IRISH MEDICINES BOARD ACT 1995

EUROPEAN COMMUNITIES (ANIMAL REMEDIES) (No. 2) REGULATIONS 2007

(S.I. No. 786 of 2007)

VPA: **10545/032/001**
Case No: 7004500

The Irish Medicines Board in exercise of the powers conferred on it by Animal Remedies (No. 2) Regulations (S.I. No. 786 of 2007) hereby grants to:

Janssen Cilag Ltd.

50-100 Holmers Farm Way, **High Wycombe**, **Buckinghamshire HP12 4EG**, **United Kingdom**

an authorisation, subject to the provisions of the said Regulations and the general conditions of the attached authorisation, in respect of the Veterinary Medicinal Product:

Janamax 0.08 %w/v Abamectin Sheep Drench

The particulars of which are set out in Part 1 and Part 2 of the said Schedule. The authorisation is also subject to any special conditions as may be specified in the said Schedule.

The authorisation,unless revoked, shall continue in force from **09/07/2008** until **12/06/2011**.

Signed on behalf of the Irish Medicines Board

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A person authorised in that behalf by the said Board.

(NOTE: This authorisation replaces any previous authorisation in respect of this product which is now null and void.)

Part II

Summary of Product Characteristics

1 NAME OF THE VETERINARY MEDICINAL PRODUCT

Janamax 0.08%w/v Abamectin Sheep Drench

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:	
Active substance:	
Abamectin	0.08% w/v
Excipeints	
Benzyl Alcohol	3.00% w/v

See Section 6.1 for full list of excipients.

3 PHARMACEUTICAL FORM

Oral solution.

4 CLINICAL PARTICULARS

4.1 Target Species

Sheep.

4.2 Indications for use, specifying the target species

A broad-spectrum endectocide of the avermectin family. For the treatment and control of the following gastro-intestinal nematodes, lungworms and nasal bots of sheep:

Gastro-intestinal nematodes:
Haemonchus contortus (adult and immature)
Ostertagia circumcincta (adult, immature and inhibited larval stages)
Ostertagia trifurcata (adult)
Trichostrongylus axei (adult)
Trichostrongylus colubriformis (adult and immature)
Cooperia curticei (adult and immature)
Nematodirus battus (adult and immature)
Nematodirus filicollis (adult)
Strongyloides papillosus (adult)
Oesophagostomum venulosum (adult)
Trichuris ovis (adult)
Chabertia ovina (adult)

Lungworms:
Dictyocaulus filiaria (adult and immature)

Nasal bot:
Oestrus ovis (all larval stages)

4.3 Contraindications

Do not concurrently treat animals with drugs which can increase GABA activity, such as barbital.

4.4 Special warnings for each target species

None known.

4.5 Special precautions for use

Special precautions for use in animals

Assess bodyweight as accurately as possible before calculating dosage. Intensive use or misuse of anthelmintics can give rise to resistance. To reduce this risk, dosing programmes should be discussed with your veterinary surgeon.
Do not use in other species.

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

Avoid contact with skin
Do not eat, drink or smoke whilst handling the product.
Operators should wear rubber gloves and boots, with a waterproof coat, when applying the product.
Protective clothing should be washed after use.
Wash hands after use.
Accidental spillage on the skin should be washed off immediately with soap and water.
If accidental eye exposure occurs, flush the eyes immediately with clean water.
In case of accidental ingestion, induce vomiting and seek medical attention.

4.6 Adverse reactions (frequency and seriousness)

The following signs of toxicity have been reported in the literature associated with excessive overdosing (20 times the recommended therapeutic dose) with abamectin formulations: Drooping of head and ears, ataxia, hypermetria, tail twitching, opisthotonus, lateral recumbency and extensor rigidity.
Proprietary data on the product showed no adverse reactions after treatments with up to 4 times the recommended therapeutic dose.

4.7 Use during pregnancy, lactation or lay

Do not use in ewes producing milk for human consumption. Proprietary data showed that treatment of pregnant ewes over mid to late gestation was safe.

4.8 Interaction with other medicinal products and other forms of interaction

None known.

4.9 Amounts to be administered and administration route

For oral administration only. Suitable for use with standard drenching equipment.

The recommended dose level is 200 μg abamectin per kg bodyweight (1 ml of product/ 4 kg bodyweight).

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

Trials showed that a dose of 800 μg/kg caused no adverse reactions, with the exception of pupillary dilation, in treated sheep.

4.11 Withdrawal Period(s)

Sheep must not be treated within 16 days of slaughter for human consumption.

Do not use in ewes producing milk for human consumption either during lactation or within 16 days of lambing.

5 PHARMACOLOGICAL or IMMUNOLOGICAL PROPERTIES

Summary presentation of the active:

Name: Abamectin

ATC Vet classification: QP54A

Action: Abamectin binds selectively and with high affinity to glumate-gated chloride ion channels in invertebrate nerve and muscle cells. This leads to an increased permeability of the cell membrane to chloride ions with hyperpolarisation of the nerve or muscle cell resulting in paralysis and death of parasite.

