



GET MORE PROFIT *out of*

YOUR PASTURE.

The benefits of deworming cows with LONGRANGE® (eprinomectin)
with up to 150 days of parasite control in a single dose.^{1,2}



IMPORTANT SAFETY INFORMATION: Do not treat within 48 days of slaughter. Not for use in female dairy cattle 20 months of age or older, including dry dairy cows, or in veal calves. Post-injection site damage (e.g., granulomas, necrosis) can occur. These reactions have disappeared without treatment.

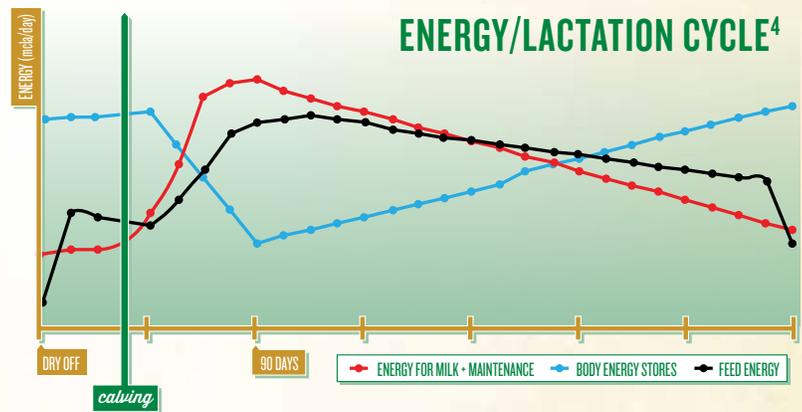
FOCUSING YOUR DEWORMING PROTOCOL JUST ON CALVES? PARASITES MAY BE SUCKING AWAY AT YOUR PROFITABILITY.



Deworming cows to manage for early conception

Cows that conceive late, calve late – and that can decrease weaning weights by as much as 40 or more lbs.³ Managing for conception should not only target ways to get cows to breed back, but breed back as early as possible.

LENGTH OF CALVING SEASON ¹	140 DAYS		60 DAYS ³	
	NUMBER	WEIGHT	NUMBER	WEIGHT
CALVES BORN IN				
20 DAYS ▶	25	540	50	540
40 DAYS ▶	22	510	30	510
60 DAYS ▶	18	480	20	480
80 DAYS ▶	12	450	---	---
100 DAYS ▶	10	420	---	---
120 DAYS ▶	8	390	---	---
140 DAYS ▶	5	360	---	---
OVERALL ▶	100	478 _{LBS.}	100	519 _{LBS.}



Peak lactation comes approximately 85 days post calving. With it comes a feed shortfall and loss of body energy stores. But this is also the optimum point at which to breed back a cow.

CALVING TIME TO BREEDING	PREGNANT ⁵			
	From 1st service (%)	After onset of breeding (%) 20 days	90 days	Cows not showing heat (%)
LOSING WEIGHT	43%	29%	72%	14%
NO WEIGHT CHANGE	60%	57%	82%	0%
DIFFERENCE	17%	28%	10%	14%

