Extended-Release Injectable Parasiticide
5% Sterile Solution
For the Treatment and Control of Internal and External Parasites of Cattle on Pasture with Persistent Effectiveness
Not for use in female dairy cattle 20 months of age or older, including dry dairy cows. Not for use in calves to be processed for veal. Not for use in breeding bulls, or in calves less than 3 months of age. Not for use in cattle managed in feedlots or under intensive rotational grazing.

CAUTION: Federal law restricts this drug to use by or on the order of a licensed veterinarian.

DESCRIPTION
LONGRANGE™ (eprinomectin) is a ready-to-use, sterile injectable preparation containing eprinomectin, a member of the macrocyclic lactone class of antiparasitics. Each mL of LONGRANGE contains 50 mg of eprinomectin in a co-solvent system of N-methyl-2-pyrrolidone (30% v/v) and triacetin (qs), along with 50 mg of poly-lactide-co-glycolic acid 75:25 (PLGA), a polymer that allows a slow release of eprinomectin from the formulation, thereby maintaining a prolonged duration of product effectiveness. Butylated hydroxytolene (0.2 mg/mL) acts as an antioxidant in the formulation.

The chemical name of eprinomectin is 4′-deoxy-4′-epacetylamino-avermectin B1. It is a semi-synthetic member of the avermectin family of compounds consisting of a mixture of two homologous components, B1a and B1b, which differ by a single methyl group at C-20.

INDICATIONS FOR USE
LONGRANGE, when administered at the recommended dose volume of 1 mL per 110 lb (50 kg) body weight, is effective in the treatment and control of the following internal and external parasites of cattle:

Gastrointestinal Roundworms
- Cooperia oncopora – Adults and L1
- Cooperia punctata – Adults and L1
- Haemonchus placei – Adults
- Oesophagostomum radiatum – Adults
- Ostertagia ostertagi – Adults
- Trichostrongylus axei – Adults and L1
- Trichostrongylus colubriformis – Adults

Lungworms
- Dictyocaulus viviparus
- Oesophagostomum venulosum

Lungworms
- Dicyclopia viviparum

Persistent Activity
LONGRANGE has been proven to effectively protect cattle from reinfection with the following parasites for the indicated amounts of time following treatment:

<table>
<thead>
<tr>
<th>Parasites</th>
<th>Durations of Persistent Effectiveness</th>
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<tbody>
<tr>
<td>Gastrointestinal Roundworms</td>
<td></td>
</tr>
<tr>
<td>Cooperia oncopora</td>
<td>100 days</td>
</tr>
<tr>
<td>Cooperia punctata</td>
<td>100 days</td>
</tr>
<tr>
<td>Haemonchus placei</td>
<td>120 days</td>
</tr>
<tr>
<td>Oesophagostomum radiatum</td>
<td>120 days</td>
</tr>
<tr>
<td>Ostertagia ostertagi</td>
<td>120 days</td>
</tr>
<tr>
<td>Trichostrongylus axei</td>
<td>100 days</td>
</tr>
<tr>
<td>Trichostrongylus colubriformis</td>
<td>100 days</td>
</tr>
</tbody>
</table>

DOSAGE AND ADMINISTRATION
LONGRANGE™ (eprinomectin) should be given only by subcutaneous injection in front of the shoulder at the recommended dosage level of 1 mg eprinomectin per kg body weight (1 mL per 110 lb body weight).

Each mL of LONGRANGE contains 50 mg of eprinomectin, sufficient to treat 110 lb (50 kg) body weight. Divide doses greater than 10 mL between two injection sites to reduce occasional discomfort or site reaction.

LONGRANGE is to be given subcutaneously only. Animals should be appropriately restrained to achieve the proper route of administration. Inject under the loose skin in front of the shoulder (see illustration) using a 16 or 18 gauge, ½ to ¾ inch needle. Sanitize the injection site by applying a suitable disinfectant. Clean, properly disinfected needles should be used to reduce the potential for injection site infections.

50 mL bottle size: Use only polycarbonate syringes. Not for use with polycarbonate syringe material. If syringe material is not known, contact the provider of the disposable syringe system. Each mL of 50 mL bottle size bottles contain sufficient solution to treat 10, 50, and 100 head of cattle.

