ANTHELMINTIC DRUGS FOR SHEEP AND GOATS

Currently in Canada, there are three anthelmintic drugs (dewormers) licensed for use in sheep, specifically ivermectin drench and injectable (e.g. Ivomec®, Merial Canada Inc.), closantel drench (Flukiver™, Elanco Canada Limited) and a combination drench containing derquantel and abamectin (Startect™, Zoetis Canada Limited). There are no anthelmintics licensed for use in goats in Canada.

Veterinarians licensed by the province in which they practice have the ability to prescribe anthelmintics that are licensed for use in other livestock species. But with this ability comes the responsibility for assuring safety (to both people and animals), efficacy (must actually work against the parasites) and appropriate withdrawal times for meat and milk. Your flock veterinarian can obtain scientifically valid meat and milk withdrawals by contacting CgFARAD (https://cgfarad.usask.ca/language.php) prior to dispensing the anthelmintic for use. Please be aware that when a drug is not licensed for use in a particular species (e.g. goats), there is no established maximum residue limit (MRL) of that drug allowed in meat or milk. This means that if an anthelmintic is detected in (e.g.) goat milk, even if the level is lower than that allowed for cow’s milk (for example), this is a violable residue and the milk will be discarded and the owner possibly fined.

Anthelmintics are divided into broad spectrum - i.e. those able to kill a wide variety of parasites, and narrow spectrum - those only able to kill one or two types of parasites. The following is a short discussion on how the various drugs work and their range of activity.

BROAD-SPECTRUM ANTHELMINTICS

MACROCYCLIC LACTONES (ML)

This group contains the avermectins (ivermectin, doramectin, eprinomectin) and the milbemycins (moxidectin). These compounds are derived from specific species of the Streptomyces bacteria and all work similarly. MLs have activity against most nematodes including the L4 stage, but not tapeworms or flukes. The MLs block the transmission of electrical activity in the nerves and muscles of the parasite, causing paralysis. The mechanism is such that they do not pose a risk to mammals. They are not ovicidal, i.e. do not kill eggs passed by the parasite. They also have activity against some arthropod ectoparasites, specifically sucking lice and nose bots (Oestrus ovis), as well as some activity against keds (Melophagus ovinus) and mange (Chorioptes, Sarcoptes and Psoroptes). Because of this spectrum of activity, drugs in this class are sometimes called endectocides.

When administered, the drugs are stored in fat tissue and then slowly released into the body. These pharmacokinetic properties result in long meat and milk withdrawal times (ivermectin = 15 days meat withdrawal for drench and 35 days for injectable). Moxidectin is considered to have significant prolonged activity - approximately 35 days when administered as an injection, and 21 days when administered as a drench, against Teladorsagia and Haemonchus. Neither form is available in Canada and cannot be imported under the new regulations for “Personal importation of certain drugs for food-producing animals” as they do not meet the requirements of being a “List B” drug.

Eprinomectin pour-on (Eprinex® Multi 5 mg/ml pour-on for beef and dairy cattle, sheep and goats, Merial Animal Health Limited) is licensed for sheep and goats in the United Kingdom for adult GIN parasites (not immature and not external parasites) but is not in Canada so its use is considered extra-label drug use (ELDU). Use of pour-on products in small ruminants is generally discouraged because absorption may be different. With this product, the wool / hair must be parted on the backbone and the nozzle placed against the skin, to make sure the product contacts the skin directly. If your veterinarian chooses to use eprinomectin, the topical dose is twice that of cattle (1 mg/kg bw). Your veterinarian should contact CgFARAD to determine the appropriate meat / milk withdrawal for small ruminants when used at this dosage.

1https://www.canada.ca/en/public-health/services/antibiotic-antimicrobial-resistance/animals/personal-importation-certain-drugs-food-producing-animals.html#a3
Section 4: Anthelmintic Drugs for Sheep and Goats

**Spiroindole – ML combination**

Recently a new combination anthelmintic product was developed and licensed for use in sheep in Canada, Startect™ (Zoetis Canada Ltd.). The product contains both derquantel, the first drug of the novel spiroindole class and abamectin, an ML in the same class as ivermectin. It is the first combination anthelmintic available in Canada for ruminants. It is not licensed and should not be used in goats, as there is no safety or efficacy data for that species.

