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Update on Parasite Control in Small Ruminants 2006

Addressing the Challenges Posed By Multiple-Drug Resistant Worms

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Abstract

Gastrointestinal nematode (GIN) parasites are the single most important health problem of sheep and goats. Traditionally, parasites have been controlled by frequent administration of anthelmintic drugs. However, the emergence of multiple-drug resistant parasites now threatens this paradigm of control and new approaches are required. Anthelmintics can no longer be thought of as an inexpensive management tool to be used as needed to maximize animal productivity. Instead anthelmintics must be thought of as extremely valuable and limited resources that should be used prudently. In response to this changing paradigm of anthelmintic use, new recommendations for parasite control have been proposed. The basis of this approach is to use the knowledge we have about the parasite, the animal, and the drugs, to develop strategies that maximize the effectiveness of treatments while also decreasing the development of drug resistance. The term "Smart Drenching" is often used to describe this approach to worm control. Due to the complexities of instituting such a program, successful implementation will only be possible with the help and active involvement of small ruminant veterinarians and other animal health professionals. Additionally, new innovative schemes using novel and sustainable approaches must be implemented. There are a number of new non-chemical technologies that will become increasingly important in GIN control programs both in the short and long term future. However, it is highly likely that any new technologies or developments in non-chemical GIN control methods will be less effective than chemical control has been (prior to emergence of drug resistant parasites). Therefore, as novel non-chemical control modalities become available and widely applied, anthelmintics will still be required for life-saving therapy when control fails. Unless veterinarians take an active and leading role in the education of small ruminant owners and help to implement these new approaches to parasite control, there may be no effective anthelmintics remaining when that time comes.

Introduction

There are many important diseases of sheep and goats, but none are as ubiquitous or present as direct a threat to the health of goats as internal parasites. Control of internal parasites is therefore of primary concern in any small ruminant health management program, and is critical to profitability. Gastrointestinal nematodes (GIN) that infect sheep and goats include *Haemonchus contortus*, *Trichostrongylus colubriformis*, *T. axei*, *Teladorsagia* (*Ostertagia*) *circumcincta*, *Cooperia* spp., *Oesophagostomum*, *Trichuris ovis*, *Strongyloides papillosus*, and *Bunostomum*. Although all of these parasites can contribute to the overall problem of gastrointestinal parasitism, it is the highly pathogenic blood-sucking parasite *H. contortus* that by far is the most prevalent and important in most regions of the US, and especially in the southern states.

Diagnosis of haemonchosis is made based upon the characteristic clinical signs of anemia, submandibular anemia, weight loss, and ill thrift along with finding large numbers of eggs in the feces. Female *Haemonchus* produce approximately 5,000 eggs per day and goats can be infected with thousands of these worms. This results in tens to hundreds of thousands of eggs being shed onto pasture by each animal each day. Because the life cycle is so short (< 3 weeks), this cycle of infection - pasture contamination - reinfection - more pasture contamination - can rapidly transform pastures into very dangerous places for goats. This is especially true in a warm environment such as Georgia, because transmission of *H. contortus* occurs virtually year-round.

As is the case for most parasitic diseases, haemonchosis is most severe in young animals during their first year on pasture. However, since immunity to GI nematodes in goats is slow to develop and is incomplete, even mature goats are at considerable risk. Furthermore, any one or combination of a number of factors such as poor nutrition, concurrent disease, stress, overstocking, or pregnancy/lactation can cause a loss of immunity to parasites. It is well established that ewes and does lose much of their protective immunity to GIN around the time of kidding/lambing (-2 to +8 weeks) causing the number of parasites infecting the does to increase. Subsequently, parasite egg production and contamination of the environment with infective larvae increases, creating a dangerous situation for the highly susceptible young kids. This phenomenon, known as the periparturient rise (PPR) is an extremely important part of the epidemiology of *Haemonchus* and must be considered when designing control programs.

