HFA-305

Approval Date: APR 2 3 2007

FREEDOM OF INFORMATION SUMMARY

ORIGINAL ABBREVIATED NEW ANIMAL DRUG APPLICATION

ANADA 200-436

NOROMECTIN Plus Injection for Cattle
ivermectin and clorsulon

Indications for use: For the treatment and control of internal parasites, including adult liver flukes, and external parasites in cattle.

Sponsored by:

Norbrook Laboratories, Ltd.

2007.200.436

FOIS 1

FREEDOM OF INFORMATION SUMMARY

1. GENERAL INFORMATION:

a. File Number:	ANADA 200-436
b. Sponsor:	Norbrook Laboratories, Ltd. Station Works Newry BT35 6JP Northern Ireland Drug Labeler Code: 055529
US Agent:	Norbrook, Inc. Bill Zollers, Ph.D. Directory of Regulatory Affairs – USA & Canada 9733 Loiret Boulevard Lenexa, KS 66219
c. Established Name:	Ivermectin and Clorsulon
d. Proprietary Name:	NOROMECTIN Plus Injection for Cattle
e. Dosage Form:	Sterile solution
f. How Supplied:	50 mL and 100 mL rubber-capped bottles; 250 mL and 500 mL rubber-capped bottles designed for use with automatic syringe equipment.
g. How Dispensed:	OTC
h. Amount of Active Ingredients:	10 mg/mL (1%) of ivermectin and 100 mg/mL (10%) of clorsulon
i. Route of Administration:	Injection
j. Species/Class:	Cattle. Exception: Not approved for use in lactating dairy cattle or pre-ruminant calves.
k. Recommended Dosage:	1 mL per 110 lbs (50 kg) of body weight, or 200 mcg ivermectin and 2 mg clorsulon per kg, given subcutaneously behind the shoulder.

l. Pharmacological Category: Parasiticide

m. Indications: NOROMECTIN Plus Injection for Cattle is indicated for the effective treatment and control of the following parasites in cattle:

Gastrointestinal Roundworms (adults and fourth-stage larvae):
Ostertagia ostertagi (including inhibited *O. ostertagi*)
O. lyrata
Haemonchus placei
Trichostrongylus axei
T. colubriformis
Cooperia oncophora
C. punctata
C. pectinata
Bunostomum phlebotomum
Nematodirus helvetianus (adults only)
N. spathiger (adults only)
Oesophagostomum radiatum

Lungworms (adults and fourth-stage larvae):
Dictyocaulus viviparus

Liver Flukes:
Fasciola hepatica (adults only)

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

Sucking Lice:
Linognathus vituli
Haematopinus eurysternus
Solenopotes capillatus

Mange Mites (cattle scab):
Psoroptes ovis (syn. *P. communis* var. *bovis*)
Sarcoptes scabiei var. *bovis*

Persistent Activity
Ivermectin and clorsulon injection has been proved to effectively control infections and to protect cattle from reinfection with *Dictyocaulus viviparus* and *Oesophagostomum radiatum* for 28 days after treatment; *Ostertagia ostertagi, Trichostrongylus axei, Cooperia punctata* for 21 days after treatment; *Haemonchus placei* and *Cooperia oncophora* for 14 days after treatment.

n. Pioneer Product: IVOMEC Plus Injection for Cattle; ivermectin and clorsulon; NADA 140-833; Merial, Ltd.

2. TARGET ANIMAL SAFETY AND DRUG EFFECTIVENESS:

Under the provisions of the Federal Food, Drug, and Cosmetic Act, as amended by the Generic Animal Drug and Patent Term Restoration Act (GADPTRA) of 1988, an Abbreviated New Animal Drug Application (ANADA) may be submitted for a generic version of an approved new animal drug (pioneer product). New target animal safety and effectiveness data and human food safety data (other than tissue residue data) are not required for approval of an ANADA.

Ordinarily, the ANADA sponsor is required to show that the generic product is bioequivalent to the pioneer, which has been shown to be safe and effective. If bioequivalence is demonstrated through a clinical endpoint study, then a tissue residue study to establish the withdrawal time for the generic product should also be conducted. For certain dosage forms, the agency will grant a waiver from the requirement of an *in vivo* bioequivalence study (55 FR 24645, June 18, 1990; Fifth GADPTRA Policy Letter; Bioequivalence Guideline, October 9, 2002).

Based on the formulation characteristics of the generic product, Norbrook Laboratories, Ltd. was granted a waiver from the requirement of an *in vivo* bioequivalence study for the generic product NOROMECTIN Plus Injection for Cattle (ivermectin and clorsulon). The generic product is administered as a sterile solution, contains the same active ingredients in the same concentration and dosage form as the pioneer product, and contains no inactive ingredients that may significantly affect the absorption of the active ingredient. The pioneer product, IVOMEC Plus Injection for Cattle (ivermectin and clorsulon), the subject of Merial, Ltd., NADA 140-833, was approved on September 17, 1990.

3. *HUMAN SAFETY:*

- **Tolerances for Residues:**

  The tolerance established for the pioneer product applies to the generic product. Tolerances of 100 parts per billion (ppb) and 10 ppb are established for 22, 23-dihydroavermectin B_1a (marker residue) in the liver (target tissue) and muscle, respectively, of cattle under 21 CFR 556.344. The Acceptable Daily Intake (ADI) for total residues of ivermectin is 1 microgram per kilogram of body weight per day. Tolerances of 1 part per million (ppm) and 0.1 ppm are established for parent clorsulon (marker residue) in the kidney (target tissue) and muscle, respectively, of cattle under 21 CFR 556.163. The Acceptable Daily Intake (ADI) for total residues of clorsulon is 8 micrograms per kilogram of body weight per day.

- **Withdrawal Times:**

  Because a waiver of the *in vivo* bioequivalence study was granted, the withdrawal times are those previously assigned to the pioneer product.

  The withdrawal time of 49 days has been established for ivermectin and clorsulon in cattle for slaughter (21 CFR 522.1193). A withdrawal period for milk has not been established, and a withdrawal period for pre-ruminating calves has not been established.

- **Regulatory Method for Residues:**

  The analytical methods for detection of ivermectin in tissues are HPLC methods with fluorescence detection. The analytical method for detection of clorsulon in tissues is UV-LC Finish or Determinative Assay. These methods are found on file at the Center for Veterinary Medicine, 7500 Standish Place, Rockville, MD 20855.

