

Date of Approval Letter: APR 1 1999

FREEDOM OF INFORMATION SUMMARY

SUPPLEMENTAL NEW ANIMAL DRUG APPLICATION

NADA 128-409

IVOMEC[®] Injection for Cattle
(ivermectin)

“...has been proved to effectively control infections and to protect from reinfection with *Dictyocaulus viviparus* for 28 days after treatment.”

Sponsored by:

MERIAL LIMITED

I. GENERAL INFORMATION

NADA Number: 128-409

Sponsor: Merial Limited 2100 Ronson Road
Iselin, New Jersey 08830

Established Name: ivermectin

Trade Name: IVOMEC® Injection for Cattle and Swine

Marketing Status: over-the-counter (OTC)

Effect of Supplement: Extend the period of persistent activity against *Dictyocaulus viviparus* from 21 days to 28 days after treatment.

II. INDICATIONS FOR USE: For the treatment and control of the following in cattle.

Gastrointestinal roundworms	<i>Ostertagia ostertagi</i>	Adults and fourth-stage larvae
	<i>Ostertagia ostertagi</i>	Inhibited fourth-stage larvae
	<i>Ostertagia lyrata</i>	Adults and fourth-stage larvae
	<i>Haemonchus placei</i>	Adults and fourth-stage larvae
	<i>Trichostrongylus axei</i>	Adults and fourth-stage larvae
	<i>Trichostrongylus colubriformis</i>	Adults and fourth-stage larvae
	<i>Cooperia oncophora</i>	Adults and fourth-stage larvae
	<i>Cooperia punctata</i>	Adults and fourth-stage larvae
	<i>Cooperia pectinata</i>	Adults and fourth-stage larvae
	<i>Oesophagostomum radiatum</i>	Adults and fourth-stage larvae
	<i>Bunostomum phlebotomum</i>	Adults and fourth-stage larvae
	<i>Nematodirus helvetianus</i>	Adults
	<i>N. spathiger</i>	Adults
Lungworms	<i>Dictyocaulus viviparus</i>	Adults and fourth-stage larvae
Grubs	<i>Hypoderma bovis</i>	
	<i>H. lineatum</i>	
Sucking Lice	<i>Linognathus vituli</i>	
	<i>Haematopinus eurysternus</i>	
	<i>Solenopotes capillatus</i>	
Mange mites	<i>Psoroptes ovis</i> (syn. <i>P. communis</i> var. <i>bovis</i>)	
	<i>Sarcoptes scabiei</i> var. <i>bovis</i>	

IVOMEC® Injection has been proved to effectively control infections and to protect cattle from re-infection with *Dictyocaulus viviparus* for 28 days after treatment; *Ostertagia ostertagi* for 21 days after treatment; *Oesophagostomum radiatum*, *Haemonchus placei*, *Trichostrongylus axei*, *Cooperia punctata*, and *Cooperia oncophora* for 14 days after treatment.

III. DOSAGE FORM, ROUTE OF ADMINISTRATION, AND DOSAGE

- A. Dosage Form: IVOMEK® Injection is a sterile solution containing 10 mg ivermectin/mL.
- B. Route of Administration: IVOMEK® Injection should be administered by subcutaneous injection.
- C. Approved Dose: 200 mcg ivermectin/kg body weight (1 mL/110 lb body weight)

IV. EFFECTIVENESS

Data demonstrating the effectiveness of IVOMEK® Injection for Cattle for previously approved indications are discussed in the parent NADA 128-409 FOI Summary (approval date February 7, 1984, and in the supplemental NADA 128-409 FOI Summary (approval date February 24, 1997). Data from the following dose confirmation trials demonstrate that IVOMEK® Injection for Cattle given at the recommended dosage controls infection and protects against reinfection with *Dictyocaulus viviparus* for 28 days after treatment.

Note: Nematode percentage efficacies were calculated if there were six adequately infected controls using the following formula:

$$\frac{[\text{Arithmetic mean number of nematodes in control cattle} - (\text{Arithmetic mean number of nematodes in ivermectin-treated cattle})]}{(\text{Arithmetic mean number of nematodes in control cattle})} \times 100 = \text{Percent Effectiveness}$$

A. Dose Confirmation: Trial ASR 15065

1. Investigator: Bruce N. Kunkle, D.V.M., M.S. Ph.D., Merial Limited, Fulton, Missouri
2. General design:
 - a. Purpose: To evaluate the persistent efficacy of ivermectin against artificially induced infections of *Dictyocaulus viviparus*.
 - b. Animals: Thirty (30) Holstein calves (10 per group). Animals were approximately 4 to 5 months old and weighed 157 to 234 kg at the start of the study. Animals were free of patent infections at the time of treatment, having been raised under parasite-free conditions and treated with fenbendazole on Days -41 and -18.
 - c. Controls: Control animals received the vehicle for IVOMEK Injection for Cattle at 1 mL/50 kg body weight. One group received a medication which is not pertinent to this document.

- d. Infection: Infective larvae were given to each animal daily, starting on the day after treatment, according to the following schedule: *Dictyocaulus viviparus* (50 larvae per day for 28 days).
 - e. Test article administration: The approved formulation of injectable solution containing 10 mg ivermectin per mL was administered by subcutaneous injection. One mL/50 kg body weight (200 mcg ivermectin/kg body weight) was given once.
 - f. Pertinent variables measured: Worm counts were determined at necropsy which was 49 to 50 days after treatment, 21 to 22 days after the last *Dictyocaulus viviparus* larvae were administered.
3. Results – *Dictyocaulus viviparus* was present in adequate numbers for a determination of efficacy.

Table 4.1. Arithmetic mean worm counts of *Dictyocaulus viviparus* recovered for each group and percent efficacy

Parasite	Arithmetic Mean		Percent efficacy
	Control	IVOMEK	
<i>Dictyocaulus viviparus</i>	20.3	0.0	100

4. Adverse reactions: No adverse reactions to treatment were observed.
 5. Conclusion: This study is adequate to establish a level of persistent efficacy for *Dictyocaulus viviparus* for 28 days.
- B. Dose Confirmation: Trial ASR 15100
1. Investigator: Edward G. Johnson, D.V.M., Johnson Research, Parma, Idaho
 2. General design:
 - a. Purpose: To evaluate the persistent efficacy of ivermectin against artificially induced infections of *Dictyocaulus viviparus*.
 - b. Animals: Twenty (20) Holstein calves (10 per group). Animals were no more than 8 months old and weighed 187 to 254 kg at the start of the study. Animals were free of patent infections at the time of treatment, having been raised under parasite-free conditions.
 - c. Controls: Vehicle for IVOMEK Injection SC at 1 mL/50 kg body weight.
 - d. Infection: Infective larvae were given to each animal daily, starting on the day after treatment, according to the following schedule: *Dictyocaulus viviparus* (100 larvae per day for 28 days).

- e. Test article administration: The approved formulation of injectable solution containing 10 mg ivermectin per mL was administered by subcutaneous injection. 1 mL/50 kg body weight (200 mcg ivermectin/kg body weight) was given once.
 - f. Pertinent variables measured: Worm counts were determined at necropsy which was 49 days after treatment and 21 days after the last *Dictyocaulus viviparus* larvae were administered.
3. Results: - *Dictyocaulus viviparus* was present in adequate numbers for a determination of efficacy.