DOSAGE AND ADMINISTRATION
LONGRANGE has been proven to effectively protect cattle from reinfection with the following internal and external parasites of cattle:

Persistent Activity
LONGRANGE effectively controls all stages of cattle grubs. However, proper timing of treatment is important. For the most effective results, cattle should be treated as soon as possible after the end of the heel fly (warble fly) season. Destruction of Helodermus larvae (cattle grubs) at the period when these grubs are in vital areas may cause undesirable host-parasite reactions, including the possibility of fatalities. Killing Helodermus larvae when it is in the tissue surrounding the esophagus (gullet) may cause salivation and bloat; killing H. bovis when it is in the vertebral canal may result in its degeneration or paralysis. These reactions are not specific to treatment with LONGRANGE, but can occur with any successful treatment of grubs. Cattle should be treated either before or after these stages of grub development. Consult your veterinarian concerning the proper time for treatment.

ENVIRONMENTAL HAZARDS
Studies indicate that when eprinomectin comes in contact with soil, it readily and tightly binds to the soil and becomes inactive over time. Free eprinomectin may adversely affect fish and certain aquatic organisms. Do not contaminate water by direct application or by improper disposal of drug containers. Dispose of containers in an approved landfill or by incineration.

As with other avermectins, eprinomectin is excreted in the dung of treated animals and can inhibit the reproduction and growth of pest and beneficial insects that use dung as a source of food and for reproduction. The magnitude and duration of such effects are species and life-cycle specific. When used according to label directions, the product is not expected to have an adverse impact on populations of dung-dependent insects.

Other Warnings: Underdosing and/or subtherapeutic concentrations of extended-release anthelmintic products may encourage the development of parasite resistance. It is recommended that parasite resistance be monitored following the use of any anthelmintic with the use of a fecal egg count reduction test program.

CLINICAL PHARMACOLOGY
Due to its unique formulation characteristics, when LONGRANGE is injected subcutaneously in the shoulder area of cattle, a polymeric PLGA matrix is formed. The biodegradable matrix solidifies in vivo to form an in situ forming gel, which allows a gradual release of eprinomectin from the formulation. The rate-limiting step is diffusion of the drug through the gel matrix. Because of its mechanism of release, absorption characteristics can be highly dependent upon the injection technique used and the corresponding surface to volume ratio of the drug.

Clinical efficacy of avermectins and milbemycins is closely related to their pharmaco kinetic behavior, and the time of parasite exposure to active drug concentrations is relevant to obtain optimal and persistent antiparasitic activity.

Mean Eprinomectin B1 Plasma Concentration Versus Time (Supporting Information)

<table>
<thead>
<tr>
<th>Mode of Action</th>
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| The macrocyclic lactones have a unique mode of action. Compounds of this class bind selectively and with high affinity to glutamate–gated chloride ion channels that are present in invertebrate nerve and muscle cells. This leads to an increase in the permeability of the cell membrane to chloride ions with hyperpolarization of the nerve or muscle cell, resulting in paralysis and death of the parasite.

Compounds of this class may also interact in other ligand-gated chloride ion channels, such as those gated by the neurotransmitter gamma-aminobutyric acid (GABA).

The margin of safety for compounds of this class is at least partially attributable to the fact that mammals do not have glutamate–gated chloride ion channels, and that the macrocyclic lactones have low affinity for other mammalian ligand-gated channels and do not readily cross the blood-brain barrier.

TARGET ANIMAL SAFETY
Clinical studies have demonstrated the wide margin of safety of LONGRANGE™ (eprinomectin). Overdosing at 3 to 5 times the recommended dose resulted in a statistically significant reduction in average weight gain when compared to the group tested at label dose. Treatment-related lesions observed in most cattle administered the product included swelling, hyperemia, or necrosis in the subcutaneous tissue of the skin. The administration of LONGRANGE at 3 times the recommended therapeutic dose had no adverse reproductive effects on beef cows at all stages of breeding or pregnancy or on their calves. Not for use in bulls, as reproductive safety testing has not been conducted in males intended for breeding or actively breeding. Not for use in calves less than 3 months of age because safety testing has not been conducted in calves less than 3 months of age.

HOW SUPPLIED
LONGRANGE is available in three ready-to-use glass bottle sizes. The 50, 250, and 500 mL bottles contain sufficient solution to treat 10, 50, and 100 head of cattle, respectively. The 250 and 500 mL bottles are supplied in a removable plastic protector.

STORAGE
Store at 77°F (25°C) with excursions between 59°F and 86°F (15°C and 30°C). Protect from light.

NADA #141-327, Approved by FDA

Made in Canada.
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