4. *AGENCY CONCLUSIONS:*

This ANADA submitted under section 512(b) of the Federal Food, Drug, and Cosmetic Act satisfies the requirements of section 512(n) of the act and demonstrates that the injectable product NOROMECTIN Plus Injection for Cattle, when used under its proposed conditions of use, is safe and effective for its labeled indications.

5. ATTACHMENTS:

Facsimile generic labeling and currently approved pioneer labeling are attached as follows:

Generic Labeling for ANADA 200-436:
NOROMECTIN Plus Injection for Cattle (ivermectin and clorsulon) – container and carton label – 50 mL, 100 mL, 250 mL, 500 mL; insert

Pioneer Labeling for NADA 140-833:
IVOMEC Plus Injection for Cattle (ivermectin and clorsulon) – container and carton label – 50 mL, 200 mL, 500 mL; insert

Noromectin® PLUS

Injection for Cattle

1% w/v ivermectin and 10% w/v clorsulon in a sterile solution

ANADA 200-436
Approved by the FDA

50 mL

Norbrook

For the treatment and control of internal parasites, including adult liver flukes, and external parasites.

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

Do not contaminate water. Dispose of containers in an approved landfill or by incineration.

See package insert for complete indications, precautions, warnings, residue information, 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 49 days of slaughter. Because a withdrawal time in milk has not been established, do not use in female dairy cattle of breeding age. A withdrawal period has not been established for this product in pre-ruminating calves. Do not use in calves to be processed for veal.

PRECAUTIONS
For subcutaneous injection in cattle only.
Protect product from light.

Store at 15-30° C (59-86° F).

Made in the UK.

Norbrook Laboratories Limited,
Newry, Co. Down, Northern Ireland

900000L01

Lot No & Exp Date ▼

000016

Noromectin® PLUS

Injection for Cattle

1% w/v ivermectin and
10% w/v clorsulon
in a sterile solution

ANADA 200-406
Approved by the FDA

100 mL

Norbrook

For the treatment and control of internal parasites, including adult liver flukes, and external parasites.

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

Do not contaminate water. Dispose of containers in an approved landfill or by incineration.

See package insert for complete indications, precautions, warnings, residue information, 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 49 days of slaughter. Because a withdrawal time in milk has not been established, do not use in female dairy cattle of breeding age. A withdrawal period has not been established for this product in pre-ruminating calves. Do not use in calves to be processed for veal.

PRECAUTIONS
For subcutaneous injection in cattle only.
Protect product from light.

Store at 15-30° C (59-86° F)

Made in the UK.

Norbrook Laboratories Limited,
Newry, Co. Down, Northern Ireland.

000000L01

Lot No & Exp Date ▼

000017

Noromectin® PLUS

Injection for Cattle

1% w/v ivermectin and
10% w/v clorsulon
in a sterile solution

ANADA 200-436
Approved by the FDA

250 mL

Norbrook

For the treatment and control of internal parasites, including adult liver flukes, and external parasites.

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

Do not contaminate water. Dispose of containers in an approved landfill or by incineration.

See package insert for complete indications, precautions, warnings, residue information, 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 49 days of slaughter. Because a withdrawal time in milk has not been established, do not use in female dairy cattle of breeding age. A withdrawal period has not been established for this product in pre-ruminating calves. Do not use in calves to be processed for veal.

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

Store at 15-30° C (59-86° F).

Made in the UK.

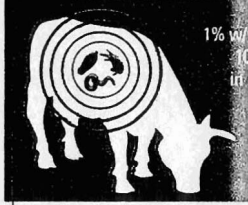
Norbrook Laboratories Limited,
Newry, Co. Down, Northern Ireland.

000000L01

Lot No & Exp Date ▼

Noromectin® PLUS

Injection for Cattle



1% w/v ivermectin and
10% w/v clorsulon
in a sterile solution

ANADA 200-436
Approved by the FDA

500 mL

Norbrook

For the treatment and control of internal parasites, including adult liver flukes, and external parasites.

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

Do not contaminate water. Dispose of containers in an approved landfill or by incineration.

See package insert for complete indications, precautions, warnings, residue information, 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 49 days of slaughter. Because a withdrawal time in milk has not been established, do not use in female dairy cattle of breeding age. A withdrawal period has not been established for this product in pre-ruminating calves. Do not use in calves to be processed for veal.

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

Store at 15-30° C (59-86° F).

Made in the UK.

Norbrook Laboratories Limited,
Newry, Co. Down,
Northern Ireland.

000000L01

Lot No & Exp Date ▼

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000020

Noromectin® PLUS

Injection for Cattle

1% w/v ivermectin and 10% w/v clorsulon in a sterile solution

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

INDICATIONS

Noromectin Plus (ivermectin and clorsulon) is indicated for the treatment and control of gastrointestinal round-worms (including inhibited *Ostertagia ostertagi* larvae), lungworms, adult liver flukes, grubs (note insert precautions), sucking lice, and mange mites (cattle scab (note insert indications)).

See package insert for complete indications and use directions. The dosage level of clorsulon supplied by Noromectin Plus is effective only against adult liver flukes (*Fasciola hepatica*).

RECOMMENDED DOSE

Noromectin Plus should be given only by subcutaneous injection at a dose volume of 1 mL per 110 lb (50 kg) body weight. This volume will deliver 10 mg ivermectin and 100 mg clorsulon.

This bottle is designed for use with automatic syringe equipment or with single dose syringes. It contains enough solution to treat ten 550 lb cattle. For example:

Body Weight (lb)	Dose (mL)	Doses per Pack
220	2	25
330	3	16
440	4	12
550	5	10
660	6	8
770	7	7
880	8	6
990	9	5
1100	10	5

Divide doses greater than 10 mL between two injection sites to reduce occasional transitory discomfort or site reaction.

Noromectin® PLUS

Injection for Cattle

1% w/v ivermectin and 10% w/v clorsulon in a sterile solution

Noromectin Plus (ivermectin and clorsulon) combines ivermectin for internal and external parasite control and clorsulon, which effectively controls adult liver flukes.

Made in the UK.

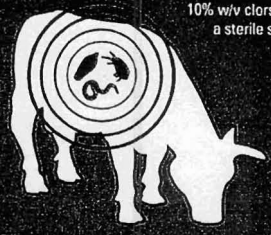
Norbrook Laboratories Limited

ANADA 200-436 Approved by the FDA

Noromectin® PLUS

Injection for Cattle

1% w/v ivermectin and 10% w/v clorsulon in a sterile solution



Treats 10 - 550 lb Cattle

For the treatment and control of internal parasites, including adult liver flukes, and external parasites.

