

Heartworm Management

Last reviewed: August 2019

3225 Alphawood Dr. Apex, NC 27539 info@sheltervet.org The ASV supports the application of the American Heartworm Society guidelines for the prevention, diagnosis, and management of canine and feline heartworms.^{1,2} The ASV also acknowledges that every shelter may not always be able to meet these practices. Resource allocation, capacity for care, compromised welfare brought on by prolonged shelter stays, and risks to population health may warrant alternative approaches to heartworm management.

Regardless of geographic location, sheltering organizations are urged to maintain all dogs, cats, and ferrets on heartworm preventive medications year-round in order to protect individual animal health and welfare and limit disease transmission within the shelter and community. The ASV encourages sheltering organizations to perform screening tests on at-risk dogs. The ASV also encourages all sheltering organizations to institute therapy for infected dogs to reduce pathology and infective potential. Alternatives to maintenance of infected dogs within the shelter population, such as transfer to partnering agencies with the capacity to begin treatment, are strongly recommended.*

Organizations choosing to treat and/or adopt infected dogs should ensure that:

- their resources and mission allow for the humane care of exercise-restricted dogs with extended lengths of stay,
- the heartworm management protocol employed minimizes risk of transmission to other animals in the shelter and the community,
- the heartworm management protocol is initiated in a timely manner to limit the potential for further transmission in the shelter and the community
- resources diverted toward heartworm management do not compromise care of other shelter animals,
- shelter staff, volunteers, and adopters are educated on the importance of adhering to each component of the management protocol, and
- potential adopters are informed of the specific management protocol undertaken and are encouraged to consult with their veterinarian for further guidance.

*When transporting heartworm-positive dogs, shelters should reference published recommendations for Minimizing Heartworm Transmission in Relocated Dogs.³

References

- 1. American Heartworm Society. Current Canine Guidelines for the Prevention, Diagnosis, and Management of Heartworm Infection in Dogs. Revised 2018. Available online at: <u>https://heartwormsociety.org/images/pdf/2018-AHS-Canine-Guidelines.pdf</u>
- 2. American Heartworm Society. Current Feline Guidelines for the Prevention, Diagnosis, and Management of Heartworm Infection in Cats. Revised 2014. Available online at: <u>https://heartwormsociety.org/images/pdf/2014-AHS-Feline-Guidelines.pdf</u>
- 3. American Heartworm Society and Association of Shelter Veterinarians. Minimizing Heartworm Transmission in Relocated Dogs. Available online at: <u>https://d3ft8sckhnqim2.cloudfront.net/images/A-News/SKO_Transport_Guidelines_for_Web_G.pdf?1519746757</u>

The mission of the ASV is to advance and support the practice of shelter medicine in order to improve community animal health and well-being.

Heartworm Management in Animal Shelters

Last reviewed: August 2019

The management of heartworm disease is a substantial and increasing concern for animal shelters across the United States (<u>Donnett 2018</u>; <u>Fagre 2017</u>; <u>Proctor 2017</u>; <u>Laderman-Jones 2016</u>; <u>AHS-ASV 2014</u>; <u>Polak 2014</u>; <u>Colby 2011</u>). For this reason, the ASV supports thoughtful application and implementation of the American Heartworm Society guidelines for the prevention, diagnosis, and management of canine and feline heartworms (<u>AHS 2018</u>; <u>AHS 2014</u>).

The ASV also acknowledges that shelters may not always be able to meet these practices as issues of resource allocation, capacity for care, compromised welfare brought on by prolonged shelter stays, and risks to population health may warrant alternative approaches to disease management. A "least harms" approach that employs broader treatment options and management practices may be required in many clinical sheltering scenarios in order to protect and improve both individual and community animal health and well-being.

Management approaches that differ from standard recommendations should only be undertaken with a thorough understanding of the risks and benefits to both individual animals as well as the shelter and community animal population and in consultation with a veterinarian. Such approaches should include evaluation of scientific evidence where available as well as direct knowledge of the allocation and restriction of resources faced by each individual sheltering organization.

Prevention

Heartworms and their vectors have been found in all 50 states and incidence of infection continues to increase (<u>AHS</u> <u>2018</u>; <u>Rehm 2017</u>; <u>Bowman 2009</u>). Additionally, the influence of microclimates, biological adaptations of mosquito vectors, and variations in biological characteristics of mosquito vectors ensure year-round risk of transmission regardless of geographic location (<u>AHS 2018</u>). For these reasons, sheltering organizations are urged to maintain all at-risk dogs, cats, and ferrets on heartworm preventive medications year-round in order to protect individual animal health and welfare and limit disease transmission within the shelter and community.

