
An injection of life against Leishmaniasis
LetiFend®
VACCINE
TECHNOLOGY
DNA
RECOMBINANT
Excellent tolerability
SAFETY
72%
LEISHMANIASIS PREVENTION
EFFICACY
1 dose per year
CONVENIENCE
PROTECTION FROM
28 days
SPEED
NO INTERFERENCE WITH DIAGNOSIS
RELIABILITY
LETI

LetiFend®, a new recombinant v against canine leishmaniasis

Safety: Excellent tolerability shown in a wide range of breeds and ages.[1,2]

Efficacy: 72% prevention of canine leishmaniasis in areas at high risk of infection by *Leishmania infantum.*[1]

Convenience: A single annual dose confers immunity for 365 days.[1,2]

Speed: Protection against development of the disease from 28 days after vaccination.[1,2]

Reliability: Specific immune response to vaccination that does not interfere with the serologic diagnosis of the disease.[1,2,3]

vaccine

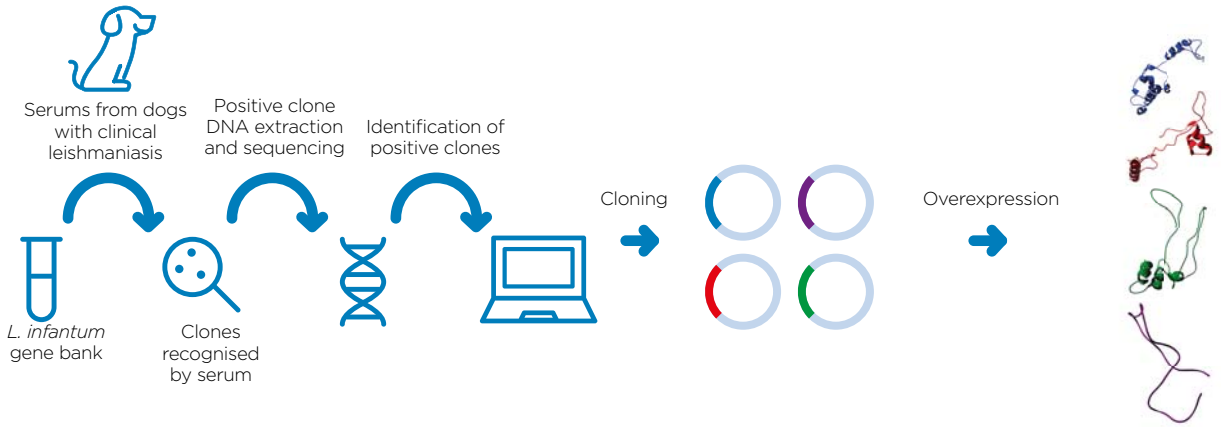
LetiFend®

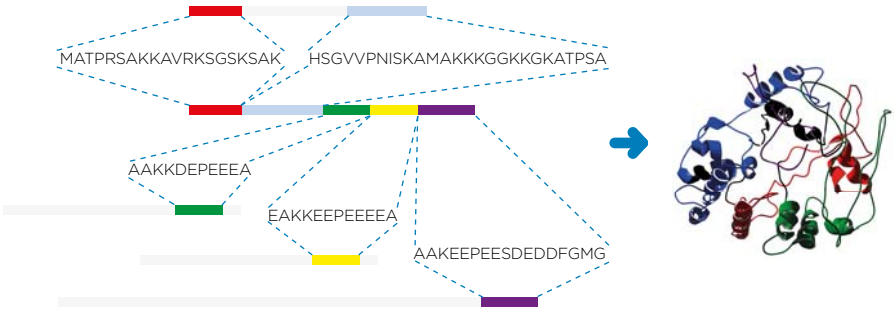
VACCINE TECHNOLOGY DNA RECOMBINANT

Innovation against canine leishmaniasis

- **LetiFend®**, a product obtained through **recombinant DNA technology**, the active substance of which is **Protein Q**.