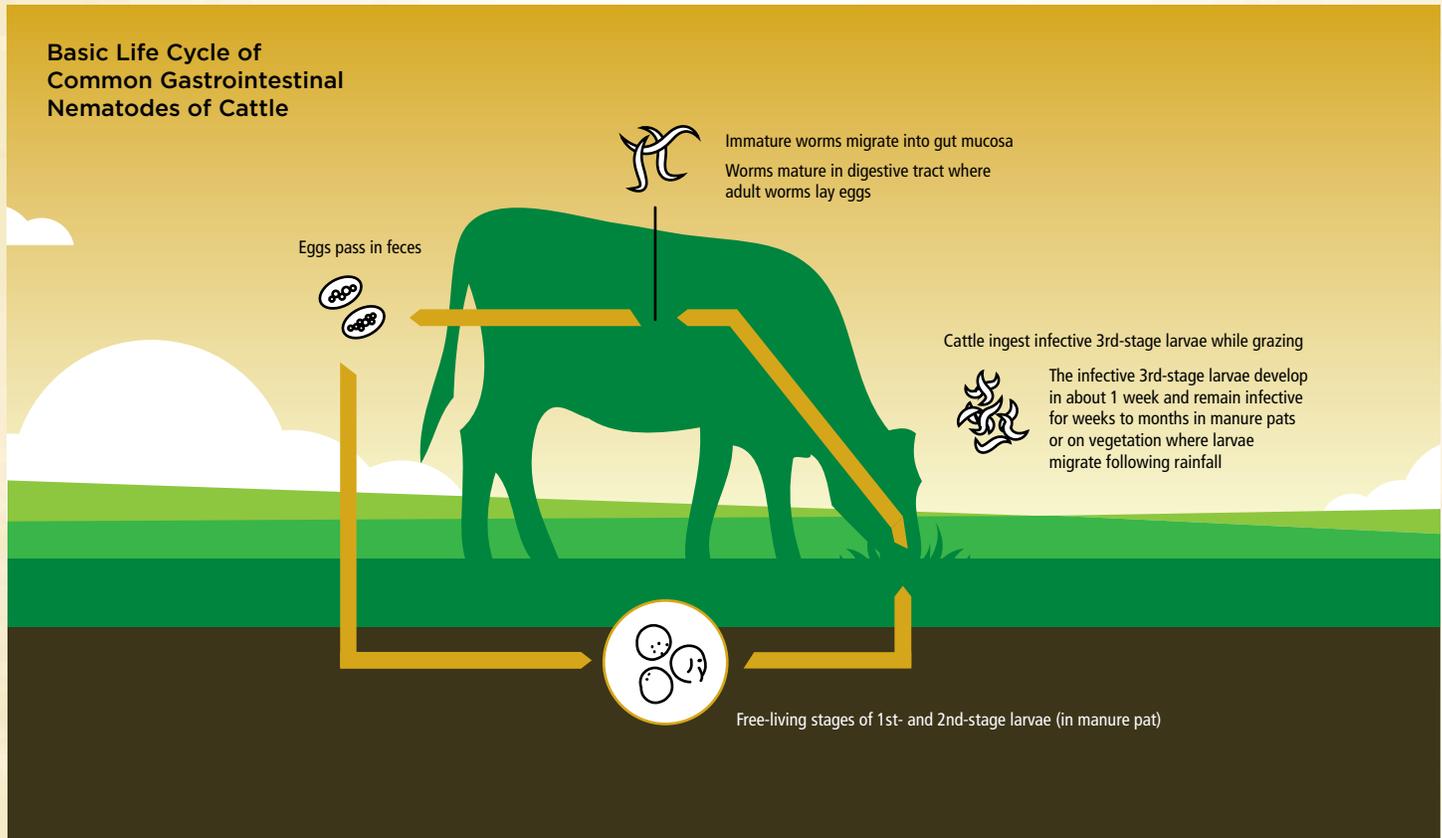
Effect of weight gain on pregnancy

Because of these energy shortfalls, however, cows are often losing weight at this point. Cows that are losing weight at breeding are 17 percent less likely to conceive at first service, and 14 percent won't show heat at all.⁵ **Stabilizing weight through day 85 is the key.**

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Parasite infections in cows reduce feed efficiency and appetite⁶

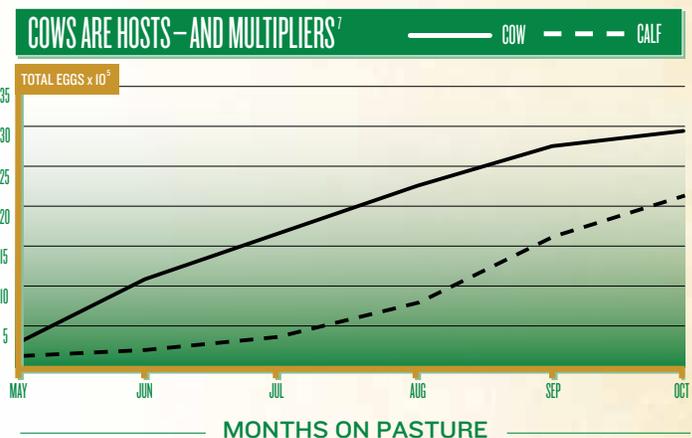
Effective parasite control at peak lactation can help stabilize the cow's weight so she has the energy to conceive. Because **conventional dewormers only last 14 to 42 days**, treating cows at turnout means those products are no longer working at peak lactation. And bringing cows up every 14 to 42 days to retreat is just not practical or economical. **Only LONGRANGE delivers up to 150 days of parasite control in a single dose.**^{1,2}



Deworming cows to manage for cleaner pastures⁷

Initially, the only larvae on the grass are those that have overwintered in the soil. Without a host, these larvae begin starving to death once the temperature and their metabolism starts to increase. This takes place *before* calves start grazing.