Shelters are encouraged to use FDA-approved heartworm preventive products according to labeled directions whenever possible. However, extra-label use of ivermectin is a common method of heartworm prevention in animal shelters (<u>AHS-ASV 2014</u>; <u>Colby 2011</u>). Such use should only be considered when access to FDA-approved products is not available or feasible. In addition, such preventive protocols should only be employed under the guidance of a veterinarian with direct knowledge of the sheltering program and its animal population. Steps should be taken to minimize risks of toxicity (e.g., dilution of stock product and the use of dosing charts) and with recognition that the dose to be administered varies widely based on intended effect (e.g., heartworm preventive vs. endoparasiticide vs. ectoparasiticide vs. microfilaricide) (Budde 2017).

Diagnostic Testing

The ASV encourages sheltering organizations to perform screening tests on at-risk dogs in order to identify those that are infected. In animal shelters, the decision to pursue diagnostic screening tests, including those for heartworm disease, should consider availability and accuracy of testing methodologies, and the impact of testing on shelter operations, animal health, and human health.

Heartworm infection in cats and ferrets is a more difficult diagnosis, often requiring serology and thoracic radiography +/- echocardiography. Because these species do not pose a risk for heartworm transmission, testing is usually reserved for those exhibiting suggestive clinical signs.

In animal shelters, consideration should be given to antigen testing in tandem with microfilaria testing. Although antigen testing is the most sensitive diagnostic method, microfilaria testing can serve as confirmation of a positive antigen test, help identify infected dogs in the presence of antigen blocking, allow for estimation of the microfilarial burden, and identify dogs that serve as reservoirs for further transmission (<u>AHS 2018</u>).

A concentration technique such as the modified Knott test is the most accurate means of microfilaria testing (Box 1); however, microscopic examination of a drop of fresh blood under a coverslip or examination of a blood sample for movement above the buffy coat in a hematocrit tube can aid in identification of microfilaria. Although insensitive when low numbers (50-100/ml) of microfilariae are present, in such patients the potential for severe reaction after

microfilaricide administration and the threat of acting as a reservoir of infection are low (<u>AHS 2018</u>). Based on analysis of a Mississippi shelter dog blood bank, blood smear evaluation can be expected to identify 38% of antigen positive samples, whereas modified Knott testing should identify 58% of antigen positive samples (<u>Donnett 2018</u>).

Management of Infected Dogs

Regardless of the specific disease management protocol undertaken, the ASV encourages sheltering organizations to institute therapy for infected dogs to reduce pathology and infective potential. Alternatives to maintaining unmanaged, infected dogs within the shelter population are strongly recommended. These would ideally include timely transfer to partnering agencies or informed adopters with the capacity to begin treatment; however, humane euthanasia, particularly for dogs that are symptomatic or have additional medical or behavioral concerns, may be appropriate.

In an effort to decrease length of stay, many in-shelter treatment protocols opt to alter the standard pre-melarsomine treatment recommendations. The use of macrocyclic lactones during the two-month pre-adulticidal treatment phase serves to reduce new infections and eliminate existing susceptible larvae (<u>AHS 2018</u>). Owing to the high efficacy of multiple doses of macrocyclic lactone preventives, particularly on younger heartworms, one theory contends that this pre-treatment phase is unnecessary, can result in greater worm mass at the time of adulticidal therapy, and contributes to further damage to the cardiopulmonary system (<u>Bowman 2017</u>).

Similarly, alterations of the recommended dosage (10 mg/kg BID for 30 days) of doxycycline pre-treatment are common. To date, one study has evaluated the impact of alterations in this dosage on canine heartworm disease management. In that report, although dogs receiving 10 mg/kg of doxycycline had increased gastrointestinal side effects, they had decreased time to amicrofilaremia and negative antigen testing as compared to those receiving 5 mg/kg doxycycline for 28 days; none of these relationships were statistically significant (Savadelis 2018). One report of human filariasis treatment found that a 3-week duration of doxycycline therapy reduced microfilarial counts but did not alter adult parasite viability (Turner 2006). Standard recommendations also call for completion of the course of doxycycline prior to melarsomine administration to allow for metabolism of *Wolbachia* organisms, separate the host's immune response to those metabolites from that of the heartworms themselves (AHS 2018). However, there are no studies evaluating the impact of timing of administration of doxycycline relative to melarsomine treatment.

