PROHEART® SR-12 10MG/ML INJECTION FOR DOGS
Moxidectin

Product Description:

ProHeart SR-12 consists of 2 separate vials that require mixing prior to administration.

One vial (contains 10% w/w moxidectin sterile microspheres) is white to off-white powder with slight aggregation which deagglomerates upon gentle shaking.

The second vial (contains sterile vehicle for constitution with the microspheres) is a clear to translucent, slightly viscous liquid with transient threadlike strands which may appear upon gently mixing (swirling).

Each mL of constituted suspension contains 10 mg moxidectin (10mg/mL). In clear or open container, the mixed constituted suspension is white to off-white, uniform in consistency and without visible particle aggregates (the product may appear as a hazy to milky suspension).

Pharmacodynamics:
Moxidectin is a semi-synthetic methoxime derivative of nemadectin which is a fermentation product of *Streptomyces cyaneogriseus subspecies noncyanogenus*. Moxidectin is a pentacyclic 16-membered lactone macrolide.
Moxidectin has activity resulting in paralysis and death of affected parasites. The stage of the canine heartworm affected at the recommended dose rate of 0.5 mg/kg is the tissue larval stage. The larval and adult stages of the canine hookworms, *A. caninum* and *U. stenocephala*, are susceptible.

Pharmacokinetics:

Following injection with ProHeart SR-12, serum levels peaked at 7-21 days post-treatment. All dogs had detectable serum levels at 337 days. In addition, observed C_{max} values following three administrations 6 month apart appear to show little or no accumulation.

Indications:

For the 12 month prevention of heartworm *(Dirofilaria immitis)* disease in dogs.

Control of canine hookworms *(Ancylostoma caninum* and *Uncinaria stenocephala)* including adult and the L4 larval stages at the time

of treatment and to provide persistent control of re-infection by these two species of hookworms for up to four months.

Recommended Dose:

Recommended for use in dogs from 12 weeks of age.

The recommended subcutaneous dose is 0.05 mL of the constituted suspension/kg body weight. This amount of suspension will provide 0.5 mg moxidectin/kg body weight. To ensure accurate dosing, calculate each dose based on the dog's weight at the time of treatment.

The following table provides a guide for weight specific dose volumes.

Dog Weight (in kg)	Dose Volume* (mL/Dog)
1 kg	0.05
5 kg	0.25
10 kg	0.50
15 kg	0.75
20 kg	1.00
25 kg	1.25
30 kg	1.50
35 kg	1.75
40 kg	2.00
45 kg	2.25
50 kg	2.50
55 kg	2.75
60 kg	3.00
65 kg	3.25
Dogs over 65 kg receive 0.25mL for each additional 5 kg body mass.	

**All dogs should be dosed at 0.05 mL suspension/kg body weight.*

General Directions on PROHEART SR-12 Injection:

1. The following features of the pharmacology of PROHEART SR-12 Injection should be taken into consideration when designing a heartworm prevention program to suit individual dogs:

- In adult dogs (over 9 months of age) dogs of all types PROHEART SR-12 Injection will provide at least 12 months protection against heartworm disease
- In growing pups the dilution effect of increasing body mass may affect the duration of protection of the recommended dose of PROHEART SR-12: the recommended dose will protect pups of all breeds of 3-6 months of age for at least 6 months and pups of 6-9 months of age for at least 9 months
- Dogs or pups may be safely retreated with PROHEART SR-12 Injection at the recommended dose rate at less than the intervals indicated above to synchronise with other routine procedures
- The retrospective activity (reach back effect) of PROHEART SR-12 Injection will kill the immature larval stages of *Dirofilaria immitis* resulting from infections acquired within the 3 months preceding the administration of a recommended dose
- The following recommended programs are a guide only and may be appropriately adapted by the veterinarian to suit individual cases or clinic protocols.

