ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

GUARDIAN SR 3.4 mg/ml powder and solvent for suspension for injection for dogs

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active substance:
Per 100 g of microsphere:
Moxidectin 10 g
When reconstituted with vehicle (17 ml) the final suspension contains 3.4 mg/moxidectin/ml.

Qualitative composition of excipients and other constituents	**Quantitative composition if that information is essential for proper administration of the veterinary medicinal product**
Excipients (microspheres)	
Glyceryl tristearate q.s.	100 g
Vehicle	
Hydroxypropyl methyl cellulose	
Methyl p-hydroxybenzoate	0.00189 g/ml
Propyl p-hydroxybenzoate	0.00022 g/ml
Sodium chloride	
Water for injection	

Microspheres: white to off-white free flowing powder. Slight aggregation may be observed which can be removed by shaking.
Vehicle: clear and colourless liquid.

3. CLINICAL INFORMATION

3.1 Target species

Dogs.

3.2 Indications for use for each target species

For the prevention of heartworm (*D. immitis*) in dogs.
For the prevention of cutaneous lesions and dermatitis caused by *D. repens.*
For the treatment of larval and adult infections of canine hookworms (*Ancylostomum caninum* and *Uncinaria stenocephala*) present at time of prevention of heartworm.

3.3 Contraindications

Do not use in dogs less than twelve weeks of age.
Do not administer by intravenous route.
Do not use in cases of hypersensitivity to the active substance or to any of the excipients.

3.4 Special warnings

None.

3.5 Special precautions for use

Special precautions for safe use in the target species:

The veterinary medicinal product should be only used in dogs tested negative for the presence of heartworm infection. Prior to initiating treatment with the veterinary medicinal product, infected dogs should be treated to remove adult heartworm and microfilaria. These treatments should be carried out under the responsibility of the veterinary surgeon.

The veterinary medicinal product is safe for use in ivermectin-sensitive dogs.

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

Avoid contact with skin and eyes.
Wash hands after use.
Take care to avoid self-injection. In case of accidental self-injection, seek medical advice immediately and show the package leaflet or the label to the physician. Treat any specific signs symptomatically.

Special precautions for the protection of the environment:

Not applicable.

3.6 Adverse events

Target species: dogs.

Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Injection site inflammation[1], Injection site pain[1] Diarrhoea, Vomiting Angioedema, Anaphylaxis, Hypersensitivity reaction[2], Urticaria Ataxia[3], Tremor[3] Pruritus Lethargy

[1]May be observed 2 – 3 weeks after injection.
[2]May include local reaction (e.g. face, mucosae, legs, testicle, palpebral, lip)
[3]Signs are transient.

Reporting adverse events is important. It allows continuous safety monitoring of a veterinary medicinal product. Reports should be sent, preferably via a veterinarian, to either the marketing authorisation holder or the national competent authority via the national reporting system. See also the package leaflet for respective contact details.

3.7 Use during pregnancy, lactation or lay

Pregnancy and lactation:

The veterinary medicinal product can be used during pregnancy and lactation.

3.8 Interaction with other medicinal products and other forms of interaction

None known.

3.9 Administration routes and dosage

The veterinary medicinal product should be administered at dose of 0.17 mg of moxidectin per kg bodyweight as single dose by subcutaneous injection, i.e. 0.05 ml of the final suspension for injection per kg bodyweight. When administered within one month of the starting activity of the intermediate host (mosquito), the veterinary medicinal product has shown persistent efficacy over the seasonal period of risk for heartworm caused by *D. immitis* and cutaneous lesions caused by *D. repens* in Europe.
Persistent preventative efficacy of the veterinary medicinal product versus *A. caninum* and *U. stenocephala* has not been determined.

For growing dogs between 12 weeks and 9 months of age the following procedure is indicated: Administer the full dose of constituted veterinary medicinal product considering the body weight of the dog at time of treatment. Do not overdose in anticipation of the pup's expected future weight. Because of the rapid change in bodyweight expected for puppies of 12 weeks of age, an additional treatment might be required to insure full protection. Use according to a risk assessment by a responsible veterinarian. Subsequently seasonal treatment may coincide with the dogs annual vaccination.

The following table may be used as a guide to dosage:

Dog b.w. (kg)	**Dose volume (mL)**	**Dog b.w. (kg)**	**Dose volume (mL)**
1	0.05	35	1.75
5	0.25	40	2.00
10	0.50	45	2.25
15	0.75	50	2.50
20	1.00	55	2.75
25	1.25	60	3.00
30	1.5	65	3.25

Dogs over 65 kg receive 0.25 mL for each additional 5 kg body mass.

