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23 August 2004

Dr. Lonnie Luther
Quality Assurance Support Team (HFV-102) Room 387
FDA Center for Veterinary Medicine
7500 Standish Place
Rockville, MD 20855

Dear Dr. Luther,

Please find enclosed a suitability petition submitted on behalf of Ancare New Zealand Limited of New Zealand. Ancare requests consideration of this suitability petition to file an ANADA for a different concentration of active in Ivermectin Pour-On for Cattle.

Please call if you have questions.

Sincerely,

Robert Holmes
Business Development Manager
Ancare New Zealand Ltd.

2004P-0383

CPI



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SUITABILITY PETITION

IDENTIFICATION OF PETITIONER:

This Suitability Petition is submitted on behalf of Ancare New Zealand Limited of New Zealand under Section 512 (n)(3) of the Federal Food, Drug, and Cosmetic Act.

ACTION REQUESTED:

The petitioner requests permission from the Commissioner to file an Abbreviated New Animal Drug Application (ANADA) for a different concentration of an approved pioneer product. The pioneer product is Merial's IVOMEC® (ivermectin) Pour-On for Cattle, approved by the Food and Drug Administration under NADA 140-841. A copy of the pioneer product labeling is provided (**Attachment 1**).

The ANADA will provide for ivermectin pour-on for cattle containing 10 mg ivermectin per mL of pour-on for topical administration to cattle rather than the 5 mg/mL concentration of the pioneer product. Both the proposed and the pioneer products are delivered topically. Both the proposed and pioneer products are provided to affected animals at the rate of 500 mcg ivermectin per kilogram of body weight for the effective control of the listed parasites.

The product labeling will provide for indications, recommended dosages, and precautions identical to the pioneer product. Draft labeling for the proposed product is provided (**Attachment II**).

The proposed product label will differ from the pioneer product specifically as follows:

- 1) The generic product will contain 10 mg/mL ivermectin rather than 5 mg/mL and the dosage instructions will recommended 0.5 mL for each 22 pounds of body weight rather than 1 mL for each 22 pounds.
- 2) The product will be delivered using a container and metering system that can be set to deliver half of the volumes required for the less concentrated pioneer product. The container types and net contents of the containers will differ from the pioneer product. Actual containers are yet to be determined.
- 3) The vehicle for the formulation will not be alcohol-based as used by the pioneer product. As such, cautions on the labeling addressing flammability will be eliminated for the generic product and storage recommendations may be revised depending upon stability characteristics.

STATEMENT OF GROUNDS:

The proposed product contains the same active ingredient and will be labeled with the same indications, recommended dose rates, contraindications, precautions and warnings as the approved pioneer product. Because the same amount of active drug will be delivered topically, the clinical effect for both drugs is expected to be similar.

ENVIRONMENTAL IMPACT:

The action of submitting this Suitability Petition and its review by the FDA - Center for Veterinary

Medicine is not expected to have an environmental impact. The action requested qualifies for categorical exclusion under 21 CFR Part 25.30(h) from the requirement for an environmental assessment and, to the best of the sponsor's knowledge, no extraordinary circumstances exist.

ECONOMIC IMPACT:

An "Economic Impact" analysis of this action will be provided if requested by the Commissioner.

CERTIFICATION:

Ancare New Zealand Limited certifies that this suitability petition contains all information known to them which is unfavorable to the petition.


Robert Holmes

Business Development Manager
Ancare New Zealand Ltd.
First Floor, 17 Shea Terrace
Takapuna, Auckland
PO Box 36240, Northcote
Auckland, New Zealand

08/23/04
Date

Attachments

1. Pioneer Product Label
2. Proposed Product Label

ATTACHMENT 1
Pioneer Product Labeling



09158202



9158202



09158202



9158202

IVOMEC[®]
(ivermectin)



pour-on for cattle

Contains 5 mg ivermectin/mL

Parasiticide

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

Introduction

IVOMEC[®] (ivermectin) Pour-On delivers internal and external parasite control in one convenient low-volume application. Discovered and developed by scientists from Merck Research Laboratories, IVOMEC Pour-On contains ivermectin, a unique chemical entity.

Indications

IVOMEC Pour-On applied at the recommended dose level of 500 mcg/kg is indicated for the effective control of these parasites.