2. Starting pups on a PROHEART SR-12 Injection program

- Pups will ideally receive their first treatment with PROHEART SR-12 Injection at 3 months of age. This will give them at least 6 months protection against heartworm disease and also inactivate any heartworm infection acquired since birth. This administration can be timed to coincide with the 3 months vaccination
- Use a dose rate based on the dog's body weight at the time of treatment (ie. do not overdose in anticipation of the pup's expected future weight)
- Re-treatment or (if treatment at 3 months was missed) initial treatment may be carried out at 6 months of age (or at a time close to that) to coincide with admission for neutering. This will give at least 9 months further protection enabling the next treatment to be administered at 15 months of age to coincide with an annual health check or revaccination
- Note that if initial treatment is administered after 3 months of age, heartworm infections acquired more than 3 months previously may not be fully controlled
- After 15 months of age, annual re-treatment should be administered as described for adult dogs below.

3. Starting adult dogs on a PROHEART SR-12 Injection program

- Dogs over 9 months of age may be started on a PROHEART SR-12 Injection program at any time in accordance with the following guidelines:
- A complete heartworm disease prevention program includes a periodic physical examination and a test for the presence of adult heartworm
- All dogs not currently on a heartworm prevention program should be tested for the presence of adult heartworms. Whilst PROHEART SR-12 Injection is safe in heartworm positive dogs, it should only be used in dogs testing negative for circulating microfilariae and / or adult heartworm antigen. Infected dogs should be treated to remove adult heartworms and microfilariae before initiating treatment with PROHEART SR-12 Injection.
- If PROHEART SR-12 Injection is replacing a monthly heartworm preventive medication, the first administration of PROHEART SR-12 Injection should ideally be given within one month of the last treatment. However, because of its retrospective activity, PROHEART SR-12 Injection is efficacious against heartworm infection acquired within the 3 months prior to administration. Therefore, there is continuity of coverage if given within 90 days of the previous treatment. If more than 90 days have elapsed since the previous treatment, PROHEART SR-12 Injection can be administered but it is recommended that the dog be tested for the presence of adult heartworm 6 months later and treatment instituted if necessary.
- Dogs on daily heartworm prevention may commence treatment with PROHEART SR-12 Injection at any time.

4. Annual re-treatment

- A repeat annual dose of PROHEART SR-12 Injection should ideally be given on the anniversary of the dog's previous treatment with the product. However, because of its retrospective activity, PROHEART SR-12 Injection is efficacious against heartworm infection acquired within the 3 months prior to administration so there is continuity of coverage if re-treatment is given within 90 days of the anniversary of the previous treatment.
- If more than 90 days have elapsed since the anniversary of the previous treatment, PROHEART SR-12 Injection can be administered, but it is recommended that the dog be tested for the presence of adult heartworm 6 months later and treatment instituted if necessary.

Route of Administration:
Subcutaneous Injection

Contraindications: Do not use in case of hypersensitivity to the active substance or to any of the excipients.

Warnings & Precautions:

HUMAN WARNINGS:
Not for human use. If contact with your skin occurs, wash thoroughly with water. May be irritating to the eyes. If product accidentally gets into your eyes, flush eyes thoroughly with water. In case of accidental ingestion, or if skin or eye irritation occurs, contact a doctor for treatment advice and show the package insert to the doctor. Take care to avoid accidental self-injection. In case of accidental self-injection, seek medical advice and show the package insert or the label to the doctor.

WARNINGS:
Do not administer ProHeart SR-12 to dogs who are sick, debilitated, underweight or who have a history of weight loss.
Always review with owners before administering ProHeart SR-12. The owner should be advised to observe their dog for adverse drug events.

