

Demodicosis, Sarcoptes and ear mite (Otodectes) treatment protocol recommendations

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Demodectic mange

Preamble

- **This information is for Veterinarians only and to be used by owners SOLELY as general information. Demodectic mange is a complex disease that is due to an immune defect and may be complicated by severe infection. Consult with your Veterinarian.**
- Since the unavailability of canine amitraz wash, there is no registered high efficiency treatment for demodectic mange available. All effective treatments (75%+ resolution rate) currently involve drugs not registered for demodicosis or the use of dose regimes outside registered guidelines.
- All studies indicate there is no treatment that is 100% successful in all cases. Success is defined as clinical and paristological resolution with no re-occurrence within 12 months
- Juvenile and adult onset demodicosis are two different manifestations. The prognosis with adult onset demodicosis where a primary cause cannot be identified and rectified is more guarded.

Reasons for treatment failure

- The most common reason is not treating for long enough. Until at least 2 negative scrapings 3-4 weeks apart. This often means 12 weeks +
- Lack of compliance
- Resistance. In some cases one “mectin” will fail while another member of the class will work. Sometimes amitraz “ +/- “mectin” will work where a “mectin” has failed
- Poor storage. “Mectins” are light sensitive. Amitraz oxidizes.

Fluralaner Bravecto® and Afoxalaner Nexgard® for demodectic mange treatment

Nexgard (afoxalaner) and Bravecto (fluralaner) are isoxazolines that are a novel class of parasiticides that are potent inhibitors of γ -aminobutyric acid (GABA)-gated chloride channels (GABA_ACl_s) and l-glutamate-gated chloride channels (GluCl_s) in both arthropods (ticks) and insects (fleas, blow/biting flies and mosquitoes)

Ivermectin and related macrocyclic lactones primarily act on glutamate-gated chloride channels (GluCl_s) and with the exception of Selamectin (Revolution) have little action against fleas. Topical Selamectin has no action against Demodex.

There is starting to be significant evidence that isoxazolines are highly efficient against canine demodicosis at the standard flea dose rate, Bravecto every 3 months; Nexgard on day 0, 14, 28 and then monthly.

The timelines expected are:

By 28 days significant improvement in clinical signs and a significant reduction in mite numbers

Day 60 Almost complete clearance

Day 90 Complete clearance

Naturally, given that the disease is as a result of an immunodeficit, it is likely that isoxazolines will not clear 100% of cases but neither will amitraz, ivermectin or moxidectin

It would seem logical to use isoxazolines as first line treatment

- Bravecto/Nexgard are registered for dogs but not for Demodex. These compounds are neither registered nor safe to use in cats.
- There are no p-glycoprotein competition issues as with macrocyclic lactones.
- Check in 2 weeks if pyoderma otherwise a regime of monthly scrapes until 2 negative scrapes 1 month apart
- If cleared, maintain on Bravecto/Nexgard long term as a flea control agent
- Whether Bravecto every 3 months or Nexgard monthly is more effective for demodicosis is yet to be determined.

Ivermectin and related compounds (Macrocyclic lactones)

These can be subdivided into two groups

Avermectins : Derivatives of fungus *Streptomyces avermectilis*. Ivermectin and doramecin

Non-Avermectins : Moxidectin, milbamecin

A success rate of 90% can be expected with ivermectin, doramecin and oral moxidectin based on clearance of infestation and no re-occurrence within 12 months

CNS TOXICITY

All members of this group can cause potentially fatal CNS depression due to failure of the p-glycoprotein pump removing drug from CNS. This may be caused by

- Genetic defect associated with the MDR- $\Delta 1$ (ABCB1-D1) gene. Particularly common in collies, shelties and other herding breeds but seen in ALL BREEDS
- Non-MDR associated pump defects

- Drug competition for p-glycoprotein. There are many drugs that compete for this pump. Ketoconazole, itraconazole and cyclosporine are common skin drugs that, if given with ivermectins, can cause fatal results
- There have been reports of ivermectin toxicity in conjunction with Spinosad (Comfortis). The mechanism of this is related to competition for p-glycoprotein.