Gastrointestinal Roundworms

- Ostertagia ostertagi* (adults and L₄)
(including inhibited stage)
- Haemonchus placei* (adults and L₄)
- Trichostrongylus axei* (adults and L₄)
- T. colubriformis* (adults and L₄)
- Cooperia* spp. (adults and L₄)
- Strongyloides papillosus* (adults)
- Oesophagostomum radiatum* (adults and L₄)
- Trichuris* spp. (adults)

Lungworms

- Dictyocaulus viviparus* (adults and L₄)

Cattle Grubs

- Hypoderma bovis* (parasitic stages)
- H. lineatum*

Mites

- Sarcoptes scabiei* var. *bovis*

Lice

- Linognathus vituli*
- Haematopinus eurysternus*
- Damalinia bovis*
- Solenopotes capillatus*

Horn Flies

- Haematobia irritans*

Persistent Activity

IVOMEC Pour-On has been proved to effectively control infections and to protect cattle from re-infection with *Ostertagia ostertagi*, *Oesophagostomum radiatum*, *Haemonchus placei*, *Trichostrongylus axei*, *Cooperia punctata* and *Cooperia oncophora* for 14 days after treatment

Treatment of Cattle for Horn Flies

IVOMEC Pour-On controls horn flies (*Haematobia irritans*) for up to 28 days after dosing. For best results IVOMEC Pour-On should be part of a parasite control program for both internal and external parasites based on the epidemiology of these parasites. Consult your veterinarian or an entomologist for the most effective timing of applications.

Dosage

The dose rate is 1 mL for each 22 lb of body weight. The formulation should be applied along the topline in a narrow strip extending from the withers to the tailhead.

Administration

Squeeze-Measure-Pour System (8.5 fl oz/250 mL Bottle with 25 mL Metering Cup)

Attach the metering cup to the bottle.

Set the dose by turning the top section of the cup to align the correct body weight with the pointer on the knurled cap. When body weight is between markings, use the higher setting.

Hold the bottle upright and squeeze it to deliver a slight excess of the required dose as indicated by the calibration lines.

By releasing the pressure, the dose automatically adjusts to the correct level. Tilt the bottle to deliver the dose. The off (STOP) position will close the system between dosing.

Squeeze-Measure-Pour System (33.8 fl oz/1 Liter Bottle with 50 mL Metering Cup)

Attach the metering cup to the bottle.

Set the dose by turning the top section of the cup to align the correct body weight with the pointer on the knurled cap. When body weight is between markings, use the higher setting.

Hold the bottle upright and squeeze it to deliver a slight excess of the required dose as indicated by the calibration lines.

By releasing the pressure, the dose automatically adjusts to the correct level. Tilt the bottle to deliver the dose. When 220 lb (10 mL) or 330 lb (15 mL) dose is required, turn the pointer to "STOP" before delivering the dose. The off (STOP) position will close the system between dosing.

Collapsible Pack (84.5 fl oz/2.5 L Pack and 169 fl oz/5 L Pack)

Connect the applicator gun to the collapsible pack as follows:

Attach the open end of the draw-off tubing to the dosing equipment. (Because of the solvents used in the formulation, only the Protector Drench Gun from Instrument Supplies Limited, or equivalent, is recommended. Other applicators may exhibit compatibility problems resulting in locking, incorrect dosage or leakage.)

Replace the shipping cap with the draw-off cap and tighten down. Attach draw-off tubing to the draw-off cap.

Gently prime the applicator gun, checking for leaks.

Follow the manufacturer's directions for adjusting the dose.

When the interval between uses of the applicator gun is expected to exceed 12 hours, disconnect the gun and draw-off tubing from the product container and empty the product from the gun and tubing back into the product container. To prevent removal of special lubricants from the Protector Drench Gun, the gun and tubing must not be washed.

IVOMEC and Cattle Head Logo are registered trademarks of Merck & Co., Inc., Whitehouse Station, N.J., U.S.A.

Mode of Action

Ivermectin as a member of the avermectin family kills certain parasitic roundworms and ectoparasites, such as mites, lice, horn flies and other insects. Its action is unique to the avermectin class of antiparasitic agents. This action involves a chemical that serves as a signal from one nerve cell to another, or from a nerve cell to a muscle cell. This chemical, a neurotransmitter, is called gamma-aminobutyric acid or GABA.

In roundworms, ivermectin stimulates the release of GABA from nerve endings and enhances binding of GABA to special receptors at nerve junctions, thus interrupting nerve impulses — thereby paralyzing and killing the parasite.

The enhancement of the GABA effect in arthropods such as mites, lice, and horn flies resembles that in roundworms except that nerve impulses are interrupted between the nerve ending and the muscle cell. Again, this leads to paralysis and death.

Ivermectin has no measurable effect against flukes or tapeworms, presumably because they do not have GABA as a nerve impulse transmitter.

The principal peripheral neurotransmitter in mammals, acetylcholine, is unaffected by ivermectin. Ivermectin does not readily penetrate the central nervous system of mammals where GABA functions as a neurotransmitter.

Safety

Studies conducted in the U.S.A. have demonstrated the safety margin for ivermectin. Based on plasma levels, the topically applied formulation is expected to be at least as well tolerated by breeding animals as is the subcutaneous formulation which had no effect on breeding performance.

WARNING: Cattle must not be treated within 48 days of slaughter for human consumption. Because a withdrawal time in milk has not been established, do not use in female dairy cattle of breeding age.

WARNING! NOT FOR USE IN HUMANS.

This product should not be applied to self or others because it may be irritating to human skin and eyes and absorbed through the skin. To minimize accidental skin contact, the user should wear a long-sleeved shirt and rubber gloves. If accidental skin contact occurs, wash immediately with soap and water. If accidental eye exposure occurs, flush eyes immediately with water and seek medical attention.

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

WARNING! FLAMMABLE!

**KEEP AWAY FROM HEAT, SPARKS, OPEN FLAME,
AND OTHER SOURCES OF IGNITION.**

PRECAUTIONS

Store away from excessive heat (104°F/40°C) and protect from light.

Use only in well-ventilated areas or outdoors.

Close container tightly when not in use.

Cattle should not be treated when hair or hide is wet since reduced efficacy may be experienced.

Do not use when rain is expected to wet cattle within six hours after treatment.

This product is for application to skin surface only. Do not give orally or parenterally.

Cloudiness in the formulation may occur when IVOMEC® (ivermectin) Pour-On is stored at temperatures below 32°F. Allowing to warm at room temperature will restore the normal appearance without affecting efficacy.

Antiparasitic activity of ivermectin will be impaired if the formulation is applied to areas of the skin with mange scabs or lesions, or with dermatoses or adherent materials, e.g., caked mud or manure.

Ivermectin has been associated with adverse reactions in sensitive dogs; therefore, IVOMEC Pour-On is not recommended for use in species other than cattle.

When to Treat Cattle with Grubs

IVOMEC Pour-On effectively controls all stages of cattle grubs. However, proper timing of treatment is important. For the most effective results, cattle should be treated as soon as possible after the end of the heel fly (warble fly) season. While this is not peculiar to ivermectin, destruction of *Hypoderma* larvae (cattle grubs) at the period when these grubs are in vital areas may cause undesirable host-parasite reactions. Killing *Hypoderma lineatum* when it is in the esophageal tissues may cause bloat; killing *H. bovis* when it is in the vertebral canal may cause staggering or paralysis. Cattle should be treated either before or after these stages of grub development.

Cattle treated with IVOMEC Pour-On at the end of the fly season may be re-treated with IVOMEC during the winter without danger of grub-related reactions. For further information and advice on a planned parasite control program, consult your veterinarian.

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 or certain water-borne organisms on which they feed. Do not permit cattle to enter lakes, streams or ponds for at least six hours after treatment. 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.

Package Information

IVOMEC Pour-On is available in an 8.5 fl oz/250 mL bottle with a squeeze-measure-pour system (Product 41309A), a 33.8 fl oz/1 L bottle with a squeeze-measure-pour system (Product 41310A), or in an 84.5 fl oz/2.5 L collapsible pack (Product 41311A), and a 169 oz/5 L collapsible pack (Product 41350A) intended for use with appropriate automatic dosing equipment.



Merck & Co., Inc.
Rahway, New Jersey 07065-0912, U.S.A.

U.S. Pat 4,199,569
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November 1998

ATTACHMENT 2
Proposed Generic Product Label

ANADA XXX-XXX, Approved by FDA

TRADENAME (ivermectin)

Pour-On for Cattle

Contains 10 mg ivermectin/mL

Parasiticide

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

Introduction

TRADENAME (ivermectin) Pour-on delivers internal and external parasite control in one convenient low-volume application. TRADENAME contains ivermectin, a unique chemical entity.

Indications

TRADENAME Pour-On applied at the recommended dose level of 500 mcg/kg is indicated for the effective control of these parasites.

Gastrointestinal Roundworms

<i>Ostertagia ostertagi</i> (including inhibited stage)	(adults and L4)
<i>Haemonchus placei</i>	(adults and L4)
<i>Trichostrongylus axei</i>	(adults and L4)
<i>T. colubriformis</i>	(adults and L4)
<i>Cooperia</i> spp.	(adults and L4)
<i>Strongyloides papillosus</i>	(adults)
<i>Oesophagostomum radiatum</i>	(adults and L4)
<i>Trichuris</i> spp.	(adults)

Lungworms

<i>Dictyocaulus viviparus</i>	(adults and L4)
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Cattle Grubs

<i>Hypoderma bovis</i>	(parasitic stages):
<i>H. lineatum</i>	

Mites

<i>Sarcoptes scabiei</i> var. <i>bovis</i> .
--

Lice

<i>Linognathus vituli</i>
<i>Haematopinus eurysternus</i>
<i>Damalinia bovis</i>
<i>Solenopotes capillatus</i>

Horn Flies

<i>Haematobia irritans</i>

Persistent Activity

TRADENAME Pour-On has been proved to effectively control infections and to protect cattle from re-infection with *Ostertagia ostertagi*, *Oesophagostomum radiatum*, *Haemonchus placei*, *Trichostrongylus axei*, *Cooperia punctata* and *Cooperia oncophora* for 14 days after treatment.

Treatment of Cattle for Horn Flies

TRADENAME Pour-On controls horn flies (*Haematobia irritans*) for up to 28 days after dosing. For best results TRADENAME Pour-On should be part of a parasite control program for both internal and external parasites based on the epidemiology of these parasites. Consult your veterinarian or an entomologist for the most effective timing of applications.

Dosage

The dose rate is 0.5 mL for each 22lb of body weight. The formulation should be applied along the top line in a narrow strip from the withers to the tailhead.

Administration

[CONTAINER, METERING EQUIPMENT AND INSTRUCTIONS YET TO BE DETERMINED]

Mode of Action

Ivermectin as a member of the avermectin family kills certain parasitic roundworms and ectoparasites, such as mites, lice, horn flies and other insects. Its action is unique to the avermectin class of antiparasitic agents. This action involves a chemical that serves as a signal from one nerve cell to another, or from a nerve cell to a muscle cell. This chemical, a neurotransmitter, is called gamma-aminobutyric acid or GABA.

In roundworms, ivermectin stimulates the release of GABA from nerve endings and enhances binding of GABA to special receptors at nerve junctions, thus interrupting nerve impulses - thereby paralyzing and killing the parasite.

The enhancement of the GABA effect in arthropods such as mites, lice, and horn flies resembles that in roundworms except that nerve impulses are interrupted between the nerve ending and the muscle cell. Again, this leads to paralysis and death.

Ivermectin has no measurable effect against flukes or tapeworms, presumably because they do not have GABA as a nerve impulse transmitter.

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Safety

Studies conducted in the U.S.A. have demonstrated the safety margin for ivermectin. Based on plasma levels, the topically applied formulation is expected to be at least as well tolerated by breeding animals as is the subcutaneous formulation which had no effect on breeding performance.

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This product should not be applied to self or others because it may be irritating to human skin and eyes and absorbed through the skin. To minimize accidental skin contact, the user should wear a long-sleeved shirt and rubber gloves. If accidental skin contact occurs, wash immediately with soap and water. If accidental eye exposure occurs, flush eyes immediately with water and seek medical attention.

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

PRECAUTION

Store away from excessive heat (104°F/40°C) and protect from light. [ACTUAL STORAGE RECOMMENDATIONS TO BE VERIFIED VIA STABILITY STUDIES]

Close container tightly when not in use.

Cattle should not be treated when hair or hide is wet since reduced efficacy may be experienced.

Do not use when rain is expected to wet cattle within six hours after treatment.

This product is for application to skin surface only. Do not give orally or parenterally.

Cloudiness in the formulation may occur when TRADENAME (ivermectin) Pour-On is stored at temperatures below 32°F. Allowing to warm at room temperature will restore the normal appearance without affecting efficacy.

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Ivermectin has been associated with adverse reactions in sensitive dogs; therefore, TRADENAME Pour-On is not recommended for use in species other than cattle.

When to Treat Cattle with Grubs

Ivermectin pour-on effectively controls all stages of cattle grubs. However, proper timing of treatment is important. For the most effective results, cattle should be treated as soon as possible after the end of the heel fly (warble fly) season. While this is not peculiar to ivermectin, destruction of *Hypoderma* larvae (cattle grubs) at the period when these grubs are in vital areas may cause undesirable host-parasite reactions. Killing *Hypoderma lineatum* when it is in the esophageal tissues may cause bloat; killing *H. bovis* when it is in the vertebral canal may cause staggering or paralysis. Cattle should be treated either before or after these stages of grub development.

Cattle treated with ivermectin pour-on at the end of the fly season may be re-treated with ivermectin pour-on during the winter without danger of grub-related reactions. For further information and advice on a planned parasite control program, consult your veterinarian.

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 or certain water-borne organisms on which they feed. Do not permit cattle to enter lakes, streams or ponds for at least six hours after treatment. 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.

Presentation

TRADENAME Pour-On is available in.... [ACTUAL CONTAINERS ARE YET TO BE DETERMINED]