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MUTUAL RECOGNITION PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

VERSICAN PLUS BB ORAL lyophilisate and solvent for oral suspension for dogs

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MODULE 1

PRODUCT SUMMARY

EU Procedure number	FR/V/0401/001/MR
Name, strength and pharmaceutical form	VERSICAN PLUS Bb ORAL – lyophilisate and solvent for oral suspension
Applicant	ZOETIS
Active substance(s)	live attenuated *Bordetella bronchiseptica* strain 92B
ATC Vetcode	QI07AE01
Target species	dogs
Indication for use	Active immunisation of dogs of 8 weeks of age or older to reduce clinical signs and excretion following infection with *Bordetella bronchiseptica* Onset of immunity : 3 weeks Duration of immunity : 12 months

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MODULE 2

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

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MODULE 3

PUBLIC ASSESSMENT REPORT

Legal basis of original application	Full application in accordance with Article 12 (3) of Directive 2001/82/EC as amended.
Date of completion of the original mutual recognition procedure	06/2019
Date product first authorised in the Reference Member State (MRP only)	12/2018
Concerned Member States for original procedure	Austria, Belgium, Bulgaria, Croatia, Czech republic, Cyprus, Denmark, Estonia, Finland, Germany, Greece, Hungary, Ireland, Italy, Latvia, Lithuania, Luxemburg, The Netherlands, Norway, Poland, Portugal, Romania, Slovenia, Slovakia, Spain, Sweden, United Kingdom

I. SCIENTIFIC OVERVIEW

VERSICAN PLUS Bb ORAL is a monovalent attenuated vaccine to be used by oral route for active immunisation of dogs from 8 weeks of age to reduce clinical signs and excretion following infection with *Bordetella bronchiseptica.* Vaccination is to be administered as a single dose from 8 weeks of age and annual revaccination is recommended.

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 dogs; 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.

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II. QUALITY ASPECTS

A. Composition

The product contains a lyophilisate fraction including live attenuated *Bordetella bronchiseptica*, strain 92B (between 1.4 10^8 to 5.5 10^9 colony forming units) to be reconstituted in the enclosed solvent.

Containers/closure system consist of colourless glass vials closed with rubber stoppers and aluminium cap.

Plastic box with 5 vials of 1 dose of lyophilisate and 5 vials of 1 dose of solvent
Plastic box with 10 vials of 1 dose of lyophilisate and 10 vials of 1 dose of solvent
Plastic box with 25 vials of 1 dose of lyophilisate and 25 vials of 1 dose of solvent

The choice of the vaccine strain and formulation is 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.
The product is manufactured in accordance with the European Pharmacopoeia and relevant European guidelines.

C. Control of Starting Materials

The active substance is attenuated *Bordetella bronchiseptica*. It complies with in-house specification, adequate to control the quality of the material. It is manufactured in accordance with the principles of good manufacturing practice. Master and Working seeds are handled according to the Seed lot system as described in the relevant guideline. Batch analytical data demonstrating compliance with this specification have been provided.

Starting materials of non-biological origin used in production comply with pharmacopoeia monographs.

Biological starting materials used are in compliance with the relevant Ph. Eur. Monographs and guidelines and are appropriately screened for the absence of

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extraneous agents according to the Ph. Eur; 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

A variety of tests are 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. The tests include in particular those for appearance, residual humidity, purity, identity and titration (freeze-dried fraction) or sterility, nitrates, fill volume and bacterial endotoxins (solvent).

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.

G. Stability

Stability data on the active substance have been provided in accordance with applicable European guidelines, demonstrating the stability of the active substance when stored under the approved conditions.

Stability data on the finished product have been provided in accordance with applicable European guidelines, demonstrating the stability of the product throughout its shelf life when stored under the approved conditions. An overage at formulation of active ingredient is applied in order to guarantee the minimal immunising titre during the vaccine shelf-life.

Shelf life of the veterinary medicinal product as package for sale: 24 months.
Shelf-life after reconstitution according to directions : use immediately.

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III. SAFETY ASSESSMENT

Safety studies were conducted using maximal content of the active ingredient in the vaccine.

