ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Hippomectin 12 mg/g Oral Gel for horses.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active substances:
Per gram:
Ivermectin 12 mg

Excipients:
For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Oral Gel.
Almost colourless to slightly yellow, opalescent gel.

4. CLINICAL PARTICULARS

4.1 Target species

Horses.

4.2 Indications for use, specifying the target species

The product is indicated for the treatment of parasitic infestations in horses due to:

Large strongyles
Strongylus vulgaris (adults and arterial larval stages)
S. edentatus (adults & tissue larval stages)
S. equinus (adults)
Triodontophorus spp. (adults)
Triodontophorus brevicauda
Triodontophorus serratus
Craterostomum acuticaudatum, (adults)

Small Strongyles (adult and fourth stage larvae including benzimidazole-resistant strains)
Coronocyclus spp
Coronocyclus coronatus
Coronocyclus labiatus
Coronocyclus labratus
Cyathostomum spp
Cyathostomum catinatum
Cyathostomum pateratum
Cylicocyclus spp
Cylicocyclus ashworthi
Cylicocyclus elongatus
Cylicocyclus insigne
Cylicocyclus leptostomum
Cylicocyclus nassatus
Cylicocyclus radiatus
Cylicostephanus spp
Cylicostephanus asymetricus
Cylicostephanus bidentatus
Cylicostephanus calicatus
Cylicostephanus goldi

Cylicostephanus longibursatus
Cylicostephanus minutus
Cylicodontophorus spp
Cylicodontophorus bicornatus
Gyalocephalus capitatus
Parapoteriostomum spp
Parapoteriostomum euproctus
Parapoteriostomum mettami
Petrovinema spp
Petrovinema poculatum
Poteriostomum spp
Poteriostomum imparidentatum

Pinworms (adult and L4 stages)
Oxyuris equi

Ascarids (adult stages)
Parascaris equorum

Stomach wurms (adults stages)
Trichostrongylus axei, Habronema muscae

Intestinal threadworms (adult stages)
Strongyloides westeri

Skin nematodes (microfilariae)
Onchocerca sp.

Stomach bots (all larval stages)
Gasterophilus spp.

Lungworms (adult and L4 stages)
Dictyocaulus arnfieldi

4.3 Contraindications

Do not use in foals under 2 weeks of age.
Do not use in horses known to be hypersensitive to the active ingredients or any of the other Ingredients.

4.4 Special warnings for each target species

During healing of skin lesions caused by *Habronema* accompanied with important tissue changes, an adjusted treatment can be useful supplemental to use of this product. Re-infections and preventive measurements should also be considered.
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 body weight, 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."
Resistance to ivermectin has been reported in Parascaris equorum in horses in a number of countries including ones in the EU. Therefore the use of this product should be based on national (regional, farm) epidemiological information about susceptibility of nematodes 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 all non target species. Cases of intolerance are reported in dogs, especially Collies, Old English Sheepdogs and related breeds or crosses, and also in turtles and tortoises.
Dogs and cats should not be allowed to ingest spilled gel or have access to used packaging due to the potential for adverse effects related to ivermectin toxicity.

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

Wash hands after use.
Do not smoke, eat or drink while handling the product.

This product may cause eye irritation, skin irritation and skin sensitization.
Avoid contact with skin and eyes.
Wash hands or any exposed area after use.
In the event of eye contact flush the eye with copious amount of clean water and seek medical advice.

In case of accidental ingestion or eye irritation, seek medical help and show the doctor the package insert.

4.6 Adverse reactions (frequency and seriousness)

Some horses carrying heavy infection of *Onchocerca* microfilariae have experienced oedema and pruritus following dosing, assumed to be the result of death of large numbers of microfilariae. These signs resolve within a few days but symptomatic treatment may be advisable.

4.7 Use during pregnancy and lactation

Can be used during pregnancy and lactation.

4.8 Interaction with other medicinal products and other forms of interaction

None known.

4.9 Amounts to be administered and administration route

Dosage
Administer orally to horses over 2 weeks of age at the recommended dose level of 0,2 mg ivermectin per kg body weight as a single dose.