50 mL

Norbrook®

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Noromectin® PLUS

Injection for Cattle

1% w/v ivermectin and 10% w/v clorsulon in a sterile solution

TAKE TIME OBSERVE LABEL DIRECTIONS

ANIMAL SAFETY

In breeding animals (bulls and cows), ivermectin and clorsulon used at the recommended level had no effect on breeding performance.

WARNING

NOT FOR USE IN HUMANS.

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

RESIDUE INFORMATION:

Do not treat cattle within 49 days of slaughter. Because a withdrawal time in milk has not been established, do not use in female dairy cattle of breeding age. A withdrawal period has not been established for this product in pre-ruminating calves. Do not use in calves to be processed for veal.

PRECAUTIONS

For subcutaneous injection in cattle only.

This product is not for intravenous or intramuscular use.

Protect product from light.

Store at 15-30° C (59-86° F).

Noromectin Plus (ivermectin and clorsulon) Injection for Cattle has been developed specifically for use in cattle **only**. This product should not be used in other animal species as severe adverse reactions, including fatalities in dogs, may result.

Do not contaminate water by direct application or by improper disposal of drug containers. Dispose of containers in an approved landfill or by incineration.

Noromectin® PLUS

Injection for Cattle

1% w/v ivermectin and 10% w/v clorsulon in a sterile solution

50 mL

Lot No & Exp Date ▼

000021

Noromectin® PLUS

Injection for Cattle

1% w/v ivermectin and 10% w/v clorsulon in a sterile solution

Lot No & Exp Date ▼

100 mL

Noromectin® PLUS

Injection for Cattle

1% w/v ivermectin and 10% w/v clorsulon in a sterile solution

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

INDICATIONS
Noromectin Plus (ivermectin and clorsulon) is indicated for the treatment and control of gastrointestinal round-worms (including inhibited *Ostertagia ostertagi* larvae), lungworms, adult liver flukes, grubs (note insert precautions), sucking lice, and mange mites (cattle scab (note insert indications)).

See package insert for complete indications and use directions. The dosage level of clorsulon supplied by Noromectin Plus is effective only against adult liver flukes (*Fasciola hepatica*).

RECOMMENDED DOSE
Noromectin Plus should be given only by subcutaneous injection at a dose volume of 1 mL per 110 lb (50 kg) body weight. This volume will deliver 10 mg ivermectin and 100 mg clorsulon.

This bottle is designed for use with automatic syringe equipment or with single dose syringes. It contains enough solution to treat twenty 550 lb cattle. For example:

Body Weight (lb)	Dose (mL)	Doses per Pack
220	2	50
330	3	33
440	4	25
550	5	20
660	6	16
770	7	14
880	8	12
990	9	11
1100	10	10

Divide doses greater than 10 mL between two injection sites to reduce occasional transitory discomfort or site reaction.

Noromectin® PLUS

Injection for Cattle

1% w/v ivermectin and 10% w/v clorsulon in a sterile solution

Noromectin Plus (ivermectin and clorsulon) combines ivermectin for internal and external parasite control and clorsulon, which effectively controls adult liver flukes.

Made in the UK.

Norbrook Laboratories Limited

ANADA 200-436 Approved by the FDA

Noromectin® PLUS

Injection for Cattle

1% w/v ivermectin and 10% w/v clorsulon in a sterile solution

Treats 20 - 550 lb Cattle

For the treatment and control of internal parasites, including adult liver flukes, and external parasites.

100 mL

Norbrook

Noromectin® PLUS

Injection for Cattle

1% w/v ivermectin and 10% w/v clorsulon in a sterile solution

TAKE TIME — OBSERVE LABEL DIRECTIONS

ANIMAL SAFETY
In breeding animals (bulls and cows), ivermectin and clorsulon used at the recommended level had no effect on breeding performance.

WARNING
NOT FOR USE IN HUMANS.
Keep this and all drugs out of the reach of children.

RESIDUE INFORMATION:
Do not treat cattle within 49 days of slaughter. Because a withdrawal time in milk has not been established, do not use in female dairy cattle of breeding age. A withdrawal period has not been established for this product in pre-ruminating calves. Do not use in calves to be processed for veal.

PRECAUTIONS
For subcutaneous injection in cattle only.
This product is not for intravenous or intramuscular use.
Protect product from light.

Store at 15-30° C (59-86° F)

Noromectin Plus (ivermectin and clorsulon) Injection for Cattle has been developed specifically for use in cattle only. This product should not be used in other animal species as severe adverse reactions, including fatalities in dogs, may result.
Do not contaminate water by direct application or by improper disposal of drug containers. Dispose of containers in an approved landfill or by incineration.

BEST AVAILABLE COPY

Noromectin® PLUS

Injection for Cattle

1% w/v ivermectin and 10% w/v clorsulon in a sterile solution

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

INDICATIONS:
Noromectin Plus (ivermectin and clorsulon) is indicated for the treatment and control of gastrointestinal round-worms (including inhibited *Ostertagia ostertagi* larvae), lungworms, adult liver flukes, grubs (note insert precautions), sucking lice, and mange mites (cattle scab (note insert indications)). See package insert for complete indications and use directions.

The dosage level of clorsulon supplied by Noromectin Plus is effective only against adult liver flukes (*Fasciola hepatica*).

RECOMMENDED DOSE:
Noromectin Plus should be given only by subcutaneous injection at a dose volume of 1 mL per 110 lb (50 kg) body weight. This volume will deliver 10 mg ivermectin and 100 mg clorsulon.

This bottle is designed for use with automatic syringe equipment only. It contains enough solution to treat fifty 550 lb cattle. For example:

Body Weight (lb)	Dose (mL)	Doses per Pack
220	2	25
330	3	83
440	4	62
550	5	50
660	6	41
770	7	35
880	8	31
990	9	27
1100	10	25

Divide doses greater than 10 mL between two injection sites to reduce occasional transitory discomfort or site reaction.

Noromectin® PLUS

Injection for Cattle

1% w/v ivermectin and 10% w/v clorsulon in a sterile solution

Noromectin Plus (ivermectin and clorsulon) combines ivermectin for internal and external parasite control and clorsulon, which effectively controls adult liver flukes.

Made in the UK.

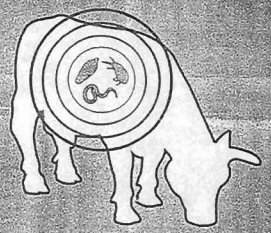
Norbrook Laboratories Limited.

