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DECENTRALISED PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

CANIGEN L – CANIXIN L – VIRBAGEN CANIS L

MODULE 1

PRODUCT SUMMARY

EU Procedure number	FR/V/0310/001/DC
Name, strength and pharmaceutical form	CANIGEN L Suspension for injection, for dogs
Applicant	VIRBAC, France
Active substance(s)	Inactivated *Leptospira interrogans* serogroup Canicola serovar canicola, strain 601903 Inactivated *Leptospira interrogans* serogroup Icterohaemorrhagiae serovar icterohaemorrhagiae, strain 60189
ATC Vetcode	QI07AB01
Target species	dogs
Indication for use	For active immunisation of dogs from 8 weeks of age to: - prevent mortality and reduce infection, clinical signs, kidney colonisation, renal lesions and urine shedding of *Leptospira* Canicola - reduce infection, clinical signs, kidney colonisation and urine shedding of *Leptospira* Icterohaemorrhagiae

MODULE 2

The Summary of Product Characteristics (SPC) for this product is available on the website http://www.ircp.anmv.anses.fr/

MODULE 3

PUBLIC ASSESSMENT REPORT

Legal basis of original application	Decentralised application in accordance with Article of Directive 2001/82/EC as amended.
Date of completion of the original decentralised procedure	25/01/2017
Date product first authorised in the Reference Member State (MRP only)	
Concerned Member States for original procedure	AT, BE, BG, CY, CZ, DE, DK, EE, EL, ES, FI, HR, HU, IE, IT, LT, LU, LV, NL, NO, PL, PT, RO, SE, SI, SK and UK

I. SCIENTIFIC OVERVIEW

The vaccine is a non-adjuvanted vaccine against leptospirosis. The product consists in a suspension containing the inactivated leptospira antigens *Leptospira* Canicola & *Leptospira* Icterohaemorrhagiae. The vaccine is recommended for puppies from 8 weeks of age as 2 injections by the SC route at an interval of 3-4 weeks. An annual single booster is also recommended.

This vaccine is included in the applicant's canine vaccine range from the same applicant and is included in the applicant's program aiming to have harmonized European authorisations for its canine vaccines.

The product is produced and controlled using validated methods and tests, which ensure the consistency of the product released on the market.
It has been shown that the product can be safely used in the target species. Some minor transient reactions were commonly observed (local swellings or weakness). Hyperthermia, local pain or digestive signs were reported in very rare cases. All those signs resolved and disappeared spontaneously within few days and without any additional treatment. These reactions have been described in the SPC and are regarded as acceptable post-vaccination reactions for a canine vaccine.
The product is safe for the user, and for the environment, when used as recommended. Suitable warnings and precautions are indicated in the SPC.
The efficacy of the product was demonstrated according to the claims made in the SPC.
The overall benefit-risk analysis is in favour of granting a marketing authorisation.

II. QUALITY ASPECTS

A. Composition

The product is a liquid suspension containing the following inactivated active ingredients:

ingredients	Quantity per dose
Leptospira Canicola	conferring ≥ 80% protection*
Leptospira Icterohaemorrhagiae	conferring ≥ 80% protection*

*According to Ph. Eur. monograph 447, Hamster potency test

The vaccine is filled in 3 ml insulin type flasks made of neutral borosilicate type 1 glass closed with a butyl elastomer stopper. The particulars of the containers and controls performed are provided and conform to regulation.

The choice of the vaccine strains, the production process and the formulation are justified.

The inactivation process and the detection limit of the control of inactivation are correctly validated.

B. Method of Preparation of the Product

The product is manufactured fully in accordance with the principles of good manufacturing practice from a licensed manufacturing site.

The product is manufactured in accordance with the European Pharmacopoeia and relevant European guidelines.

C. Control of Starting Materials

The active substances *(Leptospira* Canicola & *Leptospira* Icterohaemorragiae) are established active substances described in the European Pharmacopoeia. The active substances are manufactured in accordance with the principles of good manufacturing practice.

The master and working seeds have been produced according to the Seed Lot System as described in the relevant guideline. The active substance specifications are considered adequate to control the quality of the material. Analytical batch data demonstrating compliance with these specifications have been provided.

Starting materials of non-biological origin used in production comply with relevant European pharmacopoeia monographs where these exist, or in-house specifications.

Biological starting materials used are in compliance with the relevant Ph. Eur. Monographs and guidelines and are appropriately screened for the absence of extraneous agents; any deviation was adequately justified.

Specific Measures concerning the Prevention of the Transmission of Animal Spongiform Encephalopathies

Scientific data and/or certificates of suitability issued by the EDQM have been provided and compliance with the Note for Guidance on Minimising the Risk of Transmitting Animal Spongiform Encephalopathy Agents via Human and Veterinary Medicinal Products has been satisfactorily demonstrated.

D. Control tests during production

The tests performed during production are described and the results of 3 consecutive runs, conforming to the specifications, are provided.