Table 4.2. Arithmetic mean worm counts of *Dictyocaulus viviparus* recovered for each group and percent efficacy

Parasite	Arithmetic Mean		Percent efficacy
	Control	IVOMEC	
<i>Dictyocaulus viviparus</i>	14.7	0.0	100

- 4. Adverse reactions: No adverse reactions were observed during these studies.
- 5. Conclusion: This study is adequate to establish a level of persistent efficacy for *Dictyocaulus viviparus* for 28 days.

V. ANIMAL SAFETY

As discussed in the parent NADA 128-409 FOI Summary (approval date February 7, 1984).

VI. HUMAN SAFETY

A. Toxicology, Acceptable Daily Intake (ADI), and Target Tissue Tolerance

The basic toxicology and residue chemistry studies that support the use of ivermectin in cattle are summarized in the FOI Summaries for the original and supplemental approvals of the parenteral and oral dosage forms of ivermectin under NADA 128-409 and NADA 137-006. An ADI of 1 mcg/kg/day and the safe concentrations for total residues were assigned to cattle on the basis of the toxicology studies. The residues and metabolism studies established 100 ppb as the tolerance for residues of ivermectin B1a (the marker residue) in liver (the target tissue).

B. Assignment of a Muscle Tolerance

A muscle tolerance of 10 ppb ivermectin B1a was assigned following review of a number of pivotal residue studies with the various dosage forms of the drug, which contained values for ivermectin B1a in cattle muscle.

Data in two total residue studies, RN-189 (NADA 137-006) and RN-190 (NADA 128-409) showed that the B1a component of ivermectin represents approximately 70% of the residues present in muscle tissue in the first one or two weeks post dosing. Those results confirm that ivermectin B1a can serve as the marker residue in muscle tissue.

The muscle tolerance value of 10 ppb was obtained using the values for ivermectin B1a in study CA-129, the withdrawal study submitted with the original NADA 128-409 for the injectable formulation in cattle. Of all the studies examined, the muscle residue data in CA-129 were best suited for the muscle tolerance assignment. CA-129 was the withdrawal study with the highest residue values and was the only study that reported values in muscle at relatively short withdrawal times. The 10 ppb tolerance represents the upper tolerance limit obtained by CVM's standard statistical procedure (99% tolerance limit with 95% confidence) at approximately 22 days of withdrawal.

That interval was chosen for the tolerance assignment rather than the withdrawal time of 35 days so that the tolerance value would be well above the limit of quantitation of the assay in muscle. The choice of 10 ppb as the muscle tolerance for ivermectin makes it possible to identify animals that have been treated with the drug and slaughtered shortly thereafter.

The 10 ppb muscle tolerance applies to samples collected remotely from sites of injection with the injectable product. Muscle tissue collected at the site of injection of the ivermectin injectable product may contain ivermectin residues that significantly exceed 10 ppb, even though the animals were withheld from slaughter for the required period. A higher safe concentration for residues at injection site is allowed based on acute toxicity considerations and the minimal chance of that type tissue being

consumed in a single serving. See the FOI Summary for a Supplement to NADA 128-409 approved on September 12, 1994, for a statement on the human food safety assessment of ivermectin injection site residues.

VII. AGENCY CONCLUSIONS

The data submitted in support of this supplemental NADA satisfy the requirements of section 512 of the Federal Food, Drug, and Cosmetic Act and implementing regulations at Part 514 of Title 21, Code of Federal Regulations (21 CFR 514) to demonstrate that IVOMEK® 1% Injection Solution for Cattle, when used under the proposed conditions of use, is safe and effective to control infections and to protect cattle from reinfection with *Dictyocaulus viviparus* for 28 after treatment.

For cattle, a tolerance of 100 ppb for 22, 23-dihydro-ivermectin B1a (marker residue of ivermectin) in liver (target tissue) is codified at 21 CFR 556.334. The preslaughter withdrawal time is 35 days following one subcutaneous injection of IVOMEK® 1% Injection for Cattle, as specified at 21 CFR 522.1192. Although no new toxicology or residue chemistry studies were submitted with this supplement, CVM used the opportunity to assign a tolerance for residues of ivermectin in cattle muscle. A value of 10 ppb ivermectin B1a is assigned as the tolerance in cattle muscle tissue.

The agency has concluded that this product shall retain over-the-counter marketing status because adequate directions for use have been written for the layman and the conditions for use prescribed on the label are likely to be followed in practice.

In accordance with 21 CFR 514.106(b)(2), this is a Category II change which did not require a reevaluation of the safety or effectiveness data in the parent application.

The agency has determined under 21 CFR 25.33(a)(1) that this action is of a type that does not individually or cumulatively have a significant impact on human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

Under section 512(c)(2)(F)(iii) of the FFDCA, this approval for food producing animals qualifies for THREE (3) years of marketing exclusivity beginning on the date of approval because the supplemental application contains substantial evidence of the effectiveness of the drug involved, any studies of animal safety, or, in the case of food producing animals, human food safety studies (other than bioequivalence or residue studies) required for the approval of the application and conducted or sponsored by the applicant. The THREE years of marketing exclusivity applies only to the new claim for which the supplemental application is approved.

IVOMEK® 1% Injection for Cattle is under U.S. patent number 4,199,569, which expires on October 3, 1999, and patent number 4,853,372, which expires August 1, 2006.

VIII. APPROVED PRODUCT LABELING (attached)

- A. Facsimile base label and package outsert – 1,000 mL container
- B. Facsimile bottle label and package insert – 50, 200, 500 mL containers
- C. Facsimile box carton – 50 mL container

<p>INDICATIONS For the treatment and control of gastrointestinal roundworms, lungworms, lice, and mange mites. See package insert for complete indications and use directions.</p> <p>RECOMMENDED DOSE Cattle: 1 mL per 110 lb body weight Swine: 1 mL per 75 lb body weight</p> <p>IVOMEC is a registered trademark of Merial.</p> <p>Lot No & Exp Date ▼</p>	<p>Product 41380</p> <p>ivomec[®] (ivermectin)</p> <p>Injection for Cattle and Swine</p>	<p>WARNING Not for use in humans. Keep this and all drugs out of the reach of children.</p> <p>RESIDUE INFORMATION: Do not treat cattle within 35 days of slaughter. Because a withdrawal time in milk has not been established, do not use in female dairy cattle of breeding age. Do not treat swine within 18 days of slaughter.</p> <p>PRECAUTIONS: For subcutaneous injection in cattle and swine only. Protect product from light.</p>
<p>8913004F U.S. Pat 4,199,569</p>	<p>50 mL</p>	 <p>Merial Limited, Isevin, NJ, U.S.A.</p>

Component shown at 120%
of actual size.

Product
41380

50 mL

Ivomec
(ivermectin)
Injection
for Cattle and Swine
1% Sterile Solution

Ivomec
(ivermectin)

Injection
for Cattle and Swine

Consult your veterinarian for assistance in the diagnosis, treatment, and control of parasitism.

INDICATIONS

Cattle: Treatment and control of gastrointestinal roundworms (including inhibited *Ostertagia ostertagi*), lungworms, grubs (note insert precautions), sucking lice, and mange mites in cattle.

Swine: Treatment and control of gastrointestinal roundworms, lungworms, lice, and mange mites in swine.