If a dosage of the veterinary medicinal product is substituting for monthly heartworm preventative treatment, its first dose should be administered within one month from last treatment.

Each package contains moxidectin 10% microspheres and vehicle vials with needles for air inflow and syringe.

Mixing instructions:
1. Withdraw 17 ml of sterile vehicle from the vial labelled **Vehicle for** GUARDIAN SR 3.4 mg/ml powder and solvent for suspension for injection for dogs and do not use any other vehicle.
2. Insert the vent needle provided in the package into the vial labelled **microspheres** for GUARDIAN SR 3.4 mg/ml powder and solvent for suspension for injection for dogs to facilitate the exit of air and then of the veterinary medicinal product.
3. Gently transfer the sterile vehicle into the microsphere vial, (if added too quickly some of vehicle could come out).
4. Once the sterile vehicle has been added, remove the vent and transfer needles from the microsphere vial.
5. Shake the microsphere vial thoroughly until an evenly mixed suspension is ready.
6. Allow the suspension to stand for at least 10 minutes to allow large air bubbles to dissipate.
7. Record the date of mixing on the microsphere vial for shelf life purpose.
8. Before every use, gently swirls the mixture to achieve a uniform suspension.
9. Administer promptly after filling the syringe. If administration is delayed, gently rock the syringe prior to injection to maintain an even suspension of microsphere and ensure accurate dosing.
10. Use an appropriately sized sterile syringe with an 18 G or 20G x 1 inch needle for administration. (A 20 gauge needle is recommended for dogs less than 20 kg, and an 18 gauge for those over 20 kg).

Once reconstituted, the veterinary medicinal product should appear as a white suspension, uniform in consistency and without visible aggregates . The closures should not be punctured more than 16 times.

3.10 Symptoms of overdose (and where applicable, emergency procedures and antidotes)

Granulomatous lesions were discovered, which were usually well-defined and small in size, in about half the subjects treated with a dosage equal to or higher than 0.17 mg/kg (recommended dose) and in most of the subjects treated with a dosage equal to or higher than 0.5 mg/kg (three or more times the recommended commercial dose). The average severity of the lesions was recorded as "mild" in the subjects treated with a dosage equal to or higher than 0.17 mg/kg and "moderate" in those treated with a dosage equal to or higher than 0.5 mg/kg**.**

3.11 Special restrictions for use and special conditions for use, including restrictions on the use of antimicrobial and antiparasitic veterinary medicinal products in order to limit the risk of development of resistance

For administration only by a veterinarian.

3.12 Withdrawal periods

Not applicable.

4. PHARMACOLOGICAL

4.1 ATCvet code: QP54AB02

4.2 Pharmacodynamic

Moxidectin is a parasiticide active against a wide range of internal and external parasites and it is a second generation macrocyclic lactone of the milbemycin family. Its principal mode of action is to open the chloride channels on the postsynaptic junction to allow the inflow of chloride ions and induce an irreversible resting state. This result in a flaccid paralysis and eventual death of the parasites exposed to the compound. There is no evidence that moxidectin has any other pharmacological effect on any mammalian organ or tissue. Moxidectin at dose of 0.17 mg/kg b.w. is effective in controlling the infection of *D. immitis* larvae in tissular migration. At recommended dosage moxidectin does not have any activity against adult forms of dirofilarial parasites. Moxidectin is also effective against some gastrointestinal parasites of dogs present at the time of prevention of heartworm.

4.3 Pharmacokinetic

Moxidectin is a highly lipophilic compound with residues found predominantly in fat when compared to other tissues. Following injection with the veterinary medicinal product, moxidectin is absorbed from the injection site and undergoes limited biotransformation by hydroxylation in the body. The expectation is that this hydroxylation occurs in the liver. The only significant route of excretion is in the faeces.The mean moxidectin serum concentrations have been measured in dogs following treatment with the veterinary medicinal product. Serum moxidectin levels were dose dependent. The highest average concentration of moxidectin was observed at the first measurement post-treatment (7-8 days). Peak moxidectin concentrations were 4.9 – 5.6 ppb and decreased continually during the balance of the study. Dogs treated with 0.17 mg moxidectin/kg BW had measurable serum moxidectin levels above the method Limit of Quantitation (0.5 ppb) through 204-238 days.

