ANNEX I

LIST OF THE PHARMACEUTICAL FORMS, STRENGTHS, ROUTES OF ADMINISTRATION, PACKAGING AND PACKAGE SIZES OF THE VETERINARY MEDICINAL PRODUCT IN THE MEMBER STATES

ANNEX I

Marketing Authorisation Holder (Name and address):

Reference Member State:

IRELAND
Cross Vetpharm Group Ltd (Bimeda)
Broomhill Road
Tallaght
Dublin 24
Ireland

Concerned Member State:

BELGIUM
Cross Vetpharm Group Ltd (Bimeda)
Broomhill Road
Tallaght
Dublin 24
Ireland

Presentations:

Member State	Invented Name	Strength	Pharmaceutical Form	Target Species	Route of administration	Packaging	Content	Package-size
Ireland	Porcimectin Injection	1 % w/v (10 mg/ml)	Solution for injection	Pigs	Subcutaneous injection	Bottle (Polyethylene)	50 ml	1 bottle
Ireland	Porcimectin Injection	1 % w/v (10 mg/ml)	Solution for injection	Pigs	Subcutaneous injection	Bottle (Polyethylene)	250 ml	1 bottle
Ireland	Porcimectin Injection	1 % w/v (10 mg/ml)	Solution for injection	Pigs	Subcutaneous injection	Bottle (Polyethylene)	500 ml	1 bottle
Belgium	Porcimec P	1 % w/v (10 mg/ml)	Solution for injection	Pigs	Subcutaneous injection	Bottle (Polyethylene)	50 ml	1 bottle
Belgium	Porcimec P	1 % w/v (10 mg/ml)	Solution for injection	Pigs	Subcutaneous injection	Bottle (Polyethylene)	250 ml	1 bottle
Belgium	Porcimec P	1 % w/v (10 mg/ml)	Solution for injection	Pigs	Subcutaneous injection	Bottle (Polyethylene)	500 ml	1 bottle

ANNEX II

SCIENTIFIC CONCLUSIONS PRESENTED BY THE EMEA

SCIENTIFIC CONCLUSIONS

The basis for the arbitration procedure was the concern raised by Belgium, that plasmatic levels of anthelminthics that have been produced by means of fermentation techniques, such as the macrocyclic lactones (e.g. ivermectin) have no direct correlation with the efficacy of these products *in situ*. The applicant was requested to provide evidence of correlation of plasma concentrations with clinical efficacy against parasites included in the indications on the SPC.

The CVMP considered the written response provided by the Applicant, the joint Rapporteur-Co-Rapporteur's assessment report on the response of the Applicant and the comments from CVMP members, including references to published literature in this field.

Taking into account

- that the application was submitted in accordance with the current guidelines (EMEA/CVMP/016/00 and VICH GL7);
- that bioequivalence with the reference product has been proven;
- that the clinical effect of ivermectin is related to plasma pharmacokinetics;

the CVMP agreed that no dose confirmation study is required to show clinical efficacy.

Therefore, the CVMP has recommended the granting of the Marketing Authorisation(s) for which the Summary of Product Characteristics is set out in Annex III for Porcimectin injection.

ANNEX III

SUMMARY OF PRODUCT CHARACTERISTICS OF THE REFERENCE MEMBER STATE

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF VETERINARY MEDICINAL PRODUCT

Porcimectin Injection, 1%, Solution for Injection for swine

2. QUALITATIVE AND QUANTITATIVE COMPOSITION IN TERMS OF THE ACTIVE SUBSTANCES AND CONSTITUENTS OF THE EXCIPIENTS, KNOWLEDGE OF WHICH IS ESSENTIAL FOR PROPER ADMINISTRATION

Active Substance

Ivermectin Ph. Eur. 1.0 %w/v (10 mg/ml)

3. PHARMACEUTICAL FORM

Solution for injection

4. PHARMACOLOGICAL PROPERTIES, AND IN SO FAR AS THIS INFORMATION IS USEFUL FOR THERAPEUTIC PURPOSES, PHARMACOKINETICS PARTICULARS

4.1 Pharmacodynamic properties

Ivermectin is a member of the avermectin group. 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-gates 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.

ATC vet code: QP54AA01

4.2 Pharmacokinetic properties

At a dose level of 0.3 mg ivermectin per kg bodyweight, a mean Cmax of 6.94 ng/ml was reached at a mean Tmax of 86.75 hours, and the mean elimination half life was 133.56 hours.
Biliary excretion, followed by elimination in faeces is probably the major route of ivermectin excretion in pigs. While the major single component excreted was unaltered drug, the major metabolite in swine are 3'' -O-desmethyl-H_2B_{1a} and 3'' -O-desmethyl-H_2B_{1b}.

