ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

LETIFEND lyophilisate and solvent for solution for injection for dogs

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each dose of 0.5 ml contains:

Active substance:
Leishmania infantum, strain MON-1, recombinant protein Q ≥ 36.7 ELISA units (EU)*

*Antigen content determined in an ELISA against an internal standard.

Excipients:

Qualitative composition of excipients and other constituents
Lyophilisate:
Sodium chloride
Arginine hydrochloride
Boric acid
Solvent:
Water for injections

White lyophilisate.

3. CLINICAL INFORMATION

3.1 Target species

Dogs.

3.2 Indications for use for each target species

For active immunisation of non-infected dogs from 6 months of age to reduce the risk of developing an active infection and/or clinical disease after exposure to *Leishmania infantum.*

The efficacy of the vaccine was demonstrated in a field study where dogs were naturally exposed to *Leishmania infantum* in zones with high infection pressure over a two years period.

In laboratory studies including experimental challenge with *Leishmania infantum*, the vaccine reduced the severity of the disease, including clinical signs and parasite burden in spleen and lymph nodes.

Onset of immunity: 4 weeks after vaccination.

Duration of immunity: 1 year after vaccination.

3.3 Contraindications

Do not use in cases of hypersensitivity to the active substance or to any of the excipients.

3.4 Special warnings

Vaccinate healthy and non-infected animals only.

The vaccine is safe in infected dogs. Re-vaccination of infected dogs did not worsen the course of the disease (during the 2-month observation period). No efficacy has been demonstrated in these animals.

A test for the detection of Leishmania infection is recommended prior to vaccination.
The impact of the vaccine in terms of public health and control of the human infection cannot be estimated from available data.

3.5 Special precautions for use

Special precautions for safe use in the target species:

De-worming of infested dogs prior to vaccination is recommended.
It is essential that measures to reduce exposure to sand-flies are employed in vaccinated animals.

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

Not applicable.

Special precautions for the protection of the environment:

Not applicable.

3.6 Adverse events

Dogs.

Very common (>1 animal / 10 animals treated):	Injection site scratching[1]
Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Hypersensitivity reactions[2]: allergic skin reaction (e.g. allergic oedema, urticaria, allergic pruritus) or anaphylaxis Lethargy[3], hyperthermia[3] Vomiting[3], diarrhoea[3]

[1] Spontaneous resolution observed within 4 hours.
[2] Appropriate symptomatic treatment should be administered.
[3] Treatment should be administered as needed.

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 its local representative or the national competent authority via the national reporting system. See the package leaflet for respective contact details.

3.7 Use during pregnancy, lactation or lay

The safety of the veterinary medicinal product has not been established during pregnancy or lactation. The use is not recommended during pregnancy and lactation.

3.8 Interaction with other medicinal products and other forms of interaction

No information is available on the safety and efficacy of this vaccine when used with any other veterinary medicinal product. A decision to use this vaccine before or after any other veterinary medicinal product therefore needs to be made on a case by case basis.

3.9 Administration routes and dosage

Subcutaneous use.

Primary vaccination scheme:
A single dose of 0.5 ml to be administered to dogs from 6 months of age.

Re-vaccination scheme:
A single dose of 0.5 ml to be given annually thereafter.

Method of administration:
Reconstitute one vial of the white lyophilisate using 0.5 ml of solvent.
Shake gently to give a clear solution and administer immediately the entire content (0.5 ml) of the reconstituted product.

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

Following administration of a double dose of the vaccine, no adverse reactions other than those mentioned in section 3.6 were observed.

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

Not applicable.

3.12 Withdrawal periods

Not applicable.

4. IMMUNOLOGICAL INFORMATION

4.1 ATCvet code: QI07AO01

To stimulate active immunity against disease caused by *Leishmania infantum* parasites.