ANADA 200-439 Approved by the FDA

Noromectin® PLUS

Injection for Cattle

1% w/v ivermectin and 10% w/v clorsulon in a sterile solution



Treats 50 - 550 lb Cattle

For the treatment and control of internal parasites, including adult liver flukes, and external parasites.

250 mL

Norbrook

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Noromectin® PLUS

Injection for Cattle

1% w/v ivermectin and 10% w/v clorsulon in a sterile solution

TAKE TIME: OBSERVE LABEL DIRECTIONS

ANIMAL SAFETY:
In breeding animals (bulls and cows), ivermectin and clorsulon used at the recommended level had no effect on breeding performance.

WARNING
NOT FOR USE IN HUMANS.
Keep this and all drugs out of the reach of children.

RESIDUE INFORMATION:
Do not treat cattle within 49 days of slaughter. Because a withdrawal time in milk has not been established, do not use in female dairy cattle of breeding age. A withdrawal period has not been established for this product in pre-ruminating calves. Do not use in calves to be processed for veal.

PRECAUTIONS
Use automatic syringe equipment only.
For subcutaneous injection in cattle only.
This product is not for intravenous or intramuscular use.
Protect product from light.

Store at 15-30° C (59-86° F).

Noromectin Plus (ivermectin and clorsulon) Injection for Cattle has been developed specifically for use in cattle **only**. This product should not be used in other animal species as severe adverse reactions, including fatalities in dogs, may result.
Do not contaminate water by direct application or by improper disposal of drug containers. Dispose of containers in an approved landfill or by incineration.

Noromectin® PLUS

Injection for Cattle

1% w/v ivermectin and 10% w/v clorsulon in a sterile solution

Made in the UK.

Norbrook Laboratories Limited.

LOT No. & Exp. Date

250 mL

BEST AVAILABLE COPY

000023

500 mL

Noromectin PLUS

Injection for Cattle

1% w/v ivermectin and 10% w/v clorsulon in a sterile solution

Lot No & Exp. Date ▼

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Noromectin® PLUS

Injection for Cattle

1% w/v ivermectin and 10% w/v clorsulon in a sterile solution

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

INDICATIONS

Noromectin Plus (ivermectin and clorsulon) is indicated for the treatment and control of gastrointestinal round-worms (including inhibited *Ostertagia ostertagi* larvae), lungworms, adult liver flukes, grubs (note insert precautions), sucking lice, [illegible] (cattle scab (note insert indications)). [illegible] insert for complete indications and use directions.

The dosage level of clorsulon supplied by Noromectin Plus is effective only against adult liver flukes (*Fasciola hepatica*).

RECOMMENDED DOSE

Noromectin Plus should be given only by subcutaneous injection at a dose volume of 1 mL per 110 lb (50 kg) body weight. This volume will deliver 10 mg ivermectin and 100 mg clorsulon.

This bottle is designed for use with automatic syringe equipment only. It contains enough solution to treat one hundred 550 lb cattle. For example:

Body Weight (lb)	Dose (mL)	Doses per Pack
220	2	250
330	3	166
440	4	125
550	5	100
660	6	83
770	7	71
880	8	62
990	9	55
1100	10	50

Divide doses greater than 10 mL between two injection sites to reduce occasional transitory discomfort or site reaction.

Noromectin® PLUS

Injection for Cattle

1% w/v ivermectin and 10% w/v clorsulon in a sterile solution

Noromectin Plus (ivermectin and clorsulon) combines ivermectin for internal and external parasite control and clorsulon which effectively controls adult liver flukes.

Made in the UK

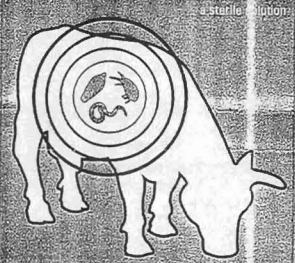
Norbrook Laboratories Limited

ANADA 200-436 Approved by the FDA

Noromectin® PLUS

Injection for Cattle

1% w/v ivermectin and 10% w/v clorsulon in a sterile solution



Treats 100 - 550 lb Cattle

For the treatment and control of internal parasites, including adult liver flukes, and external parasites.

500 mL

Norbrook

Noromectin® PLUS

Injection for Cattle

1% w/v ivermectin and 10% w/v clorsulon in a sterile solution

TAKE TIME OBSERVE LABEL DIRECTIONS

ANIMAL SAFETY

In breeding animals (bulls and cows), ivermectin and clorsulon used at the recommended level had no effect on breeding performance.

WARNING

NOT FOR HUMAN USE

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

RESIDUE INFORMATION:

Do not treat cattle within 49 days of slaughter. Because a withdrawal time in milk has not been established, do not use in female dairy cattle of breeding age. A withdrawal period has not been established for this product in pre-ruminating calves. Do not use in calves to be processed for veal.

PRECAUTIONS

Use automatic syringe equipment only.
For subcutaneous injection in cattle only.
This product is not for intravenous or intramuscular use.
Protect product from light.

Store at 15-30° C (59-86° F)

Noromectin Plus (ivermectin and clorsulon) Injection for Cattle has been developed specifically for use in cattle only. This product should not be used in other animal species as severe adverse reactions, including fatalities in dogs, may result.
Do not contaminate water by direct application or by improper disposal of drug containers. Dispose of containers in an approved landfill or by incineration.

ANADA 200-436 Approved by the FDA

Noromectin® PLUS

Injection for Cattle

1% w/v ivermectin and 10% w/v clorsulon in a sterile solution

For the effective treatment and control of internal parasites, including adult liver flukes, and external parasites. Consult your veterinarian for assistance in the diagnosis, treatment and control of parasitism.

INTRODUCTION

The ability of ivermectin to deliver internal and external parasite control has been proven in cattle markets around the world. Now, Norbrook Laboratories Limited combines ivermectin with clorsulon, an effective adult flukicide.

A single injection of Noromectin Plus (ivermectin and clorsulon) offers all the benefits of an ivermectin injection plus control of adult *Fasciola hepatica.*

The dosage level of clorsulon supplied by Noromectin Plus is effective only against adult liver flukes *(Fasciola hepatica).*

PRODUCT DESCRIPTION

Noromectin Plus is a ready-to-use sterile solution containing 1% w/v ivermectin, 10% clorsulon, 40% glycerol formal, and propylene glycol, q.s. ad 100%. It is formulated to deliver the recommended dose level of 200 mcg ivermectin/kg and 2 mg clorsulon/kg given subcutaneously behind the shoulder at the rate of 1 mL per 110 lb (50 kg) body weight.