Melarsomine dihydrochloride is the only treatment labeled for use as an adulticide and is the safest, most efficacious, and fastest way to ensure clearance of adult heartworms. Other therapeutic combinations may be effective adulticides; however, these all require a substantially prolonged treatment course and their safety has not been evaluated. There is evidence of greater risk of short-term complications of some protocols as compared with melarsomine (Ames 2017). For these reasons, the pros and cons of alternative treatment regimens should be carefully weighed (**Table 1**).

When definitive adulticidal therapy with melarsomine cannot be provided immediately, heartworm-positive dogs should be started on a 4-week course of doxycycline and a monthly preventive with a macrocyclic lactone until such treatment can be provided. To prevent rebound of Wolbachia populations, the course of doxycycline should be repeated every 12 months (McCall 2014). Exercise restriction should be also maintained during this time.

The American Heartworm Society recommends that all dogs be treated with three doses of melarsomine for the safest and most efficacious adulticidal therapy. This course of treatment, consisting of one injection followed by two injections given 24 hours apart 1 month later, has been shown to result in the death of 99% of immature adult heartworms (Keister 1992).

For dogs with asymptomatic, mild, or moderate disease, melarsomine dihydrochloride is also labeled for two treatments given 24 hours apart. Limiting the treatment course to two treatments has been shown to result in the death of approximately 91% of immature adult heartworms and reduces the length of stay of the animal in the shelter system (Keister 1992).

Non-arsenical adulticidal protocols are universally less effective than those incorporating melarsomine, may not eliminate all heartworms even after prolonged treatment courses of up to 30 months, and their success is highly dependent upon the age of the heartworms when treatment is initiated (McCall 2005; McCall 2001). During this lengthy treatment period, existing heartworms will continue to damage the heart, lungs, and pulmonary vasculature. Strict exercise restriction is recommended for the entire time that the animal harbors worms. Because of the prolonged duration of management and the increased risk of adverse medical and behavioral effects, this approach is generally not recommended.

Minimizing length of stay in shelters is the key to ensuring good medical and behavioral health and welfare. When

choosing a treatment course in the shelter, efficacy, clinical safety, and duration of treatment must all be considered. Regardless of the course pursued, clear documentation of all treatments provided and recommendations for follow-up after adoption should be provided to each adopter.

Considerations for Animal Relocation Programs

Minimizing disease transmission, including heartworms, is an essential component of shelter medicine practice. Relocation of heartworm-positive dogs should be reconsidered unless life-saving opportunities and resources will be provided at the destination, are not available in the source community, and such relocation is permissible under applicable law.

Administering doxycycline in combination with a macrocyclic lactone eliminates most circulating microfilariae (McCall 2008), thus breaking the cycle of transmission. Furthermore, after such treatment any remaining microfilariae are unlikely to develop into adult worms even if ingested by a mosquito and transmitted to another canid (McCall 2014). It is not known how early after initiation of doxycycline treatment Wolbachia are reduced to a level that affects their viability; therefore, the use of a tested repellent/ectoparasiticide can block transmission to dogs and mosquitoes and should be considered for added protection (McCall et al., 2017a; McCall et al., 2017b). When transporting heartworm-positive and recently treated dogs, shelters should reference the recommendations for Minimizing Heartworm Transmission in Relocated Dogs for further guidance.

Adopter Education

Shelters must ensure that shelter staff, volunteers, and potential adopters are educated on the current heartworm status of the dog, cat, or ferret as well as the importance of adhering to each component of the management protocol.

The Heartworm Disease Resource Task Force, a collaboration between AHS and ASV, have released six downloadable brochures for shelters to provide to adopters based on several common scenarios. Titles include:

- <u>What you need to know about heartworm disease and your newly adopted cat</u>
- Adopting a dog from a shelter that does not test for or treat canine heartworm disease
- Adopting a dog from a shelter that tests but does not treat heartworm disease
- Adopting a dog that has tested positive and been treated for canine heartworm disease
- Are you adopting a dog from another area of the country?
- What does a negative heartworm test mean?

When applicable, these brochures should be included in adoption packets.