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities

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

5.2 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 36 months
Shelf life after reconstitution according to directions: 28 days stored at 2-8°C

5.3 Special precautions for storage

After reconstitution the product has to be kept at temperature of 2 °C – 8 °C.
Do not store above 25 °C
Do not freeze.
Keep the container in the outer carton in order to protect from light.

5.4 Nature and composition of immediate packaging

Moxidectin Microsphere Vial:
Brown coloured glass vial of 20 ml containing not less than 538 mg of moxidectin microsphere (equal to 59.2 mg of moxidectin).
Closure capped with a red aluminium flip-off seal.

Vehicle vial:
Colourless glass vial containing not less than 17 ml of vehicle.
Closure capped with a green aluminium flip-off seal.

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

Medicines should not be disposes of via wastewater or household waste.

Use take-back schemes for the disposal of any unused veterinary medicinal product or waste materials derived thereof in accordance with local requirements and with any national collection systems applicable to the veterinary medicinal product concerned.

The veterinary medicinal product should not enter water courses as Moxidectin may be dangerous for fish and other aquatic organisms.

6. NAME OF THE MARKETING AUTHORISATION HOLDER

To be completed nationally.

7. MARKETING AUTHORISATION NUMBER(S)

To be completed nationally.

8. DATE OF FIRST AUTHORISATION

To be completed nationally.

9. DATE OF THE LAST REVISION OF THE SUMMARY OF THE PRODUCT CHARACTERISTICS

To be completed nationally

10. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCTS

Veterinary medicinal product subject to prescription.

Detailed information on this veterinary medicinal product is available in the Union Product Database (https://medicines.health.europa.eu/veterinary).

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

Box for Moxidectin Microsphere Vial and Vehicle vial

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

GUARDIAN SR 3.4 mg/ml powder and solvent for suspension for injection

2. STATEMENT OF ACTIVE SUBSTANCES

Per 100 g of microsphere:
Moxidectin 10 g

3. PACKAGE SIZE

20 ml

4. TARGET SPECIES

Dogs

5. INDICATIONS

6. ROUTES OF ADMINISTRATION

Subcutaneous.

7. WITHDRAWAL PERIODS

8. EXPIRY DATE

Exp. {mm/yyyy}

Once reconstituted, use by…
Shelf life after reconstitution according to directions: 28 days stored at 2-8°C

9. SPECIAL STORAGE PRECAUTIONS

After reconstitution the product has to be kept at temperature of 2 °C – 8 °C.
Do not store above 25 °C
Do not freeze.
Keep the container in the outer carton in order to protect from light.

10. THE WORDS “READ THE PACKAGE LEAFLET BEFORE USE”

Read the package leaflet before use.

11. THE WORDS “FOR ANIMAL TREATMENT ONLY”

For animal treatment only.

12. THE WORDS “KEEP OUT OF THE SIGHT AND REACH OF CHILDREN”

Keep out of the sight and reach of children.

13. NAME OF THE MARKETING AUTHORISATION HOLDER

To be completed nationally

14. MARKETING AUTHORISATION NUMBERS

To be completed nationally

15. BATCH NUMBER

Lot {number}

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

Moxidectin Microsphere Vial

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

GUARDIAN SR

2. QUANTITATIVE PARTICULARS OF THE ACTIVE SUBSTANCES

Active Ingredients per 100 g of microsphere:
Moxidectin 10 g

3. BATCH NUMBER

Lot {number}

4. EXPIRY DATE

Exp. {mm/yyyy}

Once reconstituted use by…

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

Vehicle Vial

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

GUARDIAN

2. QUANTITATIVE PARTICULARS OF THE ACTIVE SUBSTANCES

Vehicle per 100 ml
Sodium chloride 0.9 g

3. BATCH NUMBER

Lot {number}

4. EXPIRY DATE

Exp. {mm/yyyy}

Once reconstituted use by…

B. PACKAGE LEAFLET

PACKAGE LEAFLET

1. Name of the veterinary medicinal product

GUARDIAN SR 3.4 mg/ml powder and solvent for suspension for injection for dogs

2. Composition

Active substance:
Per 100 g of microsphere:
Moxidectin 10 g
When reconstituted with vehicle (17 ml) the final suspension contains 3.4 mg/moxidectin/ml.