Ivermectin

- The most frequently used compound world-wide and what I recommend as initial therapy.
- I do not dilute it with anything. No stability studies for individual products and diluents. Use the large animal injectable form orally and, for small patients, use a 1ml syringe to measure dose
- The standard dose varies in the literature from 300-600mcg/kg daily. I tend towards 450mcg/kg daily
- Weekly injections are useless
- Build up protocol essential, even in MDR normal/normal dogs. Start at 50mcg/kg and increase by 50mcg/kg until treatment dose achieved

Doramectin

- Used weekly at 600mcg/kg by injection
- Some reports that effective at 300mcg/kg 2x week orally
- No safer than ivermectin. Must do build up protocol with ivermectin first
- May work in ivermectin failures (or vice versa)
- Some clients are better served by weekly injections, esp if cant be relied on to give orally or close monitoring needed.

Moxidectin orally

- As it is not an avermectin, it may work in ivermectin resistant cases
- Build up protocol to final dose of 400mcg/kg daily

Moxidectin spot on (Advocate)

- Efficiency when used every four weeks not borne out in field use.
- Increased efficiency when used every 7 to 10 days.
- Cure rates of the order of 70% can be achieved when used weekly .
- More effective in mild cases than in severe cases.

Milbamycin

- Effective at 1 to 2 mg per kilogram daily.
- High cost.
- May be safer in sensitive dogs at lower dose rates. Reactions occur in dogs homozygous for the MDR genetic defect when treated at 1 to 2 mg per kilogram .

Amitraz

- Registered product but availability issues.
- Large animal product available for off-label use. Note concentration of large animal products is NOT the same as the small animal product.
- Full label safety precautions need to be observed.
- As effective as ivermectin.
- Efficiency increases at higher concentrations and reduced intervals.
- Registered dose 0.05%. Some clinicians use up to 0.075% weekly. Intensive protocol treating alternate halves of the body every three days with 0.125% have been reported.
- Toxicity increases in small dogs.
- Must not be used in the case of owners or patients that are diabetic or are on monoamine oxidase inhibitors.
- Alpha-2 agonist properties mean extreme caution with anaesthesia and contraindication for use with xylazine or metatomidine.
- Can be combined with ivermectin for refractory cases.
- Solutions can be made with propylene glycol for daily local treatment difficult areas such as feet.

Recommendations for treatment

1. Assume all cases have an accompanying pyoderma and treat for at least three weeks with cephalexin 25 mg per kilogram twice a day or 1 to 2 injections of Convenia two weeks apart.
2. In the case of adult onset Demodex infestation, look for an underlying disease process.
3. It would seem logical to use isoxazolaners as first line treatment
4. Warn owners that no treatment individually is 100% effective in all cases.
5. If using ivermectin daily, build up to a final dose of 450 µg per kilogram per day.
 - a. An MDR test should be offered in all cases and insisted on if any chance of Collie or herding breed cross. EDTA sample to Gribbles labelled as ivermectin sensitivity test . If client refuses the test, it should be noted on the file.
 - b. Dogs homozygous for an MDR defect should not be treated with ivermectin.
 - c. Genetically normal dogs must still be subjected to a build up protocol.
 - d. Informed consent to risks and off label use must be recorded on the file.
6. If the taste of ivermectin is too distasteful or client compliance is a concern, begin with doramectin. A build up protocol is essential.
7. Skin scrapings to monitor progress begun at three weeks and then continued on a three weekly basis.
8. If after six weeks of treatment there is no significant decrease in mite numbers and especially if nymph forms (six legs) or eggs are present, there is an indication to change drugs.
9. Continue treatment until two or preferably three negative scrapings three weeks apart.
10. Warn owners that relapses may occur.