Adopters must be informed of the specific disease management protocol undertaken with full disclosure of medical records and encouraged to consult with their veterinarian for further guidance.

Summary Statement

The management of heartworm disease in animal sheltering organizations requires different strategies than those used in private practice or other individually-owned pet scenarios. Existing evidence-based guidelines provide a rational basis on which to develop management goals that protect both individual and community animal health and welfare. Regardless of the specific strategies employed, consideration should be paid to prevention of disease and transmission of infection, establishing a reliable diagnosis in at-risk animals, limiting disease progression in affected animals, and taking steps to ensure that disease treatment is provided in a timely, safe, and effective manner.



The American Heartworm Society endorses the ASV position statement on heartworm management and its comprehensive approach towards prevention, diagnosis and management of heartworm disease in pets in shelter populations.

References

- American Heartworm Society. 2018. Current Canine Guidelines for the Prevention, Diagnosis, and Management of Heartworm (*Dirofilaria immitis*) Infection in Dogs. Available online at: <u>https://www.heartwormsociety.org/images/</u> pdf/2018-AHS-Canine-Guidelines.pdf
- American Heartworm Society. 2014. Current Feline Guidelines for the Prevention, Diagnosis, and Management of Heartworm (*Dirofilaria immitis*) Infection in Cats. Available online at: <u>https://www.heartwormsociety.org/images/</u> pdf/2014_AHS_Feline_Guidelines.pdf
- 3. American Heartworm Society and Association of Shelter Veterinarians. 2014. Heartworm Disease Management in North American Shelters. Available online at: <u>https://www.sheltervet.org/assets/hwdiseasesurveyresults.pdf</u>
- 4. Ames MK, VanVranken, P, Plath C, et al. 2017. Use of moxidectin/imidacloprid and doxycycline for non-arsenical heartworm adulticidal therapy. *Proceedings*, 2017 ACVIM Forum.
- 5. Bendas AJ, Medes-de-Almeida F, Von Simson C, et al. Heat pretreatment of canine samples to evaluate efficacy of imidacloprid + moxidectin and doxycycline in heartworm treatment. *Parasit Vectors* 10:246.
- 6. Bowman DD. 2012. Heartworms, macrocyclic lactones, and the specter of resistance to prevention in the United States. *Parasit Vectors* 5:138.
- 7. Bowman DD, Drake J. 2017. Examination of the "susceptibility gap" in the treatment of canine heartworm infection. *Parasit Vectors* 10(S2):513.
- 8. Bowman D, Little SE, Lorentzen L, et al. 2009. Prevalence and geographic distribution of *Dirofilaria immitis*, Borrelia burgdorferi, Ehrlichia canis, and Anaplasma phagocytophilum in dogs in the United States: results of a national clinic-based serologic survey. *Vet Parasitol* 160(1-2):138-48.
- 9. Budde JA, Waller, Koch SN. 2017. Ivermectin. In: Plumb's Veterinary Drugs.
- 10. Case JL, Tanner PA, Keister DM, et al. 1995. A clinical fireld trial of melarsomine dihydrochloride (RM340) in dogs with severe (Class 3) heartworm disease. Proceedings of the Heartworm Symposium '95. p. 201-19.
- 11. Chandrashekar R, Beall MJ, Saucier J, et al. Experimental *Dirofilaria immitis* infection in dogs: Effects of doxycycline and Advantage Multi[®] administration on immature adult parasites. *Vet Parasitol* 205(1-2):93-98.
- 12. Colby KN, Levy JK, Dunn KF, et al. 2011. Diagnostic, treatment, and prevention protocols for canine heartworm infection in animal sheltering agencies. *Vet Parasitol* 176(4):333-41.
- 13. Donnett U, Hubbard K, Woodruff K, et al. 2018. Prevalence of canine heartworm infection in Mississippi animal shelters. *Vet Parasitol* 259:68-73.
- 14. Fagre A, Olea-Popelka F, Ruch-Gallie R. 2017. Intake procedures in Colorado animal shelters. Animals 7(5).
- 15. Grandi G, Quintavalla C, Mavropoulou A, et al. A combination of doxycycline and ivermectin is adulticidal in dogs with naturally acquired heartworm disease (*Dirofilaria immitis*). *Vet Parasitol* 169(3-4):347-51.
- Keister DM, Dzimianski MT, McTier TL, et al. 1992. Dose selection and confirmation of RM 340, a new filaricide for the treatment of dogs with immature and mature *Dirofilaria immitis*. Proceedings of the Heartworm Symposium '92. p. 225-9.
- 17. Kramer L, Grandi G, Passeri B, et al. 2011. Evaluation of lung pathology in *Dirofilaria immitis*-experimentally infected dogs treated with doxycycline or a combination of doxycycline and ivermectin before administration of melarsomine dihydrochloride. *Vet Parasitol* 176(4):357-60.
- 18. Laderman-Jones BE, Hurley KF, Kass PH. 2016. Survey of animal shelter managers regarding shelter veterinary medical services. *Vet J* 210:68-76.
- 19. McCall JW, Varloud M, Hodgkins E, et al. 2017a. Shifting the paradigm in *Dirofilaria immitis* prevention: blocking transmission from mosquitoes to dogs using repellents/insecticides and macrocyclic lactone prevention as part of a multimodal approach. *Parasit Vectors* 10(S2): 525-36.
- 20. McCall JW, Hodgkins E, Varloud M, et al. 2017b. Blocking the transmission of heartworm (*Dirofilaria immitis*) to mosquitoes (*Aedes aegypti*) by weekly exposure for one month to microfilaremic dogs treated once topically with dinotefuran-permethrin-pyriproxyfen. *Parasit Vectors* 10(S2): 511-20.