PRECAUTIONS:
Prior to administration of ProHeart SR-12, the health of the patient should be assessed by a thorough medical history, physical examination and diagnostic testing as indicated (see WARNINGS).
Caution should be used when administering ProHeart SR-12 in dogs with pre-existing allergic disease, including food allergy and flea allergy dermatitis (see WARNINGS).
Caution should be used when administering ProHeart SR-12 concurrently with vaccinations.
Prior to administration of ProHeart SR-12, dogs should be tested for existing heartworm infections. Infected dogs should be treated with an adulticide to remove adult heartworms. ProHeart SR-12 is not effective against adult *D. immitis*. Caution should be used when administering ProHeart SR-12 to heartworm positive dogs.

For Animal Use Only
Controlled Medicine / Ubat Terkawal
Keep out of reach of children / Jauhi dari kanak-kanak

Interactions with Other Medicaments:

Concurrent administration of selamectin and ProHeart SR-12 is safe in puppies from 12 weeks of age.

However, the safety of concurrent treatment with Revolution® (selamectin) and Proheart SR-12 Injection has not been demonstrated in macrocyclic lactone sensitive breeds e.g. sensitive collies.

Incompatibilities: ProHeart SR-12 Injection must not be mixed with other medications in the syringe.

Pregnancy and Lactation:

Proheart SR-12 Injection may be used in breeding dogs of either sex at any stage of the reproductive cycle and in lactating bitches.

Side Effects:

A well-controlled field study was conducted, including a total of 593 dogs (297 received two doses of ProHeart SR-12, 12 months apart and 296 received a monthly oral heartworm preventive as active control) ranging in age from 1 to 14 years. Over the 605-day study period, all observations of potential adverse reactions were recorded.

Number of Dogs* with Adverse Reactions Reported During the Field Study with Proheart SR-12

Adverse Reaction	**Proheart SR-12 n=297 (%)**	**Ivermectin and Pyrantel Pamoate; n=296 (%)**
Vomiting	75 (25.3)	78 (26.4)
Lethargy	46 (15.5)	34 (11.5)
Diarrhea (with and without blood)	43 (14.5)	46 (15.5)
Anorexia	41 (13.8)	31 (10.5)
Seizures	10 (3.4)	7 (2.4)
Hepatopathy	8 (2.7)	3 (1.0)
Hypersalivation	7 (2.4)	3 (1.0)
Hypersensitivity Reactions	6 (2.0)	4 (1.4)

*Some dogs may have experienced more than one adverse reaction or more than one occurrence of the same adverse reaction during the study.

Two ProHeart SR-12 (moxidectin) - treated dogs experienced anaphylactoid/ hypersensitivity-related clinical signs within the first 24 hours following the initial treatment. Both dogs responded to symptomatic treatment. One dog experienced hives and facial swelling that resolved in 24 hours. The second dog experienced redness and swelling of the face and paws, followed by vomiting, polydipsia, and elevated heart rate and was treated symptomatically. Signs resolved within 4 days. One dog was pre-treated before the second injection of ProHeart SR-12, and neither dog had a reaction to the second dose 12 months later.

One active control-treated dog experienced anaphylactoid/hypersensitivity-related clinical signs within the first 24 hours. The dog was withdrawn from the study prior to the second monthly dose.

Mild injection site reactions occurred in six ProHeart SR-12-treated dogs and were observed from one to seven days post dosing and included warmth, swelling and pruritus. One of these cases included mild pruritus at the injection site that resolved spontaneously within 24 hours of administration.

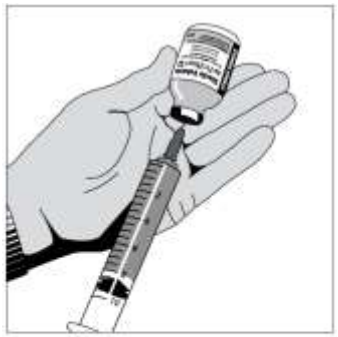
Overdose:
Subcutaneous administration of ProHeart SR-12 to male and female Beagle dogs at 0.5, 1.5, or 2.5 mg/kg on Days 1, 183, and 365 was well tolerated and did not result in any systemic adverse effects.

