LONGRANGE® (eprinomectin) is a ready-to-use, sterile injectable preparation containing eprinomectin, a member of the macrocyclic lactone class of antiparasitics. In cattle, LONGRANGE contains 50 mg of eprinomectin in a gel-based system of N-methyl-2-pyrrolidone (30% v/v) and triacetin (20%), 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. Bulky hydrated lactate (0.2 mg/mL) acts as an antioxidant in the formulation. The chemical name of eprinomectin is 4‘-deoxy-4‘-epi-acetylanamnivoranic acid B. It is a semi-synthetic member of the avermectin family of compounds consisting of a mixture of two homologous components, B1a and B1b, which are derived by a single methylene group at C4.

**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:

<table>
<thead>
<tr>
<th>Parasite / Stage</th>
<th>Body Weight (lb)</th>
<th>Dose Volume (mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastrointestinal Roundworms</td>
<td>100 days</td>
<td>150 days</td>
</tr>
<tr>
<td>Adults and L4</td>
<td>100 days</td>
<td>150 days</td>
</tr>
<tr>
<td>Ostertagia lyrata</td>
<td>100 days</td>
<td>150 days</td>
</tr>
<tr>
<td>Haemonchus placei</td>
<td>100 days</td>
<td>150 days</td>
</tr>
<tr>
<td>Cooperia punctata</td>
<td>100 days</td>
<td>150 days</td>
</tr>
<tr>
<td>Trichostrongylus axei</td>
<td>100 days</td>
<td>150 days</td>
</tr>
<tr>
<td>Trichostrongylus colubriformis</td>
<td>100 days</td>
<td>150 days</td>
</tr>
<tr>
<td>Lungworms</td>
<td>100 days</td>
<td>150 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.

**WARNINGs AND PRECAUTIONS**

Withdrawal Periods and Residue Warnings

Animals intended for human consumption must not be slaughtered within 48 days of the last treatment. This drug product is not approved for use in farm-dairy cattle 20 months of age or older, including dry dairy cows. Use in these cattle may cause drug residues in milk and in calves born to these cows. A withdrawal period has not been established for pre-ruminating calves. Do not use in calves to be processed for veal.

**User Safety Warnings**

For Use in Humans. Keep this and all drugs of this class out of the reach of children. The material safety data sheet (MSDS) contains more detailed occupational safety information. To report adverse effects, to obtain an MSDS, or for assistance, contact Merial at 1-888-637-4251. For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-4ETS, or http://www.fda.gov/AnimalVeterinary.

**Animal Safety Warnings and Precautions**

The product is likely to cause tissue damage at the site of injection, including possible granulomas and necrosis. These reactions have disappeared without treatment. Local tissue reaction may result in trim loss of edible tissue at slaughter.

Observe cattle for injection site reactions. If injection site reactions are suspected, consult your veterinarian. This product is not for intravenous or intraruminal use. If injected intravenously, over light, LONGRANGE® eprinomectin has been developed specifically for use in cattle only. This product should not be used in other animal species.

**When to Treat Cattle with Grub**

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 Hypoderma lines (cattle grubs) at the period when these grubs are in vital areas may cause undesirable host-parasite reactions, including the possibility of fatalities. Killing Hypoderma lines when it is in the tissue surrounding the esophagus [gullet] may cause salivation and bloating. Killing H. bovis when it is in the vertebral canal may cause staggering 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. Insecticidal activity of 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.

**Other Warnings:**

LONGRANGE is available in three ready-to-use glass bottle sizes. The 100, 250, and 500 mL bottles contain sufficient solution to treat 20, 50 and 100 head of 100 lbs body weight, respectively. The 250 and 500 mL bottles are supplied in a removable plastic protector.

**Storage**

Store at 27° F (−2°C) with excursions between 59° and 86° F (15° and 30° C). Protect from light.

**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 action, absorption characteristics can be highly dependent upon the injection technique used and the corresponding surface to volume ratio of the gel. Clinical efficacy of avermectins and milbemycins is closely related to their pharmacokinetic behavior, and the time of parasite exposure to active drug concentrations is relevant to obtain optimal and persistent anti-parasitic activity (Lange et al., 1997; Lutzick et al., 1999; Lutzick et al., 2004; Shoop et al., 1996). Lutzick et al. (1998) indicated that plasma concentrations between 0.5 and 1 ng/mL would represent the minimal drug level required for optimal nematocidal activity, while others have suggested minimum levels of 1 to 2 ng/mL. Pharmacokinetic studies of LONGRANGE in cattle indicate that effective plasma levels remain for an extended period of time (at least 100 days).

**Mode of Action**

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 to 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 400% of the 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.