MODE OF ACTION

Ivermectin is a member of the macrocyclic lactone class of endectocides which have a unique mode of action. Compounds of the 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 margin of safety for compounds of this class 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.

Clorsulon is rapidly absorbed into the circulating blood. Erythrocytes with bound drug as well as plasma are ingested by *Fasciola hepatica.* Adult *Fasciola hepatica* are killed by clorsulon because of inhibition of enzymes in the glycolytic pathway, which is their primary source of energy.

INDICATIONS

Noromectin Plus Injection is indicated for the effective treatment and control of the following parasites in cattle:

Gastrointestinal Roundworms (adults and fourth-stage larvae):
Ostertagia ostertagi (including inhibited *O. ostertagi*)
O. lyrata
Haemonchus placei
Trichostrongylus axei
T. colubriformis
Cooperia oncophora
C. punctata
C. pectinata
Bunostomum phlebotomum
Nematodirus helvetianus (adults only)
N. spathiger (adults only)
Oesophagostomum radiatum

Lungworms (adults and fourth-stage larvae):
Dictyocaulus viviparus

Liver Flukes:
Fasciola hepatica (adults only)

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

Sucking Lice:
Linognathus vituli
Haematopinus eurysternus
Solenopotes capillatus

Mange Mites (cattle scab*):
Psoroptes ovis (syn. *P. communis* var. *bovis*)
Sarcoptes scabiei var. *bovis*

Persistent Activity

Ivermectin and clorsulon injection has been proved to effectively control infections and to protect cattle from reinfection with *Dictyocaulus viviparus* and *Oesophagostomum radiatum* for 28 days after treatment; *Ostertagia ostertagi, Trichostrongylus axei* and *Cooperia punctata* for 21 days after treatment; *Haemonchus placei,* and *Cooperia oncophora* for 14 days after treatment.

* Ivermectin has been approved as a scabicide by USDA/APHIS. Federal regulations require that cattle infested with or exposed to scabies (i.e., infestations with *Psoroptes ovis*) be treated. Ivermectin when used according to label instructions meets this requirement. Treated cattle may be shipped interstate, but they must not be mixed with other cattle for 14 days following treatment. The federal regulations make no restriction on the movement of cattle not affected with or exposed to scabies. However, individual states have additional regulations to govern the interstate shipment of cattle and the regulatory veterinarian in the state of destination should be consulted for applicable regulations on the use of ivermectin in the control of scabies.

DOSAGE

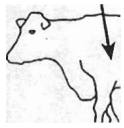
Noromectin Plus should be given only by subcutaneous injection at a dose volume of 1 mL per 110 lb (50 kg) body weight. This volume will deliver 10 mg ivermectin and 100 mg clorsulon. For example:

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

ADMINISTRATION

Noromectin Plus (ivermectin and clorsulon) Injection is to be given subcutaneously only. Animals should be appropriately restrained to achieve the proper route of administration. Use of a 16-gauge, 1/2" to 3/4" sterile needle

is recommended. Inject the solution subcutaneously (under the skin) behind the shoulder (see illustration).



Any single-dose syringe or standard automatic syringe equipment may be used with the 50 mL or 100 mL pack size. When using the 250 mL or 500 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.

The viscosity of the product increases in cool temperatures. Administering Noromectin Plus at temperatures of 5 °C (41 °F) or below may be difficult. Users can make dosing easier by warming both the product and injection equipment to about 15 °C (59 °F).

ANIMAL SAFETY
In breeding animals (bulls and cows), ivermectin and clorsulon used at the recommended level had no effect on breeding performance.

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 Norbrook, Inc. at 1-913-599-5777.

RESIDUE INFORMATION: Do not treat cattle within 49 days of slaughter. Because a withdrawal time in milk has not been established, do not use in female dairy cattle of breeding age. A withdrawal period has not been established for this product in pre-ruminating calves. Do not use in calves to be processed for veal.

PRECAUTIONS
Transitory discomfort has been observed in some cattle following subcutaneous administration. Soft-tissue swelling at the injection site has also been observed. These reactions have disappeared without treatment. Divide doses greater than 10 mL between two injection sites to reduce occasional discomfort or site reaction. Different injection sites should be used for other parenteral products.

Noromectin Plus Injection has been developed specifically for use in cattle **only**. This product should not be used in other animal species as severe adverse reactions, including fatalities in dogs, may result.

For subcutaneous injection in cattle **only**.

This product is not for intravenous or intramuscular use.

When to Treat Cattle with Grubs
Noromectin Plus 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 undesirable host-parasite reactions including the possibility of fatalities. Killing *Hypoderma lineatum* when it is in the tissue surrounding the esophagus (gullet) may cause bloat; killing *H. bovis* when it is in the vertebral canal may cause staggering or paralysis. These reactions are not specific to treatment with Noromectin Plus, 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 Noromectin Plus after the end of the heel fly season may be retreated with ivermectin during the winter for internal parasites, mange mites, or sucking lice, without danger of grub-related reactions. A planned parasite control program is recommended.

STORAGE
Protect product from light.
Store at 15-30° C (59-86° F).

ENVIRONMENTAL SAFETY
Studies indicate that when ivermectin comes in contact with soil it readily and tightly binds to the soil and becomes inactive over time. Free ivermectin may adversely affect fish and certain aquatic organisms. Do not permit water runoff from feedlots to enter lakes, streams, or ponds. 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, ivermectin 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.

HOW SUPPLIED
Noromectin Plus Injection 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.

The 100 mL pack is a multiple-dose, rubber-capped bottle. Each bottle contains sufficient solution to treat 20 head of 550 lb (250 kg) cattle.

The 250 mL pack is a multiple-dose, rubber-capped bottle designed for use with automatic syringe equipment. Each bottle contains sufficient solution to treat 50 head of 550 lb (250 kg) cattle.

The 500 mL pack is a multiple-dose, rubber-capped bottle designed for use with automatic syringe equipment. Each bottle contains sufficient solution to treat 100 head of 550 lb (250 kg) cattle.

Made in the UK.

Norbrook Laboratories Limited,
Newry, Co. Down, Northern Ireland.

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Norbrook®

Consult your veterinarian for assistance in the diagnosis, treatment, and control of parasitism.
Do not contaminate water. Dispose of containers in an approved landfill or by incineration.
See package insert for complete indications, precautions, warnings, residue information, 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 49 days of slaughter. Because a withdrawal time in milk has not been established, do not use in female dairy cattle of breeding age. A withdrawal period has not been established for this product in preruminating calves. Do not use in calves to be processed for veal.

