ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

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1. NAME OF THE VETERINARY MEDICINAL PRODUCT

LEISGUARD 5 mg/ml Oral Suspension for Dogs

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active substance:

Domperidone	5 mg

Excipients:

Methyl parahydroxybenzoate (E218)	1.80 mg
Propyl parahydroxybenzoate	0.20 mg
Quinoline yellow (E104)	0.20 mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Oral suspension
Yellow suspension

4. CLINICAL PARTICULARS

4.1. Target species

Dogs

4.2. Indications for use, specifying the target species

To reduce the risk of developing an active infection and clinical disease in case of contact with *Leishmania infantum*, through the enhancement of the cell-mediated immune response.

The efficacy of the product has been demonstrated in dogs under multiple natural parasite exposure in zones with high infection pressure.

Control of clinical progression of canine leishmaniosis at early stages of the disease (dogs with low to moderate positive antibody levels and mild clinical signs such as peripheral lymphadenopathy or papular dermatitis).

4.3. Contraindications

Do not use whenever stimulation of gastric motility might be dangerous eg. In the presence of gastrointestinal haemorrhage, mechanical obstruction or perforation.
Do not use in animals with a known hypersensitivity to domperidone or to any of the excipients.
Do not use in animals with prolactin-secreting pituitary tumor.
Domperidone is metabolized by the liver, therefore it should not be administered to patients with liver failure.

4.4. Special warnings for each target species

In case of severe infections, adequate aetiological treatment should be established in order to lower the parasitic load prior to consider a treatment with this veterinary medicinal product. In all cases, and taking into account the highly variable evolution of the disease, close patient follow up is recommended in order to adapt the treatment to the clinical stage of the animal, as required.

4.5. Special precautions for use

Special precautions for use in animals:
Administration of this veterinary medicinal product produces a transitory increase in plasma prolactin and could induce endocrine disturbances such as galactorrhoea. Therefore it should be used with caution in animals with previous episodes of pseudopregnancy.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
People with known hypersensitivity to domperidone or to any of the excipients should avoid contact with the veterinary medicinal product.
In case of accidental ingestion, seek medical advice and show the package leaflet or the label to the physician.
If you develop symptoms following exposure such as skin rash, you should seek medical advice and show this warning to the physician. Swelling of the face, lips or eyes, or difficulty with breathing are more serious symptoms and require urgent medical attention.
Do not smoke, eat or drink while handling the product.

4.6. Adverse reactions (frequency and seriousness)

In rare occasions, mammary gland disorders (mammary hyperplasia and milk production increase) have been observed. This is considered a consequence of the prolactine peaks induced by domperidone, which disappear after treatment discontinuation
In rare occasions, apathy and digestives signs (abdominal pain, diarrhoea, emesis, appetite loss) have been observed. These signs disappear once the treatment is withdrawn.

In very rare occasions, behavioural disorders have been observed.

***** The frequency of adverse reactions is defined using the following convention:
very common (more than 1 animal in 10 animals displaying adverse reactions during the course of one treatment)
common (more than 1 but less than 10 animals in 100 animals)
uncommon (more than 1 but less than 10 animals in 1,000 animals)
rare (more than 1 but less than 10 animals in 10,000 animals)
very rare (less than 1 animals in 10,000 animals, including isolated reports)

4.7. Use during pregnancy, lactation or lay

Pregnancy - Reproduction studies were performed in laboratory animals with no evidence of drug related teratogenic or embryotoxic effects. Signs of maternal toxicity were not seen in laboratory animals at doses 20 times higher than the recommended dose. However, there are no adequate and well controlled studies in pregnant bitches; therefore this drug should be used during pregnancy only in accordance with the benefit/risk assessment by the responsible veterinarian.

Lactation - Administration of domperidone to lactating females of several species has been shown to induce an increase of milk production. Administration of Leisguard to lactating bitches is likely to induce the same effect.

4.8. Interaction with other medicinal products and other forms of interaction

Cabergoline is a dopamine agonist that inhibits prolactin release from the pituitary gland. Therefore, its effects are antagonistic to those of domperidone.
Do not administer with stomach antacids such as omeprazole, cimetidine, or antacids
Domperidone should not be used with dopaminergic drugs such as dopamine or dobutamine

4.9. Amounts to be administered and administration route

0.5 mg/kg/d, equivalent to 1 ml/10 kg of Leisguard, once daily, during 4 consecutive weeks.

Leisguard may be administered directly into the mouth or mixed with food. To ensure a correct dosage, body weight should be determined as accurately as possible

Shake well before use.

There are several schedules of dosing:

A) for reducing the risk of developing an active infection and clinical disease in case of contact with Leishmania infantum,

In seronegative animals that have never showed any sign of *Leishmania spp.* infection, but live or travel to an endemic area, domperidone treatments should be programmed, taking into account the temporary prevalence of leishmaniosis vectors *(Phlebotomus spp.)* in the geographic area of the patient location or destination.

In high prevalence areas or in climates with a long infective season, one treatment every four months should be administered. In the Mediterranean area, it would be advised to treat in June, October and February.
In low prevalence areas, one treatment period at the beginning of the infective season and another treatment shortly after the end may suffice.