Anthelmintics Used in the Control of Gastrointestinal Nematodes in Sheep and Goats (see Table 1)

The number of FDA-approved drugs available for use in the treatment of haemonchosis (and other gastrointestinal parasites) in goats is severely limited. Currently only 4 drugs are approved for use in goats: morantel (Rumatel Medicated Premix-88®); thiabendazole (TBZ: Omnizole®, others); fenbendazole (FBZ: Safe-Guard®, Panacur®) and phenothiazine (Feno-Drench Suspension®), with thiabendazole no longer marketed. This list is further limited in usefulness since drug resistance to benzimidazoles (TBZ, FBZ, and related compounds) and phenothiazine is very common. Other unapproved drugs that are effective for the treatment of gastrointestinal parasites (if worms are not resistant) in goats include: ivermectin (Ivomec®), doramectin (Dectomax®), moxidectin (Cydectin®), albendazole (Valbazen®), other benzimidazoles, and levamisole (Tramisol®, Levasol®). In sheep, the 4 most commonly used anthelmintics; ivermectin, albendazole, levamsiole and moxidectin are all FDA approved so extra-label use is less of an issue. However, in goats extra-label use is important because use of drugs other than what is

indicated on the label is legally restricted and improper usage could lead (in theory) to regulatory action. The FDA does allow limited extra-label use of drugs, but this use is an exclusive privilege of the veterinary profession and is only permitted when a *bona fide* veterinarian-client-patient relationship exists and an appropriate medical diagnosis has been made.[3] Because effective control of internal parasites of goats usually can only be accomplished using drugs in an extra-label manner, involvement of a veterinarian in the implementation of a parasite control program for goats is not only advisable but is legally required. For sheep, veterinary involvement is still highly recommended, but extra-label drug use is much less important an issue. It is important that milk and meat withholding times after treatment with anthelmintics are stringently adhered to (Table 1).

It is generally recommended that all anthelmintics be given orally to small ruminants. Pour-on anthelmintics are poorly absorbed in small ruminants and have a low bioavailability, so they should never be used by that route unless specifically treating for ectoparasites. Sheep should be dosed using the appropriate label directions (all FDA approved sheep anthelmintics come in an oral drench formulation). However, when using drugs in an extra-label manner in goats it is extremely important that the sheep or cattle (label) dose is **not** used (see below for 1 exception). As a general rule goats metabolize anthelmintic drugs much more rapidly than other livestock and require a higher dosage to achieve proper efficacy.[14,28] A rule of thumb is that goats should be given a dose 1.5 – 2 times higher than for sheep or cattle. A 1.5X dose (5.45 mg/lb; 12 mg/kg) is recommended for levamisole, because a 2X dose is approaching a level that may be toxic in goats. Furthermore, because of the risk of toxicity with levamisole, it is recommended that it only be administered orally in goats and that individual goats be weighed prior to treatment to determine the appropriate dose.[11] For all other drugs it is recommended that a 2X dose be given to goats. However, there is one exception to this recommendation – when treating goats with moxidectin. It is recommended that the cattle injectable formulation of moxidectin (recently approved by FDA) be used in goats because moxidectin has a superior pharmacokinetic profile in goats when administered by subcutaneous injection as compared to when administered orally. Subsequently, moxidectin should be administered to goats by subcutaneous injection using the cattle dose (0.09 mg/lb; 0.2 mg/kg). This is the one exception where the cattle dose should be used in goats. However, if moxidectin is administered orally to goats (no longer recommended) a 2X dose (0.18 mg/lb; 0.4 mg/kg) should be given. In sheep it is recommended that the FDA approved sheep oral drench be used according to label directions (0.09 mg/lb; 0.2 mg/kg).