Qualitative composition of excipients and other constituents	**Quantitative composition if that information is essential for proper administration of the veterinary medicinal product**
Excipients (microspheres)	
Glyceryl tristearate q.s.	100 g
Vehicle	
Hydroxypropyl methyl cellulose	
Methyl p-hydroxybenzoate	0.00189 g/ml
Propyl p-hydroxybenzoate	0.00022 g/ml
Sodium chloride	
Water for injection	

Microspheres: white to off-white free flowing powder. Slight aggregation may be observed which can be removed by shaking.
Vehicle: clear and colourless liquid.

3. Target species

Dogs.

4. Indications for use

For the prevention of heartworm (*D. immitis*) in dogs.
For the prevention of cutaneous lesions and dermatitis caused by *D. repens.*
For the treatment of larval and adult infections of canine hookworms (*Ancylostomum caninum* and *Uncinaria stenocephala*) present at time of prevention of heartworm.

5. Contraindications

Do not use in dogs less than twelve weeks of age.
Do not administer by intravenous route.
Do not use in cases of hypersensitivity to the active substance or to any of the excipients.

6. Special warnings

Special warnings:
None.

Special precautions for safe use in the target species:
The veterinary medicinal product should be only used in dogs tested negative for the presence of heartworm infection. Prior to initiating treatment with the veterinary medicinal product, infected dogs should be treated to remove adult heartworm and microfilaria. These treatments should be carried out under the responsibility of the veterinary surgeon.

The veterinary medicinal product is safe for use in ivermectin-sensitive dogs.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
Avoid contact with skin and eyes
Wash hands after use
Take care to avoid self-injection. In case of accidental self-injection, seek medical advice immediately and show the package leaflet or the label to the physician. Treat any specific signs symptomatically.

Special precautions for the protection of the environment:
Not applicable.

Pregnancy and lactation:
The veterinary medicinal product can be used during pregnancy and lactation.

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

Overdose:
Granulomatous lesions were discovered, which were usually well-defined and small in size, in about half the subjects treated with a dosage equal to or higher than 0.17 mg/kg (recommended dose) and in most of the subjects treated with a dosage equal to or higher than 0.5 mg/kg (three or more times the recommended commercial dose). The average severity of the lesions was recorded as "mild" in the subjects treated with a dosage equal to or higher than 0.17 mg/kg and "moderate" in those treated with a dosage equal to or higher than 0.5 mg/kg.

Special restrictions for use and special conditions for use:
For administration only by a veterinarian.

Major incompatibilities:
Do not mix with other substances.
In the absence of compatibility studies, this veterinary medicinal product must not be mixed with other veterinary medicinal products.

7. Adverse events

Target species: dogs.

Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Injection site inflammation[1], Injection site pain[1] Diarrhoea, Vomiting Angioedema, Anaphylaxis, Hypersensitivity reaction[2], Urticaria

	Ataxia[3], Tremor[3] Pruritus Lethargy

[1]May be observed 2 – 3 weeks after injection.
[2]May include local reaction (e.g. face, mucosae, legs, testicle, palpebral, lip)
[3]Signs are transient.

Reporting adverse events is important. It allows continuous safety monitoring of a product. If you notice any side effects, even those not already listed in this package leaflet, or you think that the medicine has not worked, please contact, in the first instance, your veterinarian. You can also report any adverse events to the marketing authorisation holder using the contact details at the end of this leaflet, or via your national reporting system.

8. Dosage for each species, routes and method of administration

The veterinary medicinal product should be administered at a dose of 0.17 mg of moxidectin per kg bodyweight as single dose by subcutaneous injection, i.e. 0.05 ml of the final suspension for injection per kg bodyweight. When administered within one month of the starting activity of the intermediate host (mosquito), the veterinary medicinal product has shown persistent efficacy over the seasonal period of risk for heartworm caused by *D. immitis* and cutaneous lesions caused by *D. repens* in Europe.
Persistent preventative efficacy of the veterinary medicinal product versus *A. caninum* and *U. stenocephala* has not been determined.

For growing dogs between 12 weeks and 9 months of age, the following procedure is indicated. Administer the full dose of constituted veterinary medicinal product considering the body weight of the dog at time of treatment. Do not overdose in anticipation of the pup's expected future weight. Because of the rapid change in bodyweight expected for puppies of 12 weeks of age, an additional treatment might be required to insure full protection. Use according to a risk assessment by a responsible veterinarian. Subsequently seasonal treatment may coincide with the dogs annual vaccination.