Diagnostic tools designed to detect *Leishmania* antibodies (SLA or IFAT or rk-39 rapid diagnostic tests) should be suitable to enable discrimination between dogs vaccinated with this vaccine and dogs infected with *Leishmania infantum*.

The efficacy of the vaccine was demonstrated in a field study where seronegative dogs from a variety of breeds were naturally exposed to *Leishmania infantum* in zones with high infection pressure over a two year period. The data has shown that a vaccinated dog has 9.8 times less risk to develop clinical signs, 3.5 times less risk of having detectable parasites and 5 times less risk to develop clinical disease than a non-vaccinated dog.

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities

Do not mix with any other veterinary medicinal product, except the solvent supplied for use with the veterinary medicinal product.

5.2 Shelf life

Lyophilisate:
Shelf life of the veterinary medicinal product as packaged for sale: 4 years.

Solvent:
Shelf life of the solvent: 5 years.

Shelf life after reconstitution according to directions: use immediately.

5.3. Special precautions for storage

Store in a refrigerator (2 ºC – 8 ºC).
Do not freeze.

5.4 Nature and composition of immediate packaging

Lyophilisate vial
Type I glass vials containing 1 dose of vaccine.

Solvent vial
Type I glass vials containing 0.8 ml of solvent.

Vials are both closed with a bromobutyl stopper and an aluminium cap.

Pack sizes:
Plastic box containing 1 vial of 1 dose of lyophilisate and 1 vial of 0.8 ml of solvent.
Plastic box containing 4 vials of 1 dose of lyophilisate and 4 vials of 0.8 ml of solvent.
Plastic box containing 5 vials of 1 dose of lyophilisate and 5 vials of 0.8 ml of solvent.
Plastic box containing 10 vials of 1 dose of lyophilisate and 10 vials of 0.8 ml of solvent.
Plastic box containing 20 vials of 1 dose of lyophilisate and 20 vials of 0.8 ml of solvent.
Plastic box containing 25 vials of 1 dose of lyophilisate and 25 vials of 0.8 ml of solvent.
Plastic box containing 50 vials of 1 dose of lyophilisate and 50 vials of 0.8 ml of solvent.
Plastic box containing 100 vials of 1 dose of lyophilisate and 100 vials of 0.8 ml of solvent.

Not all pack sizes may be marketed.

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 disposed 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.

6. NAME OF THE MARKETING AUTHORISATION HOLDER

LETI Pharma, S.L.U.

7. MARKETING AUTHORISATION NUMBER(S)

EU/2/16/195/001-008

8. DATE OF FIRST AUTHORISATION

Date of first authorisation: 20/04/2016

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

DD/MM/YYYY

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 II

OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

None

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

Plastic box

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

LETIFEND lyophilisate and solvent for solution for injection

2. STATEMENT OF ACTIVE SUBSTANCES

Each dose of 0.5 ml contains:
Leishmania infantum, strain MON-1, recombinant protein Q ≥ 36.7 EU

3. PACKAGE SIZE

1 vial of lyophylisate and 1 vial of solvent (1 dose)
4 vials of lyophylisate and 4 vials of solvent (4 doses)
5 vials of lyophylisate and 5 vials of solvent (5 doses)
10 vials of lyophylisate and 10 vials of solvent (10 doses)
20 vials of lyophylisate and 20 vials of solvent (20 doses)
25 vials of lyophylisate and 25 vials of solvent (25doses)
50 vials of lyophylisate and 50 vials of solvent (50 doses)
100 vials of lyophylisate and 100 vials of solvent (100 doses)

4. TARGET SPECIES

Dogs.

5. INDICATIONS

6. ROUTES OF ADMINISTRATION

Subcutaneous use.

7. WITHDRAWAL PERIODS

8. EXPIRY DATE

Exp {mm/yyyy}

Once reconstituted use immediately.

9. SPECIAL STORAGE PRECAUTIONS

Store in a refrigerator.
Do not freeze.

