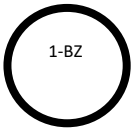
Broad-spectrum Anthelmintics

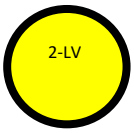
The broad-spectrum anthelmintics can be divided into **five groups** based on chemical structure and mode of action Each are denoted by a colour symbol and identifier as shown below:

Group 1 - BZ, **Benzimidazole** ('white').



These are effective against nematodes and are ovicidal, although individual generic products may vary in efficacy against some nematode species, particularly *N. battus*. Most are efficacious against tapeworms. After administration, the 1-BZ passes into the rumen which acts as a reservoir, allowing gradual release into the bloodstream. It is therefore essential the dose is given over the back of the tongue, so it does not bypass the rumen because the longer the 1-BZs remain in the animal the more effective they are. The 1-BZs act by inhibiting tubulin activity in intestinal cells of nematodes or tegumental cells of cestodes, preventing uptake of glucose. *There is one 1-BZ anthelmintic (triclabendazole), which is narrow spectrum (liver fluke only) and differs from all the other 1-BZs, in many respects, but is classed with them because of its chemical structure.*

Group 2 - LV, Levamisole (LV) ('yellow')

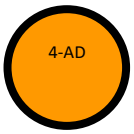


This group now comprises just one active molecule levamisole, an imidazothiazole (2-LV). This acts rapidly on the nerve ganglia of the parasite, causing paralysis. At normal therapeutic dosages, side effects are rarely seen, but the therapeutic safety index for 2-LV is low compared to other anthelmintics, so an overdose may occasionally result in the appearance of cholinergic-type symptoms such as salivation, muscular tremors and head shaking. Levamisole is rapidly absorbed and excreted, with most of the dose lost from the system within 24 hours so it is not essential to maintain high concentrations in the sheep for protracted periods. Levamisole is **not** ovicidal.

Group 3 - ML, **Macrocyclic lactones** ('clear')

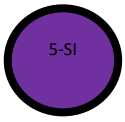
This group includes the avermectins (ivermectin/doramectin/abamectin) and the milbemycin (moxidectin). These compounds are highly lipophilic and are stored in fat tissue from where they are slowly released. They act on glutamate gated Cl- channels and γ-aminobutyric acid (GABA) neurotransmission sites in nematodes, blocking inter-neuronal stimulation of inhibitory motor neurones, leading to a flaccid paralysis of the helminth. Products in this group are available in oral and injectable formulations, the latter being active against sheep scab.

Group 4 – AD, Amino-acetonitrile derivatives ('orange')



Launched on to the UK market in 2010, this was the first new anthelmintic group for over 30 years. It is effective against all Gastro-intestinal (GI) nematode species and those resistant to the three original groups above. It is not effective against lungworm. Monepantel is the first of the derivatives in the AD group to reach the market. Its mode of action is similar to the paralysis of the 2-LV group, but it acts via a previously unknown nicotinic acetylcholine receptor site which is nematode specific and confers a very high safety index.

Group 5-SI, Spiroindoles ('purple')



Derquantel, from the new spiroindole group, was launched in 2012 and is a dual active preparation, combined with abamectin, a 3-ML. This is the first time two broad spectrum anthelmintics have been combined into a product for the UK market. Derquantel is a nicotinic cholinergic antagonist, having a novel action which blocks neuromuscular transmission, inducing flaccid paralysis in the nematode.
(Note: at the time of this update this product is only available on a Special Import Certificate from VMD).

Multiple Active Anthelmintics

To avoid confusion in the UK, we use the term 'multi-active' for products containing more than one active against the **same** target parasite. The first (and to date only) such product in this group is the 5-SI derquantel + abamectin product (Startect™) which was launched on to the UK market in March 2012. Any other subsequent such products will also be described as 'multiple actives' so they can be differentiated from the combination products described above. This allows prescribers to distinguish

between these products and avoid unnecessary use of the combinations which leads to over-use of anthelmintics.

Table 22. Broad Spectrum Anthelmintic preparations for sheep.

Compound	Spectrum of Activity	*Activity against*			Comments
		Tela Trich Nem Coop Chab Oes	*Haemonchus contortus*	*Fasciola hepatica*	
Group 1 BZ, Benzimidazoles		All 1-BZ are oral formulations			
Albendazole	Broad	+	+	+ > 10 w	50% higher dose rate required for fluke
Fenbendazole	Broad	+	+		
Mebendazole	Broad	+	+		Variable activity against *N. battus*
Ricobendazole	Broad	+	+	+ > 10 w	50% higher dose rate required for fluke
Oxfendazole	Broad	+	+		
Triclabendazole	Narrow			+ > 2 d	
Group 2 – LV, Levamisole					
Levamisole	Broad	+	+		Oral formulation
Group 3 – ML, Macrocyclic lactones					
Ivermectin	Broad	+	+		Endectocidal activity. Injectable and oral formulations.
Moxidectin	Broad	+	+		Endectocidal activity. Persistent activity against some nematodes. Injectable and oral formulations
Doramectin	Broad	+	+		Endectocidal activity Injectable only.
Eprinomectin	Broad	+	+		POM-VPS only Pour-on
Group 4 – AD, Amino-Acetonitrile Derivative					
Monepantel	Broad	+	+		Oral Formulation
Group 5 – SI, Spiroindoles					
Derquantel	Broad	+	+		Oral Formulation

 # Only as a dual active product in conjunction with abamectin a 3-ML

Check the most up to date information and product SPCs on the VMD website at:
https://www.vmd.defra.gov.uk/productinformationdatabase/

Activity against Nematodirus battus

The 1-BZ group possesses high activity against the adult and immature larvae of *N battus,* although some of the earlier 1-BZs (mebendazole) have variable activity against immature stages. The 3-MLs have variable activity against *Nematodirus* species, including *N battus.* Both ivermectin and moxidectin given orally have activity against adult and immature stages of *N. battus*, whilst doramectin given by injection at increased dose rate is active against adult and L4 larvae of this species. Moxidectin, (oral or injectable) while effective, has no persistent activity against *N battus*.

Cestodes (*Moneizia spp* tapeworms)

The 1-BZs are generally effective in treating tapeworm infections.

Activity against hypobiotic larvae

Albendazole, fenbendazole, oxfendazole, levamisole, doramectin, ivermectin, moxidectin, monepantel and the dual active containing derquatel + abamectin are all effective against arrested fourth stage (L4) larvae of the abomasal parasites.

Injectable formulations of 3-MLs

Ivermectin (IVM), doramectin (DOR) and moxidectin (MOX) are available for sheep either as injectable formulations, or oral drenches (except DOR). Administration by injection leads to better absorption and a longer half-life than oral treatment.

Only products containing MOX have licensed claims for persistent activity in sheep. MOX (1% injection) prevents re-infection with 3-ML-susceptible *Teladorsagia* spp and *H contortus* for five weeks and *Trichostrongylus colubriformis* for two weeks. A longer acting injectable formulation (2%) of moxidectin protects sheep against infection or re-infection with *Teladorsagia circumcincta* (97 days), *H contortus* (111 days) and *Trichostrongylus colubriformis* (44 days). MOX has no persistent activity against *Nematodirus battus.*

The *injectable* products also have activity against sheep scab (*Psoroptes ovis*) and increasing use for the control and treatment of scab is cause for concern with respect to the acceleration in the development of AR in nematode species.

Click here for a full listing of anthelmintic products available for sheep.