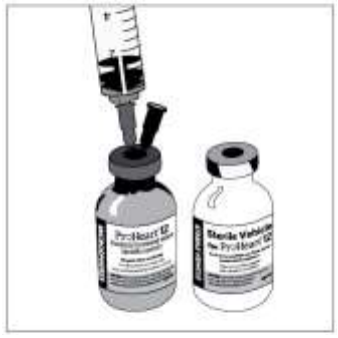
ProHeart SR-12-related findings included edema and thickening of the injection sites that was not associated with adverse clinical signs. These results support the safety of ProHeart SR-12 when administered to dogs at a dosage of 0.5 mg/kg once every 12 months.

Instructions for Use:

CONSTITUTION PROCEDURES:

ProHeart SR-12 must be prepared at least 30 minutes prior to the first use.
Items needed to constitute ProHeart SR-12:
• Sterile vehicle vial- included
• Microspheres vial- included
• Vent needle (25G)- included
• Sterile 10 mL syringe for transfer- not included
• Transfer needle (18G or 20G) - not included





(1) Shake the microsphere vial to break up any aggregates prior to constitution.

(2) Using an 18G or 20G needle and sterile syringe withdraw 8 mL of the unique sterile vehicle from the vial.
There is more sterile vehicle supplied than the 8 mL required.

(3) Insert the enclosed 25G vent needle into the microsphere vial.

(4) Slowly transfer the 8 mL of sterile vehicle into the microsphere vial through the stopper using the transfer needle and syringe.

(5) Once the sterile vehicle has been added, remove the vent and transfer needles from the microsphere vial. Discard unused sterile vehicle and needles.

(6) Shake the microsphere vial vigorously until a thoroughly mixed suspension is produced. The product may appear as a hazy to milky suspension.

(7) Record the time and date of mixing on the microsphere vial.

(8) Allow suspension to stand for at least 30 minutes to allow large air bubbles to dissipate.

(9) **Before every use, gently swirl the mixture to achieve uniform suspension.** The product may appear as a hazy to milky suspension.
The microspheres and vehicle will gradually separate on standing.

(10) Use a 1 mL or 3 mL syringe and an 18G or 20G needle for dosing. Dose promptly after drawing into dosing syringe.
If administration is delayed, gently roll the dosing syringe prior to injection to maintain a uniform suspension and accurate dosing.

(11) Refrigerate the unused product. The constituted product remains stable for 8 weeks in a refrigerator. Avoid direct sunlight.

INJECTION TECHNIQUE:

ProHeart SR-12 must be prepared at least 30 minutes prior to the first use by adding the sterile vehicle to the microspheres.

Swirl the constituted product vial gently before every use to uniformly re-suspend the microspheres.

Withdraw 0.05 mL of suspension/kg body weight into an appropriately sized syringe fitted with an 18G or 20G hypodermic needle. Dose promptly after drawing into dosing syringe. If administration is delayed, gently roll the dosing syringe prior to injection to

maintain a uniform suspension and accurate dosing.

Using aseptic technique, inject the product subcutaneously in the left or right side of the dorsum of the neck cranial to the scapula. No more than 3 mL should be administered in a single site. The location(s) of each injection (left or right side) should be noted so that prior injection sites can be identified and the next injection can be administered on the opposite side.

Storage Condition: Store at or below 30°C. Do not expose to light for extended periods of time.

Shelf Life (as packaged for sale): 3 years.

Shelf-life after first opening of container:
After constitution, the product is stable for 8 weeks stored under refrigeration at 2° to 8°C.

Shelf-life after reconstitution or dilution:

After constitution, the product is stable for 8 weeks stored under refrigeration at 2° to 8°C.

Pack Size:
ProHeart SR-12 is available in 1's - pack size consisting of:
1 vial of Moxidectin sterile microspheres
1 vial of Sterile Vehicle (SR Vehicle)

Disposal: The material should be disposed in compliance with national and regional requirements.

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