- 21. McCall JW, Ryan WG, Roberts RE, et al. 1998. Heartworm adulticidal activity of prophylactic doses of ivermectin (6 ug/kg) plus pyrantel administered monthly to dogs. *Proceedings* Recent Advances in Heartworm Disease: Symposium '98. p. 209-215.
- 22. McCall JW. 2005. The safety-net story about macrocyclic lactone heartworm preventives: a review, an update, and recommendations. *Vet Parasitol* 133(2-3):197-206.
- 23. McCall JW, Genchi C, Kramer L, et al. 2008. Heartworm and Wolbachia: therapeutic implications. *Vet Parasitol* 158(3):204-14.
- 24. McCall JW, Guerrero J, Roberts RE, et al. 2001. Further evidence of clinical prophylactic, retroactive (reach-back) and adulticidal activity of monthly administrations of ivermectin (Heartgard Plus) in dogs experimentally infected with heartworms. In: Recent Advances in Heartworm Disease Symposium '01. American Heartworm Society, 198-200.
- 25. McCall JW, Kramer L, Genchi C, et al. 2014. Effects of doxycycline on heartworm embryogenesis, transmission, circulating microfilaria, and adult worms in microfilaremic dogs. *Vet Parasitol* 206 (1-2):5-13.
- 26. McCall JW, Kramer L, Genchi C, et al. 2011. Effects of doxycycline on early infections of *Dirofilaria immitis* in dogs. *Vet Parasitol* 176(4):361-7.
- 27. Nelson CT, Myrick ES, Nelson TA. 2017. Clinical benefits of incorporating doxycycline into a canine heartworm treatment protocol. *Parasit Vectors* 10(S2):515.
- 28. Polak KC, Smith-Blackmore M. 2014. Animal shelters: managing heartworms in resource-scarce environments. *Vet Parasitol* 206(1-2):78-82.
- 29. Proctor S, Crawford S. 2017. Dog importation into New Hampshire: A parasitic disease risk assessment of dog rescue activity. *Proceedings*, ABVP Symposium, p. 412.
- 30. Rehm C, Carithers D. 2017. Beyond the map: The state of heartworm incidence in the United States. Today's *Veterinary Practice*. September/October 2017.
- 31. Savadelis MD, Day KM, Bradner JL, et al. 2018. Efficacy and side effects of doxycycline versus minocycline in the three-dose melarsomine canine adulticidal heartworm treatment protocol. *Parasit Vectors* 11:671-8.
- 32. Savadelis MD, Ohmes CM, Hostetler JA, et al. Assessment of parasitological findings in heartworm-infected beagles treated with Advantage Multi[®] for dogs (10% imidacloprid + 2.5% moxidectin) and doxycycline. *Parasit Vectors* 10:245.
- 33. Turner JD, Mand S, Debrah AY, et al. 2006. A randomized, double-blind clinical trial of a 3-week course of doxycycline plus albendazole and ivermectin for the treatment of *Wuchereria bancrofti* infection. *Clin Infect Dis* 42(8):1081-9.