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

LETI Pharma, S.L.U.

14. MARKETING AUTHORISATION NUMBERS

EU/2/16/195/001	1 dose
EU/2/16/195/002	4 doses
EU/2/16/195/003	5 doses
EU/2/16/195/004	10 doses
EU/216/195/005	20 doses
EU/2/16/195/006	25 doses
EU/2/16/195/007	50 doses
EU/2/16/195/008	100 doses

15. BATCH NUMBER

Lot {number}

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

Vial of lyophilisate

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

LETIFEND lyophilisate

2. QUANTITATIVE PARTICULARS OF THE ACTIVE SUBSTANCES

Leishmania infantum, strain MON-1, recombinant protein Q

3. BATCH NUMBER

Lot {number}

4. EXPIRY DATE

Exp {mm/yyyy}

Once reconstituted use immediately.

5. NAME OF THE MARKETING AUTHORISATION HOLDER

Company logo (LETI Pharma, S.L.U.)

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

Vial of solvent

1. NAME OF THE SOLVENT

LETIFEND solvent

2. TARGET SPECIES

3. BATCH NUMBER

Lot {number}

4. EXPIRY DATE

Exp {mm/yyyy}

5. NAME OF THE MARKETING AUTHORISATION HOLDER

Company logo (LETI Pharma, S.L.U.)

B. PACKAGE LEAFLET

PACKAGE LEAFLET

1. Name of the veterinary medicinal product

LETIFEND lyophilisate and solvent for solution for injection for dogs

2. Composition

Each dose of 0.5 ml contains:

Active substance:
Leishmania infantum, strain MON-1, recombinant protein Q: ≥ 36.7 ELISA units (EU)*

*Antigen content determined in an ELISA against an internal standard.

White lyophilisate.

3. Target species

Dogs.

4. Indications for use

For active immunisation of non-infected dogs from 6 months of age to reduce the risk of developing an active infection and/or clinical disease after exposure to *Leishmania infantum.*

The efficacy of the vaccine was demonstrated in a field study where dogs were naturally exposed to *Leishmania infantum* in zones with high infection pressure over a two years period.

In laboratory studies including experimental challenge with *Leishmania infantum*, the vaccine reduced the severity of the disease, including clinical signs and parasite burden in spleen and lymph nodes.

Onset of immunity: 4 weeks after vaccination.

Duration of immunity: 1 year after vaccination.

5. Contraindications

Do not use in cases of hypersensitivity to the active substance or to any of the excipients.

6. Special warnings

Vaccinate healthy and non-infected animals only.

The vaccine is safe in infected dogs. Re-vaccination of infected dogs did not worsen the course of the disease (during the 2-month observation period). No efficacy has been demonstrated in these animals.

A test for the detection of Leishmania infection is recommended prior to vaccination.

The impact of the vaccine in terms of public health and control of the human infection cannot be estimated from available data.

Special precautions for safe use in the target species:
De-worming of infested dogs prior to vaccination is recommended.
It is essential that measures to reduce exposure to sand-flies are employed in vaccinated animals.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
Not applicable.

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

Pregnancy and lactation:
The safety of the veterinary medicinal product has not been established during pregnancy or lactation. Therefore, the use is not recommended during pregnancy and lactation.

Interaction with other medicinal products and other forms of interaction:
No information is available on the safety and efficacy of this vaccine when used with any other veterinary medicinal product. A decision to use this vaccine before or after any other veterinary medicinal product therefore needs to be made on a case by case basis.

Overdose:
Following administration of a double dose of the vaccine, no adverse reactions other than those mentioned in section 7 were observed.

Major incompatibilities:
Do not mix with any other veterinary medicinal product, except solvent supplied for use with the medicinal product.

7. Adverse events

Dogs.