That means that cows are the true source of pasture, and eventually, calf infestation. As cows eat the larvae, the parasite life cycle continues, and the cows load the pasture with new eggs that hatch over the summer. These are the larvae that eventually infect the calves.

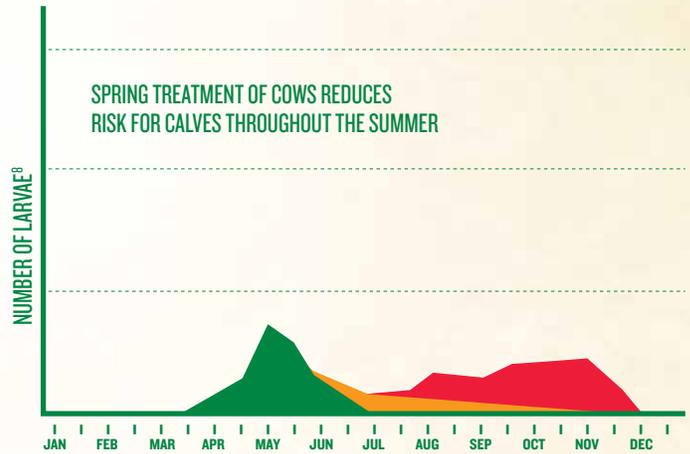
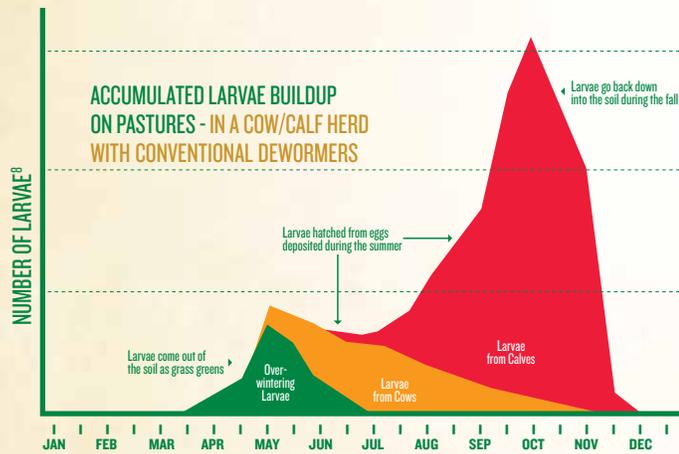


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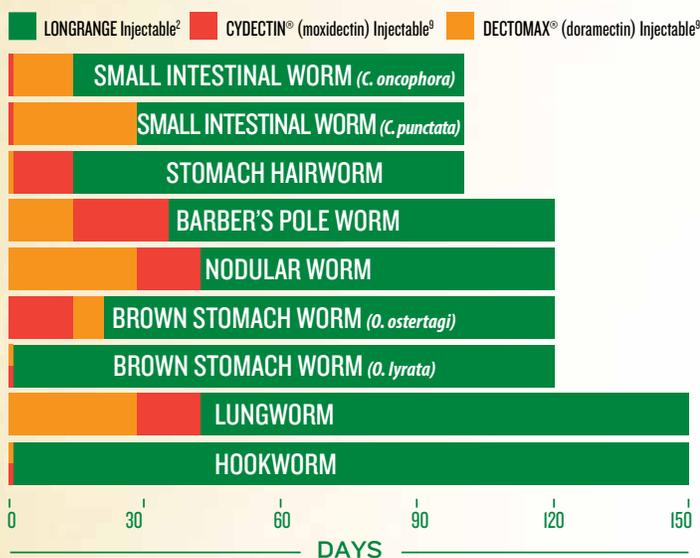
The problem with conventional dewormers

Deworming cows results in fewer eggs being deposited on the pasture for a period of time depending on the dewormer's persistence. However, conventional dewormers only last a short time. So even if cows were dewormed at turnout, the dewormer has worn off by the time parasite larvae reach their heaviest concentration.

While deworming cows with a conventional dewormer slightly delays the accumulation of larvae, the cows are quickly reinfected by the overwintering parasites. By the end of the grazing season, larvae numbers approximate untreated herds.



Only LONGRANGE delivers up to 150 days of parasite control in a single dose.^{1,2}



It takes about 100 days of continuous control to break the parasite life cycle.^{10,11} But you can see from the chart that conventional dewormers don't work nearly that long. When you treat cows with LONGRANGE, you get true season-long control with one convenient injection.

