samples (5 samples out of 128) presented concentrations widely below the published maximum residue level (MRL) (Figure 2).

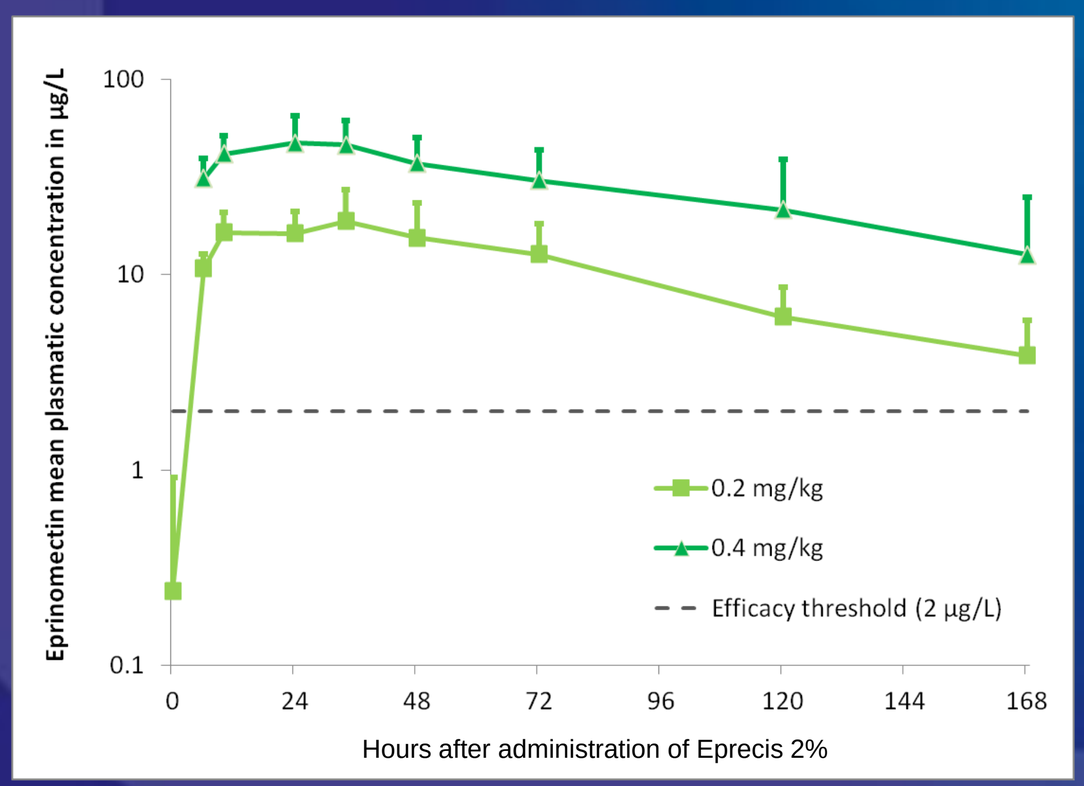

Figure 1. Mean plasmatic concentration of eprinomectin following administration of 0.2 or 0.4 mg/kg of Eprecis 2%

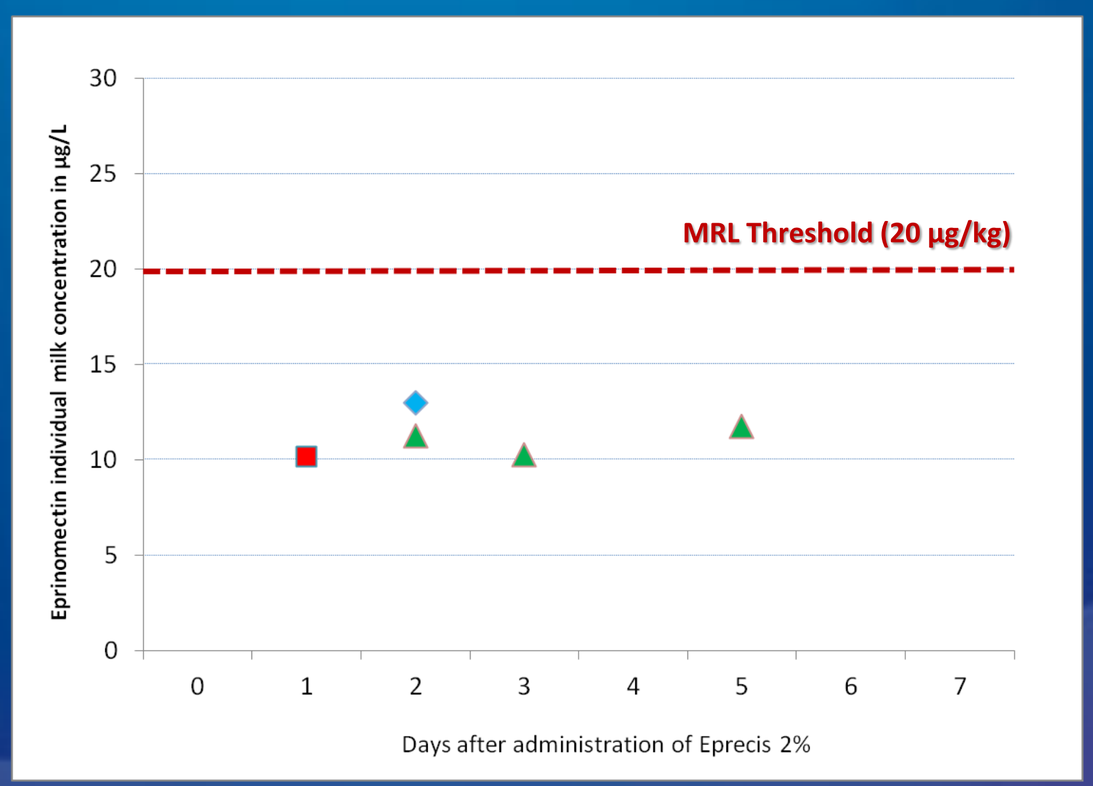

Figure 2. Individual milk residue profile following administration of 0.2 mg/kg of Eprecis 2%

Finally, in comparison with the topical formulation dosed at 1.0 mg/kg (Eprinex® Pour-on, Merial)[2], subcutaneous formulation dosed at 0.2 mg/kg showed a higher *AUClast* (73.3 vs 48.8 day*ng/mL) and *Cmax* (19.5 vs 6.2 ng/mL), demonstrating a greater bioavailability with 5 times less active ingredient.

Conclusions

Based on this pharmacokinetic study, subcutaneous administration of Eprecis 2% is expected to be efficacious in sheep for the control of endoparasites at 0.2 mg/kg. At this dose rate, no eprinomectin residue above the MRL was detected in the milk of treated ewes. Moreover, this dose rate was associated with greater bioavailability than the recently registered pour-on formulation which dose rate is 1 mg/kg.

1. Lifschitz, A. *et al.* Pharmacokinetic evaluation of four ivermectin generic formulations in calves. *Veterinary Parasitology* **119,** 247–257 (2004).
2. Hamel, D. et al. Eprinomectin pour-on (EPRINEX® Pour-on, Merial): efficacy against gastrointestinal and pulmonary nematodes and pharmacokinetics in sheep. BMC Vet. Res. 13, 148 (2017).