Very common (>1 animal / 10 animals treated):	Injection site scratching[1]
Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Hypersensitivity reactions[2]: allergic skin reaction (e.g. allergic oedema -swelling-, urticaria -rash-, allergic pruritus -itching-) or anaphylaxis Lethargy[3] -inactivity-, hyperthermia[3] -fever Vomiting[3], diarrhoea[3]

[1] Spontaneous resolution observed within 4 hours.
[2] Appropriate symptomatic treatment should be administered as needed.
[3] Treatment should be administered as needed.

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 or the local representative of the marketing authorisation holder using the contact details at the end of this leaflet, or via your national reporting system: {national system details}

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

Subcutaneous use.

Primary vaccination scheme:
A single dose of 0.5 ml to be administered to dogs from 6 months of age.

Re-vaccination scheme:
A single dose of 0.5 ml to be given annually thereafter.

9. Advice on correct administration

Reconstitute one vial of the white lyophilisate using 0.5 ml of the solvent. Shake gently to give a clear solution, and administer immediately the entire content (0.5 ml) of the reconstituted product.

10. Withdrawal periods

Not applicable.

11. Special storage precautions

Keep out of the sight and reach of children.

Store in a refrigerator (2 ºC – 8 ºC).
Do not freeze.

Do not use this veterinary medicinal product after the expiry date which is stated on the label after Exp. The expiry date refers to the last day of that month.

Shelf life after reconstitution according to directions: use immediately.

12. Special precautions for disposal

Medicines should not be disposed 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 applicable national collection systems. These measures should help to protect the environment.

13. Classification of veterinary medicinal products

Veterinary medicinal product subject to prescription.

14. Marketing authorisation numbers and pack sizes

EU/2/16/195/001-008

Pack sizes:
Plastic box containing 1 vial of 1 dose of lyophilisate and 1 vial of 0.8 ml of solvent.
Plastic box containing 4 vials of 1 dose of lyophilisate and 4 vials of 0.8 ml of solvent.
Plastic box containing 5 vials of 1 dose of lyophilisate and 5 vials of 0.8 ml of solvent.
Plastic box containing 10 vials of 1 dose of lyophilisate and 10 vials of 0.8 ml of solvent.
Plastic box containing 20 vials of 1 dose of lyophilisate and 20 vials of 0.8 ml of solvent.
Plastic box containing 25 vials of 1 dose of lyophilisate and 25 vials of 0.8 ml of solvent.

Plastic box containing 50 vials of 1 dose of lyophilisate and 50 vials of 0.8 ml of solvent.
Plastic box containing 100 vials of 1 dose of lyophilisate and 100 vials of 0.8 ml of solvent.

Not all pack sizes may be marketed.

15. Date on which the package leaflet was last revised

DD/MM/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 manufacturer responsible for batch release:

LETI Pharma, S.L.U.
C/ Del Sol 5, Polígono Industrial Norte
Tres Cantos
28760 Madrid
SPAIN

Local representatives and contact details to report suspected adverse reactions:

België/Belgique/Belgien
LETI Pharma, S.L.U.
C/ Del Sol 5, Polígono Industrial Norte
Tres Cantos 28760 Madrid
(SPANJE/ESPAGNE/SPANIEN)
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For any information about this veterinary medicinal product, please contact the local representative of the marketing authorisation holder.

17. Other information

To stimulate active immunity against disease caused by *Leishmania infantum* parasites.

Diagnostic tools designed to detect *Leishmania* antibodies (SLA or IFAT or rk-39 rapid diagnostic tests) should be suitable to enable discrimination between dogs vaccinated with this vaccine and dogs infected with *Leishmania infantum*.

The efficacy of the vaccine was demonstrated in a field study where seronegative dogs from a variety of breeds were naturally exposed to *Leishmania infantum* in zones with high infection pressure over a two year period. The data has shown that a vaccinated dog has 9.8 times less risk to develop clinical signs, 3.5 times less risk of having detectable parasites and 5 times less risk to develop clinical disease than a non-vaccinated dog.