RECOMMENDED DOSE

Cattle: 1 mL per 110 lb body weight
Swine: 1 mL per 75 lb body weight

See package insert for complete indications and use directions.

PRECAUTIONS

For subcutaneous injection in cattle and swine only.
Protect product from light.

IVOMEc (ivermectin) Injection for Cattle and Swine has been developed specifically for use in cattle, swine, reindeer, and American bison only. This product should not be used in other animal species as severe adverse reactions, including fatalities in dogs, may result.

IVOMEc and Cattle Head Logo are registered trademarks of Merial.
U.S. Pat. 4,199,569 Made in U.S.A.
84237F

Ivomec
(ivermectin)
Injection
for Cattle and Swine



WARNING
Not for use in humans.
Keep this and all drugs out of the reach of children.

RESIDUE INFORMATION: Do not treat cattle within 35 days of slaughter. Because a withdrawal time in milk has not been established, do not use in female dairy cattle of breeding age. Do not treat swine within 18 days of slaughter.



Product
41380

Ivomec
(ivermectin)

Injection
for Cattle and Swine

NADA 128-499
Approved by the FDA

1% Sterile Solution



A Parasiticide for the Treatment and Control of Internal and External Parasites of Cattle and Swine.

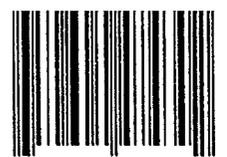
50 mL



Ivomec
(ivermectin)
Injection
for Cattle and Swine
Lot No & Exp Date ▼



Merial Limited
Iselin, NJ, U.S.A.



3 50604-47430 2

Product 41383

Ivomec[®]
(ivermectin)

Injection for Cattle and Swine

1% Sterile Solution

Consult your veterinarian for assistance in the diagnosis, treatment, and control of parasitism.

INDICATIONS

Cattle: Treatment and control of gastrointestinal roundworms (including inhibited *Ostertagia ostertagi*), lungworms, grubs (note insert precautions), sucking lice, and mange mites in cattle.

Swine: Treatment and control of gastrointestinal roundworms, lungworms, lice, and mange mites in swine.

RECOMMENDED DOSE

Cattle: 1 mL per 110 lb body weight

Swine: 1 mL per 75 lb body weight

See package insert for complete indications and use directions.

Lot No &
Exp Date ▶

500 mL

WARNING

Not for use in humans.

Keep this and all drugs out of the reach of children.

RESIDUE INFORMATION: Do not treat cattle within 35 days of slaughter. Because a withdrawal time in milk has not been established, do not use in female dairy cattle of breeding age.

Do not treat swine within 18 days of slaughter.

PRECAUTIONS

Use automatic syringe equipment only. For subcutaneous injection in cattle and swine only. Protect product from light.

Merial Limited, Iselin, NJ, U.S.A.

8913204F

IVOMEc is a registered trademark of Merial.



U.S. Pat. 4,199,569

Product
41382

ivomec[®]
(ivermectin)

Injection for Cattle and Swine

1% Sterile Solution

Consult your veterinarian for assistance in the diagnosis, treatment, and control of parasitism.

INDICATIONS

Cattle: Treatment and control of gastrointestinal roundworms (including inhibited *Ostertagia ostertagi*), lungworms, grubs (note insert precautions), sucking lice, and mange mites in cattle.

Swine: Treatment and control of gastrointestinal roundworms, lungworms, lice and mange mites in swine.

See package insert for complete indications and use directions.

RECOMMENDED DOSE

Cattle: 1 mL per 110 lb body weight

Swine: 1 mL per 75 lb body weight

WARNING

Not for use in humans.

Keep this and all drugs out of the reach of children.

RESIDUE INFORMATION: Do not treat cattle within 35 days of slaughter. Because a withdrawal time in milk has not been established, do not use in female dairy cattle of breeding age.

Do not treat swine within 18 days of slaughter.

PRECAUTIONS

Use automatic syringe equipment only. For subcutaneous injection in cattle and swine only. Protect product from light.

Merial Limited, Iselin, NJ, U.S.A.

IVOMEC is a registered trademark of Merial.

Lot No & Exp Date ▼ 8913104F

200 mL U.S. Pat 4,199,569



Component shown at
120% of actual size.

Product
41384

ivomec[®]
(ivermectin)

Injection for Cattle and Swine

1% Sterile Solution

Consult your veterinarian for assistance in the diagnosis, treatment, and control of parasitism.

INDICATIONS

Cattle: Treatment and control of gastrointestinal roundworms (including inhibited *Ostertagia ostertagi*), lungworms, grubs (note insert precautions), sucking lice, and mange mites in cattle.

Swine: Treatment and control of gastrointestinal roundworms, lungworms, lice, and mange mites in swine.

RECOMMENDED DOSE

Cattle: 1 mL per 110 lb body weight

Swine: 1 mL per 75 lb body weight

See package insert for complete indications and use directions.

Lot No &
Exp Date ▶

1000 mL

WARNING

Not for use in humans.

Keep this and all drugs out of the reach of children.

RESIDUE INFORMATION: Do not treat cattle within 35 days of slaughter. Because a withdrawal time in milk has not been established, do not use in female dairy cattle of breeding age.

Do not treat swine within 18 days of slaughter.

PRECAUTIONS

Use automatic syringe equipment only.

For subcutaneous injection in cattle and swine only.

Protect product from light.

Merial Limited, Iselin, NJ, U.S.A.

8913305F

IVOMEc is a registered trademark of Merial.



U.S. Pat. 4,199,569

When using the 1000 mL pack size, use only automatic syringe equipment. As with any injection, sterile equipment should be used. The injection site should be cleaned and disinfected with alcohol before injection. The rubber stopper should also be disinfected with alcohol to prevent contamination of the contents. Mild and transient pain reactions may be seen in some swine following subcutaneous administration.

Recommended Treatment Program

Swine: At the time of initiating any parasite control program, it is important to treat all breeding animals in the herd. After the initial treatment, use IVOMECS (ivermectin) injection regularly as follows:

BREEDING ANIMALS
Sows: Treat prior to farrowing, preferably 7-14 days before, to minimize infection of piglets.

Gilts: Treat 7-14 days prior to breeding.

Boars: Treat 7-14 days prior to farrowing.

Frequency and need for treatments are dependent upon exposure.
 Treat at least two times a year.

FEEDER PIGS

(Weaners/Growers/Finishers)
 All weaners/feeder pigs should be treated before placement in clean quarters.
 Pigs exposed to contaminated soil or pasture may need retreatment if reinfestation occurs.

NOTE:
 (1) IVOMECS (ivermectin) injection has a persistent drug level sufficient to control mite infestations throughout the egg to adult life cycle. However, since the ivermectin effect is not immediate, care must be taken to prevent reinfestation from exposure to untreated animals or contaminated facilities. Generally, pigs should not be moved to clean quarters or exposed to uninfested pigs for approximately one week after treatment. Sows should be treated at least one week before farrowing to minimize transfer of mites to newborn baby pigs.
 (2) Louse eggs are unaffected by IVOMECS injection and

may require up to three weeks to hatch. Louse infestations developing from hatching eggs may require retreatment.

(3) Consult a veterinarian for aid in the diagnosis and control of internal and external parasites of swine.