11. Dogs with juvenile onset generalised demodectic mange should be neutered and not used for breeding.

Sarcoptic Mange and ear mites (Otodectes)

Selamectin spot-on (Revolution / Stronghold ® Zoetis) has a label registration for treatment of sarcoptic mange. Because it needs to be systemically absorbed, selamectin is only effective if applied directly on the skin and hence it is advisable to clip a small window to ensure effective application. On an off label basis, many dermatologists (including the author) prefer to use selamectin on a fortnightly basis for 6 weeks then monthly.

Treatment with the imidacloprid/moxidectin (Advocate ®) is highly effective against *Sarcoptes scabiei* and almost complete resolution of clinical signs within 50 to 64 days after the initial treatment is reported.

Both the above spot on products have registered efficacy against ear mites. In a published field study, mite clearance on Day 28 was 71% for the imidacloprid+moxidectin group and 69% for the selamectin group. Mite clearance on Day 56 was 82% for the imidacloprid+moxidectin group and 74% for the selamectin group.

Both afoxaloner and fluralaner have been shown to be effective against canine sarcoptic mange in published clinical trials at standard flea dose rates (monthly and three monthly respectively)

Fluralaner was effective in eliminating scabies mites within 14 days and significantly resolved the clinical signs associated with sarcoptic mange within 21 days after a single dose. In a trial of experimentally infected dogs treated with afoxaloner monthly, clinical and paristological cure was achieved by day 28

Sarolaner (Simparica™, Zoetis) has shown similar results with respect to demodicosis and sarcoptic mange. Furthermore, in a study, 32 dogs with induced infestations of *Otodectes cynotis* were treated with oral sarolaner (2mg/kg) as a single treatment on Day 0 or as a two dose regime (Days 0 and 30), or a placebo group for each of the dose regimes. Sarolaner administered at 2mg/kg as a single oral dose resulted in a 98.2% reduction at Day 30 and two doses of sarolaner, administered one month apart, resulted in a 99.5% reduction in ear mites at Day 60 compared to placebo controls.

References:

Arther RG et al: Clinical evaluation of the safety and efficacy of 10% imidacloprid + 2.5% moxidectin topical solution for the treatment of ear mite (*Otodectes cynotis*) infestations in dogs. *Vet Parasitol.* 2015 May 30;210(1-2):64-8. doi: 10.1016/j.vetpar.2015.02.022. Epub 2015 Mar 2.

Becskei C et al: Efficacy and safety of a novel oral isoxazoline, sarolaner (Simparica™), for the treatment of sarcoptic mange in dogs. Vet Parasitol. 2016 May 30;222:56-61. doi: 10.1016/j.vetpar.2016.02.017. Epub 2016 Feb 20.

Beugnet F, Halos L, Larsen D & de Vos C: Efficacy of oral afoxolaner for the treatment of canine generalised demodicosis. Parasite, 2016, 23, 14.

Beugnet F et al : Efficacy of **afoxolaner** in a clinical field study in dogs naturally infested with *Sarcoptes scabiei*. Parasite. 2016;23:26

Fourie JJ et al (2015) Efficacy of orally administered fluralaner (Bravecto(TM)) or topically applied imidacloprid/moxidectin (Advocate®) against generalized demodicosis in dogs. Parasitic Vectors Mar 28;8:187. doi: 10.1186/s13071-015-0775-8.

Hutt JH, Prior IC, Shipstone MA (2015) Treatment of canine generalized demodicosis using weekly injections of doramectin: 232 cases in the USA (2002-2012). Vet Dermatol. 2015 Jul 20. doi: 10.1111/vde.12223. [Epub ahead of print]

Mueller, R. S et al (2012), Treatment of demodicosis in dogs: 2011 clinical practice guidelines. Veterinary Dermatology. doi: 10.1111/j.1365-3164.2011.01026.x

Romero C, Heredia R, Pineda J, Serrano JA, Mendoza GD, Trápala P, Cordero AM. Efficacy of fluralaner in 17 dogs with sarcoptic mange. Vet Dermatol. 2016 Aug 11. doi: 10.1111/vde.12363. [Epub ahead of print]