# Anthelmintic treatment in horses: the extra-label use of products and the danger of under-dosing

S Matthee[a]

**ABSTRACT**

Anthelmintic products form the basis of helminth control practices on horse stud farms at present. Regular evaluation of the efficacy of these products is advisable, as it will provide information on the worm egg reappearance period and the resistance status in the worm population. The aim of this study was to evaluate the efficacy of doramectin, pyrantel pamoate, ivermectin and moxidectin on a Thoroughbred stud farm in the Western Cape Province, South Africa. The study also compared the anthelmintic efficacy of two moxidectin formulations administered at their recommended dosages (an injectable, at 0.2 mg/kg, not registered for horses, and an oral gel at 0.4 mg/kg, registered for horses). Two mixed-sex groups of 30 yearlings and 40 weaners were tested in 2001 and 2002, respectively, divided into 3 and 4 groups of equal size. In 2001, moxidectin was one of 3 drugs administered orally and at a dose rate of 0.4 mg/kg. In 2002, pyrantel pamoate and ivermectin were orally administered at 19 and 0.2 mg/kg. Moxidectin and doramectin (the latter not registered for horses) were administered by intramuscular injection at a dose of 0.2 mg/kg, the dosage registered for other host species. The faecal egg count reduction test was used to determine the anthelmintic efficacies in both years. Each animal acted as its own control and the arithmetic mean faecal egg count and lower 95 % confidence limit was calculated for each of the groups. A 100 % reduction in the faecal egg counts and a 100 % lower 95 % confidence limit was recorded for moxidectin (0.4 mg/kg) in 2001. In 2002, a 99 % and 96 % reduction was recorded for pyrantel pamoate and ivermectin, respectively. In the same year doramectin and moxidectin (both injectable and given at 0.2 mg/kg) did not have any effect on worm egg counts. Of the 4 drugs tested in 2002, only pyrantel pamoate recorded lower 95 % confidence limits above 90 %.

**Key words**: anthelmintic treatment, *Equus caballus,* faecal egg count reduction, under-dosing.

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The betting turnover by the South African horse racing industry is estimated at 5.5 billion rand for the year 2001/2002 (C Hall, South African Jockey Club, pers. comm., 2002). As expected, the breeding of top-quality horses comes at a cost, one aspect of which is providing high-quality feed that will maximize growth and development in young horses. It is well-known that large burdens of helminth parasites (*i.e.* worms) can cause weight loss, diarrhoea, colic and even death in especially young horses[11]. It is for this reason that intensive horse farming practices largely rely on the use of anthelmintics for fast and effective worm control[13]. According to 35 of 57 respondents to a questionnaire survey on helminth control practices on Thoroughbred stud farms, predominantly in the Western Cape and KwaZulu-Natal provinces, the estimated expenditure on anthelmintics is roughly R21 422 per annum (range R400 to R60 000 depending of the number of horses and the treatment frequency on the farms)[12]. The economic viability of anthelmintics is threatened by the development of resistance in the worms to these products. Although the development of anthelmintic resistance is inevitable, there are several practices that can potentially contribute to and/or facilitate its development[1,10,16]. These include a high frequency of anthelmintic treatment, the use of the same drug class every year, high stocking rates and the administration of incorrect dosages[10,16]. Apart from these factors, the questionnaire survey conducted in 2000/2001 revealed that many of the stud farms use 'unregistered products' (*i.e.* products that are registered but not registered for use in horses) and/or 'unregistered drug formulations' (products that are registered for horses but the specific drug formulation is not)[12]. The threat of anthelmintic resistance is not only restricted to horses in South Africa but also to other species. Recent surveys, using faecal egg count reduction tests (FECRT) on small domestic ruminants, both in the summer and winter rainfall regions, indicated resistance to at least one drug on 90 % of the farms studied[6,14,15].