Special Minor Use

Reindeer: For the treatment and control of warbles (*Oedemegena tarandi*) in reindeer, inject 200 micrograms ivermectin per kilogram of body weight, subcutaneously. Follow use directions for cattle as described under ADMINISTRATION.

American Bison: For the treatment and control of grubs (*Hypoderma bovis*) in American bison, inject 200 micrograms ivermectin per kilogram of body weight, subcutaneously. Follow use directions for cattle as described under ADMINISTRATION.

RESIDUE INFORMATION: Do not treat reindeer or American bison within 8 weeks (56 days) of slaughter.

WARNING

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, obtain an MSDS or for assistance, contact Merial at 1-888-637-4251.

RESIDUE INFORMATION: Do not treat cattle within 35 days of slaughter.
 Because a withdrawal time in milk has not been established, do not use in female dairy cattle of breeding age.
 Do not treat swine within 18 days of slaughter.

PRECAUTIONS

Transitory discomfort has been observed in some cattle following subcutaneous administration. A low

incidence of soft tissue swelling at the injection site has been observed. These reactions have disappeared without treatment. For cattle, divide doses greater than 10 mL between two injection sites to reduce occasional discomfort or site reaction.

Use sterile equipment and sanitize the injection site by applying a suitable disinfectant. Clean, properly disinfected needles should be used to reduce the potential for injection site infections.

Observe cattle for injection site reactions. Reactions may be due to clostridial infection and should be aggressively treated with appropriate antibiotics. If injection site infections are suspected, consult your veterinarian.

This product is not for intravenous or intramuscular use.

Protect product from light.

IVOMECS injection for Cattle and Swine has been developed specifically for use in cattle, swine, reindeer, and American bison only. This product should not be used in other animal species as severe adverse reactions, including fatalities in dogs, may result.

When to Treat Cattle with Grubs

IVOMECS effectively controls all stages of cattle grubs. However, proper timing of treatment is important. For 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 the 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 stegomyia or paralysis. These reactions are not specific to treatment with IVOMECS, 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.

Cattle treated with IVOMECS after the end of the heel fly season may be retreated with IVOMECS during the winter for internal parasites, mange mites, or sucking lice without danger of grub-related reactions. A planned parasite control program is recommended.

Environmental Safety

Studies indicate that when ivermectin comes in contact with the soil, it readily and tightly binds to the soil and becomes inactive over time. Free ivermectin may adversely affect fish and certain water-borne organisms on which they feed. Do not permit water runoff from feedlots or production sites to enter lakes, streams, or ponds. Do not contaminate water by direct application or by the improper disposal of drug containers. Dispose of containers in an approved landfill or by incineration.

HOW SUPPLIED

IVOMECS (ivermectin) Injection for Cattle and Swine is available in a 1000 mL soft, collapsible pack designed for use with automatic syringe equipment. Each pack contains sufficient solution to treat 200 head of 550 lb (250 kg) cattle or 2000 head of 38 lb (17.3 kg) swine.

(Merial Limited, Registered in England and Wales [Reg. No. 3332751] with registered offices at 27 Knightsbridge, London, SW1X 7OT, England and domiciled in Delaware, USA as Merial LLC.)

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 Iselin, NJ, U.S.A.
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 Made in U.S.A.
 January 1999
 All Rights Reserved.

Product 41280

Ivomec
 (ivermectin)

Injection
 for Cattle and Swine

1% Sterile Solution

A Parasiticide for the Treatment and Control of Internal and External Parasites of Cattle and Swine.



Merial Limited
 Iselin, NJ, U.S.A.
 NADA 144-383
 Approved by the FDA

Consult your veterinarian for assistance in the diagnosis, treatment and control of parasitism.

1000 mL

MERIAL

2.375"

2.25"

2.25"

2.375"

2.5"

IVOMEC[®]

(ivermectin)

Injection

for Cattle and Swine

INTRODUCTION

IVOMEC[®] (ivermectin) is an injectable parasiticide for cattle and swine. One low-volume dose effectively treats and controls the following internal and external parasites that may impair the health of cattle and swine: gastrointestinal roundworms (including inhibited *Ostertagia oestertagi* in cattle), lungworms, grubs, sucking lice, and mange mites of cattle; and gastrointestinal roundworms, lungworms, lice, and mange mites of swine. Discovered and developed by scientists from Merck Research Laboratories, ivermectin is a novel chemical entity. Its convenience, broad-spectrum efficacy, and safety margin make IVOMEC injection a unique product for parasite control of cattle and swine.

PRODUCT DESCRIPTION

Ivermectin is derived from the avermectins, a family of potent, broad-spectrum antiparasitic agents isolated from fermentation of *Streptomyces avermitilis*.

IVOMEC injection is a clear, ready-to-use, sterile solution containing 1% ivermectin, 40% glycerol formal, and propylene glycol, q.s. ad 100%. IVOMEC injection is formulated to deliver the recommended dose level of 200 mcg ivermectin/kilogram of body weight in cattle when given subcutaneously at the rate of 1 mL/110 lb (50 kg). In Swine, IVOMEC injection is formulated to deliver the recommended dose level of 300 mcg ivermectin/kilogram body weight when given subcutaneously in the neck at the rate of 1 mL per 75 lb (33 kg).

IVOMEC, Cattle Head Logo and Pig Head Logo are registered trademarks of Merck.

MODE OF ACTION

Ivermectin is a member of the macrocyclic lactone class of anticholinergics which have a unique mode of action. Compounds of this class bind selectively and with high affinity to glutamate-gated chloride ion channels which occur 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 with other ligand-gated chloride channels, such as those gated by the neurotransmitter gamma-aminobutyric acid (GABA).

The wide margin of safety is attributable to the fact that mammals do not have glutamate-gated chloride channels, the macrocyclic lactones have a low affinity for other mammalian ligand-gated chloride channels and they do not readily cross the blood-brain barrier.

INDICATIONS

Cattle:
IVOMEC (ivermectin) Injection is indicated for the effective treatment and control of the following harmful species of gastrointestinal roundworms, lungworms, grubs, sucking lice, and mange mites in cattle:

- Gastrointestinal Roundworms (adults and fourth-stage larvae):
 - Ostertagia oestertagi* (including inhibited *O. oestertagi*)
 - O. lyrus*
 - Haemonchus placei*
 - Trichostrongylus axei*
 - T. colubriformis*
 - Coprepes oocophorus*
 - C. punctata*
 - C. pectinatus*
 - Oesophagostomum radiatum*
 - Bunostomum phlebotomum*
 - Haematodius haematodes* (adults only)
 - N. spathiger* (adults only)
- Lungworms (adults and fourth-stage larvae):
 - Dicrocoelium viviparum*
- Cattle Grubs (parasitic stages):
 - Hypoderma bovis*
 - H. lineatum*

Sucking Lice:

- Lymnephilus abissi*
- Haematopinus eurysternus*
- Solenopotes appollatus*
- Mites (scabiei):
 - Sarcoptes ovis* (syn. *P. communis* var. *bovis*)
 - Sarcoptes scabiei* var. *bovis*

Persistent Itchiness:

IVOMEC Injection has been proved to effectively control infections and to protect cattle from re-infection with *Dicrocoelium viviparum* for 28 days after treatment; *Ostertagia oestertagi* for 21 days after treatment; *Oesophagostomum radiatum*, *Haemonchus placei*, *Trichostrongylus axei*, *Coprepes punctata*, and *Coprepes oocophorus* for 14 days after treatment.