Ivermectin and doramectin are avermectin drugs that have excellent efficacy against all stages of parasites in the host (if not resistant), and also have persistent activity when given by parenteral administration. Because doramectin has a much longer persistence but no significant improvement in efficacy compared to ivermectin, it will select for resistance more rapidly. Since resistance to either ivermectin or doramectin confers resistance to the other, it is my opinion that doramectin should not be used in small ruminants for GIN control. However, doramectin injectable may be the treatment of choice for sheep scab (Psoroptes ovis) because its long persistence will clear the infection with a single treatment. Also, because of its longer persistence, doramectin would be the treatment of choice for prophylactic treatment against *Parelaphostrongylus tenuis* in camelids. Moxidectin, a milbemycin, is a very closely related compound with similar spectrum of activity, but which is more lipophilic than the avermectins and therefore has an even longer persistent activity.[15] Moxidectin is also more potent against many nematodes and therefore will often kill worms that are resistant to the avermectin drugs. However, because multiple-drug resistance is such a widespread problem and moxidectin resistance is frequently reported, moxidectin should be used only with careful consideration in order to preserve its effectiveness (see below).

Anthelmintic Resistance: An Emerging Problem That Is Changing Our Approach For Controlling *Haemonchus* In Small Ruminants

Only a few years ago, recommendations for control of *H. contortus* in goats were based on the premise that anthelmintics should be used in a strategic manner to maximize animal productivity. This approach was used because it is known that subclinical parasitic infections are responsible for significant economic loss; once clinical disease is noticed in a group of animals much economic loss in terms of animal productivity has already occurred in some animals. Parasite control was therefore aimed at preventing animals from becoming highly parasitized, thereby maximizing productivity. Key to the success of this program was the availability of inexpensive and effective anthelmintics, since this approach required the frequent use of these drugs. We now know that this strategy has turned out to be shortsighted and unsustainable. The prevalence of multi-drug resistant nematodes (particularly *H. contortus* but also others) is extremely high any we are at risk of having no effective anthelmintics to use in the near future. In 2001, we published the first report of multiple-drug resistant *H. contortus* to all 3 available drug classes in the U.S. (moxidectin remained effective).[32] In 2001 we also completed the largest U.S. study to date on the prevalence of anthelmintic resistance in GIN in goats. Ninety percent of all farms tested in Georgia had *H. contortus* resistant to both ivermectin and albendazole. A further 30% of farms had *H. contortus* that were resistant to levamisole.[27] Moxidectin was the only drug effective on all farms, meaning that on 30% of farms it was the only drug that was fully effective. However, the problem of resistance continues to worsen; a follow-up study performed in 2003 demonstrated that 50% of farms tested with a history of moxidectin use over the previous 2 -3 years had moxidectin-resistant worms.[19] Unfortunately, this situation is not static, but instead worsens every year. Last year we diagnosed the first case of total anthelmintic failure (resistance to all available anthelmintics) in the US on a goat farm in Arkansas.[20] Importantly, we did not seek out this farm, but discovered it on a routine diagnostic DrenchRite test that the consulting veterinarian sent in because of ongoing parasite problems.

The rapid increasein moxidectin resistance is not surprising given the fact that ivermectin and moxidectin are closely related drugs that have the same mechanisms of action and resistance; resistance to one drug in this class confers resistance to all of them.[26,31] Dose-titration studies have demonstrated that the same resistance ratios (dose required to kill resistant worms:dose required to kill susceptible worms) exist for ivermectin and moxidectin. Therefore, ivermectin-resistant worms are technically also moxidectin-resistant. The reason that moxidectin remains effective against ivermectin-resistant worms is simply a matter of potency. Moxidectin is just a more potent drug so that therapeutic doses are still capable of killing worms that have become resistant to ivermectin. Unfortunately, this efficacy has proven to be short-lived, therefore use of moxidectin must be carefully managed to maintain its efficacy. Moxidectin is highly persistent in animal tissues, preventing the establishment of IVM-sensitive (IVM-S) *H. contortus* in sheep for 35 days.[1,21] We recently reported the results of a study in goats that demonstrated that although moxidectin had 100% efficacy against IVM-resistant (IVM-R) adult worms, incoming IVM-R L_3 infective larvae were only killed for a few days following treatment.[17] Since the persistent activity of moxidectin prevents IVM-S L_3 from establishing for up to 5 weeks, treatment with moxidectin will allow sheep and goats to become infected with a pure IVM-R population of worms over an approximately 4-week period. In this exclusive niche, one can expect a rapid accumulation of IVM-resistant genes within a population

of parasites, further accelerating the selection for resistance.