The aim of this study was to evaluate the efficacy of doramectin (not registered for horses), pyrantel pamoate, ivermectin and moxidectin. The anthelmintic efficacy of moxidectin administered at two dosages (a 0.2 mg/kg injectable as registered for cattle, sheep and ostriches and a 0.4 mg/kg oral gel as registered for horses) was also compared. The study involved 70 Thoroughbred horses on a stud farm in the Western Cape Province during 2001 and 2002. The farm stocks approximately 200 horses that are kept on approximately 50 ha of pastures (30 ha are irrigated). Most of the weaners and yearlings are kept in groups of 6–8 on the irrigated pastures. Faeces are removed from the pastures at 7–14-day intervals. The anthelmintics used on the farm from 1997 to 2000 included pyrantel pamoate, fenbendazole, praziquantel, moxidectin, doramectin and ivermectin. Adult mares, yearlings and weaners are dewormed every month. No evaluation of anthelmintic efficacy took place on the farm until 2000, when the farm participated in a questionnaire survey on helminth control practices[12]. In 2001, 30 yearling horses from the same farm formed part of the 1st anthelmintic efficacy test. The animals were divided into 3 equal groups. Oxibendazole (Seroh paste, Virbac), moxidectin (Equest Gel, Fort Dodge and Bayer) and ivermectin (Eqvalan paste, Merial) were administered orally and at dose rates of 10, 0.4 and 0.2 mg/kg[12]. In 2002 the farm manager suspected a worm problem as a number of weaners were in poor condition (*e.g.* underweight, pot-bellied, dull coats). A 2nd anthelmintic evaluation test was undertaken on the farm and the efficacy of 4 drugs regularly

[a]Department of Zoology, University of Stellenbosch, Private Bag X1, Matieland, 7602 South Africa.
E-mail: smatthee@sun.ac.za

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Table 1: **Faecal egg count** (FEC) **reduction and lower 95 % confidence limits** (LCL) **following anthelmintic treatment in horses.**

| Year | Drug | *n* | Dosage | Formulation | Mean FEC (day 0) | Mean FEC (days 10–14) | Mean % reduction | LCL (%) | Res[f] |
|---|---|---|---|---|---|---|---|---|---|
| 2001 | Moxidectin[a] | 10 | 0.4 | Oral paste | 935 | 0 | 100 | 100 | S |
| | Ivermectin[b] | 10 | 0.2 | Oral paste | 1125 | 0 | 100 | 100 | S |
| 2002 | Moxidectin[c] | 10 | 0.2 | I/m injection | 585 | 605 | –3 | –146 | R |
| | Doramectin | 10 | 0.2 | I/m injection | 567 | 584 | –3 | –111 | R |
| | Pyrantel pamoate | 9[e] | 19 | Oral dose | 564 | 5 | 99 | 94 | S |
| | Ivermectin[d] | 10 | 0.2 | Oral paste | 595 | 25 | 96 | –4 | SR |

[a]0.4 mg/kg (Equest gel), [b]0.2 mg/kg (Eqvalan paste), [c]0.2 mg/kg (Cydectin injectable), [d]0.2 mg/kg (Equimax oral paste); [e]on days 10–14 only 9 samples were processed.
[f]Res = resistant status, S = susceptible, SR = suspected resistance, R = resistant.

used on the farm, was assessed. This time, 40 weaners were divided into 4 equal groups. Pyrantel pamoate (Nemex-H powder, Pfizer) and ivermectin (Equimax oral paste, Virbac) were administered orally at doses of 19 and 0.2 mg/kg. Doramectin (Dectomax LA Injection, Pfizer) and moxidectin (Cydectin injectable, Fort Dodge) were administered by intramuscular injection at dosages of 0.2 mg/kg for both (neither of the two formulations are registered for use in horses). All dosages (in 2001 and 2002) were based on the individual weight of the animals using the Equi-feeds weigh band (95 % accuracy; F E van Niekerk, University of Stellenbosch, pers. comm., 2001). Each animal acted as its own control and the arithmetic means were used to calculate the percentage reduction between pre- and post-treatment worm egg counts for each animal (FECRT)[2,3]. Only the strongyle egg count was used in the calculation of the FECRTs. Resistance was 'confirmed' when faecal egg count reduction (FECR) was less than 95 % and the lower 95 % confidence limit (LCL) was less than 90 % (see Coles *et al.*[2] for calculation of LCL). If only one of the conditions was met, resistance was noted as 'suspected', but not confirmed. The reason for such a strict measure is that the sensitivity of the tests is limited and it can only detect resistant worms when they have reached reasonable abundance in the population[7].

The following equation was used to determine the percentage reduction[2]:

$$\%R = 100(1–Xt/Xc),$$

where $X$ is the arithmetic mean, $t$ is the post-treatment group worm egg count at 10–14 days and $c$ is the pre-treatment group worm egg count.