Administration
To ensure administration of a correct dose, body weight 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 overdosing.
Each syringe contains 120 mg ivermectin sufficient for the treatment of 600 kg bodyweight, or 160 mg ivermectin sufficient for the treatment of 800 kg bodyweight.
Each weight marking on the syringe plunger will deliver sufficient paste to treat 100 kg bodyweight.
The calculated dose is provided by adjusting the ring on the plunger according to the body weight of the horse. Remove the plastic cap from the tip of the nozzle. Make sure the horse's mouth contains no

feed. Insert the syringe into the horse's mouth at the interdental space. Advance the plunger as far as it will go, depositing the medication on the base of the tongue.

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

Mild transitory signs (slowed pupillary light response and depression) have been seen at a dose of 1.8 mg/kg (9 times the recommended dose level). Other signs seen at higher doses include mydriasis, ataxia, tremors, stupor, coma and death. The less severe signs have been transitory. No antidote has been identified; however, symptomatic therapy may be beneficial.

4.11 Withdrawal period(s)

Meat and offal: 18 days
Not permitted for use in mares producing milk for human consumption.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Endectocides

ATCvet code: QP54AA01

5.1 Pharmacodynamic properties

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.

5.2 Pharmacokinetic particulars

In the horse the maximum plasma concentration (average of 32 ng/ml) is reached 6 hours after administration of a dose rate of 0.3 mg ivermectin per kg bodyweight.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Hydroxyethylcellulose
Anise oil
Propylene glycol (E1520).

6.2 Incompatibilities

Do not mix this product with other veterinary medicinal products.

6.3 Shelf life

Shelf-life of the veterinary medicinal product as packaged for sale: 3 years.
Shelf-life after first opening the immediate packaging: 8 weeks.

6.4 Special precautions for storage

Do not store above 25°C.
Do not refrigerate or freeze.

6.5 Nature and composition of immediate packaging

Pre-filled multi-dose (LDPE) syringe with adjustable screw ring closed with a (PE) cap, packed in a cardboard box.
Each syringe contains 10 g or 13.3 g gel.

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

.Do not contaminate surface waters or ditches with product or used container since ivermectin is EXTREMELY DANGEROUS TO FISH AND AQUATIC LIFE.
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

Le Vet B.V.
Wilgenweg 7
3421 TV Oudewater
The Netherlands
tel: +31 (0)348 565858
fax: +31 (0)348 565454
e-mail: info@levetpharma.com

8. MARKETING AUTHORISATION NUMBER(S)

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

10 DATE OF REVISION OF THE TEXT

PROHIBITION OF SALE, SUPPLY AND/OR USE

Not applicable.

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

(OUTER CARTON / CARDBOARD BOX)

Read the package leaflet before use.

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Hippomectin 12 mg/g Oral Gel for horses
(Ivermectin)

2. STATEMENT OF ACTIVE AND OTHER SUBSTANCES

Active substances per gram:
Ivermectin 12 mg

3. PHARMACEUTICAL FORM

Oral gel.

4. PACKAGE SIZE

Multi-dose syringe with 10 gram / 13.3 gram gel.

5. TARGET SPECIES

Horses.

6. INDICATION(S)

-

7. METHOD AND ROUTE(S) OF ADMINISTRATION

For oral administration.

8. WITHDRAWAL PERIOD

Meat and offal: 18 days
Not permitted for use in mares producing milk for human consumption.

9. SPECIAL WARNING(S), IF NECESSARY

-

10. EXPIRY DATE

EXP month/year .....
Shelf-life after first opening the immediate packaging: 8 weeks.

11. SPECIAL STORAGE CONDITIONS

Do not store above 25°C.
Do not refrigerate or freeze.

12. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCTS OR WASTE MATERIALS, IF ANY

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

13. THE WORDS "FOR ANIMAL TREATMENT ONLY" AND CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE, if applicable

For animal treatment only.
To be supplied only on veterinary prescription.

14. THE WORDS "KEEP OUT OF THE REACH AND SIGHT OF CHILDREN"

Keep out of the reach and sight of children.

15. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Marketing Authorisation Holder
Name: Le Vet B.V.
Address: Wilgenweg 7
3421 TV Oudewater
The Netherlands

16. MARKETING AUTHORISATION NUMBER(S)

17. MANUFACTURER'S BATCH NUMBER

Batch number .....