Derquantel acts as an antagonist at the nicotinic cholinergic receptors; it blocks contraction of the somatic muscle of the parasite resulting in flaccid paralysis. When combined with abamectin, which also causes paralysis of the parasite but by a different method, the product is very effective at killing a wide range of internal nematode parasites including some inhibited stages of those parasites, but not flukes or tapeworms. It has also been demonstrated to be effective against GIN parasites that are resistant to other anthelmintics, including MLs. At the point of writing, resistance of parasites to this combination has not been demonstrated anywhere in the world.

**BENZIMIDAZOLES (BZ)**

These are also known as “white” drenches. This group of chemicals is effective against all GIN and somewhat against adult tapeworms. The drugs are deposited in the rumen and are slowly released into the gastrointestinal tract. They act on the intestinal cells of the nematode and the skin cells of the tapeworms, inhibiting polymerisation of microtubules. This, in turn, inhibits uptake of glucose and causes starvation. They kill not only the adult forms but also the immature stages (L4). They are also ovicidal - with activity against eggs being passed by nematodes and tapeworms.

Currently, fenbendazole is the chemical most commonly used from this group for sheep (Safeguard® 10% suspension, Merck Animal Health) followed by albendazole (Valbazen®, Zoetis Canada Inc.). Both of these products are available as drenches and are licensed for cattle but not sheep or goats in Canada. Albendazole also has activity against adult flukes, but should not be used during breeding or the first 45 days of pregnancy because of toxicity to the foetus in early pregnancy. Generally, however, the BZ class of drugs are very safe with low levels of toxicity. The dosage used in sheep is the same as the cattle dosage but goats metabolize the drug quickly and require the dosage to be doubled.

**IMIDAZOTHIAZOLES (LV) AND TETRAHYDROPYRIMIDINES**

This group contains levamisole, pyrantel and morantel. They are also known as “yellow” drenches. Levamisole is no longer licensed in Canada (since 2005) but is still in use in other countries. It is also used as an immunomodulator in humans and for the treatment of specific types of cancer. The difference between the dose that is toxic to animals versus the dose that is efficacious against GIN, is very narrow making overdose and poisoning a risk. Prior to this drug being taken off the market, the most commonly reported adverse drug reaction in any animal was from the use of levamisole in goats. Because of the narrow safety margin, its use is not recommended. It also cannot be imported under the new regulations for “Personal importation of certain drugs for food-producing animals” as it doesn’t meet the requirements of being a “List B” drug.

Levamisole works by paralysing the parasite so that it is removed rapidly from the gut. It works well against a broad range of adult worms but less so against the immature stages (e.g. L4). However, it is particularly effective against lungworm. Signs of toxicity in animals include salivation, slow heart rate and muscle tremors with occasional death. Morantel can be used to treat GIN but is not effective against the immature forms. Pyrantel is rarely used in livestock.

**AMINO-ACETONITRILE DERIVATIVES (AAD)**

The first product from this new class of drugs (monepantel) was released March 31, 2009 in New Zealand and the UK (Zolvix®, Elanco Animal Health) but not in Canada. This was the first new class of anthelmintics developed in 25 years and has excellent activity against resistant strains of GIN as well as immature forms of nematodes, and in particular Haemonchus. The drug is also of low toxicity as it targets a unique, nematode-specific class of acetylcholine receptor subunits. Unfortunately, since its release there have been many reports of resistance in small ruminant GIN. This reminds us how important it is to use these drugs properly. Zolvix cannot be imported for own use as it doesn’t meet the criteria of a “List B” drug.
NARROW-SPECTRUM ANTHelmINTICS

These drugs only act against a few types of parasites.

CLOSANTEL

This product was recently licensed in Canada for the control of Haemonchus contortus (Flukiver™, Elanco Animal Health). The drug is effective only against internal parasites that ingest blood. In sheep and goats, this is Haemonchus (including larval stages) and the liver fluke Fasciola hepatica. It acts by inhibiting ATP synthesis in the parasite’s mitochondria affecting its energy metabolism. It also has persistent activity by strongly binding to the host's plasma proteins (albumin) so is delivered directly to the parasite ingesting the blood. Closantel is very persistent but not active against the non-feeding immature stages of H. contortus.