E. Control Tests on the Finished Product

The tests performed on the final product conform to the relevant requirements; any deviation from these requirements is justified. The tests include in particular:

- Physicochemical tests,
- Identification and assay of the active ingredient
- Bacterial and fungal sterility according to Ph. Eur.
- Control of inactivation

F. Batch to batch consistency

The demonstration of the batch to batch consistency is based on the results of 3 batches produced according to the method described in the dossier. Other supportive data provided confirm the consistency of the production process.

G. Stability

Stability data have been provided in accordance with applicable European guidelines, demonstrating the stability of vaccine (24 months) when stored under the approved conditions (2-8°C).

III. SAFETY ASSESSMENT

Vaccine batches used in the following studies are representative of the production process. Most of the studies have been conducted using a multivalent vaccine of the same canine vaccine range.

Laboratory trials

Safety of the vaccine is supported by investigations conducted in laboratory studies (3 and 4 repeated administrations of multivalent vaccine in groups of 10 puppies – 20 vaccinated puppies). The investigation was performed according to the recommendations of Directive 2001/82/EC as amended, the relevant guidelines and according to the relevant European Pharmacopoeia monographs when applicable.
Transient mild local reactions after vaccination have been observed in most of the vaccinated dogs. These reactions have been adequately described in the SPC and package leaflet.

In the absence of any demonstration data, it is recommended not to use the vaccine during pregnancy or lactation.

The excipients used are in annex II of MRL regulation and live components are not associated to zoonotic disease. Based on this information, no withdrawal period is proposed.

Safety and efficacy data demonstrate that this vaccine can be mixed before administration with live vaccine from the same applicant containing canine distemper virus, canine adenovirus, canine parvovirus and canine parainfluenza virus. No specific assessment of the interaction of this product with other medicinal product was made. Appropriate warning is included in the SPC.

Field studies

Safety of the vaccine was confirmed in field situation where 26 puppies aged 8 weeks from 6 veterinary clinics were vaccinated as recommended. In addition, pharmacovigilance data available for this vaccine or multivalent vaccines of the same applicant's canine range which are authorised for years in many European countries support the safety of this vaccine.
Most of the vaccinated dogs presented transient mild local reactions. In very rare cases, general post vaccine reactions could be observed in vaccinated dogs, including hyperthermia, limited and brief digestive signs such as vomiting, diarrhoea or signs of lethargy. All these reactions resolve spontaneously within few days and are regarded as not uncommon and acceptable post-vaccination reactions for a canine vaccine. They are adequately described in the SPC.

Ecotoxicity

The applicant provided a first phase environmental risk assessment in compliance with the relevant guideline which showed that no further assessment is required.

Warnings and precautions as listed on the product literature are adequate to ensure safety to the environment when the product is used as directed.

IV. CLINICAL ASSESSMENT (EFFICACY)

Laboratory Trials

The efficacy of the product has been demonstrated in laboratory studies in accordance with the relevant requirements which show the efficacy of the vaccine with regard to the claims. Most of the studies were conducted using a multivalent vaccine of the same canine vaccine range.

Efficacy of the vaccine against *Leptospira* Canicola and *Leptospira* Icterohaemorrhagiae (prevention of mortality, reduction of infection, clinical signs, kidney colonisation, renal lesions and urine shedding) is established in clinical studies including challenge performed 5 weeks after vaccination for *Leptospira* Canicola (12 vaccinated dogs – 12 controls) and 2 weeks after vaccination for *Leptospira* Icterohaemorrhagiae (6 vaccinated dogs – 6 controls). In these studies, prevention of mortality, reduction of infection, clinical signs, kidney colonisation, renal lesions and urine shedding has been established for *L.* Canicola and reduction of infection, clinical signs, kidney colonisation and urine shedding was established for *L.* Icterohaemorrhagiae.
Duration of immunity has been established through challenge protection study conducted one year after vaccination including for each serovar 6 vaccinated puppies and 6 controls. In these studies there was no significant difference between vaccinated and control dogs in reduction of kidney colonisation for *L.* Canicola and *L.* Icterohaemorrhagiae nor in renal lesions and urine shedding for *L.* Canicola.

Field Trials

Laboratory studies are completed by field studies relying on observation of the serological response after vaccination of 62 puppies of minimal age, various breeds and from 6 veterinary clinics. Supportive pharmacovigilance data are also provided for this vaccine and multivalent vaccines of the same canine vaccine range which are authorised for years in many European countries.

V. OVERALL CONCLUSION AND BENEFIT– RISK ASSESSMENT

The data submitted in the dossier demonstrate that when the product is used in accordance with the Summary of Product Characteristics, the benefit-risk profile for the target species is favourable and the quality and safety of the product for humans and the environment is acceptable.

MODULE 4

POST-AUTHORISATION ASSESSMENTS

The SPC and package leaflet may be updated to include new information on the quality, safety and efficacy of the veterinary medicinal product. The current SPC is available on the veterinary Heads of Agencies website (http://www.hma.eu/vmriproductindex.html).

This section contains information on significant changes which have been made after the original procedure which are important for the quality, safety or efficacy of the product.

<None>