5. CLINICAL PARTICULARS

5.0 Target Species:

Pigs

Porcimectin Injection for pigs can be given to all ages of animals including piglets.

5.1 Indications For Use

Porcimectin Injection is indicated for the effective treatment and control of the following harmful parasites of pigs:

Gastrointestinal roundworms: (Adults and fourth stage larvae):

Ascaris suum
Hyostrongylus rubidus
Oesophagostomum spp.
*Strongyloides ransomi (*adults and somatic larval stages)

Lungworms:
Metastrongylus spp. (adult)

Lice:
Haematopinus suis

Mange mites:
Sarcoptes scabiei var. *suis*

5.2 Contra-indications

Do not use in case of known hypersensitivity to the active ingredient.
Do not administer by the intravenous or intramuscular route.
Porcimectin Injection for Pigs has been formulated specifically for use in this species. Avermectins may not be well tolerated in all non-target species (cases of intolerance with fatal outcome are reported in dogs especially Collies, Old English Sheepdogs and related breeds or crosses, and also in turtles/tortoises).

Do not use in cats and dogs.

5.3 Undesirable Effects

Mild and transient pain reactions may be seen in some pigs following subcutaneous injection at injection site. All these reactions disappeared without treatment

5.4 Special Precautions for Use

Assess bodyweight as accurately as possible before calculating the dosage.

5.5 Use During Pregnancy and Lactation:

Porcimectin Injection for pigs can be used in breeding sows and boars and will not affect fertility.

Do not administer Porcimectin Injection during the first 40 days of pregnancy.

5.6 Interaction with Other Medicaments and other Forms of Interactions

Porcimectin Injection can be used concurrently without adverse effects with foot and mouth disease vaccine or clostridial vaccine, given at separate injection sites.

5.7 Posology and Method of Administration

Each ml contains 10 mg of ivermectin sufficient to treat 33 kg of bodyweight of pigs. The injection may be given with any standard automatic or single-dose or hypodermic syringe. Use of 17 gauge x ½ inch needle is suggested. Replace with a fresh sterile needle after every 10 to 12 animals. Injection of wet or dirty animals is not recommended. If using a single-dose hypodermic syringe, use a separate sterile needle to withdraw Porcimectin Injection from the container.

In pigs, the recommended dosage level is 300 mcg ivermectin per kg bodyweight. This is equivalent to 1 ml per 33 kg bodyweight. The recommended route of administration is by subcutaneous injection into the neck.

Young Pigs*:*
In young pigs, especially those below 16 kg for which less than 0.5 ml Porcimectin Injection is indicated, dosing accuracy is important. The use of a syringe that can accurately deliver as little as 0.1 ml is recommended.

5.8 Overdose

A dose of 30 mg ivermectin per kg (100 x the recommended dose of 0.3 mg per kg) injected subcutaneously to pigs caused lethargy, ataxia, bilateral mydriasis, intermittent tremors, laboured breathing and lateral recumbency.

5.9 Special Warnings for each Target Species

Details provided above apply. See also points 5.2, 5.3 and 5.5.

5.10 Withdrawal Periods

Meat: 28 days

5.11 Special Precautions to be taken by the person administering the product to animals

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

6. PHARMACEUTICAL PARTICULARS

6.1 Incompatibilities

None known.

6.2 Shelf-life

Shelf-life: 2 years.
Shelf-life after first broaching: 28 days.

6.3 Special Precautions for Storage

None.

6.4 Nature and Contents of Container

Multidose high density polyethylene bottles of 50 ml, 250 ml and 500 ml sealed with bromobutyl seals and aluminium overseals, containing a clear, colourless sterile solution.

6.5 Name or Style and Permanent address or Registered Place of Business of the Holder of the Authorisation to place the Product on the Market

Bimeda,
(a division of Cross Vetpharm Group Limited)
Broomhill Road, Tallaght,
Dublin 24,
Ireland.

6.6 Special Precautions for the disposal of unused product or waste material, if any

Any unused veterinary product or waste material derived from the product should be disposed of in accordance with local requirements. The product should not enter water courses as this may be dangerous to fish and other aquatic organisms.

7. Additional Information

Marketing Authorisation Number