Swine:

IVOMEC Injection is indicated for the effective treatment and control of the following harmful species of gastrointestinal roundworms, lungworms, lice, and mange mites in swine:

- Gastrointestinal Roundworms:
 - Large roundworm, *Ascaris suum* (adults and fourth-stage larvae)
 - Red stomach worm, *Trichostrongylus rubicatus* (adults and fourth-stage larvae)
 - Nodular worm, *Oesophagostomum* spp. (adults and fourth-stage larvae)
 - Threadworm, *Strongylidae ranosomi* (adults)
- Somatic Roundworms Larvae:
 - Threadworm, *Strongylidae ranosomi* (somatic larvae)
 - Sows must be treated at least seven days before farrowing to prevent infection in piglets.
- Lungworms:
 - Metastrongylus* spp. (adults)
- Lice:
 - Haematopinus suis*
 - Mange mites:
 - Sarcoptes scabiei* var. *suis*

DOSAGE

Cattle:
IVOMEC (ivermectin) Injection should be given only by subcutaneous injection under the loose skin in

front of or behind the shoulder at the recommended dose level of 200 mcg of ivermectin per kilogram of body weight. Each mL of IVOMEC contains 10 mcg of ivermectin, sufficient to treat 110 lb (50 kg) of body weight (maximum 10 mL per injection site).

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

Swine:

IVOMEC (ivermectin) Injection should be given only by subcutaneous injection in the neck of swine at the recommended dose level of 300 mcg of ivermectin per kilogram (2.2 lb) of body weight. Each mL of IVOMEC contains 10 mcg of ivermectin, sufficient to treat 75 lb of body weight.

Body Weight (lb)	Dose Volume (mL)
Growing Pigs	19
	38
	75
	150
Breeding Animals (Sows, Gilts, and Boars)	225
	300
	375
	450

ADMINISTRATION

Cattle:
IVOMEC Injection is to be given subcutaneously only, to reduce risk of potentially fatal clostridial infection of the injection site. Animals should be appropriately restrained to achieve the proper route of administration. Use of a 16-gauge, 1/2 to 3/4" needle is suggested. Inject under the loose skin in front of or behind the shoulder (see illustration).



When using the 1000 mL pack size, use only automatic syringe equipment.

Use sterile equipment and sanitize the injection site by applying a suitable disinfectant. Clean, properly disinfected needles should be used to reduce the potential for injection site infections.

No special handling or protective clothing is necessary.

Swine:

IVOMEC (ivermectin) Injection is to be given subcutaneously in the neck. Animals should be appropriately restrained to achieve the proper route of administration. Use of a 16- or 18-gauge needle is suggested for sows and boars, while an 18- or 20-gauge needle may be appropriate for young animals. Inject under the skin, immediately behind the ear (see illustration).



2.5"

2.375"

2.25"

2.25"

2.375"



NADA 140-088, Approved by the FDA 001 04 99

Ivomec[®] Injections

for Cattle and Swine
1% Sterile Solution

A Parasiticide for the Treatment and Control of Internal and External Parasites of Cattle and Swine
Consult your veterinarian for assistance in the diagnosis, treatment and control of parasitism.

INTRODUCTION
IVOMEC[®] (ivermectin) is an injectable parasiticide for cattle and swine. One low-volume dose effectively treats and controls the following internal and external parasites that may impact the health of cattle and swine: gastrointestinal roundworms (including inhibited *Ostertagia ostertagi* in cattle), lungworms, grubs, sucking lice, and mange mites (including sarcoptic mange mites); and external parasites (including head lice, lice, and ticks).
Merial Research Laboratories, Ivermectin is a novel chemical entity. Its convenience, broad spectrum efficacy, and safety margin make IVOMEC[®] injection a unique product for parasite control of cattle and swine.

PRODUCT DESCRIPTION
Ivermectin is derived from the avermectins, a family of potent, broad-spectrum antiparasitic agents isolated from fermentation of *Streptomyces avermectin*.
IVOMEC[®] injection is a clear, ready-to-use, sterile solution containing 1% ivermectin, 40% glycerol formal, and propylene glycol, q.s. ad 100%. IVOMEC[®] injection is formulated to deliver the recommended dose level of 300 mcg ivermectin/kg of body weight in cattle when given subcutaneously at the rate of 1 mL/71 lb (30 kg) in Swine. IVOMEC[®] injection is formulated to deliver the recommended dose level of 300 mcg ivermectin/kg of body weight when given subcutaneously in the neck at the rate of 1 mL per 75 lb (32 kg).

MODE OF ACTION
Ivermectin is a member of the macrocyclic lactone class of antiparasitics which have a unique mode of action. Compounds of this class bind selectively and with high affinity to glutamate-gated chloride channels which occur 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 with other ligand-gated chloride channels, such as those gated by the neurotransmitter gamma-aminobutyric acid (GABA).

The wide margin of safety is attributable to the fact that mammals do not have glutamate-gated chloride channels, the macrocyclic lactone have a low affinity for mammalian ligand-gated chloride channels and they do not readily cross the blood-brain barrier.

INDICATIONS

Cattle: IVOMEC[®] injection is indicated for the effective treatment and control of the following harmful species of gastrointestinal roundworms, lungworms, grubs, sucking lice, and mange mites in cattle:
Gastrointestinal Roundworms (adults and fourth-stage larvae):
Ostertagia ostertagi (including inhibited *O. ostertagi*)
C. jejuni
Haemonchus placei
Trichostrogylus axei
T. colubriformis
Coprepes oocrochoris
C. punctata
C. pectinosa
Oesophagostomum radiatum
Aunostemon phlebotomum
Nematodirus battus (adults only)
N. spathiger (adults only)

Lungworms (adults and fourth-stage larvae):
Dicrocoelium viviparum

Cattle Grubs (parasitic stages):
Hypoderma bovis
H. lineatum

Sucking Lice:
Lictrix robustus
Haemaphysalis eurysternus
Solenopotes capillatus

Mites (scabies):
Sarcoptes ovis (syn. *P. communis* var. *bovis*)
Sarcoptes scabiei var. *bovis*

Persistent Activity
IVOMEC[®] injection has been proved to effectively control infections and to protect cattle from reinfection with *Dicrocoelium viviparum* for 21 days after treatment, *Ostertagia ostertagi* for 21 days after treatment, *Oesophagostomum radiatum*, *Haemonchus placei*, *Trichostrogylus axei*, *Coprepes punctata*, and *Coprepes oocrochoris* for 14 days after treatment.

Swine: IVOMEC[®] injection is indicated for the effective treatment and control of the following harmful species of gastrointestinal roundworms, lungworms, lice, and mange mites in swine:
Gastrointestinal Roundworms:
Large roundworm, *Ascaris suum* (adults and fourth-stage larvae)
Red stomach worm, *Hydrocotyle rubicula* (adults and fourth-stage larvae)
Nodular worm, *Oesophagostomum* spp. (adults and fourth-stage larvae)
Threadworm, *Strongylus ransomi* (adults)

Somatic Roundworm Larvae:
Threadworm, *Strongylus ransomi* (somatic larvae)
Sows must be treated at least seven days before farrowing to prevent infection in piglets.