NADA 140-833
Approved by the FDA Product **4130612**

Ivomec® *Plus*

(1% w/v ivermectin and 10% w/v clorsulon in a sterile solution)

Injection for Cattle

For the treatment and control of internal parasites, including adult liver flukes, and external parasites.

50 mL

1021-1050-00 Rev. 08-2004

Lot No:

Exp Date:

PRECAUTIONS
For subcutaneous injection in cattle only.
Protect product from light.

IVOMEC is a registered trademark of Merial Limited.
Made in The Netherlands.
U.S. Pat. 4,199,569 & 4,853,372
Merial Limited, Duluth, Georgia, U.S.A.
H23868(US)

MERIAL

696604/070904C

NADA 140-833. Approved by the FDA

Product **413076**

Ivomec® *Plus*

(1% w/v ivermectin and 10% w/v clorsulon in a sterile solution)

Injection for Cattle

For the treatment and control of internal parasites, including adult liver flukes, and external parasites.

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

Do not contaminate water. Dispose of containers in an approved landfill or by incineration.

See package insert for complete indications, precautions, warnings, residue information, and use directions.

WARNING
NOT FOR USE IN HUMANS.
Keep this and all drugs out of the reach of children.

IVOMEC is a registered trademark of Merial Limited.
Made in The Netherlands.
U.S. Pat. 4,199,569 & 4,853,372.
1021-1055-00 Rev. 08-2004

200 mL

RESIDUE INFORMATION: Do not treat cattle within 49 days of slaughter. Because a withdrawal time in milk has not been established, do not use in female dairy cattle of breeding age. A withdrawal period has not been established for this product in pre-ruminating calves. Do not use in calves to be processed for veal.

Lot No:

Exp Date

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

H23869(US)

Merial Limited
3239 Satellite Blvd.
Duluth, Georgia
30096-4640, U.S.A.

MERIAL

69606/080904C

Product

NADA 140-833. Approved by the FDA

Product **413086**

Ivomec® *Plus*

(1% w/v ivermectin and 10% w/v clorsulon in a sterile solution)

Injection for Cattle

For the treatment and control of internal parasites, including adult liver flukes, and external parasites.

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

- Do not contaminate water. Dispose of containers in an approved landfill or by incineration.

See package insert for complete indications, precautions, warnings, residue information, 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 49 days of slaughter. Because a withdrawal time in milk has not been established, do not use in female dairy cattle of breeding age. A withdrawal period has not been established for this product in pre-ruminating calves. Do not use in calves to be processed for veal.

500 mL

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

IVOMEC is a registered trademark of Merial Limited.
Made in The Netherlands.
U.S. Pat. 4,199,569 & 4,853,372.

H23871(US)

Lot No:

Exp Date

1021-1059-00
Rev. 08-2004

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Duluth, Georgia
30096-4640, U.S.A.

MERIAL

H23868(US)
69605/070904E
300-720-021/050a

Ivomec® *Plus*

(1% w/v ivermectin and 10% w/v clorsulon in a sterile solution)

Injection for Cattle

WARNING
NOT FOR USE IN HUMANS.
Keep this and all drugs out of the reach of children.

RESIDUE INFORMATION: Do not treat cattle within 49 days of slaughter. Because a withdrawal time in milk has not been established, do not use in female dairy cattle of breeding age. A withdrawal period has not been established for this product in pre-ruminating calves. Do not use in calves to be processed for veal.

PRECAUTIONS

For subcutaneous injection in cattle only.

This product is not for intravenous or intramuscular use.

Protect product from light.

IVOMEC® Plus (ivermectin and clorsulon) Injection for Cattle has been developed specifically for use in cattle **only.** This product should not be used in other animal species as severe adverse reactions, including fatalities in dogs, may result.

Do not contaminate water by direct application or by improper disposal of drug containers. Dispose of containers in an approved landfill or by incineration.

1030-1051-00 Rev. 08-2004

Product
4130612

Ivomec® *Plus*

(1% w/v ivermectin and 10% w/v clorsulon in a sterile solution)

Injection for Cattle

Treats 10–550 lb Cattle

For the treatment and control of internal parasites, including adult liver flukes, and external parasites.

50 mL

MERIAL

Ivomec® *Plus*

(1% w/v ivermectin and 10% w/v clorsulon in a sterile solution)

Injection for Cattle

SEALED FOR SECURITY.

IF BROKEN, DO NOT ACCEPT.

2

Ivomec® Plus

(1% w/v ivermectin and 10% w/v clorsulon in a sterile solution)

Injection for Cattle

IVOMEC and Cattle Head Logo are registered trademarks of Merial Limited.

Made in The Netherlands.

U.S. Pat. 4,199,569 & 4,853,372

NADA 140-833, Approved by the FDA

Merial Limited
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Duluth, Georgia
30096-4640, U.S.A.

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Ivomec® Plus

(1% w/v ivermectin and 10% w/v clorsulon in a sterile solution)

Injection for Cattle

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

INDICATIONS

IVOMEC® Plus (ivermectin and clorsulon) is indicated for the treatment and control of gastrointestinal round-worms (including inhibited *Ostertagia ostertagi* larvae), lungworms, adult liver flukes, grubs (note insert precautions), sucking lice, and mange mites (cattle scab (note insert indications)). See package insert for complete indications and use directions.

The dosage level of clorsulon supplied by IVOMEC Plus is effective only against adult liver flukes (*Fasciola hepatica*).

RECOMMENDED DOSE

IVOMEC Plus should be given only by subcutaneous injection at a dose volume of 1 mL per 110 lb (50 kg) body weight. This volume will deliver 10 mg ivermectin and 100 mg clorsulon.

This bottle is designed for use with automatic syringe equipment or with single dose syringes. It contains enough solution to treat ten 550 lb cattle. For example:

Body Weight (lb)	Dose (mL)	Doses per Pack
220	2	25
330	3	16
440	4	12
550	5	10
660	6	8

Over 660 lb body weight, give 1 mL per 110 lb body weight

Divide doses greater than 10 mL between two injection sites to reduce occasional transitory discomfort or site reaction.

ANIMAL SAFETY

In breeding animal (bulls and cows), ivermectin and clorsulon used at the recommended level had no effect on breeding performance.

Lot No:

Exp Date:

50 mL

Product 4130612

SEALED FOR SECURITY.

IF BROKEN, DO NOT ACCEPT.