- **Protein Q**, the active substance in **LetiFend®**, is a protein obtained by a combination of **5 highly antigenic fragments**, fusioned and cloned in *E. coli*, from 4 *Leishmania infantum*.[4]





Selection of the 5 antigen determinants recognised by a collection of serums from dogs with clinical leishmaniasis.[5-8]

Recombinant technology: innovation in prevention

- Recombinant vaccines form part of a **new strategy** and have been designed too ensure a **targeted and effective immune response with a high level of safety**.

- It prevents the need to inject complex formulas comprising live or inactive organisms or extracts of same in the presence of adjuvants.

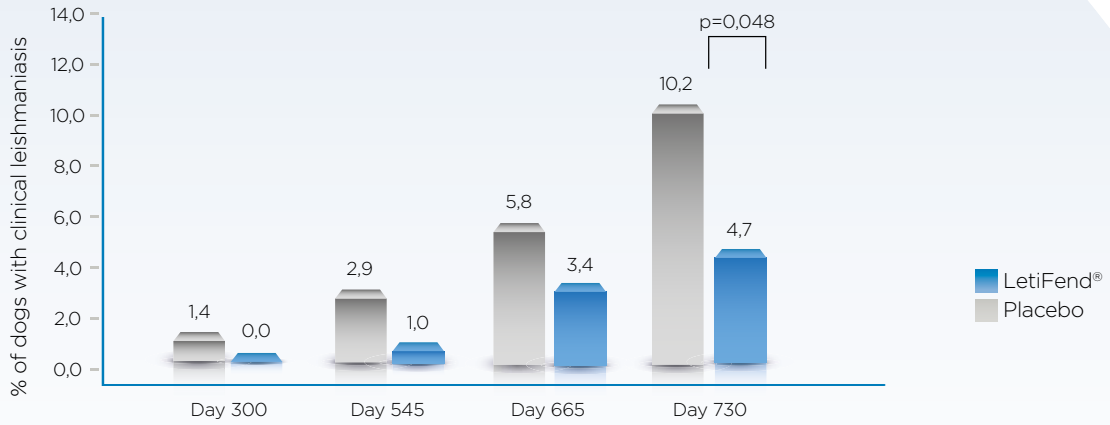
LetiFend®: clinically proven efficacy[1,2]

The efficacy of **LetiFend®** was shown in a large scale field study **with dogs of different breeds and ages** naturally exposed to infection for a two-year period. [1,2]

Field study design:

- 549 dogs of different breeds, ages and genders
- Animals that are seronegative at the start of the study
- Natural exposure to the sandfly in areas at high risk of infection (France and Spain)
- Re-vaccination after 365 days
- Evaluation of efficacy after two years
- Multicentre, randomised, double-blind, placebo-controlled study

LetiFend® showed a significant reduction in the development of canine leishmaniasis[1,2,*]



*** It was established that an animal with clinical leishmaniasis met 3 pre-defined criteria:**

1 - Presence of clinical signs attributable to the disease.
2 - Serology positive for *Leishmania*.
3 - Presence of parasites in lymph nodes or bone marrow.

72%
LEISHMANIASIS PREVENTION
EFFICACY

In high prevalence areas, **LetiFend® presents 72% clinical efficacy in the prevention of canine leishmaniasis.**[1]

LetiFend®

LetiFend® reduces the risk of developing clinical leishmaniasis[1,2]

A dog vaccinated with LetiFend® presents:[1,2]

Seriousness — 9.8 times less risk of presenting clinical signs.

Transmission — 3.5 times less risk of presenting parasites.

5 times less risk of developing clinical leishmaniasis.

Efficacy confirmed in laboratory studies

Different laboratory studies conducted with experimental infection with *Leishmania infantum* showed that **LetiFend®:**[1,2]

- ✔ Reduces **development** of the disease.
- ✔ Reduces **clinical signs**.
- ✔ Reduces **parasite burden in the spleen and lymph nodes**.
- ✔ **Protects** from 28 days.
- ✔ Duration of **immunity**: 1 year.