Larval cultures were made of the faecal material from positive animals in 2001 upon which more than 90 % of the larvae were found to be cyathostomes (also known as small strongyles and *Trichonema*). Although no larval cultures were made in 2002 it is expected that cyathostomes were once again the most prevalent worms. Pyrantel pamoate recorded FECR and LCL above 95 % and 90 %, respectively. Moxidectin, revealed a lower FECR when administered at a 0.2 mg/kg dose than at 0.4 mg/kg (Table 1). The latter dosage recorded FECR and LCL above 95 % and 90 %, respectively. FECR of ivermectin was above 95 % in both years, but LCL was below 90 % in 2002 (Table 1). Doramectin, administered at 0.2 mg/kg had no effect on the worm egg counts (Table 1).

Currently there are 3 classes of broad-spectrum anthelmintics available for use in domestic animals. These include the benzimidazoles, macrocyclic lactones and the acetylcholine receptor agonists levamisole, pyrantel and morantel[7]. Within each of these classes there are specific products, dose rates and formulations (*e.g.* oral paste, *per os* liquid and injection) registered for individual host species, based on factors such as host physiology and economic considerations[9] (Table 2). The extra-label use of products for worm control in the horse industry in South Africa is not uncommon and seems to be largely motivated by two factors: 1) the perception that registered horse products are more expensive than products registered for 'other' animal species; and 2) the ease of administration as both moxidectin (Cydectin Injectable) and doramectin (Dectomax LA Injection), that are registered for 'other' host species, are administered by intramuscular injection which also restricts wastage[12]. The extra-label use of products is illegal in terms of the Fertilizers, Farm Feeds, Agricultural Remedies and Stock Remedies Act (Act No. 36 of 1947). Moreover, concerns about this practice include the incorrect calculation of the required dosage for horses and the use of anthelmintic formulations that can potentially affect the health of the animal. Doramectin is related to ivermectin and together they belong to the avermectin group. Recent comparative pharmokinetic studies of these two products have revealed comparable results for various parameters such as maximum plasma concentrations, mean residence time and faecal concentrations (dry weight)[8]. Horse breeders in South Africa use doramectin quite extensively, although it is not registered for use in horses, but only for use in cattle, sheep and pigs (44 % of breeders that participated in a questionnaire survey used doramectin in 2000[12]). A previous study in South Africa has evaluated doramectin's efficacy in horses in a FECRT and reported that when administered intramuscularly at a dose rate of 0.2 mg/kg (which is comparable to the 0.2 mg/kg dosage for ivermectin in horses), it resulted in a 100 % reduction in FECs[4]. In contrast to these findings, doramectin did not reduce FECs in the treated horses in the present study. Unfortunately there is no empirical data available on the efficacy of doramectin in the horses when it was 1st used on the particular farm. The main differences between the two studies are that the horses used in the initial study were exposed to fewer treatments (3- to 6-month intervals) and the animals varied in age (3 months to 33 years)[4]. All the horses in the present study were Thoroughbred weaners kept on a stringent 4-week deworming schedule[12]. In addition, during the past 4 years doramectin was frequently used and administered at a 0.2 mg/kg dose rate, and the farm was stocked with large numbers of horses (>100) for several years), which could have resulted in high stocking rates on the pastures (6–8 horses/ha) and possibly high helminth infection rates in the horses. Equest gel is a registered horse product, containing moxidectin as active ingredient. The recommended method of administration and dose rate for moxidectin in horses is an oral paste and at 0.4 mg/kg. As in previous studies[5,17], this product resulted in a 100 % reduction in FECs and a LCL of 100 % in the yearlings in 2001. By contrast, when weaners were dewormed with moxidectin a year later the post-treatment FECs were higher than the pre-treatment egg counts and LCL was significantly below 90 %. These weaners were dewormed with Cydectin Injectable, which also contains moxidectin but is registered for use in cattle, sheep and ostriches. For the test in 2002 a dose rate of 1 m*l*/50 kg (as recommended by the manufacturers for cattle, sheep and ostriches) was adminis-