Lungworms:
Melospirax spp. (adults)

Lice:
Haemaphysalis suis

Mange Mites:
Sarcoptes scabiei var. *suis*

DOSEAGE
CATTLE: IVOMEC[®] injection should be given only by subcutaneous injection under the loose skin in front of or behind the shoulder at the recommended dose level of 300 mcg of ivermectin per kilogram of body weight. Each mL of IVOMEC[®] contains 10 mg of ivermectin, sufficient to treat 110 lb (50 kg) of body weight (maximum 10 mL per injection site).

Body Weight (lb) Dose Volume (mL)

220 2

330 3

440 4

550 5

660 6

770 7

880 8

990 9

1100 10

Swine: IVOMEC[®] injection should be given only by subcutaneous injection in the neck of swine at the recommended dose level of 300 mcg of ivermectin per kilogram (2.2 lb) of body weight. Each mL of IVOMEC[®] contains 10 mg of ivermectin, sufficient to treat 75 lb of body weight.

Body Weight (lb) Dose Volume (mL)

Growing Pigs 19 1/4

 38 1/2

 75 1

 150 2

Breeding Animals 225 3

(Sows, Gils, and Boars) 300 4

 375 5

 450 6

ADMINISTRATION
Cattle: IVOMEC[®] injection is to be given subcutaneously only, to reduce risk of potentially fatal clostridial infection of the injection site. Animals should be appropriately restrained to achieve the proper route of administration. Use of a 16- or 18-gauge needle is suggested. Inject under the loose skin in front of or behind the shoulder (see illustration).

When using the 200, 500 or 1000 mL pack size, use only automatic syringe equipment. Use sterile equipment and sanitize the injection site by applying a suitable disinfectant. Clean, properly disinfected needles should be used to reduce the potential for injection site infections. No special handling or protective clothing is necessary.

Swine: IVOMEC[®] (Ivermectin) injection is to be given subcutaneously in the neck. Animals should be appropriately restrained to achieve the proper route of administration. Use of a 16- or 18-gauge needle is suggested for sows and boars, while an 18- or 20-gauge needle may be appropriate for young animals. Inject under the skin, immediately behind the ear (see illustration).

When using the 200 mL, 500 mL, or 1000 mL pack size, use only automatic syringe equipment. As with any injection, sterile equipment should be used. The injection site should be cleaned and disinfected with alcohol before injection. The rubber stopper should also be disinfected with alcohol to prevent contamination of the contents. Mild and transient pain reactions may be seen in some swine following subcutaneous administration.

Recommended Treatment Program
Swine: At the time of initiating any parasite control program, it is important to treat all breeding animals in the herd. After the initial treatment, use IVOMEC[®] injection regularly as follows:
BREEDING ANIMALS
Sows: Treat prior to farrowing, preferably 7-14 days before, to minimize infection of piglets.
Gils: Treat 7-14 days prior to breeding.
Treat 7-14 days prior to farrowing.
Boars: Frequency and need for treatments are dependent upon exposure.
Treat at least two times a year.

FEEDER PIGS (Weaners/Growers/Finishers)
All weaner/feeder pigs should be treated before placement in clean quarters.
Pigs exposed to contaminated soil or pasture may need re-treatment if reinfection occurs.

NOTE:
(1) IVOMEC[®] injection has a persistent drug level sufficient to control mite infestations throughout the pig's life cycle. However, since the ivermectin effect is not immediate, care must be taken to prevent contamination from exposure to untreated animals or contaminated facilities. Generally, pigs should be moved to clean quarters or exposed to untreated pigs for approximately one week after treatment. Sows should be treated at least one week before farrowing to minimize transfer of mites to newborn baby pigs.
(2) Loose eggs are unaffected by IVOMEC[®] injection and may require up to three weeks to hatch. Loose infestations developing from hatching eggs may require re-treatment.
(3) Consult a veterinarian for aid in the diagnosis and control of internal and external parasites of swine.

Special Minor Use
Reindeer: For the treatment and control of reindeer (Cervus reindeer) in reindeer, inject 200 micrograms ivermectin per kilogram of body weight, subcutaneously. Follow use directions for cattle as described under ADMINISTRATION.
American Bison: For the treatment and control of grubs (Hypoderma bovis) in American bison, inject 200 micrograms ivermectin per kilogram of body weight, subcutaneously. Follow use directions for cattle as described under ADMINISTRATION.

RESIDUE INFORMATION: Do not treat reindeer or American bison within 8 weeks (56 days) of slaughter.

WARNING
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, obtain an MSDS or for assistance, contact Meriel at 1-888-637-4231.

RESIDUE INFORMATION: Do not treat cattle within 35 days of slaughter. Because a withdrawal time in milk has not been established, do not use in female dairy cattle of breeding age.
Do not treat swine within 18 days of slaughter.

PRECAUTIONS
Transient discomfort has been observed in some cattle following subcutaneous administration. A low incidence of soft tissue swelling at the injection site has been observed. These reactions have disappeared without treatment. For cattle, divide doses greater than 10 mL between two injection sites to reduce occasional discomfort or skin reaction.
Use sterile equipment and sanitize the injection site by applying a suitable disinfectant. Clean, properly disinfected needles should be used to reduce the potential for injection site infections.
Observe cattle for injection site reactions. Reactions may be due to chemical irritation and should be aggressively treated with appropriate antibiotics. If injection site infections are suspected, consult your veterinarian.
This product is not for intravenous or intramuscular use.
Protect product from light.
IVOMEC[®] injection for Cattle and Swine has been developed specifically for use in cattle, swine, reindeer, and American bison only. This product should not be used in other animal species as severe adverse reactions, including fatalities in dogs, may result.
When to Treat Cattle with Grubs
IVOMEC[®] effectively controls all stages of cattle grubs. However, proper timing of treatment is important. For most effective results, cattle should be treated as soon as possible after the end of the feed 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 infection. Killing Hypoderma lineatum when it is in the tissue surrounding the esophageal (gullet) may cause salivation and blood, killing H. bovis when it is in the ventral canal may cause atrophy or paralysis. These reactions are not specific to treatment with IVOMEC[®], 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.
Cattle treated with IVOMEC[®] after the end of the feed fly season may be re-treated with IVOMEC[®] during the winter for internal parasites, mange mites, or sucking lice without danger of grub-related reactions. A planned parasite control program is recommended.

Environmental Safety
Studies indicate that when ivermectin comes in contact with the soil, it readily and lightly binds to the soil and becomes inactive over time. Free ivermectin may adversely affect fish and certain water-borne organisms on which they feed. Do not permit water runoff from feedlots or production sites to enter lakes, streams, or ponds. Do not contaminate water by direct application or by the improper disposal of drug containers. Dispose of containers in an approved landfill or by incineration.

HOW SUPPLIED
IVOMEC[®] injection for Cattle and Swine is available in four ready-to-use pack sizes:
The 50 mL pack is a multiple-dose, rubber capped bottle. Each bottle contains sufficient solution to treat 10 head of 550 lb (250 kg) cattle or 100 head of 38 lb (17.3 kg) swine.
The 200 mL pack is a soft, collapsible pack designed for use with automatic syringe equipment. Each pack contains sufficient solution to treat 40 head of 550 lb (250 kg) cattle or 400 head of 38 lb (17.3 kg) swine.
The 500 mL pack is a soft, collapsible pack designed for use with automatic syringe equipment. Each pack contains sufficient solution to treat 100 head of 550 lb (250 kg) cattle or 1000 head of 38 lb (17.3 kg) swine.
The 1000 mL is a soft, collapsible pack designed for use with automatic syringe equipment. Each pack contains sufficient solution to treat 200 head of 550 lb (250 kg) cattle or 2000 head of 38 lb (17.3 kg) swine.