Making matters worse, the anthelmintic market for small ruminants is deemed too small by the pharmaceutical companies to justify the great cost associated with new drug discovery and development.[13] It is extremely unlikely, therefore, that new anthelmintics with novel modes of action will be developed and marketed in the US in the near future. This is without a doubt a severe and important problem that directly threatens the viability of the sheep/goat industry. Clearly then, major changes need to be made in the way that nematode control is practiced. Small ruminant parasitologists are now calling for a shift in the paradigm of thought used to control *H. contortus* in goats. Anthelmintics can no longer be though of as an inexpensive management tool to be used as needed to maximize animal productivity, but instead must be thought of as an extremely valuable and limited resource. We must balance our desire to maximize goat health with the reality that effective long-term control of *Haemonchus* in goats will only be possible if anthelmintics are used intelligently with prevention of resistance as a goal. To address this issue, a concept referred to as 'Smart Drenching' has been introduced. Smart drenching is an approach whereby we use the current state of knowledge regarding host physiology, anthelmintic pharmacokinetics, parasite biology, dynamics of the genetic selection process for resistance, and the resistance status of worms on the farm to develop strategies that maximize the effectiveness of treatments while also decreasing the selection of drug resistance. One of the most important aspects of smart drenching is a selective treatment approach based on the use of FAMACHA©.

Diagnosis of Anthelmintic Resistance

Before developing an effective control program for *Haemonchus* or any other GIN parasite, it is extremely important to know if resistant worms are present on a particular property, and if present, to which drugs. This can only be done 2 ways: (1) by performing a fecal egg count reduction test; or (2) by performing an *in vitro* larval development assay (LDA). The FECRT is presently the most definitive means of determining whether resistance is present on a particular property, but this test is labor intensive and therefore expensive to perform. An alternative to the FECRT is the LDA (DrenchRite®), however, the test is not suited for in-clinic use and can only realistically be performed in a parasitology diagnostic lab. A single DrenchRite test can detect resistance to benzimidazole (BZ), levamisole (LEV), BZ/LEV combinations, and avermectin/milbemycin anthelmintics from a single sample. The DrenchRite assay does not directly test for moxidectin resistance, but recent studies in our laboratory have established reliable resistance ratios based on the ivermectin dose response that enable us to accurately diagnose moxidectin resistance using this test. In the DrenchRite assay, nematode eggs are isolated from feces and placed into the wells of a microtiter plate containing growth media and varying concentrations of anthelmintic. The concentration of anthelmintic required to block development of nematode larvae is related to the *in vivo* efficacy of the drug. My laboratory currently offers this test on a limited basis for a fee $350. This cost reflects the significant equipment and supply needs, as well as the great deal of labor required to perform the DrenchRite assay. Requests for information about the DrenchRite test should be sent to Sue Howell <showell@vet.uga.edu>.

When considering the cost of the test it is important to realize that only one DrenchRite test performed on a pooled fecal sample from 10-20 goats/sheep is needed per farm, and all 3 major drug classes (including moxidectin) are tested in each assay. This is in comparison to the FECRT, where before and after treatment fecal egg counts (FEC) must be performed on individual animals from

flow-rate of the digesta.[16] Since rumen volume remains relatively constant, there is an inverse relationship between feed intake and digesta residence time. Simply restricting feed intake for 24 hours prior to treatment decreases digesta transit and increases drug availability and efficacy. This is not a theoretical issue - it has been demonstrated in both pharmacokinetic studies and field efficacy trials where this strategy significantly increased the efficacy of fenbendazole against benzimidazole field-resistant strains of GI nematodes.[16] Withholding of feed should be done when using a BZ drug or ivermectin. With moxidectin and levamisole it is not necessary to withhold feed.