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

(Pre-filled multidosis PE SYRINGE with adjustable screw ring closed with a PE cap)

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Hippomectin 12 mg/g Oral Gel for horses
(Ivermectin)

2. QUANTITY OF THE ACTIVE SUBSTANCE(S) PER GRAM

1 gram contains
Ivermectin 12 mg.

3. CONTENTS BY WEIGHT, BY VOLUME OR BY NUMBER OF DOSES

Syringe containing 10 gram / 13.3 gram gel.

4. ROUTE(S) OF ADMINISTRATION

For oral administration.

5. WITHDRAWAL PERIOD

Meat and offal: 18 days
Not authorised for use in mares producing milk for human consumption.

6. BATCH NUMBER

Batch number .....

7. EXPIRY DATE

EXP (month/year) .....
Once opened, use by 8 weeks.

8. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only.

B. PACKAGE LEAFLET

PACKAGE LEAFLET
Hippomectin 12 mg/g Oral Gel for horses

1. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER AND OF THE MANUFACTURING AUTHORISATION HOLDER RESPONSIBLE FOR BATCH RELEASE, IF DIFFERENT

Marketing authorisation holder:
Name: Le Vet B.V.
Address: Wilgenweg 7
3421 TV Oudewater
The Netherlands

Manufacturer for the batch release:
Name: Produlab Pharma B.V.
Address: Forellenweg 16
4941 SJ Raamsdonksveer
The Netherlands

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

Hippomctin 12 mg/g Oral Gel for horses
(Ivermectin)

3. STATEMENT OF THE ACTIVE SUBSTANCE(S) AND OTHER INGREDIENT(S)

Active substances per gram:
Ivermectin 12 mg

Excipients
Hydroxyethylcellulose, anise oil, propylene glycol (E1520).

Description
Almost colourless to slightly yellow, opalescent gel.

4. INDICATION(S)

The product is indicated for the treatment of parasitic infestations in horses due to:
Large strongyles
Strongylus vulgaris (adults and arterial larval stages)
S. edentatus (adults & tissue larval stages)
S. equinus (adults)
Triodontophorus spp. (adults)
Triodontophorus brevicauda
Triodontophorus serratus
Craterostomum acuticaudatum, (adults)
Small Strongyles (adult and fourth stage larvae including benzimidazole-resistant strains)
Coronocyclus spp
Coronocyclus coronatus
Coronocyclus labiatus
Coronocyclus labratus
Cyathostomum spp
Cyathostomum catinatum
Cyathostomum pateratum
Cylicocyclus spp
Cylicocyclus ashworthi

Cylicocyclus elongatus
Cylicocyclus insigne
Cylicocyclus leptostomum
Cylicocyclus nassatus
Cylicocyclus radiatus
Cylicostephanus spp
Cylicostephanus asymetricus
Cylicostephanus bidentatus
Cylicostephanus calicatus
Cylicostephanus goldi
Cylicostephanus longibursatus
Cylicostephanus minutus
Cylicodontophorus spp
Cylicodontophorus bicornatus
Gyalocephalus capitatus
Parapoteriostomum spp
Parapoteriostomum euproctus
Parapoteriostomum mettami
Petrovinema spp
Petrovinema poculatum
Poteriostomum spp
Poteriostomum imparidentatum
Pinworms (adult and L4 stages)
Oxyuris equi
Ascarids (adult stages)
Parascaris equorum
Stomach wurms (adults stages)
Trichostrongylus axei, Habronema muscae
Intestinal threadworms (adult stages)
Strongyloides westeri
Skin nematodes (microfilariae)
Onchocerca sp.
Stomach bots (all larval stages)
Gasterophilus spp.
Lungworms (adult and L4 stages)
Dictyocaulus arnfieldi

5. CONTRAINDICATIONS

Do not use in foals under 2 weeks of age.
Do not use in horses known to be hypersensitive to the active ingredients or any of the other Ingredients.

6. ADVERSE REACTIONS

Some horses carrying heavy infection of *Onchocerca* microfilariae have experienced oedema and pruritus following dosing, assumed to be the result of death of large numbers of microfilariae. These signs resolve within a few days but symptomatic treatment may be advisable.

If you notice any serious effects or other effects not mentioned in this leaflet, please inform your veterinary surgeon.