Table 2: **Avermectins, macrocyclic lactones and benzimidazoles registered for** (A) **horses and** (B) **other target species** (*e.g.* cattle)**. Wholesale unit prices from the Index of Veterinary Specialities (2002) and the product distributors for treatment of internal parasites for a 500-kg horse.**

| Name | Manufacturer | Species | Route | Active ingredient | Concentration | Dosage rate (host) | Dosage rate | Unit price | Price/500-kg host | Price/500-kg horse |
|---|---|---|---|---|---|---|---|---|---|---|
| **A: Horse** | | | | | | | | | | |
| Equest Gel | Fort Dodge | H[a] | P/O[b] | Moxidectin | 2 % m/m (2 g/100 g) | | 0.4 mg/kg | R94.67/12.2-g tube | | R94.67 |
| Eqvalan Paste | Merial | H | P/O | Ivermectin | 1.87 % m/m (1.87 g/100 g) | | 0.2 mg/kg | R74.10/6.42-g tube | | R74.10 |
| Equimax Oral Paste | Logos Agvet | H | P/O | Ivermectin | 1.2 g/100 mℓ | | 0.2 mg/kg | R102.00/10-g tube | | R80.98 |
| Equimax Tubing Liquid | Logos Agvet | H | P/O | Ivermectin | 0.8 g/l | | 1 mℓ/4 kg | R507.00/2.5 l | | R25.25 |
| Promectin Worm & Bot Paste | Kyron | H | P/O | Abamectin | 3.7 mg/g | | 0.2 mg/kg | R68.34/tube | | R68.34 |
| Ecomintic 50 | ECO, AH | H | P/O | Fenbendazole | 5 % m/v (5 g/100 mℓ) | | 0.2mℓ/kg | R107.73/l | | R10.77 |
| Ostridose | ECO, AH | H | P/O | Fenbendazole | 5 % m/v (5 g/100mℓ) | | 0.2mℓ/kg | R651.51/10l | | R6.52 |
| Qualiten | ECO, AH | H | P/O | Fenbendazole | 5 % m/v (5 g/100mℓ) | | 0.1mℓ/kg | R107.73/l | | R5.39 |
| Telmin Granules | Janssen | H | P/O | Mebendazole | 10 mg/g | | 1 g/20 kg | R33.70/20 g | | R4.23 |
| **B: Target species** | | | | | | | | | | |
| Cydectin | Fort Dodge | C[a] | Inj[b] | Moxidectin | 1 % m/v (1 g/100 mℓ) | 1 mℓ/50 kg (0.2 mg/kg) | 0.4 mg/kg | R1119.88/500mℓ | R22.40 | R44.80 |
| Dectomax | Pfizer | C | Inj | Dectomax | 1 % m/v (1 g/100 mℓ) | 1 mℓ/50 kg (0.2 mg/kg) | 0.2 mg/kg (ivermectin) | R1080.40/500mℓ | R21.61 | R21.62 |
| Ivomec Super | Merial | C | Inj | Ivermectin | 1 % m/v (1 g/100 mℓ) | 1 mℓ/50 kg (0.2 mg/kg) | 0.2 mg/kg | R524.40/200mℓ | R26.22 | R26.22 |
| Ecomintic 50 | ECO, AH | C | P/O | Fenbendazole | 5 % m/v (5 g/100 mℓ) | 0.1 mℓ/kg | 0.2 mℓ/kg | R107.73/ℓ | R5.39 | R10.77 |
| Panacur | Intervet | C | P/O | Fenbendazole | 4 % m/m (4 g/100 g) | 1.25 g/10 kg | 0.1–0.2 mℓ/kg | R211.20/kg | R13.20 | R10.56–R21.12 |

[a]H = horse; C = cattle.
[b]P/O = *per os*; Inj = injectable.

tered to the horses, as this is the dosage used by the particular breeder and by most horse breeders that use this product. When recalculated, the latter is equivalent to a 0.2 mg/kg dose rate, which explains why there was no reduction in the FECs following anthelmintic treatment. Most breeders expect to save money when using products not registered for horses, but when they use such products at the incorrect dosage or if they use products that have no effect on horse worms they will have to repeat treatment of the entire herd with a different but effective drug. Under-dosing is one of several reasons why anthelmintics do not perform the way they should, although this is often interpreted as arising from resistance to a particular product. Resistance to moxidectin (at 0.4 mg/kg), on the farm in the present study, can only be confirmed with further controlled studies. However, it must be noted that horses treated with moxidectin using the 0.2 mg/kg 'cattle' dosage will be underdosed by 50 %. Under-dosing facilitates the survival of worms that carry the resistance gene. These worms reproduce and pass on alleles that promote anthelmintic resistance development by their offspring[7].


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