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LongRange™ (eprinomectin 5%) extended-release injection parasiticide and the utility of extended-activity antiparasitics in cattle

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ABSTRACT

An extended-release injection, which is administered at a rate of 1 mg eprinomectin/kg body weight, has been developed to provide up to 150 days control of parasites of cattle. The product can facilitate the achievement of two of the fundamental aims of parasite control. The first is protection of the host against the negative impact of susceptible parasites in order to ensure control of disease and to enhance performance. The second is to reduce parasite transmission and hence the challenge to animals when grazing. In addition, farmers and veterinarians can benefit from high levels of convenience and hence compliance from a single administration, which also limits handling stress in the cattle. This introductory paper provides some perspective on the practical applications for this extended-release product under various husbandry systems and in different classes of cattle and discusses its role in sustainable parasite control.

1. Introduction

An eprinomectin extended-release injection (ERI) has been developed to provide long-term control of parasites of cattle. The product comprises a 5% sterile solution of eprinomectin that is administered at a rate of 1 mg/kg body weight, equivalent to 1 ml/50 kg body weight, by subcutaneous injection in front of the shoulder. The eprinomectin is formulated in a solvent that includes a polymer, which slowly releases the active following injection. Pharmacokinetic studies reveal a unique pattern of release with a peak in plasma concentrations of eprinomectin occurring within a few days of injection, followed by a gradual decline in concentration to ~Day 25, then staying constant to around Day 70. Thereafter, plasma concentrations rise, creating a secondary peak at ~Day 90–120 followed by a decline out to Day 160. This pharmacokinetic profile is reflected in the therapeutic and preventive efficacy of the product against ectoparasites and endoparasites, described in this volume. This profile affords the ability to effectively treat existing infections and also to prevent new infections of susceptible ectoparasites, gastrointestinal nematodes and lungworms from establishing in treated animals for species-dependent periods of between 100 and 150 days after administration.

1.1. Value of extended long-action parasite control in cattle in operations

For many livestock producers, convenience is one of the strongest drivers in the choice of products for parasite control. Convenience in this context incorporates ease of administration, minimising additional animal handling, and adaptability to various grazing and management systems. These preferences are reflected in the popularity of medium-acting (e.g., 3–6 weeks) topical anthelmintic formulations, sustained-release intra-ruminal boluses, and extended-activity injections among cattle producers. Long-acting anthelmintics can provide season-long control with a single administration, not only of parasitic gastroenteritis (PGE), but also of parasitic bronchitis. The value that producers place on the convenience and productivity benefits

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of long-action anthelmintics can be judged from the fact that such products command an important share of the market, even though the unit cost is typically higher than that of shorter-acting products.

While the main incentive for the development and use of long-acting parasiticides in cattle is the control of parasitic nematodes, they also can be valuable in the control of several species of parasitic arthropods of veterinary importance. Efficacy at, or close to, 100% against target obligate ectoparasites and protection against new infestations for several weeks or months after administration are prerequisites for effective control. These attributes are essential for use in eradication programmes for those parasites for which elimination on a regional or national basis is a realistic option, such as *Hypoderma* spp. The combination of high efficacy and ultra-long duration of activity in eprinomectin ERI makes it a valuable addition to the veterinary armamentarium for the control of some species of ectoparasites, as well as endoparasites in cattle.

The practical application and use of long-acting anthelmintic formulations in the control of parasitic nematodes in cattle rest on a number of criteria, including parasite epidemiology, seasonality of grazing, class and physiological status of the animals, and production targets. The geographical location has a strong influence because of the effect of latitude on the species of parasites present, the ecology of free-living stages, and the seasonal patterns of exposure and acquisition of infection. The main cattle farming regions of the world – North America, South America, Europe, and Australasia – include temperate, Mediterranean and sub-tropical zones, each with their own suite of parasites, periods of risk and management types.

