Comparing Pharmacokinetics of IVOMEC® (ivermectin) 1% Injection and DECTOMAX® (doramectin) 1% Injectable in Cattle

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Pharmacokinetics examines the absorption, metabolism and action of drugs. In this study commissioned by Pfizer Animal Health, Dr. P. L. Toutain of Toulouse, France compared the plasma profile resulting from a single dose of commercial injectable formulations of IVOMEC® (ivermectin) 1% Injection and DECTOMAX® (doramectin) 1% Injectable. He concluded that pharmacokinetic differences observed in the study might result in differences between the two compounds in terms of antiparasitic activity and preventive efficacy in actual use. Pharmacokinetics, however, are not the determinants of actual performance under field conditions. Only actual efficacy and spectrum studies can determine duration of effect. Conclusions about the strength and duration of activity of a product based solely on plasma profiles of products can be faulty and may not be borne out in actual product use.

The Bottom Line
This graph depicts the average amount of ivermectin and doramectin in the blood plasma of cattle when the commercial formulation of each product was given as a single subcutaneous injection at 200 mcg/kg bodyweight.

- While the graph indicates a difference in plasma blood levels, it is important to note the quicker uptake of ivermectin and, as indicated by the error bars, that the plasma levels in this study appeared to vary more among cattle treated with DECTOMAX Injectable than those treated with IVOMEC 1% Injection.

- No conclusions about strength or duration of activity under field conditions can be made from this graph. No data showing any association between plasma profiles and control of parasites has been generated in this study.

- Studies published in *The Veterinary Record* by Entrocasso *et al* provide evidence that there is no practical difference in the duration of activity between IVOMEC and DECTOMAX in controlling naturally acquired gastrointestinal parasites of cattle and the reactivation of egg-shedding after treatment.

- The real value of a parasite control product is determined by how well that product controls profit-robbing internal and external parasites of cattle. There is published evidence that parasite control with IVOMEC can result in calves with higher weaning weights as well as higher average daily gain in stocker cattle and replacement heifers.

### Plasma Profiles and Parasite Control

A clear connection between the plasma profile and efficacy of doramectin has not been demonstrated-ed. Comparisons between products based on pharmacokinetic characteristics are only relevant if any observed differences are scientifically proven to be clinically important. In order to assess the clinical importance, it is necessary to have data relating control of parasites to plasma levels of the compounds. If this relationship was firmly established for both products, comparison of plasma levels would be meaningful. However, without this correlation, any relationship between comparative plasma concentrations and comparative efficacy is speculative.

Evidence of the absence of practical differences in persistent activity under field use of injectable formulations of doramectin and ivermectin against naturally-acquired parasites has been published by Entrocasso and his colleagues.

### Factors Affecting Plasma Profile

Plasma profiles can be affected by a number of factors including the target species, the formulation, the route of administration and animal-to-animal variation. The graph indicates that both active ingredients reached certain
levels in the blood, that the formulations were probably different (which they are), and that the plasma concentrations appeared to vary from animal to animal, with more variation appearing in this graph between individual cattle treated with DECTOMAX than between those treated with IVOMEC.

Variability of the Plasma Profile
There is an intrinsic variability of the plasma profile of the macrocyclic lactone family, which includes doramectin and ivermectin. Variability of the plasma profile between animals is well documented in cattle for doramectin. In the study conducted by M. A. Nowakoski of the Pfizer Inc. Central Research Division and colleagues, wide variations in blood levels between individual cattle were demonstrated after both subcutaneous and intramuscular injection. Although the authors concluded that both routes appeared bioequivalent, they also concluded that the variability between animals precluded any meaningful assessment of certain absorption characteristics.

In the Toutain study, the extent of the variation between animals in the study is represented by the bars on either side of the average values shown in the graph. These bars are an indication of the extent to which the individual data points are different from the average value. This is known as the standard deviation. The variability is actually even greater than shown because only one-half of the actual standard deviation value has been presented. It is ordinarily standard practice to present this data as one full standard deviation not one-half the value.

Advantages of IVOMEC Products
There is clear evidence that IVOMEC brand products provide advantages to ranchers and farmers in spectrum as well as convenience. IVOMEC Plus (ivermectin/clorsulon) controls more types of internal and external parasites than any other injectable parasite control product available, offering long-acting control of the most economically important parasites of cattle: the brown stomach worm, Ostertagia ostertagi; Cooperia species; and lungworms. A single dose provides the broadest spectrum control of profit-robbing parasites, including lungworms and mature liver flukes, while also controlling external parasites such as sucking lice, mange mites, scab mites and grubs.

IVOMEC Pour-On (ivermectin) provides broad-spectrum control of internal and external parasites with easy application. It remains the only endectocide that delivers up to 28 days of horn fly control. It also controls grub and mange mites, as well as lice - even biting lice - with satisfaction guaranteed!

Conclusions
The plasma profile indicates that both ivermectin and doramectin attained certain concentrations in the plasma. The wide variability of the plasma profile from animal to animal exhibited in this study is consistent with that observed by other investigators. The differences in plasma profiles that
were observed can be attributed to differences in the formulation. However, there are no data that permits drawing any conclusions relative to plasma profiles about what parasites will be controlled, how many parasites will be killed, and how long it will take for the parasites to re-establish themselves.

The value of a parasite control product is determined by which parasites it kills and how long it will be before they become re-established. There is no evidence that differences in plasma profiles between DECTOMAX and IVOMEC provide any practical advantages in terms of strength or duration of activity. There is no evidence presented in this paper that the plasma profile of the DECTOMAX 1% Injectable makes it any better than the original formulation of IVOMEC in prolonging the re-establishment of natural parasitic infections.

IVOMEC products offer advantages over DECTOMAX in terms of convenience and spectrum. Only IVOMEC Plus controls over 30 stages of profit-robbing parasites including mature liver flukes. Only IVOMEC Pour-On provides up to 28 days of horn fly control and controls both biting and sucking lice - with satisfaction guaranteed - as part of its convenient, broad spectrum control of internal and external parasites. IVOMEC products have been proven to provide broad spectrum, convenient, long-acting control of internal and external parasites of cattle.

References


13. Hicks RB, Gill DR, Smith RA, Ball RL. The effect of ivermectin on health and performance of newly arrived stocker cattle. *Animal Science Research Reports, Oklahoma Agricultural Experiment Station*, 1986; 236-239.


*Evidence regarding improvement of age at conception for replacement heifers treated with ivermectin have not been shown to be statistically significant.

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