PROTECTION FROM **28 days** SPEED

LetiFend® has shown a high safety profile[1,2]

- **LetiFend®** has been subject to **strict controls to guarantee its safety**. In all, 827 dogs participated in **7 studies** in which it was found that **LetiFend®** is a **safe tool to combat canine leishmaniasis.**[1]

- Specific **safety studies:** 2 laboratory studies and a field study show that **LetiFend® is safe and well tolerated.**[1]

· In the field study, **there were no local or systemic undesirable effects** after vaccination, annual re-vaccination and **long-term follow-up (730 days).**[1]

· The laboratory studies evaluated safety after the administration of one dose, a double dose and repeated doses. The **only adverse effect found** after the administration of a dose was transient (<4 hours) pruritus at the injection site.[1]

Excellent tolerability

SAFETY

No serious systemic or local adverse effects were found.[1,2]

LetiFend®

Vaccination with LetiFend® does not interfere with the diagnosis of leishmaniasis[2,3]

SIN INTERFERENCIA EN EL DIAGNÓSTICO
FIABILIDAD

LetiFend®, a DIVA* vaccine that enables distinguishing between vaccinated and infected animals.[2]

*Differentiating Infected from Vaccinated Animals

- Serums of animals vaccinated with **LetiFend®** were subject to the serological tests most widely used for the diagnosis of leishmaniasis (ELISA, IFI and snap tests).

- The results showed that none of the evaluated tests were positive after analysis of the serums.[3]

LetiFend® enables the vaccination of a population of animals susceptible of catching the disease without compromising their subsequent serological diagnosis.