One generalisation that can be applied to all the regions is that younger cattle are typically more susceptible to clinical parasitic disease than adults, because they lack functional, acquired immunity to some nematode species until they have been exposed to infection for several months (Armour, 1989). Another generalisation is that, while adult cows are considered less susceptible to PGE insofar as they rarely suffer from clinical disease, they do, however, commonly harbour significant worm populations, particularly of *Ostertagia ostertagi* in the abomasum (Agneessens et al., 2000; Borgsteede et al., 2000; Burrows et al., 1980; Murphy et al., 2006). Furthermore, recent research has shown that over a third of adult cattle at slaughter have extensive gross, pathological changes in the abomasal mucosa, typical of ostertagiosis (Larraillet et al., 2012). Manifestations of gastrointestinal parasitism in cows include loss of appetite, reduced milk yield and poor reproductive efficiency (Forbes et al., 2004; Gross et al., 1999; Stromberg and Corwin, 1993).

The significance of worm burdens in adult cattle is that they may contribute to pasture contamination with infective larvae, particularly in cow-calf operations (Yazwinski and Tucker, 2006), with important epidemiological consequences for their calves (Stromberg et al., 1991). The importance of the cow as a pasture contaminator is sometimes underestimated because their faecal egg counts (FEC) are generally low. However, FEC is a measure of concentration and when the weight of faeces produced by a cow per day (~30 kg) is used to estimate the total egg output, then a cow with an FEC of say 20 eggs per gram (EPG) will deposit 600,000 eggs per day on the pasture. Furthermore, because of acquired immunity to other species, the egg output comprises largely *O. ostertagi* (Couvillion et al., 1996), one of the most pathogenic species for calves. In one study it was shown that over a grazing season, the cow was responsible for over 50% of the egg deposition on pasture, compared to her calf (Stromberg and Averbeck, 1999).

1.1.1. Young cattle

The benefits of long-term control of PGE through the strategic use of anthelmintics administered early in the main grazing season has been demonstrated repeatedly, particularly under European conditions (Shaw et al., 1998b), but in other regions as well, including in North America (Herd et al., 1987; Purvis et al., 1994). This approach is most readily applicable to fall-born calves during their first grazing season but can also be used in cattle in their second grazing season (Rickard et al., 1991; Taylor et al., 1995b).

In Europe, a significant ($P < 0.001$) positive association has been shown between the duration of nematode control, through the use of anthelmintics, and growth rates in young cattle over the grazing season (Shaw et al., 1998a). Thus, cattle in which parasite chemoprophylaxis on pasture lasted less than 15 weeks gained on average 95 kg during the grazing season, while those with control lasting longer than 15 weeks had total gains of 108 kg.

If strategic programmes are not implemented, then anthelmintics can be used once the risk of PGE increases, typically from the middle of the main period of transmission during the grazing season. Anthelmintics given during this period can help avoid disease and mitigate the impact of PGE on livestock performance (Satrija et al., 1996). Regardless of whether a strategic or a tactical approach to the use of anthelmintics in calves is used, there are advantages in terms of convenience and compliance in using long-acting products (Forbes and Rice, 2000).

In cow-calf beef systems, in addition to regional differences, husbandry also influences the epidemiology of PGE in calves, so treatment times are based more typically on management activities, such as weaning or relocation to fresh pasture. Production benefits in young cattle from the use of long-acting anthelmintics have been demonstrated under a variety of management systems, in stockers in North America (Williams et al., 1995) and in weaned calves from spring-calving beef suckler systems in Europe (Forbes et al., 2002).

An important consideration for long-acting anthelmintics is whether their use may reduce contact between the host and the parasite to a level that severely limits the development of acquired immunity and hence results in animals being more susceptible to the effects of nematode parasitism, once the period of anthelmintic activity is over. This issue has been addressed in a number of studies and the consensus is that animals treated in their first grazing season may display some reduced immune protection when subsequently artificially challenged with high infective doses of larvae. However, under normal husbandry conditions, second grazing season cattle (and adult cows) are exposed to