Why Cydectin® Long Acting Injection for Sheep is superior to Controlled Release Capsules (CRCs of Ivermectin, Abamectin or Albendazole, or combinations thereof)

Highly Potent

The basic principle underpinning strategic drenching programmes is the reduction in the larvae contaminating the pasture (Brunsdon, 1980). The most important aspect of a drench in achieving this is its potency. Potency relates to the effectiveness of the drench in killing worms. Moxidectin, the active ingredient in Cydectin®, is the most potent of all the macrocyclic lactones (MLs). Moxidectin has five times the potency of ivermectin on Teladorsagia spp (small brown stomach worm) (Shoop et al., 1993), four times the potency on Haemonchus contortus (barber’s pole worm) (Molento et al., 1999) and twice the potency on Trichostrongylus colubriformis (black scour worm) (Shoop et al., 1993). The potency of abamectin falls somewhere in between ivermectin and moxidectin.

Selection of resistance in parasites to drenches occurs at two points. The first is to the worms currently in the gut when the drench is initially given to the sheep which is known as ‘head’ selection. The ongoing presence of the drench will affect incoming larvae and this will have a secondary selection effect.

A study performed by CSIRO using a computer simulation model showed that the most important factor in delaying resistance was the initial kill of resident worms, the ‘head kill’. The tail is relatively ineffective in influencing the development of resistance (Dobson et al., 1996). As a result it has taken twice as long to develop resistance to moxidectin compared with ivermectin and abamectin.

The relationship between head kill and potency

Cydectin Long Acting Injection for Sheep (Cydectin LA) is given at five times the oral dose of Cydectin (1mg/kg vs 0.2 mg/kg) and is at its most potent at the start of the treatment.

By contrast, Controlled Release Capsules (capsules) release a daily dose that is only one tenth of the oral drench dose of the same active, so are unlikely to provide a highly effective clean out immediately after application. This will result in greater head selection.

The importance of potency and removing as many adult worms as possible at the very beginning is that it reduces the opportunity for resistant worms to lay eggs and thus prevents resistant parasites becoming dominant in the population.

Persistent anthelmintics provide protection by killing infective larvae (L3s) as they are taken up by the sheep. This is the principle by which the capsules aim to function, maintaining a consistent low level of active over a long period. This is fraught with danger as once resistance to that dose is established (Figure 1) (Barger, I., et al., 2005) resistant parasites will be continually laying eggs and resistant L3s will be maturing into egg laying adults for the full 100 days. This will result in pastures heavily contaminated by resistant parasites.

In contrast, the high initial dose of Cydectin LA means that there is only a short window in which there is an opportunity for similarly resistant parasites to establish (Barger, I., et al., 2005). Before this time the moxidectin is killing the parasites and after this window little selection is occurring as neither resistant nor susceptible larvae are killed. Figure 2 indicates how the window of selection is of similar length between Cydectin Oral and Cydectin LA.

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**Figure 1:** How capsules fail when resistance occurs

- Resistant Worms are killed
- Susceptible Worms are killed. Resistant worms survive - thus selection for resistance
- Both resistant and susceptible worms survive

**Figure 2:** Short window of opportunity where selection for resistance may occur

- Resistant Worms are killed
- Susceptible Worms are killed. Resistant worms survive - thus selection for resistance
- Both resistant and susceptible worms survive
Genetics and resistance

Parasites like any organism have two copies of a gene. When the genes are the same it is homozygous, when different heterozygous. Parasites can carry two copies of the resistant gene (homozygous) or one copy (heterozygous). Homozygotes are most resistant, heterozygotes are less resistant but carry the gene and when heterozygote parasites mate many of their young will become homozygotes, so heterozygotes are potentially very dangerous to have around. As ivermectin is not effective against heterozygote resistant parasites the use of capsules when resistance is present will lead to rapid development of a highly resistant population.

It is therefore strongly advised that ivermectin capsules should not be used when ML resistance is present. Cydectin, however, is effective against adult heterozygotes (Barnes et al., 2001). This potency means that resistance is far slower to build up when using Cydectin (Figure 3).

Resistance and best practice

It is always preferable to use the most potent chemical to prevent resistance. However if any ML resistance has been identified it is preferable to use Cydectin LA with a primer (non-ML effective drench) to maximize the head kill and then an exit drench (non-ML effective drench) once eggs start to appear. The primer drench ensures a kill of all adult parasites at the time of treatment. The exit drench is then designed to clean out any resistant worms that have established, this should be a different group to the primer drench. Worm egg counts (WECs) will enable the first appearance of eggs to be detected and a treatment should be given at that time before there is a chance of resistant parasites building up in numbers on the pasture. Thus, the benefits from the persistent activity of Cydectin LA can be obtained while limiting the further development of resistance.

• Potency is the most important factor in delaying the development of resistance. Upfront potency is far more important in preventing the selection of resistance than a period of persistent activity. This is borne out by history and also by computer modelling (Dobson, 1995)
• Capsules and Cydectin LA both have persistent activity so that is not a basis for preferentially selecting one over the other.
• Selection for resistance may occur during the entire persistent period with capsules if the active constituent falls below the effective level due to resistance.
• Unlike capsules, the high initial efficacy of Cydectin LA may be less likely to result in the development of resistance.

Other benefits

• Ease of application compared with capsules - subcutaneous injection versus capsuling sheep.
• Lack of toxicity of its residues in dung of treated animals does not endanger the survival of dung beetles, earthworms and beneficial insects in the soil ecosystem (Robinson, 2002).

For more information on Cydectin® Long Acting Injection for Sheep, contact your Territory Sales Manager who can be found at www.virbac.com.au or by calling Customer Support 1800 242 100.

REFERENCES: