SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Premadex 10 mg/ml Solution for Injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1 ml solution for injection contains:

Active substance(s):
Ivermectin……10 mg

Excipient(s):
Benzyl alcohol…….10 mg

For the full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Solution for injection
A clear, colourless solution.

4. CLINICAL PARTICULARS

4.1 Target species

Cattle, sheep and pigs.

4.2 Indications for use, specifying the target species

Cattle:

For the treatment of gastrointestinal nematodes, lungworms, eyeworms, warble flies, mites and lice (as shown below) of beef and non-lactating dairy cattle:

Gastrointestinal worms (adults and 4th stage larvae):
Ostertagia ostertagi
Ostertagia lyrata
Haemonchus placei
Trichostrongylus colubriformis
Cooperia oncophora (adults)
Cooperia punctata (adults)
Cooperia pectinata (adults)
Bunostomum phlebotomum
Oesophagostomum radiatum

Lungworms (adult and 4th stage larvae):
Dictyocaulus viviparus

Eyeworms (adult):
Thelazia spp.

Warble flies (parasitic stages):
Hypoderma bovis
H. lineatum

Mites:
Psoroptes ovis
Sarcoptes scabiei var. bovis

Sucking lice:
Linognathus vituli
Haematopinus eurysternus
Solenopotes capillatus

May also be used as an aid in the control of the mange mite *Chorioptes bovis* but complete elimination may not occur.

Treatment with Qualimec 10 mg/ml Solution for Injection at the recommended dose rate prevents re-infection with *Haemonchus placei*, *Cooperia oncophora*, *Cooperia pectinata* and *Trichostrongylus axei* for 7 days after treatment, *Ostertagia ostertagi* and *Oesophagostomum radiatum* for 14 days after treatment and *Dictyocaulus viviparus* for 21 days after treatment.

Sheep

For the treatment of psoroptic mange (sheep scab), gastrointestinal nematodes, lungworms and nasal bots of sheep:

Gastrointestinal roundworms (adults):
Ostertagia circumcincta
Haemonchus contortus
Trichostrongylus axei
T. colubriformis and T. vitrinus
Cooperia curticei
Nematodirus filicollis
Variable activity may be observed against *Cooperia curticei* and *Nematodirus filicollis*.

Lungworms:
Dictyocaulus filaria (adults)

Mange mites:
Psoroptes ovis

Nasal bot:
Oestrus ovis (all larval stages)

Pigs

For the treatment of gastro-intestinal nematodes, lungworms, lice and mange mites of pigs.

Gastro-intestinal worms (adult and fourth stage larvae):
Ascaris suum
Hyostrongylus rubidus
Oesophagostomum spp.
Strongyloides ransomi (adults).

Lungworms:
Metastrongylus spp. (adults)

Lice:
Haematopinus suis

Mange Mites:
Sarcoptes scabiei var. suis

4.3 Contraindications

Do not use in lactating dairy cows and sheep producing milk for human consumption. Do not use in non-lactating dairy cows, including pregnant dairy heifers or non-lactating dairy sheep within 60 days of calving/lambing.
Do not use in cases of known hypersensitivity to ivermectin.
Do not administer by the intravenous or intramuscular route.

4.4 Special warnings for each target species

Care should be taken to avoid the following practices because they increase the risk of development of resistance and could ultimately result in ineffective therapy:

- Too frequent and repeated use of anthelmintics from the same class, over an extended period of time
- Underdosing, which may be due to underestimation of bodyweight, misadministration of the product, or lack of calibration of the dosing device (if any)

Suspected clinical cases of resistance to anthelmintics should be further investigated using appropriate tests (e.g. Faecal Egg Count Reduction Test). Where the results of the test(s) strongly suggest resistance to a particular anthelmintic, an anthelmintic belonging to another pharmacological class and having a different mode of action should be used.

Treatment of psoroptic mange (sheep scab) with one injection is not recommended because, although clinical improvement may be seen, elimination of all mites may not occur.
Sheep scab (*Psoroptes ovis*) is an extremely contagious external parasite of sheep. Following treatment of infected sheep great care must be taken to avoid re-infestation as mites may be viable for up to 15 days off the sheep. It is important to ensure all sheep which have been in contact with infected sheep are treated. Contact between treated infected and non-treated, non-infected flocks must be avoided until at least 7 days after the last treatment.