1

H23869(US)
69608/170904E
300-720-001/093H

NADA 140-833,
Approved by the FDA

Product
413076

Ivomec® Plus

(1% w/v ivermectin and
10% w/v clorsulon in a sterile solution)

Injection for Cattle

ANIMAL SAFETY

In breeding animal (bulls and cows), ivermectin and clorsulon used at the recommended level had no effect on breeding performance.

WARNING
NOT FOR USE IN HUMANS.
Keep this and all drugs out of the reach of children.

RESIDUE INFORMATION: Do not treat cattle within 49 days of slaughter. Because a withdrawal time in milk has not been established, do not use in female dairy cattle of breeding age. A withdrawal period has not been established for this product in pre-ruminating calves. Do not use in calves to be processed for veal.

PRECAUTIONS

Use automatic syringe equipment only.
For subcutaneous injection in cattle only.
This product is not for intravenous or intramuscular use.
Protect product from light.

IVOMEC® Plus (ivermectin and clorsulon) Injection for Cattle has been developed specifically for use in cattle **only**. This product should not be used in other animal species as severe adverse reactions, including fatalities in dogs, may result.
Do not contaminate water by direct application or by improper disposal of drug containers. Dispose of containers in an approved landfill or by incineration.

1030-1056-00 Rev. 08-2004

Ivomec® Plus
(1% w/v ivermectin and
10% w/v clorsulon in a sterile solution)
Injection for Cattle

Treats 40–550 lb Cattle

For the treatment and control of internal parasites, including adult liver flukes, and external parasites.

200 mL

MERIAL

Ivomec® Plus
(1% w/v ivermectin and
10% w/v clorsulon in a sterile solution)

Ivomec® Plus

(1% w/v ivermectin and 10% w/v clorsulon in a sterile solution)

Injection for Cattle

IVOMEC® Plus (ivermectin and clorsulon) combines ivermectin for internal and external parasite control and clorsulon, which effectively controls adult liver flukes.

IVOMEC and Cattle Head Logo are registered trademarks of Merial Limited.

Made in The Netherlands.

U.S. Pat. 4,199,569 & 4,853,372

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Duluth, Georgia
30096-4640, U.S.A.

3 5060447471 5

Product 413076

Lot No:

Exp Date

200 mL

SEALED FOR SECURITY.

IF BROKEN, DO NOT ACCEPT.

Ivomec® Plus

(1% w/v ivermectin and 10% w/v clorsulon in a sterile solution)

Injection for Cattle

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

INDICATIONS

IVOMEC® Plus (ivermectin and clorsulon) is indicated for the treatment and control of gastrointestinal roundworms (including inhibited *Ostertagia ostertagi* larvae), lungworms, adult liver flukes, grubs (note insert precautions), sucking lice, and mange mites (cattle scab [note insert indications]). See package insert for complete indications and use directions.

The dosage level of clorsulon supplied by IVOMEC Plus is effective only against adult liver flukes (*Fasciola hepatica*).

RECOMMENDED DOSE

IVOMEC Plus should be given only by subcutaneous injection at a dose volume of 1 mL per 110 lb (50 kg) body weight. This volume will deliver 10 mg ivermectin and 100 mg clorsulon.

This bottle is designed for use with automatic syringe equipment only. It contains enough solution to treat forty 550 lb cattle. For example:

Body Weight (lb)	Dose (mL)	Doses per Pack
220	2	100
330	3	66
440	4	50
550	5	40
660	6	33
770	7	28
880	8	25
990	9	22
1100	10	20

Divide doses greater than 10 mL between two injection sites to reduce occasional transitory discomfort or site reaction.

NADA 140-833,
Approved by the FDA

Product
413086

Ivomec® *Plus*

(1% w/v ivermectin and 10% w/v clorsulon in a sterile solution)

Injection for Cattle

ANIMAL SAFETY

In breeding animal (bulls and cows), ivermectin and clorsulon used at the recommended level had no effect on breeding performance.

WARNING
NOT FOR USE IN HUMANS.
Keep this and all drugs out of the reach of children.

RESIDUE INFORMATION:
Do not treat cattle within 49 days of slaughter. Because a withdrawal time in milk has not been established, do not use in female dairy cattle of breeding age. A withdrawal period has not been established for this product in pre-ruminating calves. Do not use in calves to be processed for veal.

PRECAUTIONS

Use automatic syringe equipment only.

For subcutaneous injection in cattle only.

This product is not for intravenous or intramuscular use.

Protect product from light.

IVOMEC® Plus (ivermectin and clorsulon) Injection for Cattle has been developed specifically for use in cattle **only**. This product should not be used in other animal species as severe adverse reactions, including fatalities in dogs, may result.

Do not contaminate water by direct application or by improper disposal of drug containers. Dispose of containers in an approved landfill or by incineration.

1030-1061-00 Rev. 08-2004

Ivomec® *Plus*

(1% w/v ivermectin and 10% w/v clorsulon in a sterile solution)

Injection for Cattle

Treats 100–550 lb Cattle

For the treatment and control of internal parasites, including adult liver flukes, and external parasites.

500 mL

MERIAL

Ivomec® *Plus*

(1% w/v ivermectin and 10% w/v clorsulon in a sterile solution)

Injection for Cattle

Ivomec® *Plus*

(1% w/v ivermectin and 10% w/v clorsulon in a sterile solution)

Injection for Cattle

IVOMEC® Plus (ivermectin and clorsulon) combines ivermectin for internal and external parasite control and clorsulon, which effectively controls adult liver flukes.

IVOMEC and Cattle Head Logo are registered trademarks of Merial Limited.

Made in The Netherlands.

U.S. Pat. 4,199,569 & 4,853,372

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30096-4640, U.S.A.

3 50604-47472 2

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

INDICATIONS

IVOMEC® Plus (ivermectin and clorsulon) is indicated for the treatment and control of gastrointestinal round-worms (including inhibited *Ostertagia ostertagi* larvae), lungworms, adult liver flukes, grubs (note insert precautions), sucking lice, and mange mites (cattle scab [note insert indications]). See package insert for complete indications and use directions.

The dosage level of clorsulon supplied by IVOMEC Plus is effective only against adult liver flukes (*Fasciola hepatica*).

RECOMMENDED DOSE

IVOMEC Plus should be given only by subcutaneous injection at a dose volume of 1 mL per 110 lb (50 kg) body weight. This volume will deliver 10 mg ivermectin and 100 mg clorsulon.