Plus, the cows act like a parasite vacuum for the pasture because few overwintering juveniles that are ingested become adults. That means fewer eggs are shed onto the pasture to infect calves – or to overwinter to infect cows and calves next season. So you'll see the benefits in two calf crops – this year's and next's.

Now that's LONGRANGE.

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Heifer Weight Gain Trial Results¹²

In a recent trial, heifers treated with LONGRANGE had an average additional gain per head of **25.4 lbs.** over cattle treated with DECTOMAX and statistically lower egg counts.¹²

	Day 0	Day 36	Day 64	Day 113	Day 155	Gain Per Head	ADG
Average Weight (lbs.)							
LONGRANGE (302 calves)	452.9	515.1	561.5 [†]	651.6	735.5	282.6	1.82
DECTOMAX (301 calves)	454.5	513.9	562.1	630.2	711.7	257.2	1.66
Weight Difference	-1.6	1.2	-0.6	21.4*	23.8*	25.4	0.16
Average Fecal Egg Counts (eggs per gram)							
LONGRANGE (20 calves)	155.1	10.6	8.51	33.6	3.3		
DECTOMAX (20 calves)	169.1	25.0	192.5	57.3	5.9		
Difference	-14.0	-14.4**	-183.99**	-23.7**	-2.6**		

[†] Water source dry day of weighing in animals treated with LONGRANGE * Statistically significant difference ($P < 0.001$) ** Statistically significant difference ($P < 0.020$)

- 603 heifer calves given standard vaccinations and weighed individually on arrival
 - 302 head treated with a single dose of LONGRANGE according to label instructions
 - 301 head treated with a single dose of DECTOMAX Injectable according to label instructions
- Placed on adjacent equal but separate 60-acre pastures for 45 days and then transferred to adjacent equal but separate 100-acre native oat/ryegrass pastures for the rest of the 155-day study
- Both groups received equivalent supplemental feed; all animals weighed within +/- 1 day of target date

Weaning Weight Gain Trial Results — Calves on Cows¹³

In a trial of calves on cows, LONGRANGE treated steers gained as much as 40 lbs. more over steers treated with CYDECTIN + SAFE-GUARD® (fenbendazole) in 100 days.

- 361 male and female commercial beef calves
 - 137 head treated with single dose of LONGRANGE injectable
 - 227 head treated with single dose of CYDECTIN 1% injectable plus SAFE-GUARD drench administered orally
- Calves remained in cow-calf pairs on separate but equal pastures throughout study

	DAY 0	DAY 104 ADG
Average Weight (lbs.)		
LONGRANGE	374.0	2.05 lbs./day heifers 2.46 lbs./day steers*
CYDECTIN + SAFE-GUARD	310.4	1.92 lbs./day heifers 2.07 lbs./day steers

* Statistically significant difference ($P < 0.001$)

When you add up all the benefits of season-long parasite control with prescription LONGRANGE, you'll see that your cattle — and your operation — have a lot to gain. And all for just a penny a pound.

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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.

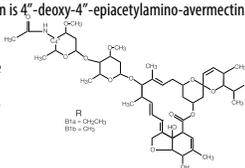
Not for use in breeding bulls, or in calves less than 3 months of age.
Not for use in cattle managed in feedlots or under intensive rotational grazing.

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 hydroxytoluene (0.2 mg/mL) acts as an antioxidant in the formulation.

The chemical name of eprinomectin is 4'-deoxy-4"-epiactylamino-avermectin B₁. It is a semi-synthetic member of the avermectin family of compounds consisting of a mixture of two homologous components, B₁ and B₂, which differ by a single methylene group at C₂₆.



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	Lungworms
<i>Bunostomum phlebotomum</i> – Adults and L ₄	<i>Dictyocaulus viviparus</i> – Adults
<i>Cooperia oncophora</i> – Adults and L ₄	
<i>Cooperia punctata</i> – Adults and L ₄	
<i>Cooperia sumabada</i> – Adults and L ₄	
<i>Haemonchus placei</i> – Adults	Grubs
<i>Oesophagostomum radiatum</i> – Adults	<i>Hypoderma bovis</i>
<i>Ostertagia lyrata</i> – Adults	
<i>Ostertagia ostertagi</i> – Adults, L ₄ , and inhibited L ₄	
<i>Trichostrongylus axei</i> – Adults and L ₄	Mites
<i>Trichostrongylus colubriformis</i> – Adults	<i>Sarcoptes scabiei</i> var. <i>bovis</i>