Proper technique when drenching animals is also very important. All anthelmintics administered orally should be delivered over the back of the tongue. Presenting a drench to the buccal cavity, rather than into the pharynx/esophagus, can stimulate closure of the esophageal groove with significant drench bypassing the rumen.[29] Absorbed drug concentrations may be higher initially, but are of such short duration that efficacy is reduced.[15] Special dosing syringes and extenders that attach to regular syringes are sold by several sheep supply companies and should be routinely used. Without any additional cost or effort, these 2 recommendations have the potential to significantly improve drug efficacy, thereby prolonging the useful life of today's anthelmintics and should be used as a matter of course.

Split and repeat dosing: As mentioned above, increasing the duration of contact between drug and parasite can significantly increase efficacy. This also can be accomplished by administering 2 doses 12 hours apart. Repeat dosing can be used as an alternative to withholding feed, or even better, in addition to withholding feed. In a recent study, the efficacy of fenbendazole increased from 50% when administered as a single dose, to 92% when 2 doses were administered 12 hours apart.[36] This approach is most likely to yield benefit when using a BZ drug. With levamisole it is recommended to wait a full 24 hr before re-dosing.

Dosing with two different drugs at same time: When drugs are still effective, treating with 2 drugs of different anthelmintic classes simultaneously can delay the development of resistance. Once resistance is present, treating with 2 drugs of different anthelmintic classes can still be of great benefit. Anthelmintics given together will produce a synergistic effect; significantly increasing the efficacy of treatment compared to the individual drugs. This synergistic effect is most pronounced when the level of resistance is low. Once high-level resistance to both drugs is present, the synergistic effect is unlikely to produce an acceptable efficacy.

Rotation of anthelmintics: I no longer recommend rotation of anthelmintics. Rotation is an overblown concept that gives farmers (and veterinarians) a false sense that they are actually doing something worthwhile in terms of resistance prevention. The common practice of rotating drugs with each treatment does not slow the development of resistance, and actually appears to increase the rate at which resistance develops by selecting for resistance to more than one drug simultaneously. When more than one anthelmintic class is effective, it has been thought in the past that performing annual (slow) rotation is beneficial in terms of delaying resistance. However, there is no direct evidence for this and recent computer models indicate no benefit of rotation. Consequently, in recent years many parasitologists believe that rotation should not be used. Instead, it is recommended that an anthelmintic be used until it is no longer effective and then drugs should be switched. The main rationale behind this approach is that it will become obvious when a drug no longer works so the farmer will always be aware of his/her situation. If a rotation is used, resistance develops slowly to all drugs and the farmer is unaware of this until multiple-drug resistance is a

serious problem. Whether rotation is used or is not used, it is important to understand that rotation is NOT a replacement for proper resistance prevention measures. It also is worth noting that many farmers do not know what products are in which drug class. There are many drugs with different brand names that belong to the same drug class - rotation between different products within the same drug class will do nothing to slow down resistance. Rotation also becomes moot when only 1 drug is effective; a situation that is becoming increasingly common.

Recent computer models that examined the effects of various worm control strategies on anthelmintic resistance suggest that the most effective approach for delaying the selection for resistance is to treat simultaneously with 2 chemically distinct anthelmintics. Although expensive and not routinely practiced, this approach deserves further attention in light of the current situation. Unfortunately, to be truly effective in preventing resistance, this approach must be implemented while the number of resistant worms is extremely low (long before detectable levels). This situation rarely exists anymore.

Reduce the frequency of treatment through the use of sound pasture management: Good pasture management can also go a long way in preventing resistance by minimizing the dependence on anthelmintics. Anthelmintics alone will not successfully control parasites. Managing pastures so that safe grazing areas are available will permit animals to be moved to a safe area, reducing the number of treatments that are needed. It is important however, that the animals not be treated immediately before the move to safe pasture unless a proportion of the animals are left untreated. Also, goats are natural browsers so browse areas should be used as much as possible. Parasite transmission is greatly reduced when goats are browsing because they are ingesting forage farther from the ground. Reducing stocking rates will decrease the number of parasites that sheep and goats are exposed to and will also improve the quality and quantity of forage available to the animals. Overstocking can often make control of *Haemonchus* nearly impossible. Also, using fewer, strategically timed treatments during high risk portions of the year i.e. young kids/lambs following weaning and lactating does around the time of kidding, in combination with the use of FAMACHA© will decrease the amount of exposure worms have to the drug and therefore significantly slow down the development of resistance.