Resistance to ivermectin has been reported in *Ostertagia circumcincta* in lambs and in *Ostertagia ostertagi* in cattle. Therefore, the use of this product should be based on local (regional, farm) epidemiological information about

susceptibility of these *helminth species* and recommendations on how to limit further selection for resistance to anthelmintics

4.5 Special precautions for use

Special precautions for use in animals

Avermectins may not be well tolerated in non-target species. Cases of intolerance with fatal results are reported in dogs – especially Collies, Old English Sheepdogs and related breeds and crosses, and also in turtles/tortoises.

Do not combine treatment with vaccination against lungworms. If vaccinated animals are to be treated, treatment should not be carried out within a period of 28 days before or after vaccination.

The shedding of nematode eggs can continue for some time after treatment.

In Cattle: To avoid secondary reactions due to the death of *Hypoderma* larvae in the oesophagus or in the spine, it is recommended to administer the product at the end of warble fly activity and before the larvae reach their resting sites.

Swab septum before removing each dose.

Special precautions to be taken by the person administering the veterinary medicinal product to animals

Do not smoke, eat or drink while handling the product.
Wash hands after use.
Take care to avoid self injection: the product may cause local irritation and/or pain at the site of injection.

4.6 Adverse reactions (frequency and seriousness)

Transitory discomfort has been observed in some animals immediately following subcutaneous administration. In cattle this may include jumping and rolling, but behaviour returns to normal after 15 minutes.

Soft tissue swelling and thickening of the skin at the injection site has been observed in treated animals. Typically these reactions are transient and disappear within one to four weeks

4.7 Use during pregnancy, lactation or lay

The product can be administered during pregnancy in cows, ewes and sows (for information on use in lactating animals, see sections 4.3 and 4.11).
The fertility of males is not affected by administration of the product.

4.8 Interaction with other medicinal products and other forms of interaction

Do not combine ivermectin treatment with vaccination against lungworms. If vaccinated animals are to be treated, treatment should not be carried out within a period of 28 days before or after vaccination (see section 4.5).

4.9 Amounts to be administered and administration route

For single administration only (except for the treatment of *Psoroptes ovis* infections in sheep).

To ensure administration of a correct dose, bodyweight should be determined as accurately as possible. Accuracy of the dosing device should be checked.

If animals are to be treated collectively rather than individually, they should be grouped according to their bodyweight and dosed accordingly, in order to avoid under- or over-dosing.

Cattle

Dosage:
1.0 ml per 50 kg bodyweight (based on a recommended dosage level of 200 micrograms ivermectin per kg bodyweight).

Administration:
Inject subcutaneously in front of, or behind, the shoulder using aseptic technique. A sterile 1.4 x 15 mm (17G x ½ inch) needle is recommended.

SHEEP

Dosage:
0.5 ml per 25 kg of bodyweight (based on a recommended level of 200 micrograms ivermectin per kg bodyweight).

Administration:
For the treatment of gastrointestinal roundworms, lungworms and nasal bots inject once subcutaneously in the neck, using aseptic precautions; a sterile 1.4 x 15 mm (17G x ½ inch) needle is recommended. For the treatment of *Psoroptes ovis* (sheep scab), two injections with a seven day interval are required to treat clinical signs of scab and to eliminate living mites.

For young lambs weighing less than 20.0 kg give 0.1 ml per 5 kg. In these lambs the use of a syringe which can deliver as little as 0.1 ml is recommended.

Pigs

Dosage:

1.5 ml per 50 kg bodyweight (based on a recommended dosage level of 300 micrograms ivermectin per kg bodyweight)

Administration:
The recommended route of administration is by subcutaneous injection into the neck using aseptic technique and a sterile 1.4 x 15 mm (17G x ½ inch) needle.
For piglets weighing less than 16 kg give 0.1 ml per 3 kg. In these piglets the use of a syringe which can deliver as little as 0.1 ml is recommended.