Additional Resources

Managing Heartworm Disease in Shelter Animals Frequently Asked Questions on Heartworm Treatment in Shelters Adopter Educational Brochures

Updates on Heartworm Disease Management for Animal Shelters

Box 1. Modified Knott Test (AHS 2018)

- 1. Mix 1.0 ml of EDTA blood with 9.0 ml of 2% formalin in a centrifuge tube.
- 2. Invert the tube several times to mix the blood and formalin solution, lysing the red blood cells.
- 3. Place the tube in a centrifuge and spin at 1100-1500 rpm for 5-8 minutes.
- 4. Pour off the liquid.
- 5. Add one drop of methylene blue stain to the sediment.
- 6. Transfer a drop of stained sediment onto a microscope slide and apply a cover slip.
- 7. Examine the slide under low power (10x objective lens) for the presence of microfilariae.
- 8. Table 1. Adulticidal Protocol Comparison

Table 1. Adulticidal Protocol Comparison

Protocol	Description	Adulticidal Efficacy	Treatment Duration	Advantages	Disadvantages	Materials Cost ^a	Cost of Care ^b	Total Cost°	References
Split dose melarsomine (3 inj.) + doxy- cycline	Melarsomine dihydrochloride 2.5 mg/kg intramuscular injection on Day 1, repeat on Days 30 and 31; doxycycline hyclate 10 mg/kg q12h orally x 30 days	No data available.	N/A	 Decreased severity of pulmonary pathology and reduced thrombi Reduced respiratory complications (6.5%) and disease-related deaths No risk of resistance 	• 2 months activity restriction	\$145	N/A	N/A	Kramer 2011 Nelson 2017
	Melarsomine dihydrochloride 2.5 mg/kg intramuscular injection on Day 1, repeat on Days 30 and 31; intermittent doxycycline hyclate 10 mg/kg/ day ^d ; ivermectin 6 mcg/kg orally weekly	93%	9 mos.	 Decreased severity of pulmonary pathology and reduced thrombi Reduced respiratory complications and disease-related deaths No risk of resistance High adulticidal efficacy 	 2 months activity restriction High cost of care (>\$150) 	\$269	\$1,350	\$1,619	McCall 2008 Kramer 2011 Nelson 2017
Split-dose melarsomine (3 inj.)	Melarsomine dihydrochloride 2.5 mg/kg intramuscular injection on Day 1, repeat on Days 30 and 31	99-100%	31 days	No risk of resistanceHigh adulticidal efficacy	 2 months activity restriction Increased coughing (7.7-20.5%) in class 3 dogs 	\$135	\$130	\$265	Keister 1992 Case 1995
	Melarsomine dihydrochloride 2.5 mg/kg intramuscular injection on Day 1, repeat on Days 30 and 31	100%	31 days	 No risk of resistance High adulticidal efficacy 	• 2 months activity restriction	\$135	\$130	\$265	McCall 2008
Standard dose melarsomine (2 inj.) + doxy- cycline	Melarsomine dihydrochloride 2.5 mg/kg intramuscular injection on Day 1, repeat on Day 2; doxycycline hyclate 10 mg/kg q12h orally x 30 days	No data available.	N/A	 1 month activity restriction No risk of resistance 	 Less adulticidal efficacy compared to split-dose protocols 	\$100	N/A	N/A	
Standard dose melarsomine (2 inj.)	Melarsomine dihydrochloride 2.5 mg/kg intramuscular injection on Day 1, repeat on Day 2	91%	48 hrs.	 1 month activity restriction No risk of resistance Low materials costs (<\$100) High adulticidal efficacy 	 Decreased efficacy compared to split-dose protocols 	\$90	\$10	\$100	Keister 1992
Single dose melarsomine (1 inj.)	Melarsomine dihydrochloride 2.5 mg/kg intramuscular injection	52%	Single treatment	 No risk of resistance Low materials costs (<\$100) Single injection 	Poor adulticidal efficacy	\$45	\$5	\$50	Keister 1992
Moxidectin + imidacloprid + doxycycline	Moxidectin (2.5 mg/kg) + imidacloprid (10 mg/kg) applied topically once per month; doxycycline hyclate 10 mg/kg q12h orally x 30 days	36%	6 mos.	Decreased upfront materials costs	 Prolonged activity restriction Poor adulticidal efficacy High cost of care (>\$150) 	\$82	\$900	\$982	Bendas 2017
	Moxidectin (2.5 mg/kg) + imidacloprid (10 mg/kg) applied topically once per month; doxycycline hyclate 10 mg/kg/ day x 15 days	62%	11 mos.	Decreased upfront materials costs	 Prolonged activity restriction Poor adulticidal efficacy High cost of care (>\$150) Increased coughing during treatment (44.4% of dogs) compared to melarsomine protocols 	\$137	\$1,650	\$1,787	Ames 2017