Novel Non-Chemical Approaches

In response to the crisis posed by drug-resistant parasites, researchers and extension personnel who have the responsibility of providing parasite control advice to the small ruminant industry have come to realize that total reliance on chemical control for parasites is no longer a viable strategy, and new innovative schemes using sustainable approaches must be implemented. There are a number of new non-chemical technologies that will become increasingly important in anti-nematode control programs both in the short and long term future.[25] These include vaccines,[22] nutritional supplementation,[10] biological agents to destroy nematode larvae,[23] bioactive forages,[4] copper oxide wire particle boluses,[9] and various genetic approaches. However, none of these by themselves is likely to provide an answer to the problems of parasite control. Instead an integrated approach that combines several of these novel methods together with limited but intelligent use of anthelmintics will be necessary.

Parasite vaccines remain an elusive goal and it will likely be many more years before effective vaccines become commercially available. Breeding for genetically resistant sheep has progressed at a slow pace, but offers great promise. Unfortunately, researchers have found that

resistance to nematodes and production traits are often in selective conflict. Bioactive forages such as those containing condensed tannins may become part of an integrated approach to GIN control. In a recent study, feeding Sericea Lespedeza (SL) hay to goats significantly ($P < 0.01$) reduced FEC and increased PCV compared with goats fed Bermuda grass (BG) hay.[30] Goats fed SL hay also had significantly fewer abomasal (*H. contortus, T. circumcincta*) and small intestinal (*T. colubriformis*) worms. In addition, a lower percentage of ova in feces from SL-fed goats developed into infective (L3) larvae. Copper oxide wire particle (COWP) boluses have demonstrated good efficacy against *H. contortus* in some studies,[7] but additional research is still required to determine proper dosage, treatment frequency, and potential negative health effects relating to copper toxicity. Data from a recent study suggest that low dose COWP may be a safe and effective means of controlling *H. contortus* in lambs.[8] COWP may therefore become an important component of integrated GIN control programs, but will require veterinary guidance due to the potential for copper toxicity.

A leading non-chemical technology that has received much attention in the past few years is the naturally occurring nematode-trapping fungus *D. flagrans*, which acts as a biological control agent. Spores of this fungus are grown on grain and fed to animals where they pass unchanged through the digestive tract and concentrate in the feces. After feces are deposited onto the pasture, the spores germinate forming hyphae that are able to trap and kill the developing larval stages of parasitic nematodes. Numerous studies have been done with most showing positive benefits,[12,24,33] although the degree of benefit has varied greatly between studies. However, problems in developing a practical and convenient means to administer the fungus have delayed development of a marketable product. This fungus remains commercially unavailable and it is unknown whether a product will be sold anytime soon.

Therefore, at the present time we are unfortunately left with few well tested options other than good management and intelligent chemical control with anthelmintics. However, veterinarians and small ruminant owners must be prepared to keep up to date with new developments that are certain to materialize in the next few years as these novel approaches are tested and validated. Much of the research in this area is being performed by members of the Southern Consortium for Small Ruminant Parasite Control. Updated information on novel approaches to parasite control can be found on their website www.scsrpc.org. In the mean time, specific strategies exist that can and should be used to maximize the effectiveness of treatments and to prevent the development of anthelmintic resistance. Foremost, anthelmintics can no longer be thought of as an inexpensive management tool to be used as needed to maximize animal productivity. Instead anthelmintics must be thought of as extremely valuable and limited resources that should be used prudently. In response to this changing paradigm of anthelmintic use, new recommendations for parasite control have been proposed. The basis of this approach is to use the knowledge we have about the parasite, the animal, and the drugs to develop strategies that maximize the effectiveness of treatments while also decreasing the development of drug resistance. The term "Smart Drenching" is often used to describe this approach to worm control.