Laboratory trials

The safety of the administration of one dose, an overdose and the repeated administration of one dose in 8 weeks old dogs is demonstrated. The investigation was performed according to the recommendations of Directive 2001/82/EC as amended and the relevant guidelines. It was concluded that the product has an acceptable safety profile. Reactions that may be observed after vaccination (rarely mild ocular discharge / very rarely mild transient diarrhoea, vomiting, nasal discharge, mild transient cough) are described in the SPC.

No investigation of effect on reproductive performance was conducted because the starting materials from which the product is derived is not considered a potential risk factor. Use of the vaccine is not recommended during gestation or lactation.

There are no data suggesting that this product might adversely affect the immune system of the vaccinated animal or its progeny therefore a specific study was not carried out.
A safety study has been conducted demonstrating that administration of VERSICAN PPLUS Bb ORAL (oral route) in combination with VERISCAN Plus DHPPi/L4R or VANGUARD 7 is safe. No data are available on the efficacy of the vaccines in case of combined vaccination. This is adequately mentioned in the SPC.

Specific studies were carried out to describe the spread, dissemination, and possibility of reversion to virulence of *Bordetella bronchiseptica.* Stability of the strain is confirmed is these studies and also by its use in the field for years in other vaccines from the applicant. The vaccinated dogs may shed the vaccine strain for 35 days in oronasal secretions and for 70 days in feces.
Vaccine strain has been shown to be safe for pigs that may be exposed. Cats exposed to the vaccine strain may show moderate clinical signs such as sneezing, nasal and ocular discharge. Immunocompromised persons are advised to avoid contact with the vaccine and vaccinated dogs during the shedding period.

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Field studies

A field study is provided conducted in USA that confirms that the vaccine administered by the oral route was safe after vaccination of 321 dogs from various sex, ages, breeds and locations. Post-vaccine reactions that were observed in vaccinated dogs do not differ from the reactions observed in laboratory and they are adequately described in the SPC. Data are also completed by pharmacovigilance review from the similar vaccine (same vaccine strain / same manufacturing process / oral route administration) commercialised in USA and Canada.

Ecotoxicity

The applicant provided a first phase environmental risk assessment in compliance with the relevant guideline. Safety of the vaccine strain has been investigated in cats and pigs. The strain poses an almost negligible risk to humans.

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)

Efficacy studies were conducted using vaccines containing the minimal content of active ingredient.

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IV.B Clinical Studies

Laboratory Trials

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

animals	vaccination	Experimental infection	RESULTS
4 groups of 16 dogs of 8 weeks of age	By the oral route, vaccine with different antigen concentrations	virulent *Bordetella bronchiseptica* strain administered 3 weeks after vaccination	Setting of the minimal immunising dose
2 groups of 16 dogs of 8 weeks of age	1 vaccinated group / 1 control	virulent *Bordetella bronchiseptica* strain administered 3 weeks after vaccination	Reduction of clinical signs and duration and amount of nasal shedding of *Bordetella bronchiseptica.*
2 groups of 16 dogs of 8 weeks of age	1 vaccinated group / 1 control	virulent *Bordetella bronchiseptica* strain administered 6 months after vaccination	Reduction of clinical signs and bacterial excretion (amount and duration)
2 groups of 16 dogs of 8 weeks of age	1 vaccinated group / 1 control	virulent *Bordetella bronchiseptica* strain administered 12 months after vaccination	Reduction of clinical signs and bacterial excretion (amount and duration)

The vaccine reduces the severity of clinical signs after infection with *Bordetella brocnhiseptica* and the excretion. Reduction of excretion is thought to decrease the spread and severity of an outbreak of *Bordetella bronchiseptica* and the vaccine may be especially recommended for dogs coming into contact with other dogs such as kennels, dog shows, puppy classes, breeding facilities etc.

IV.C. Field Trials

Field efficacy studies have not been performed with this vaccine. As efficacy laboratory studies allow to establish efficacy of the vaccination, and taking into

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account epidemiology and pathogenicity of *Bordetella bronchiseptica*, it has been considered that an additional study would be of limited value with regard to demonstration of efficacy and was not required.

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.

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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.

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