Persistent Activity

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

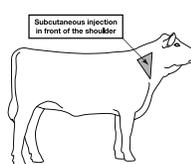
Parasites	Durations of Persistent Effectiveness
Gastrointestinal Roundworms	
<i>Bunostomum phlebotomum</i>	150 days
<i>Cooperia oncophora</i>	100 days
<i>Cooperia punctata</i>	100 days
<i>Haemonchus placei</i>	120 days
<i>Oesophagostomum radiatum</i>	120 days
<i>Ostertagia lyrata</i>	120 days
<i>Ostertagia ostertagi</i>	120 days
<i>Trichostrongylus axei</i>	100 days
Lungworms	
<i>Dictyocaulus viviparus</i>	150 days

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.

Body Weight (lb)	Dose Volume (mL)
110	1
220	2
330	3
440	4
550	5
660	6
770	7
880	8
990	9
1100	10

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 polypropylene syringes. Not for use with polycarbonate syringe material. If syringe material is not known, contact the syringe manufacturer prior to use for identification. Do not use beyond 3 months after stopper has been punctured. Discard bottle after 15 stopper punctures.
250 mL and 500 mL bottle sizes: Use only automatic syringe equipment provided by Merial. To obtain compatible equipment, contact Merial at 1-888-637-4251 or your veterinarian. LONGRANGE should not be stored in automatic syringe equipment. Automatic syringe equipment should be thoroughly cleaned after each use. Discard bottle after one stopper puncture with draw-off spike. No special handling or protective clothing is necessary.

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 female dairy cattle 20 months of age or older, including dry dairy cows. Use in these cattle may cause drug residues in milk and/or 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

Not for Use in Humans. Keep this and all drugs 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-VETS, 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 intramuscular use. Protect product from 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 Grubs

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* 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 *Hypoderma lineatum* 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 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 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. Not for use in cattle managed in feedlots or under intensive rotational grazing because the environmental impact has not been evaluated for these scenarios.

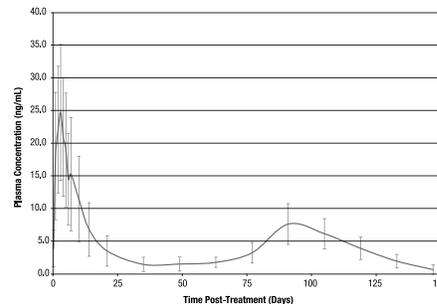
Other Warnings: Underdosing and/or subtherapeutic concentrations of extended-release anthelmintic products may encourage the development of parasite resistance. It is recommended that parasite resistance be monitored following the use of any anthelmintic with the use of a fecal egg count reduction test 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 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 antiparasitic activity (Lanusse et al., 1997; Lifschitz et al., 1999; Lifschitz et al., 2004; Shoop et al., 1996). Lifschitz et al. (1999) 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).

Mean Eprinomectin B₁ Plasma Concentration Versus Time Following a Single Subcutaneous Injection of LONGRANGE® at a Dose Rate of 1 mg Eprinomectin per kg Body Weight in Beef Cattle
(Arithmetic Mean ± Standard Deviation of the Mean, n=42)



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 the 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 550 lb (250 kg) 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° and 86° F (15° and 30° C). Protect from light.

NADA #141-327, Approved by FDA

Made in Canada.

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¹ Dependent upon parasite species, as referenced in FOI summary and LONGRANGE product label.

² LONGRANGE product label.

³ Mathematical calculations based on 140-day and 60-day calving seasons.

⁴ Coppock CE. The importance of an energy-dense diet for high-producing dairy cows. *Vet Med/Food Anim Pract.* 1990;85:429-434.

⁵ Wiltbank JN. Reproductive losses in the beef cow. Texas A&M University Experiment Station. Page 385.

⁶ Stromberg BE, Gasbarre LC. Gastrointestinal nematode control programs with an emphasis on cattle. *Vet Clin Food Anim.* 2006;22:543-565.

⁷ Stromberg BE, Averbeck GA. The role of parasite epidemiology in the management of grazing cattle. *Int J Para.* 1999;33:39.

⁸ Hildreth AVC presentation. December 2008.

⁹ CYDECTIN Injectable and DECTOMAX product labels.

¹⁰ Morley FH, Donald AD. Farm management and systems of helminth control. *Vet Parasitol.* 1980;6:105-134.

¹¹ Brunson RV. Principles of helminth control. *Vet Parasitol.* 1980;6:185-215.

¹² Data on file at Merial.

¹³ Data on file at Merial.