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DECENTRALISED PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

CANIGEN DHPPi – CANIGEN CHPPi – VIRBAGEN CANIS SHAPPi – CANIXIN DHPPi

MODULE 1

PRODUCT SUMMARY

EU Procedure number	FR/V/297/001/DC
Name, strength and pharmaceutical form	CANIGEN CHPPi Lyophilisate for suspension for injection, for dogs
Applicant	VIRBAC, France
Active substance(s)	Attenuated canine distemper virus (CDV) – Lederle strain Attenuated canine adenovirus type 2 (CAV-2) – Manhattan strain Attenuated canine parvovirus (CPV) – CPV780916 strain Attenuated canine parainfluenza virus (CPiV) – Manhattan strain
ATC Vetcode	QI07AD04
Target species	dogs
Indication for use	For active immunisation of dogs from 8 weeks of age to: - prevent mortality and clinical signs caused by canine distemper virus - prevent mortality and clinical signs caused by canine adenovirus type 1 - prevent clinical signs and mortality and reduce excretion caused by canine parvovirus in challenge studies performed with a CPV-2b strain - prevent clinical signs and reduce excretion caused by canine parvovirus in a challenge study performed with a CPV-2c strain - reduce respiratory clinical signs and viral excretion caused by canine parainfluenza virus and canine adenovirus type 2

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	25/05/2016
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, IS, IT, LT, LU, LV, MT, NL, NO, PL, PT, RO, SE, SI, SK and UK

I. SCIENTIFIC OVERVIEW

The vaccine is a multivalent live virus vaccine indicated for active immunisation of healthy puppies from 8 weeks of age and dogs against canine distemper, adenovirus hepatitis, adenovirus respiratory disease, parvovirosis and parainfluenza. It is presented in a freeze-dried form in a vial to be reconstituted with a vial of water for injection (or with inactivated vaccine from the same applicant containing *Leptospira* canicola and *Leptospira* icteroaemorrhagiae and presented in liquid form).
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; the slight reactions observed are indicated in the SPC.
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 risk/benefit analysis is in favour of granting a marketing authorisation.

II. QUALITY ASPECTS

A. Composition

The product is constituted of a freeze-dried fraction containing the following live attenuated active ingredients :

ingredients	Quantity per dose
attenuated canine distemper virus, strain Lederle	$10^{3.0}$ to $10^{4.9}$ $CCID_{50}$
attenuated canine adenovirus type 2, Manhattan strain	$10^{4.0}$ to $10^{6.0}$ $CCID_{50}$
attenuated canine parvovirus, CPV 780916 strain	$10^{5.0}$ to $10^{6.8}$ $CCID_{50}$
attenuated canine parainfluenza virus, Manhattan strain	$10^{5.0}$ to $10^{6.9}$ $CCID_{50}$
Stabilisant Buffered isotonic solution	

This fraction is to be reconstituted with the solvent provided with the vaccine (water for injection) before vaccination.

The 2 fractions are 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.

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 substance (canine distemper virus, canine adenovirus, canine parvovirus, canine parainfluenza virus) are established active substance 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. Batch analytical data demonstrating compliance with this 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.

D. 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.

E. Control tests during production

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

F. 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 :
Lyophilisate :

- Physicochemical tests,
- Identification and assay of the active ingredient
- Bacterial, fungal and mycoplasmic sterility according to Ph. Eur.
- Viral purity
- Residual humidity

Solvent :

- Appearance
- Sterility
- Volume
- endotoxins

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 on the active substances have been provided in accordance with applicable European guidelines, demonstrating the stability of the active substance (18 months) when stored under the approved conditions (2-8°C).

The vaccine must be used immediately after reconstitution.

III. SAFETY ASSESSMENT

Vaccine batches used in the following studies are representative of the production process. For the live components, vaccine batches contain the maximal claimed titres. Most of the studies have been conducted using a more valent vaccine from the same canine vaccine range.

Laboratory trials

The safety of the administration of one dose, an overdose and the repeated administration of one dose in the dogs is demonstrated in groups of 8 weeks old vaccinated dogs (1 dose, 10 doses of lyophilisate reconstituted in 2 doses of liquid fraction, administration of 3 doses 2 weeks apart). 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.

For each live strain included in the vaccine (canine distemper virus, Lederle strain – canine adenovirus type 2, Manhattan strain- canine parvovirus, CPV780916 strain and canine parainfluenza virus, Manhattan strain), specific studies were carried out to describe the spread, dissemination, reversion to virulence, biological properties, recombination or genetic reassortment of the vaccine strains. The live viral vaccinal strain canine adenovirus type 2 and canine parvovirus have been demonstrated to spread from vaccinated dogs to animals put-in contact without leading to any pathological effects for these in-contact animals.

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 inactivated leptospira suspension vaccine (Leptospira canicola & Leptospira icterohaemorrhagiae) from the same applicant. 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 puppies aged 8 weeks from 6 veterinary clinics were vaccinated as recommended. Data complete also pharmacovigilance data available for this vaccine which is authorised for years in many European countries.
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. Vaccines used in these studies were formulated to contain minimal claimed titres. Most of the studies were conducted using a more valent vaccine from the same canine vaccine range.

Efficacy of the vaccine against distemper virus (prevention of mortality and clinical signs) is established according to the requirements of the European Pharmacopoeia (monograph 448) in clinical studies including challenge performed 3 weeks after vaccination. Duration of immunity has been established through a challenge protection study conducted one year after vaccination.

Efficacy of the vaccine against canine type 1 adenovirus (prevention of mortality and clinical signs) is established according to criteria defined in the European Pharmacopoeia in the corresponding monograph (1951) in a clinical study including challenge performed 4 weeks after vaccination. 1 year duration of immunity is estimated from antibody levels that do not decline during this period.

Efficacy of the vaccine against canine type 2 adenovirus (reduction of clinical signs and viral excretion) is established according to the requirements of the European Pharmacopoeia (1951) in a clinical study including challenge performed 3 weeks

after vaccination. 1 year duration of immunity has been established through a challenge protection study conducted one year after vaccination.

Efficacy of the vaccine against parvovirus (prevention of mortality and clinical signs, reduction of excretion) is established in conformity with the European Pharmacopoeia (monograph 964) in a clinical study including challenge with parvovirus type 2b performed 3 weeks after vaccination. In an additional study including challenge with parvovirus type 2c, efficacy of the vaccine to prevent clinical signs and reduction of excretion has also been established. 1 year duration of immunity is estimated for these 2 parvovirus strains from antibody levels that do not decline during this period.

Efficacy of the vaccine against canine parainfluenza virus (reduction of clinical signs) is established in conformity with the European Pharmacopoeia (monograph 1955) in a clinical study including challenge performed 4 weeks after vaccination. Duration of immunity has been established through a challenge protection study conducted one year after vaccination.

Data and analysis of serological response have been provided that suggest that maternally derived antibodies may negatively influence the immune response to vaccination (CAV-2 and CPV in particular). Based on the available data, it is justified to recommend in presence of such antibodies to perform three vaccine injections.

Field Trials

Laboratory studies are completed by field studies relying on observation of the serological response after vaccination of puppies of minimal age, various breeds and from 6 veterinary clinics. Supportive pharmacovigilance data are also provided as this vaccine which is 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 risk benefit 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.