This bottle is designed for use with automatic syringe equipment only. It contains enough solution to treat one hundred 550 lb cattle. For example:

Body Weight (lb)	Dose (mL)	Doses per Pack
220	2	250
330	3	166
440	4	125
550	5	100
660	6	83
770	7	71
880	8	62

Divide doses greater than 10 mL between two injection sites to reduce occasional transitory discomfort or site reaction.

NADA 140-833, Approved by the FDA

IVOMEC® Plus

(1% w/v ivermectin and 10% w/v clorsulon in a sterile solution)

Injection for Cattle

For the effective treatment and control of internal parasites, including adult liver flukes, and external parasites.

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

INTRODUCTION

The ability of IVOMEC® (ivermectin) to deliver internal and external parasite control has been proven in cattle markets around the world. Now, Merial Limited combines ivermectin, the active ingredient of IVOMEC, with clorsulon, an effective adult flukicide.

A single injection of IVOMEC Plus (ivermectin and clorsulon) offers all the benefits of IVOMEC plus control of adult *Fasciola hepatica*.

The dosage level of clorsulon supplied by IVOMEC Plus is effective only against adult liver flukes *(Fasciola hepatica)*.

PRODUCT DESCRIPTION

IVOMEC Plus is a ready-to-use sterile solution containing 1% w/v ivermectin, 10% clorsulon, 40% glycerol formal, and propylene glycol, q.s. ad 100%. It is formulated to deliver the recommended dose level of 200 mcg ivermectin/kg and 2 mg clorsulon/kg given subcutaneously behind the shoulder at the rate of 1 mL per 110 lb (50 kg) body weight.

MODE OF ACTION

Ivermectin is a member of the macrocyclic lactone class of endectocides which have a unique mode of action. Compounds of the 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 margin of safety for compounds of this class 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.

Clorsulon is rapidly absorbed into the circulating blood. Erythrocytes with bound drug as well as plasma are ingested by *Fasciola hepatica*. Adult *Fasciola hepatica* are killed by clorsulon because of inhibition of enzymes in the glycolytic pathway, which is their primary source of energy.

INDICATIONS

IVOMEC Plus Injection is indicated for the effective treatment and control of the following parasites of cattle:

Gastrointestinal Roundworms (adults and fourth-stage larvae):
Ostertagia ostertagi (including inhibited *O. ostertagi*)
O. lyrata
Haemonchus placei
Trichostrongylus axei
T. colubriformis
Cooperia oncophora
C. punctata
C. pectinata
Bunostomum phlebotomum
Nematodirus helvetianus (adults only)
N. spathiger (adults only)
Oesophagostomum radiatum

Lungworms (adults and fourth-stage larvae):
Dictyocaulus viviparus

Liver Flukes:
Fasciola hepatica (adults only)

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

Sucking Lice:
Linognathus vituli
Haematopinus eurystemus
Solenopotes capillatus

Mange Mites (cattle scab*):
Psoroptes ovis (syn. *P. communis* var. *bovis*)
Sarcoptes scabiei var. bovis

Persistent Activity

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

*Ivermectin has been approved as a scabicide by USDA/APHIS. Federal regulations require that cattle infested with or exposed to scabies (i.e., infestations with *Psoroptes ovis*) be treated. Ivermectin when used according to label instructions meets this requirement. Treated cattle may be shipped interstate, but they must not be mixed with other cattle for 14 days following treatment. The federal regulations make no restriction on the movement of cattle not affected with or exposed to scabies. However, individual states have additional regulations to govern the interstate shipment of cattle and the regulatory veterinarian in the state of destination should be consulted for applicable regulations on the use of ivermectin in the control of scabies.

4130612, 413076, 413086

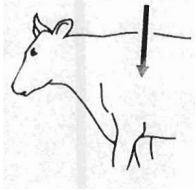
DOSAGE

IVOMEC® Plus should be given only by subcutaneous injection at a dose volume of 1 mL per 110 lb (50 kg) body weight. This volume will deliver 10 mg ivermectin and 100 mg clorsulon. For example:

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

ADMINISTRATION

IVOMEC Plus (ivermectin and clorsulon) Injection is to be given subcutaneously only. Animals should be appropriately restrained to achieve the proper route of administration. Use of a 16-gauge, 1/2" to 3/4" sterile needle is recommended. Inject the solution subcutaneously (under the skin) behind the shoulder (see illustration).



Any single-dose syringe or standard automatic syringe equipment may be used with the 50 mL pack size. When using the 200 mL, 500 mL 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.

The viscosity of the product increases in cool temperatures. Administering IVOMEC Plus at temperatures of 5°C (41°F) or below may be difficult. Users can make dosing easier by warming both the product and injection equipment to about 15°C (59°F).

ANIMAL SAFETY

In breeding animals (bulls and cows), ivermectin and clorsulon used at the recommended level had no effect on breeding performance.

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 49 days of slaughter. Because a withdrawal time in milk has not been established, do not use in female dairy cattle of breeding age. A withdrawal period has not been established for this product in pre-ruminating calves. Do not use in calves to be processed for veal.

PRECAUTIONS

Transitory discomfort has been observed in some cattle following subcutaneous administration. Soft-tissue swelling at the injection site has also been observed. These reactions have disappeared without treatment. Divide doses greater than 10 mL between two injection sites to reduce occasional discomfort or site reaction. Different injection sites should be used for other parenteral products.

IVOMEC Plus Injection has been developed specifically for use in cattle **only**. This product should not be used in other animal species as severe adverse reactions, including fatalities in dogs, may result.

For subcutaneous injection in cattle **only**.

This product is not for intravenous or intramuscular use.

When to Treat Cattle with Grubs

IVOMEC Plus 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 undesirable host-parasite reactions including the possibility of fatalities. Killing *Hypoderma lineatum* when it is in the tissue surrounding the esophagus (gullet) may cause bloat; killing *H. bovis* when it is in the vertebral canal may cause staggering or paralysis. These reactions are not specific to treatment with IVOMEC Plus, but can occur with any successful treatment of grubs. Cattle should be treated either before or after stages of grub development. Consult your veterinarian concerning the proper time for treatment.

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

Protect product from light.

Environmental Safety

Studies indicate that when ivermectin comes in contact with soil it readily and tightly binds to the soil and becomes inactive overtime. Free ivermectin

may adversely affect fish and certain aquatic organisms. Do not permit water runoff from feedlots to enter lakes, streams or ponds. 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, ivermectin 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.

HOW SUPPLIED

IVOMEC® Plus Injection 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.

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.

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.

The 1000 mL pack 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.

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