SUMMARY OF PRODUCT CHARACTERISTICS
1. NAME OF THE VETERINARY MEDICINAL PRODUCT LETIFEND freeze-dried and solvent for solution for injection for dogs **2. QUALITATIVE AND QUANTITATIVE COMPOSITION** Each 0.5 ml dose of vaccine contains: **Freeze-dried active substance:** Recombinant protein Q of *Leishmania infantum* MON 1 ≥ 36.7 ELISA units (EU)* * Antigen content determined with ELISA relative to internal standard. See 6.1 for a complete list of excipients. **3. PHARMACEUTICAL FORM** Freeze-dried product and solvent for solution for injection. White powder. **4. CLINICAL PARTICULARS 4.1 Target species** Dogs **4.2 Indications for use, specifying target species** For the active immunisation of uninfected dogs from 6 months of age, to reduce the risk of developing active infection and/or clinical disease after exposure to *Leishmania infantum*. The efficacy of the vaccine was shown in a field study in which dogs were naturally exposed to *Leishmania infantum* in areas at high risk of infection for a two-year period. In laboratory studies that included experimental infection with *Leishmania infantum*, the vaccine reduced the seriousness of the disease, and the clinical signs and parasite load in the spleen and lymph glands. Onset of immunity: 28 days after vaccination. Duration of immunity: 1 year after vaccination. **4.3 Contraindications** None. **4.4 Special warnings for each recipient species** The vaccine is safe in infected dogs. The re-vaccination of infected dogs did not aggravate the course of the disease (during the two-month observation period). Efficacy has not been shown in these animals. It is advisable to perform a leishmaniasis detection test before vaccination. The impact of the vaccine in terms of public health and control of human infection cannot be estimated with the available data. **4.5 Special precautions for use** Special precautions for use in animals. Only vaccinate healthy, uninfected animals. It is advisable to worm infested dogs before vaccination. It is essential to take steps to minimise exposure to the sandfly in vaccinated animals. Specific precautions to be taken by whoever administers the veterinary medicinal product to the animals None. **4.6 Adverse reactions (frequency and seriousness)** After the administration of the vaccine in dogs, scratches at the injection site were very commonly found. It was found that scratching spontaneously resolved within 4 hours. The frequency of undesirable effects must be classified according to the following groups: - Very common (more than 1 animal out of 10 presents undesirable effects during treatment) - Common (more than 1 but less than 10 animals out of every 100) - Uncommon (more than 1 but less that 10 animals out of every 1000) - Rare (more than 1 but less than 10 animals out of every 10 000) - Very rare (less than 1 animal out of every 10 000, including isolated cases). **4.7 Use during gestation or lactation** The safety of the veterinary medicinal product during gestation or lactation has not been shown. Its use is therefore not recommended during pregnancy or lactation. **4.8 Interaction with other drugs and other forms of interaction** There is no information available about the safety or efficacy off the use of this vaccine with another veterinary medicinal product. Decisions regarding the use of this vaccine before or after the administration of any other veterinary medicinal product must be on a case-by-case basis. **4.9 Posology and route of administration** Subcutaneous. Primary vaccination schedule: Administer a single dose of the vaccine (0.5 ml) in dogs from 6 months of age. Re-vaccination schedule: Administer a single dose of the vaccine (0.5 ml) annually. Method of administration: Dissolve a vial containing the white freeze-dried powder using 0.5 ml of solvent. Shake carefully to obtain a transparent solution and administer all (0.5 ml) the reconstituted medicinal product immediately. **4.10 Overdose (symptoms, emergency measures, antidotes) if necessary** After the administration of a double dose, the reactions are similar in nature to those found after the administration of a single dose (see section 4.6). **4.11 Wait time(s)** Not applicable. **5. IMMUNOLOGIC PROPERTIES** Pharmacotherapeutic group: immunologic medicinal products for canines (dogs). ATCvet code: QI07A To stimulate active immunity against the disease caused by *Leishmania infantum* parasites. The diagnostic tools designed to detect *Leishmania* antibodies (rk 39, IFAT or SLA snap tests) should be appropriate for distinguishing between dogs vaccinated with this medicinal product and those infected with *Leishmania infantum*. The efficacy of the vaccine was shown in a field study in which seronegative dogs of different breeds were naturally exposed to *Leishmania infantum* in areas at high risk of infection for a two-year period. The data obtained showed that vaccinated dogs have a 9.8 times lower risk of developing clinical signs, a 3.5 times lower risk of having detectable parasites and a 5 times lower risk of developing the clinical disease than unvaccinated dogs. **6. PHARMACEUTICAL PARTICULARS 6.1 List of excipients** Freeze-dried product: Sodium chloride. Arginine hydrochloride. Boric acid. Solvent: Water for injection. **6.2 Incompatibilities** Do not mix with a veterinary medicinal product other than the solvent supplied for use with the veterinary medicinal product. **6.3 Shelf life** Shelf life of the veterinary medicinal product packaged for sale: 2 years. Shelf life after reconstitution according to instructions: immediate use. **6.4. Special storage precautions** Store in refrigerator (from 2ºC to 8ºC). Do not freeze. **6.5 Nature and composition of the primary container** Vial of freeze-dried product Type I glass vial with 1 dose of vaccine; Vial of solvent Type I glass vial with 0.8 ml of solvent. Both vials are sealed with a bromo butyl stopper and an aluminium capsule. Formats: Plastic box with 1 vial containing a dose of freeze-dried product and 1 vial with 0.8 ml of solvent. Plastic box with 4 vials containing a dose of freeze-dried product and 4 vials with 0.8 ml of solvent. Plastic box with 5 vials containing a dose of freeze-dried product and 5 vials with 0.8 ml of solvent. Plastic box with 10 vials containing a dose of freeze-dried product and 10 vials with 0.8 ml of solvent. Plastic box with 20 vials containing a dose of freeze-dried product and 20 vials with 0.8 ml of solvent. Plastic box with 25 vials containing a dose of freeze-dried product and 25 vials with 0.8 ml of solvent. Plastic box with 50 vials containing a dose of freeze-dried product and 50 vials with 0.8 ml of solvent. Plastic box with 100 vials containing a dose of freeze-dried product and 100 vials with 0.8 ml of solvent. All the formats may not be marketed. **6.6 Special precautions for the disposal of unused veterinary medicinal product or the waste derived from its use** All unused veterinary medicinal products or waste derived from the same must be disposed of according to local standards. **7. MARKETING AUTHORISATION HOLDER** Laboratorios LETI, S.L. unipersonal C/ Del Sol 5, Polígono Industrial Norte Tres Cantos 28760 Madrid (SPAIN) +34 91 771 17 90 **8. MARKETING AUTHORISATION NUMBER(S)** EU/2/16/195/001-008 **9. DATE OF FIRST AUTHORISATION/RENEWAL OF AUTHORISATION** Date of first authorisation: DD/MM/YYYY **10. DATE OF REVISION OF TEXT** You will find detailed information about this veterinary medicinal product on the European Medicines Agency website http://www.ema.europa.eu/. **PROHIBITION OF SALE, DISPENSATION AND/OR USE** The manufacture, import, possession, sale, supply and/or use of LETIFEND is forbidden or could be forbidden in a Member State, in all or part of its territory, pursuant to national legislation. Whoever aims to manufacture, import, possess, sell, supply and/or use LETIFEND must consult the competent authority of the Member State regarding current vaccination policy before manufacture, import, possession, sale, supply and/or use.

