Veterinary Medicines Directorate

United Kingdom
Veterinary Medicines Directorate
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MUTUAL RECOGNITION PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Nobivac KC

PuAR correct as of 07/03/2018 when RMS was transferred to IT. Please contact the RMS for future updates

MODULE 1

PRODUCT SUMMARY

EU Procedure number	UK/V/0142/001
Name, strength and pharmaceutical form	Nobivac KC $\geq 10^{8.0}$ and $\leq 10^{9.7}$cfu[1] of live *Bordetella bronchiseptica b*acteria strain B-C2 $\geq 10^{3.0}$ and $\leq 10^{5.8}$ $TCID_{50}$[2] of live canine parainfluenza virus strain Cornell. [1]colony forming units [2]Tissue Culture Infective Dose 50%
Applicant	Intervet International BV represented by Intervet UK Ltd Walton Manor Walton Milton Keynes Bucks MK7 7AJ
Active substance(s)	$\geq 10^{8.0}$ and $\leq 10^{9.7}$cfu[1] of live *Bordetella bronchiseptica b*acteria strain B-C2 $\geq 10^{3.0}$ and $\leq 10^{5.8}$ $TCID_{50}$[2] of live canine parainfluenza virus strain Cornell. [1]colony forming units [2]Tissue Culture Infective Dose 50%
ATC Vetcode	AI07AF
Target species	Dogs
Indication for use	Active immunisation of dogs against *Bordetella bronchiseptica* and canine parainfluenza virus for periods of increased risk to reduce clinical signs induced by *B. bronchiseptica* and canine parainfluenza virus and to reduce shedding of canine parainfluenza virus. Specific claims Onset of immunity: for *Bordetella bronchiseptica*: 72 hours after vaccination; for canine parainfluenza virus: three weeks after vaccination. Duration of immunity: 1 year

MODULE 2

The Summary of Product Characteristics (SPC) for this product is available on the Heads of Medicines Agencies (veterinary) (HMA(v)) website (www.hma.eu).

MODULE 3

PUBLIC ASSESSMENT REPORT

Legal basis of original application	Mutual recognition application in accordance with Article 13 of Directive 2001/82/EC as amended.
Date of completion of the original mutual recognition procedure	19 October 2000.
Date product first authorised in the Reference Member State (MRP only)	15 November 1999
Concerned Member States for original procedure	Greece, Spain, Finland, France, Ireland, Portugal, Luxembourg, Germany, Belgium, Austria, The Netherlands
Date of completion of the repeat use mutual recognition procedure	25 July 2007
Concerned Member States for repeat use procedure	Denmark, Italy, Norway, Poland, Sweden

I. SCIENTIFIC OVERVIEW

This is a live vaccine containing *Bordetella bronchiseptica* bacterial strain B-C2 and canine parainfluenza virus strain Cornell. Live intranasal vaccines are regarded as more effective where immunity is considered to be based on local immune reactions. The product is intended to combat kennel cough, which may be very serious in young dogs, but may also affect older animals, particularly during a stay in kennels. Two or more pathogens implicated in the disease may cause severe symptoms. The two active substances included in this vaccine are considered important causes of kennel cough.

Aseptically reconstituted vaccine is shaken, and the contents used within one hour. Dogs should be at least 3 weeks of age, and unvaccinated animals should receive one dose of the product prior to the risk period, (i.e. kennelling), as specified in the SPC[1] in order to obtain the benefit of both active agents. Revaccination should occur annually.

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

[1] SPC- Summary of Product Characteristics.

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 benefit/risk analysis is in favour of granting a marketing authorisation.

II. QUALITY ASPECTS

A. Composition

The product contains $\geq 10^{8.0}$ and $\leq 10^{9.7}$cfu of live *Bordetella bronchiseptica* bacteria strain B-C2 $\geq 10^{3.0}$ and $\leq 10^{5.8}$ $TCID_{50}^2$ of live canine parainfluenza virus strain Cornell. The excipients are a gelatine-based stabiliser, sodium chloride, phosphate buffer and water for injections.

The container/closure system consists of 3 ml (single dose presentation), or 10 ml (5 and 10 dose presentation) vials of glass Type I (Ph. Eur) closed with a halogenobutyl rubber stoppers and sealed with a coded aluminium cap and accompanied by a vial of sterile diluent and applicator. The diluent supplied for reconstitution is filled into the same type container (glass Type I vial and rubber stopper), as the product.
Pack sizes: Carton boxes with 1, 5, 10, 25 or 50 x 1, 5, or 10 doses of vaccine and diluent and applicator. The particulars of the containers and controls performed are provided and conform to the regulation. The choice of the vaccine strains and the absence of preservative are justified. The product is an established pharmaceutical form and its development is adequately described in accordance with the relevant European guidelines.