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Meriel Limited, Health, NJ, U.S.A.

U.S. Pat. 4,198,549

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MERIAL

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When using the 200, 500 or 1000 mL pack size, use only automatic syringe equipment. Use sterile equipment and sanitize the injection site by applying a suitable disinfectant. Clean, properly disinfected needles should be used to reduce the potential for injection site infections. No special handling or protective clothing is necessary.

Swine: IVOMEC[®] (Ivermectin) injection is to be given subcutaneously in the neck. Animals should be appropriately restrained to achieve the proper route of administration. Use of a 16- or 18-gauge needle is suggested for sows and boars, while an 18- or 20-gauge needle may be appropriate for young animals. Inject under the skin, immediately behind the ear (see illustration).

When using the 200 mL, 500 mL, or 1000 mL pack size, use only automatic syringe equipment. As with any injection, sterile equipment should be used. The injection site should be cleaned and disinfected with alcohol before injection. The rubber stopper should also be disinfected with alcohol to prevent contamination of the contents. Mild and transient pain reactions may be seen in some swine following subcutaneous administration.

Recommended Treatment Program
Swine: At the time of initiating any parasite control program, it is important to treat all breeding animals in the herd. After the initial treatment, use IVOMEC[®] injection regularly as follows:
BREEDING ANIMALS
Sows: Treat prior to farrowing, preferably 7-14 days before, to minimize infection of piglets.
Gils: Treat 7-14 days prior to breeding.
Treat 7-14 days prior to farrowing.
Boars: Frequency and need for treatments are dependent upon exposure.
Treat at least two times a year.

FEEDER PIGS (Weaners/Growers/Finishers)
All weaner/feeder pigs should be treated before placement in clean quarters.
Pigs exposed to contaminated soil or pasture may need re-treatment if reinfection occurs.

NOTE:
(1) IVOMEC[®] injection has a persistent drug level sufficient to control mite infestations throughout the pig's life cycle. However, since the ivermectin effect is not immediate, care must be taken to prevent contamination from exposure to untreated animals or contaminated facilities. Generally, pigs should be moved to clean quarters or exposed to untreated pigs for approximately one week after treatment. Sows should be treated at least one week before farrowing to minimize transfer of mites to newborn baby pigs.
(2) Loose eggs are unaffected by IVOMEC[®] injection and may require up to three weeks to hatch. Loose infestations developing from hatching eggs may require re-treatment.
(3) Consult a veterinarian for aid in the diagnosis and control of internal and external parasites of swine.

Special Minor Use
Reindeer: For the treatment and control of reindeer (Cervus reindeer) in reindeer, inject 200 micrograms ivermectin per kilogram of body weight, subcutaneously. Follow use directions for cattle as described under ADMINISTRATION.
American Bison: For the treatment and control of grubs (Hypoderma bovis) in American bison, inject 200 micrograms ivermectin per kilogram of body weight, subcutaneously. Follow use directions for cattle as described under ADMINISTRATION.

RESIDUE INFORMATION: Do not treat reindeer or American bison within 8 weeks (56 days) of slaughter.

WARNING
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, obtain an MSDS or for assistance, contact Meriel at 1-888-637-4231.

RESIDUE INFORMATION: Do not treat cattle within 35 days of slaughter. Because a withdrawal time in milk has not been established, do not use in female dairy cattle of breeding age.
Do not treat swine within 18 days of slaughter.

PRECAUTIONS
Transient discomfort has been observed in some cattle following subcutaneous administration. A low incidence of soft tissue swelling at the injection site has been observed. These reactions have disappeared without treatment. For cattle, divide doses greater than 10 mL between two injection sites to reduce occasional discomfort or skin reaction.
Use sterile equipment and sanitize the injection site by applying a suitable disinfectant. Clean, properly disinfected needles should be used to reduce the potential for injection site infections.
Observe cattle for injection site reactions. Reactions may be due to chemical irritation and should be aggressively treated with appropriate antibiotics. If injection site infections are suspected, consult your veterinarian.
This product is not for intravenous or intramuscular use.
Protect product from light.
IVOMEC[®] injection for Cattle and Swine has been developed specifically for use in cattle, swine, reindeer, and American bison only. This product should not be used in other animal species as severe adverse reactions, including fatalities in dogs, may result.
When to Treat Cattle with Grubs
IVOMEC[®] effectively controls all stages of cattle grubs. However, proper timing of treatment is important. For most effective results, cattle should be treated as soon as possible after the end of the feed 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 infection. Killing Hypoderma lineatum when it is in the tissue surrounding the esophageal (gullet) may cause salivation and blood, killing H. bovis when it is in the ventral canal may cause atrophy or paralysis. These reactions are not specific to treatment with IVOMEC[®], 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.
Cattle treated with IVOMEC[®] after the end of the feed fly season may be re-treated with IVOMEC[®] during the winter for internal parasites, mange mites, or sucking lice without danger of grub-related reactions. A planned parasite control program is recommended.

Environmental Safety
Studies indicate that when ivermectin comes in contact with the soil, it readily and lightly binds to the soil and becomes inactive over time. Free ivermectin may adversely affect fish and certain water-borne organisms on which they feed. Do not permit water runoff from feedlots or production sites to enter lakes, streams, or ponds. Do not contaminate water by direct application or by the improper disposal of drug containers. Dispose of containers in an approved landfill or by incineration.

HOW SUPPLIED
IVOMEC[®] injection for Cattle and Swine is available in four ready-to-use pack sizes:
The 50 mL pack is a multiple-dose, rubber capped bottle. Each bottle contains sufficient solution to treat 10 head of 550 lb (250 kg) cattle or 100 head of 38 lb (17.3 kg) swine.
The 200 mL pack is a soft, collapsible pack designed for use with automatic syringe equipment. Each pack contains sufficient solution to treat 40 head of 550 lb (250 kg) cattle or 400 head of 38 lb (17.3 kg) swine.
The 500 mL pack is a soft, collapsible pack designed for use with automatic syringe equipment. Each pack contains sufficient solution to treat 100 head of 550 lb (250 kg) cattle or 1000 head of 38 lb (17.3 kg) swine.
The 1000 mL is a soft, collapsible pack designed for use with automatic syringe equipment. Each pack contains sufficient solution to treat 200 head of 550 lb (250 kg) cattle or 2000 head of 38 lb (17.3 kg) swine.

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Meriel Limited, Health, NJ, U.S.A.

U.S. Pat. 4,198,549

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MERIAL

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Component shown shown at 80% Reduction.
All copy prints Black unless otherwise Indicated.

When using the 200, 500 or 1000 mL pack size, use only automatic syringe equipment.

Use sterile equipment and sanitize the injection site by applying a suitable disinfectant. Clean, properly disinfected needles should be used to reduce the potential for injection site infections.

No special handling or protective clothing is necessary.