LetiFend®

An injection of life against Leishmaniasis

LetiFend® and its administration protocol:[1,2]

- Apply from 6 months of age.
- Indicated for uninfected dogs.
- **Application in a single annual dose, even in the first vaccination.**
- **Protection from 28 days.**
- Subcutaneous administration.
- It is advisable to supplement vaccination with repellent insecticides.[1,2,9]

1 dose per year
CONVENIENCE

Vaccination represents a turning point in the prevention of leishmaniasis and is a fundamental tool for reducing the prevalence of the disease in endemic areas.[9]

LETI code	LetiFend formats®
46010003	1 box (10 doses)
46010002	1 box (4 doses)
46010001	1 box (1 dose)

VACCINE TECHNOLOGY DNA RECOMBINANT

Excellent tolerability
SAFETY

72% LEISHMANIASIS PREVENTION
EFFICACY

1 dose per year
CONVENIENCE

PROTECTION FROM 28 days
SPEED

NO INTERFERENCE WITH DIAGNOSIS
RELIABILITY

REFERENCES:
1. Committee for medicinal products for veterinary use (CVMP) european public assessment report (EPAR) for LETIFEND. European Medicines Agency, 2016. **2.** Summary of product characteristics of LetiFend®. European Medicines Agency, 2016. **3.** Iniesta V, Solano-Gallego L, Gómez-Nieto C, Fernández-Cotrina J, Fabra M, Balsa D, Brazis P. Vaccination with LetiFend®, a novel canine leishmaniosis vaccine, does not interfere with serological diagnostic tests. Proceedings of the SEVC & AVEPA, 2016. **4.** Soto M, Requena JM, Quijada L, Alonso C. Multicomponent chimeric antigen for serodiagnosis of canine visceral leishmaniasis. J Clin Microbiol. 1998 Jan;36(1):58-63. **5.** Soto M., Requena J.M., Quijada L., Angel S.O., Gomez L.C., Guzman F., Patarroyo M.E. and Alonso C. During active viscerocutaneous leishmaniasis the anti-P2 humoral response is specifically triggered by the parasite P proteins. Clin Exp Immunol. 1995. 100:246-252. **6.** Soto M, Requena JM, Quijada L, García M, Guzman F, Patarroyo ME, Alonso C. Mapping of the linear antigenic determinants from the Leishmania infantum histone H2A recognized by sera from dogs with leishmaniasis. Immunol Lett. 1995 Dec;48(3):209-14. **7.** Soto M, Requena JM, Quijada L, Guzman F, Patarroyo ME, Alonso C. Identification of the Leishmania infantum P0 ribosomal protein epitope in canine visceral leishmaniasis. Immunol Lett. 1995 Nov;48(1):23-8. **8.** Nieto CG, García-Alonso M, Requena JM, Mirón C, Soto M, Alonso C, Navarrete I.Analysis of the humoral immune response against total and recombinant antigens of Leishmania infantum: correlation with disease progression in canine experimental leishmaniasis. Vet Immunol Immunopathol. 1999 Feb 1;67(2):117-30. **9.** EFSA AHAW Panel (EFSA Panel on Animal Health and Welfare), 2015. Scientific Opinion on canine leishmaniosis. EFSA Journal 2015; 13(4):4075.

LETI

Customer service: **+34 93 584 33 88**
Fax: **+34 93 584 33 90**
www.leti.com/salud-animal