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. Process validation data on the product have been presented in accordance with the relevant European guidelines.

C. Control of Starting Materials

The active substances are *Bordetella bronchiseptica* and canine parainfluenza virus. The active substances are manufactured in accordance with the principles of good manufacturing practice. Starting materials of non-biological origin used in production comply with pharmacopoeial monographs.

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.

The master and working seeds have been produced according to the Seed Lot System as described in the relevant guideline.

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

Scientific data and/or certificates of suitability 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 those for purity and identity of the active substances, residual moisture and visual inspection.

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 were provided in accordance with applicable European guidelines, demonstrating the stability of the active substance when stored under the approved conditions. The in-use shelf-life of the reconstituted vaccine is supported by the data provided.

H. Genetically Modified Organisms

Not applicable.

J. Other Information

Do not mix with any other vaccine or immunological product.
In freeze-dried form: 27 months at +2°C to +8°C. Reconstituted vials should be used within 1 hour.

Store at +2°C to +8°C. The vaccine should be transported under the recommended conditions.

III. SAFETY ASSESSMENT

Laboratory trials

The safety of the administration of one dose, an overdose and the repeated administration of one dose of the product in the target animal was demonstrated in an appropriate study. In a GLP[2]-compliant safety test performed in young dogs, a suitable number of animals, displaying varying seronegativity for *Bordetella* showed no adverse reactions to treatment. For the administration of a single dose, (non-GLP), a suitable number of animals contributed to additional data on the safety of the product. No adverse reactions to vaccination were seen. Where an overdose was given, the most common signs seen were ocular and nasal discharge, and slight pharyngitis. Some sneezing and coughing were observed. The SPC carried suitable warnings with regard to signs that might be seen on application or on overdose application of the product. In general, signs seen in repeated administration of one dose mimicked those of the single dose.

Reproductivity Studies

Two studies, (one additionalnon-GMP study), ascertained that no adverse reactions were seen to be due to use of the vaccine in pregnant animals.

Special Requirements for Live Vaccines

Suitable analyses were performed to assess the dissemination of the vaccine strains. The SPC carries appropriate information with regard to the spread of vaccine strains to other animals, which may occur up to six weeks after application.

Suitable data with reference to reversion to virulence and recombination or genomic reassortment of vaccine strains were provided.

Field studies

Two field studies were presented. Firstly, a field safety study was presented. A suitable number of young dogs were allocated to one of two treatment groups and vaccinated either with Nobivac KC or Intrac (a competitor product). A third group remained as non-treated controls. The product was considered safe for use, based on analysis of results obtained. A second study confirmed the high level of safety associated with this vaccine, with no adverse reactions being directly related to use of the product.

Ecotoxicity

The applicant provided a suitable environmental risk assessment in compliance with the relevant guideline which showed that no further assessment was 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:-

[2] GLP – Good Laboratory Practise.

Dispose of waste material by boiling, incineration or immersion in an appropriate disinfectant in accordance with national requirements.

IV CLINICAL ASSESSMENT (EFFICACY)

Clinical Studies

Laboratory Trials

The efficacy of the product has been demonstrated in four laboratory studies in accordance with the relevant requirements.

Studies 1 and 2

Two studies established the efficacy of the canine parainfluenza fraction of the vaccine. A suitable number of dogs, free from antibodies to canine parainfluenza were vaccinated or allocated as controls. Challenge animals were given virulent virus oro-nasally in another study, three weeks post-vaccination. Clinical examinations were performed periodically showed that the vaccine was effective in reducing preventing clinical signs and virus isolation.. Seroconversion occurred effectively in all challenged animals.

Studies 3 and 4

Two studies established the efficacy of the *Bordetella* fraction of the vaccine.
A suitable number of seronegative and culture negative animals were vaccinated prior to challenge. A portion of animals served as negative controls. All animals were challenged with virulent *Bordetella bronchiseptica*, and animals were examined periodically after challenge. . Clinical signs detected in the vaccinated puppies were milder and of shorter duration than those seen in the control puppies. Seroconversion occurred effectively in all challenged animals., with no adverse reactions attributable to the vaccine.

Field Trials

Field trials were not performed as the product is to be used in dogs housed in kennels. All necessary data were obtained during kennel-related trials.

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 Product Information Database of the Veterinary Medicines Directorate website.

(www.gov.uk/check-animal-medicine-licensed)

The post-authorisation assessment (PAA) 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.

The PAA for this product is available on the Product Information Database of the Veterinary Medicines Directorate website.

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