Group: Avermectins: Macrocyclic lactones

5.1 Pharmacodynamic properties

Macrocyclic lactones, including Abamectin, have a board spectrum of activity and are active against mature and immature nematode and arthropod parasites of mammals, fish and other vertebrates. Compounds of this class bind selectively and with high affinity to glutamate-gated chloride ion channels which occur in invertebrate nerve and muscle cells. This leads to an increase in the permeability of the cell membrane to chloride ions with hyperpolarization of the nerve or muscle cell, which results 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 neurotransmitter gamma-aminobutyric acid (GABA).

The margin of the safety for compounds of this class is attributable to the fact that mammals and other vertebrates do not have glutamate-gated chloride ion channels, the avermectin/ milbemycin compounds have a low affinity for other mammalian ligand-gated chloride channels, and they do not readily cross the blood-brain barrier.
Therefore, avermectins kill parasites without adversely affecting their hosts. Reports in the literature describing the effects of acvermectins show that concentrations required to affect vertebrates are far in excess of those required to treat relevant parasites.

5.2 Pharmacokinetic properties

The product is formulated in carrier water. Proprietary data demonstrated that after oral administration, radiolabelled abamectin was rapidly absorbed from the gastrointestinal tract into the systemic circulation. There were no apparent differences in the plasma kinetics or excretory profile following a single or mixed Abamectin form (ie Component B_{1a} alone or mixture of Components B_{1a} and B_{1b}). Greater than 80% of administered radioactivity was eliminated in faeces with elimination in urine being negligible. The half-life of elimination form the plasma was approximately 62 hours. At all time points the highest concentrations of radioactivity were present in liver and fat with much lower concentrations being present in kidney and muscle. By 10 and 14 days the concentrations of radioactivity in many kidney and fat samples were close to or below the limit of detection (approximately 0.003 µg/g). Abamectin B_{1a} was the major component in all tissues with metabolites constituting a significant proportion of the total residue in kidney at early time points and fat at the last time point. At other times in these tissues and at all times in liver and fat, minor metabolites are present which account for a small proportion of radioactivity.

Concentrations of radioactivity in all tissues were greater than those measured in plasma at the 3 and 7 day time points. These differences were greater for liver (10 fold) than for kidney (3 fold). Concentrations in muscles were only marginally above the levels observed in plasma. It is of interest that the depletion of residues in faeces was correlated to its depletion from tissues and blood. By day 14 post treatments, all levels were below detection limits. The pharmacokinetics profile was:

Parameter	Average
C_{max} (µg equivalents/g):	0.044
T_{max} (h):	24.000
$T_{1/2\ elim}$ (h):	61.800
Range (h):	12-192
AUC_{0-t} (µg equivalents/g):	3.755
$AUC_{0-\infty}$ (µg equivalents/g):	4.611

Environmental properties

Properties which contribute to the environmental safety profile of the avermectins, including abamectin, include the fact that they are hydrophobic, immobile in soil, rapidly photodegraded in water and aerobically degraded in soil less bioactive compounds; they do not bioaccumulate nor undergo translocation in the environment.

Studies in a variety of terrestrial organisms including bacteria, fungi, higher plants, arthropods, earthworms, birds and mammals have shown that abamectin shows little or no toxicity to non-target organisms, other than some coprophagous arthropod larvae. Impact on sensitive, non-target dung arthropod populations is constrained by the typical usage of avermectins.

The proposed use of the product would occur mainly in the summer months when temperatures and sunlight are at their maxima. Therefore the instability of abamectin under these conditions will ensure any residues in the environment are rapidly broken down and will not accumulate.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Benzyl Alcohol
Propylene Glycol
Glycerol Formal
Polysorbate 80
Sodium Dihydrogen Phosphate
Disodium Phosphate Dihydrate
Purified Water

6.2 Incompatibilities

None known.

6.3 Shelf-life

36 months

6.4 Special precautions for storage

Do not store above 25°C. Protect from light.

6.5 Nature and composition of immediate packaging

Clear, straw coloured liquid in 1, 2.5 and 5 L white HDPE backpacks and jerrycans.

6.6 Special precautions for the disposal of unused veterinary medicinal products or waste materials

Unused product or waste material should be disposed of in accordance with national requirements.
Abamectin is extremely dangerous to fish and other aquatic life. Do not contaminate ponds, waterways or ditches with product or empty containers. Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal products should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

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High Wycombe
Buckinghamshire
HP12 4EG
UK

8 MARKETING AUTHORISATION NUMBER(S)

VPA 10545/32/1

9 DATE OF THE FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

13th June 2006

10 DATE OF REVISION OF THE TEXT

9th July 2008