In all cases, the treatment strategy must be established by the attending veterinarian in accordance with the local incidence of the disease and temporary presence of the infective vectors.

B) For the Control of clinical progression of canine leishmaniosis at early stages of the disease

The treatment should be started immediately after diagnosis in order to help animals to self-limit the disease.

Treatment with Leisguard may be repeated as needed, in accordance with the clinical and serological follow up performed by the attending veterinarian.

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

In tolerance trials performed in dogs, this veterinary medicinal product has been administered at five times the recommended doses during periods up to one year with no noticeable adverse events.

4.11. Withdrawal period(s)

Not applicable.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Other protozoal agents
ATCvet Code: QP51AX24

5.1. Pharmacodynamic properties

Domperidone is a dopamine antagonist that promotes the release of prolactin from the pituitary gland. Its repeated daily administration results in daily regular acute and reversible peaks in prolactin blood levels with stimulatory effects on the cellular immune system, leading to activation of phagocytic leukocytes and as a result, to efficient intracellular microorganism (*Leishmania spp.*) reduction, at "in vitro" conditions. Domperidone also has anti-emetic and gastrokinetic properties due to its antagonism of dopamine receptors.

5.2. Pharmacokinetic particulars

Absorption

In fasting dogs, domperidone is rapidly absorbed reaching peak plasma concentrations (Cmax) of 16.6 ng/mL at 2 hours after oral administration. Oral absolute bioavailability of domperidone is low (24%) due to an extensive first-pass metabolism in the gut wall and liver. Domperidone's bioavailability is not affected when taken with food.

In studies performed in dogs at oral dosages between 2.5 and 40 mg/kg domperidone does not accumulate or induce its own metabolism. Domperidone is 91-93% bound to plasma proteins.

Distribution

Distribution studies with radiolabelled drug in animals have shown wide tissue distribution, although it does not readily cross the blood-brain barrier. Small amounts of drug cross the placenta in rats.

Metabolism

Domperidone undergoes rapid and extensive hepatic metabolism by hydroxylation and N-dealkylation. Aromatic hydroxylation of domperidone yields (hydroxy-domperidone) which is the main metabolite found in faeces. N-dealkylated metabolites and their conjugates can be detected in urine. None of the identified metabolites has any pharmacological activity.

Excretion

Elimination half-life (T1/2) is of 3.2 h. The distribution volume (Vd) of 3.3 L/kg, and plasma clearance (Cl) of 0.73 L/h/kg. The proportion of the drug excreted unchanged is small (15% of faecal excretion and approximately 2% of urinary excretion). The amount excreted in faeces or urine corresponds to 60% and 28% of the oral dose respectively. Very small amounts may be found in milk.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Sorbitol, liquid (non crystallising)
Microcrystalline cellulose and carmellose sodium
Methyl parahydroxybenzoate (E218)
Propyl parahydroxybenzoate
Saccharin sodium

Polysorbate 20
Quinoline yellow (E104)
Sodium hydroxide
Water, purified

6.2. Incompatibilities

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

6.3. Shelf life

Shelf-life of the veterinary medicinal product as packaged for sale: 4 years
Shelf-life after first opening the immediate packaging: 8 months

6.4. Special precautions for storage

Store in the original package.
Protect from light.

6.5. Nature and composition of immediate packaging

A 60 ml high-density polyethylene (HDPE) bottle closed with a low density polyethylene (LDPE) adapter and a HDPE child-proof screw-cap. The medicinal product is supplied with two syringes (LDPE barrel, polystyrene (PS) plunger and LDPE piston), one graduated up to 1.5 ml and the other graduated up to 5 ml.

DIVASA-FARMAVIC, S.A.:

Package sizes:
Carton box with 1 bottle of 60 ml and 2 syringes of 1.5 and 5 ml
Carton box with 2 bottles of 60 ml and 2 syringes of 1.5 and 5 ml
Carton box with 3 bottles of 60 ml and 2 syringes of 1.5 and 5 ml
Carton box with 4 bottles of 60 ml and 2 syringes of 1.5 and 5 ml

SINCROFARM, S.L.:

Package sizes:
Carton box with 2 bottles of 60 ml and 2 syringes of 1.5 and 5 ml
Carton box with 3 bottles of 60 ml and 2 syringes of 1.5 and 5 ml
Carton box with 4 bottles of 60 ml and 2 syringes of 1.5 and 5 ml

Not all pack sizes may be marketed.

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

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

Ecuphar Veterinaria S.L.U.
C/Cerdanya, 10-12 Planta 6º

08173 Sant Cugat del Vallés
Barcelona, Spain

8. MARKETING AUTHORISATION NUMBER(S)

9. DATE OF FIRST MARKETING AUTHORISATION/RENEWAL OF THE AUTHORISATION

10. DATE OF REVISION OF THE TEXT

02/2022

PROHIBITION OF SALE, SUPPLY AND/OR USE

Dispensing conditions:
To be supplied only on veterinary prescription.
Administration by a veterinary surgeon or under their direct responsibility.
For animal treatment only