Swine: IVOMEC[®] (Ivermectin) injection is to be given subcutaneously in the neck. Animals should be appropriately restrained to achieve the proper route of administration. Use of a 16- or 18-gauge needle is suggested for sows and boars, while an 18- or 20-gauge needle may be appropriate for young animals. Inject under the skin, immediately behind the ear (see illustration).

When using the 200 mL, 500 mL, or 1000 mL pack size, use only automatic syringe equipment. As with any injection, sterile equipment should be used. The injection site should be cleaned and disinfected with alcohol before injection. The rubber stopper should also be disinfected with alcohol to prevent contamination of the contents. Mild and transient pain reactions may be seen in some swine following subcutaneous administration.

Recommended Treatment Program
Swine: At the time of initiating any parasite control program, it is important to treat all breeding animals in the herd. After the initial treatment, use IVOMEC[®] injection regularly as follows:
BREEDING ANIMALS
Sows: Treat prior to farrowing, preferably 7-14 days before, to minimize infection of piglets.
Gils: Treat 7-14 days prior to breeding.
Treat 7-14 days prior to farrowing.
Boars: Frequency and need for treatments are dependent upon exposure.
Treat at least two times a year.

FEEDER PIGS (Weaners/Growers/Finishers)
All weaner/feeder pigs should be treated before placement in clean quarters.
Pigs exposed to contaminated soil or pasture may need re-treatment if reinfection occurs.

NOTE:
(1) IVOMEC[®] injection has a persistent drug level sufficient to control mite infestations throughout the pig's life cycle. However, since the ivermectin effect is not immediate, care must be taken to prevent contamination from exposure to untreated animals or contaminated facilities. Generally, pigs should be moved to clean quarters or exposed to untreated pigs for approximately one week after treatment. Sows should be treated at least one week before farrowing to minimize transfer of mites to newborn baby pigs.
(2) Loose eggs are unaffected by IVOMEC[®] injection and may require up to three weeks to hatch. Loose infestations developing from hatching eggs may require re-treatment.
(3) Consult a veterinarian for aid in the diagnosis and control of internal and external parasites of swine.

Special Minor Use
Reindeer: For the treatment and control of reindeer (Cervus reindeer) in reindeer, inject 200 micrograms ivermectin per kilogram of body weight, subcutaneously. Follow use directions for cattle as described under ADMINISTRATION.
American Bison: For the treatment and control of grubs (Hypoderma bovis) in American bison, inject 200 micrograms ivermectin per kilogram of body weight, subcutaneously. Follow use directions for cattle as described under ADMINISTRATION.

RESIDUE INFORMATION: Do not treat reindeer or American bison within 8 weeks (56 days) of slaughter.

WARNING
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, obtain an MSDS or for assistance, contact Meriel at 1-888-637-4231.

RESIDUE INFORMATION: Do not treat cattle within 35 days of slaughter. Because a withdrawal time in milk has not been established, do not use in female dairy cattle of breeding age.
Do not treat swine within 18 days of slaughter.

PRECAUTIONS
Transient discomfort has been observed in some cattle following subcutaneous administration. A low incidence of soft tissue swelling at the injection site has been observed. These reactions have disappeared without treatment. For cattle, divide doses greater than 10 mL between two injection sites to reduce occasional discomfort or skin reaction.
Use sterile equipment and sanitize the injection site by applying a suitable disinfectant. Clean, properly disinfected needles should be used to reduce the potential for injection site infections.
Observe cattle for injection site reactions. Reactions may be due to chemical irritation and should be aggressively treated with appropriate antibiotics. If injection site infections are suspected, consult your veterinarian.
This product is not for intravenous or intramuscular use.
Protect product from light.
IVOMEC[®] injection for Cattle and Swine has been developed specifically for use in cattle, swine, reindeer, and American bison only. This product should not be used in other animal species as severe adverse reactions, including fatalities in dogs, may result.
When to Treat Cattle with Grubs
IVOMEC[®] effectively controls all stages of cattle grubs. However, proper timing of treatment is important. For most effective results, cattle should be treated as soon as possible after the end of the feed 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 infection. Killing Hypoderma lineatum when it is in the tissue surrounding the esophageal (gullet) may cause salivation and blood, killing H. bovis when it is in the ventral canal may cause atrophy or paralysis. These reactions are not specific to treatment with IVOMEC[®], 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.
Cattle treated with IVOMEC[®] after the end of the feed fly season may be re-treated with IVOMEC[®] during the winter for internal parasites, mange mites, or sucking lice without danger of grub-related reactions. A planned parasite control program is recommended.

Environmental Safety
Studies indicate that when ivermectin comes in contact with the soil, it readily and lightly binds to the soil and becomes inactive over time. Free ivermectin may adversely affect fish and certain water-borne organisms on which they feed. Do not permit water runoff from feedlots or production sites to enter lakes, streams, or ponds. Do not contaminate water by direct application or by the improper disposal of drug containers. Dispose of containers in an approved landfill or by incineration.

HOW SUPPLIED
IVOMEC[®] injection for Cattle and Swine is available in four ready-to-use pack sizes:
The 50 mL pack is a multiple-dose, rubber capped bottle. Each bottle contains sufficient solution to treat 10 head of 550 lb (250 kg) cattle or 100 head of 38 lb (17.3 kg) swine.
The 200 mL pack is a soft, collapsible pack designed for use with automatic syringe equipment. Each pack contains sufficient solution to treat 40 head of 550 lb (250 kg) cattle or 400 head of 38 lb (17.3 kg) swine.
The 500 mL pack is a soft, collapsible pack designed for use with automatic syringe equipment. Each pack contains sufficient solution to treat 100 head of 550 lb (250 kg) cattle or 1000 head of 38 lb (17.3 kg) swine.
The 1000 mL is a soft, collapsible pack designed for use with automatic syringe equipment. Each pack contains sufficient solution to treat 200 head of 550 lb (250 kg) cattle or 2000 head of 38 lb (17.3 kg) swine.

[Meriel Limited, Registered in England and Wales (Reg. No. 333275)] with registered offices at 27 Knightsbridge, London, SW1X 7QT, England and domesticated in Delaware, USA as Meriel LLC.

Meriel Limited, Health, NJ, U.S.A.

U.S. Pat. 4,198,549

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MERIAL

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Product 41280

Ivomec[®]

(ivermectin)

Injection
for Cattle and Swine

1% Sterile Solution

Consult your veterinarian for assistance in the diagnosis, treatment, and control of parasitism.

INDICATIONS

Cattle: Treatment and control of gastrointestinal roundworms (including inhibited *Ostertagia ostertagi*), lungworms, grubs (note outsert precautions), sucking lice, and mange mites in cattle.

Swine: Treatment and control of gastrointestinal roundworms, lungworms, lice and mange mites in swine.

See package outsert for complete indications and use directions.

WARNING

Not for use in humans.

Keep this and all drugs out of the reach of children.

RESIDUE INFORMATION: Do not treat cattle within 35 days of slaughter. Because a withdrawal time in milk has not been established, do not use in female dairy cattle of breeding age.

Do not treat swine within 18 days of slaughter.

PRECAUTIONS

Use automatic syringe equipment only.

For subcutaneous injection in cattle and swine only.

Protect from light.

Merial Limited
Iselin, NJ, U.S.A.

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Lot No &
Exp Date

1000 mL