7. TARGET SPECIES

Horses.

8. DOSAGE FOR EACH SPECIES, ROUTE(S) AND METHOD OF ADMINISTRATION

Administer orally to horses over 2 weeks of age at the recommended dose level of 0,2 mg ivermectin per kg body weight as a single dose.

9. ADVICE ON CORRECT ADMINISTRATION

To ensure administration of a correct dose, body weight 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 overdosing.
Each syringe contains 120 mg ivermectin sufficient for the treatment of 600 kg bodyweight or 160 mg ivermectin sufficient for the treatment of 800 kg bodyweight.
Each weight marking on the syringe plunger will deliver sufficient paste to treat 100 kg bodyweight.
The calculated dose is provided by adjusting the ring on the plunger according to the body weight of the horse. Remove the plastic cap from the tip of the nozzle. Make sure the horse's mouth contains no feed. Insert the syringe into the horse's mouth at the interdental space. Advance the plunger as far as it will go, depositing the medication on the base of the tongue.

10. WITHDRAWAL PERIOD

Meat and offal: 18 days
Not authorised for use in mares producing milk for human consumption.

11. SPECIAL STORAGE PRECAUTIONS

Do not store above 25°C.
Do not refrigerate or freeze.
Keep out of the reach and sight of children.
Do not use after the expiry date stated on the label.
Shelf-life after first opening the immediate packaging: 8 weeks.

12. SPECIAL WARNING(S)

Special warnings for each target species
During healing of skin lesions caused by *Habronema* accompanied with important tissue changes, an adjusted treatment can be useful supplemental to use of this product. Re-infections and preventive measurements should also be considered.
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 body weight, 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."
Resistance to ivermectin has been reported in Parascaris equorum in horses in a number of countries including ones in the EU. Therefore the use of this product should be based on national (regional, farm) epidemiological information about susceptibility of nematodes and recommendations on how to limit further selection for resistance to anthelmintics."

Special precautions for use in animals
Avermectins may not be well tolerated in all non target species. Cases of intolerance are reported in dogs, especially Collies, Old English Sheepdogs and related breeds or crosses, and also in turtles and tortoises.
Dogs and cats should not be allowed to ingest spilled gel or have access to used packaging due to the potential for adverse effects related to ivermectin toxicity.

Special precautions to be taken by the person administering the veterinary medicinal product to animals
Wash hands after use.
Do not smoke, eat or drink while handling the product.
This product may cause eye irritation, skin irritation and skin sensitisation
Avoid contact with skin and eyes
Wash hands or any exposed area after use.
In the event of eye contact flush the eye with copious amount of clean water and seek medical advice.
In case of accidental ingestion or eye irritation, seek medical help and show the doctor the package insert.

Use during pregnancy and lactation
Can be used during pregnancy and lactation.

Overdose (symptoms, emergency procedures, antidotes)(if necessary)
Mild transitory signs (slowed pupillary light response and depression) have been seen at a dose of 1.8 mg/kg (9 times the recommended dose level). Other signs seen at higher doses include mydriasis, ataxia, tremors, stupor, coma and death. The less severe signs have been transitory. No antidote has been identified; however, symptomatic therapy may be beneficial.

Interaction with other medicinal products and other forms of interaction
None known.

Incompatibilities
Do not mix this product with other veterinary medicinal products.

13. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCT OR WASTE MATERIALS, IF ANY

Do not contaminate surface waters or ditches with product or used container since ivermectin is EXTREMELY DANGEROUS TO FISH AND AQUATIC LIFE.Medicines should not be disposed of via wastewater or household waste.
Ask your veterinary surgeon how to dispose of medicines no longer required. These measures should help to protect the environment.

14. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED

MM/DD/YYYY

15. OTHER INFORMATION

Pharmacodynamic properties
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.

Pharmacokinetic particulars
In the horse the maximum plasma concentration (average of 32 ng/ml) is reached 6 hours after administration of a dose rate of 0.3 mg ivermectin per kg bodyweight.

Package (size)
Pre-filled multi-dose (LDPE) syringe with adjustable screw ring closed with a (PE) cap, packed in a cardboard box.
Each syringe contains 10 g or 13.3 g gel.

For any information about this veterinary medicinal product, please contact the local representative of the marketing authorisation holder.