PRAZIQUANTEL

This drug acts against the adult and immature stages of tapeworms and is of most use for control of tapeworms in guardian and working dogs. It is not available for use in sheep and goats.

ROUTE OF ADMINISTRATION

DRENCH VERSUS INJECTION

Drenches are deposited in the rumen so that proper absorption can occur. Injection of anthelmintics has been shown to result in a longer action - which may be favourable in some instances, but may select for resistant nematodes because of prolonged sub-therapeutic drug levels. Therefore, use of injectable anthelmintics (i.e. ivermectin) is strongly discouraged.

USE OF POUR-ON ANTHelmINTICS

There is evidence that pour-on products are not as well absorbed in sheep and goats as in cattle. Because of the risk of sub-therapeutic dosing by this route, they are not recommended for use in either sheep or goats. For more information on eprinomectin, please read above on MLs.

USING AN ANTHelmINTIC BY A ROUTE OTHER THAN INDICATED ON THE LABEL

Use of pour-on products as an oral medication is not recommended as the absorption, efficacy, duration of action and withdrawal times cannot be predicted. This increases the risk of the parasite developing resistance to the drug. Additionally, use of injectable products as a drench may not be advisable as they have a different carrier that can affect a drug’s effectiveness.

APPROPRIATE DOSAGE OF AN ANTHelmINTIC

In table 1 is a listing of those anthelmintics that may be available for use in sheep and goats in Canada. The dosages provided are based on Canadian labels or – if not licensed in Canada, licensed recommendations from other countries where the drug is approved, or from the literature. Please note, anthelmintics not approved for that species should only be used on the advice of a licensed veterinarian and with a valid veterinary-client-patient relationship.
Table 1. Suggested dosages of anthelmintics for treatment of GIN infections (bw = body weight)

<table>
<thead>
<tr>
<th></th>
<th>Benzimidazoles</th>
<th>Avermectin</th>
<th>Closantel</th>
<th>Derquantel/Abamectin</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sheep</strong></td>
<td>5 mg/kg bw</td>
<td>0.2 mg/kg bw</td>
<td>10 mg/kg bw</td>
<td>0.2 mL/kg bw</td>
</tr>
<tr>
<td><strong>Goat</strong></td>
<td>10 mg/kg bw</td>
<td>0.3 mg/kg bw</td>
<td>10 mg/kg bw</td>
<td><strong>DO NOT USE</strong></td>
</tr>
</tbody>
</table>

**Very Important:** Please note that all dosages listed above (except derquantel / abamectin) are based on the amount of the active ingredient to be given per kilogram of body weight of the animal. Various formulations of the drugs have different concentrations of the active ingredient, and so the actual volume of drug delivered to the animal must be calculated based on the dosage, the concentration of the drug, and the weight of the animal.

**EFFICACY AGAINST...**

Table 2. Activity of Anthelmintics against the Different Parasite Classes

<table>
<thead>
<tr>
<th></th>
<th>Benzimidazoles</th>
<th>Avermectin</th>
<th>Closantel</th>
<th>Derquantel / Abamectin</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hypobiotic Larvae</strong></td>
<td>+</td>
<td>++</td>
<td>+/-</td>
<td>++</td>
</tr>
<tr>
<td><strong>Persistent Activity</strong></td>
<td>-</td>
<td>+/−</td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td><strong>Tapeworms</strong></td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td><strong>External Parasites</strong></td>
<td>−</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td><strong>Liver Flukes</strong></td>
<td>+/- *</td>
<td>-</td>
<td>++</td>
<td>-</td>
</tr>
</tbody>
</table>

+ = good activity; ++ = much activity; − = no activity; +/- = slight activity against most GIN parasites

* = albendazole has activity against adult flukes but only at double-dosage (10 mg/kg bw sheep)

Benzimidazole = fenbendazole and albendazole

Avermectin = ivermectin, doramectin, eprinomectin

Closantel in goats may have less persistent activity than in sheep

*Next section is “When treating with an anthelmintic does not work”*