When using the 200, 250 or 500ml pack sizes, use only automatic syringe equipment. For the 50ml pack size, use of a multiple dose syringe is recommended. To refill the syringe, use of a draw-off needle is recommended to avoid excessive broaching of the stopper.

4.10 Overdose (symptoms, emergency procedures, antidotes), if necessary

Clinical symptoms of ivermectin toxicity include ataxia and depression. No antidote has been identified. In case of overdose, symptomatic treatment should be given. No signs of toxicity were observed in animals treated at up to 3 times the recommended dose rate.

4.11 Withdrawal period(s)

Cattle:
Meat and offal: 49 days.
Do not use in lactating cows producing milk for human consumption. Do not use in non-lactating dairy cows, including pregnant dairy heifers, within 60 days of calving.

Sheep:
Meat and offal: 42 days.

Do not use in lactating ewes producing milk for human consumption. Do not use in sheep which are intended to produce milk for human consumption within 60 days of lambing.

Pigs:
Meat and offal: 28 days

5. PHARMACOLOGICAL PROPERTIES

Ivermectin is a mixture of two partially modified compounds of abamectin belonging to the avermectin family, which are a macrocyclic lactone group of endectocides. Abamectin is a mixture of two fermentation products of the soil organism *Streptomyces avermitilis*.

ATC vet code: QP54AA01.
Therapeutic group: Endectocide, ivermectin

5.1 Pharmacodynamic properties

Ivermectin is a macrocyclic lactone derivative and acts by inhibiting nerve impulses. It binds 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 relevant parasites. 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.

5.2 Pharmacokinetic particulars

In each of the target species the pharmacokinetic profile following subcutaneous administration was characterised as follows (pharmacokinetic parameters presented as mean values):

Following administration to cattle, Cmax was 51ng/ml, with a Tmax of 43 h, $T_{1/2}$ of 129 h and an AUC of 7398 ng.h/ml.

Following two subsequent administrations seven days apart to sheep, Cmax was 14 ng/ml, with a Tmax of 202 h, $T_{1/2}$ of 380 h and an AUC of 4686 ng.h/ml.

Following administration to pigs, Cmax was 6.35ng/ml, with a Tmax of 106 h, $T_{1/2}$ of 219 h and an AUC of 1260 ng.h/ml.

Only about 2% of the drug is excreted in urine, faecal excretion being the major route of elimination. Tissue residues of radioactivity following subcutaneous administration of tritium-labelled ivermectin are highest in liver and fat; lowest levels are found in brain.

In cattle, the residual antiparasitic effect of ivermectin is due to its persistence which in turn is due in part to its long intrinsic half life and its relatively high protein binding (90%).

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Benzyl alcohol
Ethanol 96 per cent
Water for injections
Propylene glycol

6.2 Major incompatibilities

In the absence of compatibility studies, this veterinary medicinal product must not be mixed with other veterinary medicinal products.

6.3 Shelf life

Shelf-life of the veterinary medicinal product as packaged for sale: 2 years
Shelf-life after first opening the immediate packaging: 28 days

6.4. Special precautions for storage

Store below 25°C.
Protect from direct sunlight.
Keep container in the outer carton in order to protect from light.

6.5 Nature and composition of immediate packaging

HDPE multidose container with bromobutyl rubber stopper and aluminium cap.
Pack size: 50 ml, 200 ml and 500 ml.

Clear PET multidose container with bromobutyl rubber stopper and aluminium cap.
Pack size: 50 ml, 250 ml and 500 ml.

Not all pack sizes may be marketed.

6.6 Special precautions for the disposal of unused veterinary medicinal product or waste materials derived from the use of such products

EXTREMELY DANGEROUS TO FISH AND AQUATIC LIFE. Do not contaminate surface waters or ditches with product or used container. Any unused veterinary medicinal product or waste material derived from such veterinary medicinal product should be disposed of in accordance with national requirements.

7. MARKETING AUTHORISATION HOLDER

Eco Animal Health Ltd
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100 High Street
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N14 6BN
United Kingdom

8. MARKETING AUTHORISATION NUMBER

Vm 13277/4017

9. DATE OF FIRST AUTHORISATION

17 May 2007

10. DATE OF REVISION OF THE TEXT

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