Moxidectin + imidacloprid + doxycycline (cont'd.)	Moxidectin (2.5 mg/kg) + imidacloprid (10 mg/kg) applied topically once per month; doxycycline hyclate 10 mg/kg q12h orally x 30 days	96%	10 mos.	High adulticidal efficacy	 Prolonged activity restriction High cost of care (>\$150) 	\$130	\$1,500	\$1,630	Savadelis 2017
	Moxidectin (2.5 mg/kg) + imidacloprid (10 mg/kg) applied topically once per month; doxycycline hyclate 10 mg/kg q12h orally x 30 days	100%	9 mos.	High adulticidal efficacy	 Prolonged activity restriction High cost of care (>\$150) 	\$118	\$1,350	\$1,468	Chandrashekar 2014
Moxidectin + imidacloprid	Moxidectin (2.5 mg/kg) + imidacloprid (10 mg/kg) applied topically once per month	No data available.	N/A	Decreased upfront materials costs	Prolonged activity restriction	N/A	N/A	N/A	
	Moxidectin (2.5 mg/kg) + imidacloprid (10 mg/kg) applied topically every 2 weeks	No data available.	N/A	Decreased upfront materials costs	Prolonged activity restriction	N/A	N/A	N/A	
lvermectin + doxycycline	Ivermectin (6 mcg/kg) orally once per month; doxycycline hyclate 10 mg/kg q 12h x 30 days	No data available.	N/A	Decreased upfront materials costs	 Prolonged activity restriction Potential for increased risk of resistance 	N/A	N/A	N/A	Bowman 2012
	Ivermectin (6 mcg/kg) orally q 15 days; doxycycline hyclate 10 mg/kg q 12h x 30 days	73%	10 mos.	• Low materials costs (<\$100)	 Prolonged activity restriction Potential for increased risk of resistance Poor adulticidal efficacy High cost of care (>\$150) 	\$60	\$1,500	\$1,560	Grandi 2010 Bowman 2012
	Ivermectin (6 mcg/kg) orally weekly + intermittent doxycycline 10/mg/kg/day ^d	78%	9 mos.	Decreased upfront materials costs	 Prolonged activity restriction Potential for increased risk of resistance Poor adulticidal efficacy High cost of care (>\$150) 	\$134	\$1,350	\$1,484	McCall 2008 Bowman 2012
Moxidectin	Moxidectin (0.17 mg/kg) subcu- taneous injection every 6 months	No data available.	N/A	Single injection	Prolonged activity restriction	\$20	N/A	N/A	
Ivermectin	Ivermectin (6 mcg/kg) orally once per week	20%	9 mos.	Decreased upfront materials costs	 Prolonged activity restriction Potential for increased risk of resistance Poor adulticidal efficacy High cost of care (>\$150) 	\$180	\$1,350	\$1,530	McCall 2008 Bowman 2012
	Ivermectin (6 mcg/kg) orally once per month	56%	16 mos.	• Low materials costs (<\$100)	 Prolonged activity restriction Potential for increased risk of resistance Poor adulticidal efficacy High cost of care (>\$150) 	\$80	\$2,400	\$2,480	McCall 1998 Bowman 2012
Doxycycline	Intermittent doxycycline 10 mg/kg/day ^d	9%	9 mos.	• Low materials costs (<\$100)	 Prolonged activity restriction Potential for increased risk of resistance Poor adulticidal efficacy High cost of care (>\$150) 	\$44	\$1,350	\$1,394	McCall 2008 Bowman 2012

a = Cost for treatment of a 20kg dog at the following rates: melarsomine - \$23/ml; doxycycline - \$42/30 days; labeled monthly ivermectin heartworm preventive - \$5/dose; topical moxidectin + imidacloprid - \$12/dose • b = Cost of care estimated at \$5 per day • c = Total cost = Materials cost + Cost of care • d = Intermittent doxycycline protocol = administration during weeks 1-6, 10-11, 16-17, 22-25, 28-33