The following table may be used as a guide to dosage:

Dog b.w. (kg)	**Dose volume (mL)**	**Dog b.w. (kg)**	**Dose volume (mL)**
1	0.05	35	1.75
5	0.25	40	2.00
10	0.50	45	2.25
15	0.75	50	2.50
20	1.00	55	2.75
25	1.25	60	3.00
30	1.5	65	3.25

Dogs over 65 kg receive 0.25 mL for each additional 5 kg body mass.

If a dosage of the veterinary medicinal product is substituting for monthly heartworm preventative treatment, its first dose should be administered within one month from last treatment.

Each package contains moxidectin 10% microspheres and vehicle vials with needles for air inflow and syringe.

Mixing instructions:
1. Withdraw 17 ml of sterile vehicle from the vial labelled **Vehicle for** GUARDIAN SR 3.4 mg/ml powder and solvent for suspension for injection for dogs and do not use any other vehicle.

2. Insert the vent needle provided in the package into the vial labelled **microspheres** for GUARDIAN SR 3.4 mg/ml powder and solvent for suspension for injection for dogs to facilitate the exit of air and then of the veterinary medicinal product.
3. Gently transfer the sterile vehicle into the microsphere vial, (if added to quickly some of vehicle could come out).
4. Once the sterile vehicle has been added, remove the vent and transfer needles from the microsphere vial.
5. Shake the microsphere vial thoroughly until an evenly mixed suspension is ready.
6. Allow the suspension to stand for at least 10 minutes to allow large air bubbles to dissipate.
7. Record the date of mixing on the microsphere vial for shelf life purpose.
8. Before every use, gently swirls the mixture to achieve a uniform suspension.
9. Administer promptly after filling the syringe. If administration is delayed, gently rock the syringe prior to injection to maintain an even suspension of microsphere and ensure accurate dosing.
10. Use an appropriately sized sterile syringe with an 18 G or 20G x 1 inch needle for administration. (A 20 gauge needle is recommended for dogs less than 20 kg, and an 18 gauge for those over 20 kg).

Once reconstituted, the veterinary medicinal product should appear as a white suspension, uniform in consistency and without visible aggregates.. The closures should not be punctured more than 16 times.

9. Advice on correct administration

The veterinary medicinal product should be only used in dogs tested negative for the presence of heartworm infection. Prior to initiating treatment with the product, infected dogs should be treated to remove adult heartworm and microfilaria. These treatments should be carried out under the responsibility of the veterinary surgeon.

10. Withdrawal periods

Not applicable.

11. Special storage precautions

Keep out of the sight and reach of children.
After reconstitution the product has to be kept at temperature of 2 °C – 8 °C.
Do not store above 25 °C
Do not freeze.
Keep the container in the outer carton in order to protect from light.

Do not use this veterinary medicinal product after the expiry date which is stated on the label. The expiry date refers to the last day of that month.
Shelf life after reconstitution according to directions: 28 days stored at 2-8°C

12. Special precautions for disposal

Medicines should not be disposes of via wastewater or household waste.

Use take-back schemes for the disposal of any unused veterinary medicinal product or waste materials derived thereof in accordance with local requirements and with any national collection systems applicable to the veterinary medicinal product concerned.

The veterinary medicinal product should not enter water courses as Moxidectin may be dangerous for dish and other aquatic organisms.

13. Classification of veterinary medicinal products

Veterinary medicinal product subject to prescription.

14. Marketing authorisation numbers and pack sizes

Marketing authorisation numbers to be completed nationally.

Moxidectin Microsphere Vial:
Brown coloured glass vial of 20 ml containing not less than 538 mg of moxidectin microsphere (equal to 59.2 mg of moxidectin).
Closure capped with a red aluminium flip-off seal.

Vehicle vial:
Colourless glass vial containing not less than 17 ml of vehicle.
Closure capped with a green aluminium flip-off seal.

15. Date on which the package leaflet was last revised

To be completed nationally.

<{MM/YYYY}>
<{DD/MM/YYYY}>
<{DD month YYYY}>

Detailed information on this veterinary medicinal product is available in the Union Product Database (https://medicines.health.europa.eu/veterinary).

16. Contact details

Marketing authorisation holder and contact details to report suspected adverse reactions:
To be completed nationally.

Manufacturer responsible for batch release:
Elanco France S.A.S.
26 Rue de la Chapelle
68330 Huningue
France

<17. Other information>