Conclusion

The days of being able to control GIN in small ruminants by treating with anthelmintics at frequent intervals are nearing an end. Therefore, if anthelmintics are to remain a viable component of GIN control, a fresh 'Smart Drenching' approach will be needed. Due to the

complexities of instituting such a program, successful implementation will only be possible with the help and active involvement of small ruminant veterinarians and other animal health professionals. Resistance to moxidectin has rapidly developed in the past few years and on some farms this drug has already become useless. Therefore on farms where moxidectin remains effective it should be reserved for life-saving purposes (4s and 5s, or just 5s on FAMACHA©), and should not be used for routine treatments unless there are no effective alternatives. Even where resistance exists to all drugs except moxidectin, less effective drugs may be used in animals with only a marginal need for treatment (e.g. 3s on FAMACHA©). Ultimately, GIN parasite control in small ruminants must be practiced with an eye to the future. It is quite likely that any new technologies or developments in non-chemical GIN control methods will be less effective than chemical control has been (prior to emergence of drug resistant parasites). Therefore, as novel non-chemical control modalities become available and widely applied, anthelmintics will still be required for life-saving therapy when control fails. Unless we dramatically change the ways we use anthelmintics, there may be no effective anthelmintics remaining when that time comes.

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Table 1: Commonly used anthelmintics in sheep and goats.

Drug	Class	Approved Sheep	Goats	Dosage (mg/kg)	How Supplied	Prevalence of Resistance*	Meat WDT‡	Milk WDT For Goats‡	Remarks
Ivermectin	AM	Yes	No	Sheep 0.2 Goats 0.4	Sheep oral drench	high	Sheep 11 days Goats 14 days	Not Approved 8 days	Injectable formulation not recommended
Doramectin	AM	No	No	Sheep 0.2 Goats 0.4	Cattle injectable	high	ND	NE	Not rec'd because residual activity promotes resistance
Moxidectin	AM	Yes	No	Sheep 0.2 Goats 0.2	Sheep oral drench Cattle injectable	moderate	Sheep 14 days Goats 30 days	NE NE	Use in targeted treatment program (e.g. FAMACHA) to preserve efficacy. Kills avermectin-resistant worms but resistance to moxidectin may develop fairly rapidly if over-used.
Levamisole	I/T	Yes	No	Sheep 8.0 Goats 12.0	Soluble drench powder	low	Sheep 3 days Goats 4 days	NE	Be careful of toxicity from overdosing in goats Recommended to weigh goats before treatment
Morantel	I/T	No	Yes	10	Feed premix	moderate to high	30 days	0 days	Approved for use in lactating goats
Fenbendazole	BZ	No (Approved in Big-horned sheep and wildlife)	Yes	Sheep 5.0 Goats 5.0**	Paste Suspension feed block Mineral Pellets	high	Goats 6 days† (only for suspension) 16 days‡	Not Approved 0 days† 4 days‡	**label dose is 5.0 mg/kg but 10 mg/kg is recommended. †listed WDT are for the 5 mg/kg dose. ‡ at the 10 mg/kg dose, these extended WDT should be used
Albendazole	BZ	Yes	No	Sheep 7.5 Goats 15-20	Paste Suspension	high	Sheep 7 days Goats 9 days	NE 7 days	Don't use within 30 days of conception

AM = Avermectin/Milbemycin
BZ = Benzimidazole
I/T = Imidazothiazole/Tetrahydropyrimidine
WDT = Withdrawal time
NE = Milk WDT has not been established in goats; product should not be used in lactating dairy goats
ND = Meat withdrawal time has not been established.
*In the southern United States. Prevalence of resistance has not been established elsewhere.
‡ Where drug is not FDA approved, the listed WDT are based on recommendations of FARAD. These are considered a minimum time interval and it is recommended to extend these times if possible.