The European Agency for the Evaluation of Medicinal Products
Veterinary Medicines Evaluation Unit

EMEA/MRL/523/98-FINAL
November 1998

COMMITTEE FOR VETERINARY MEDICINAL PRODUCTS

PRAZIQUANTEL (extension to sheep milk)

SUMMARY REPORT (2)

1. Praziquantel is an anthelmintic used in both human and veterinary medicine, it is a racemate derivative of pyrazinoisoquinoline and is effective against many species of cestodes and trematodes. Praziquantel affects the integumental membrane of the parasite, disrupting the regulatory processes and inducing spastic paralysis of the parasite's musculature. It is indicated for use in non-lactating sheep as a single oral dose of 3.75 mg/kg bw and in horses as a single oral dose of 1 mg/kg bw.

   An ADI of 0.17 mg/kg bw had previously been established by the Committee for Veterinary Medicinal Products.

   Currently, praziquantel is included in Annex II of Council Regulation (EEC) No 2377/90 in accordance with the following table:

Pharmacologically active substance(s)	Target Species	Other provisions
Praziquantel	Ovine	For use in non-lactating sheep only
Praziquantel	Equidae	

   The ADI was established at 0.17 mg/kg bw.

2. An application has now been submitted for an extension of the MRLs to sheep milk. Praziquantel is indicated as a single oral dose of 3.75mg/kg bw in sheep including lactating animals.

3. Radiolabelled studies with ^{14}C-Praziquantel in rats, dogs, monkeys and sheep show rapid and extensive metabolism with no unmetabolised compound present in any of the excretion products. All major metabolites were hydroxylated derivatives of the parent compound. Metabolism data in man also indicate rapid and extensive metabolism.

4. Radiolabelled metabolism studies with ^{14}C-Praziquantel in lactating sheep also demonstrate extensive metabolism; parent compound was not detected in milk of sheep given 3.75 mg/kg bw; 11 metabolites were found of which 8 were identified and characterised. All metabolites found in milk were also found to exist in edible tissues of treated sheep.

5. Radiolabelled residue depletion studies with ^{14}C-Praziquantel in lactating sheep given 3.75 mg/kg bw show that residues in sheep milk are rapidly depleted. At 8 hours post treatment, the maximum level present in milk was 1.6 µg equivalents/ml; at 48 hours the maximum level was 0.2 µg equivalents/ml and by 72 hours it had declined to a maximum of 0.04 µg equivalents/ml.

6. Assuming a worst case scenario where maximum residues were present in edible tissues and in milk, the daily intake of residues 8 hours after treatment is less than 2.5 mg/day which represents less than 30% of the ADI.

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Conclusions and Recommendation

Having considered the criteria for inclusion of a substance in Annex II of Council Regulation (EEC) No. 2377/90 and in particular that:

- praziquantel is extensively metabolised and rapidly excreted in sheep,
- total residues from both edible tissues and milk of sheep at 8 hours post treatment represent less than 30% of the ADI,

the Committee for Veterinary Medicinal Products considers that there is no need to establish a MRL for Praziquantel and recommends to amend the current entry for praziquantel for ovine in Annex II of Council Regulation (EEC) No. 2377/90 in accordance with the following table:

Pharmacologically active substance(s)	Animal Species	Other provisions
Praziquantel	Ovine	