Veterinary Medicines Directorate

United Kingdom
Veterinary Medicines Directorate
Woodham Lane
New Haw
Addlestone
Surrey KT15 3LS

NATIONAL PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Protivity Lyophilisate and Solvent for Suspension for Injection for Cattle

Date Created: May 2024

MODULE 1

PRODUCT SUMMARY

Name, strength and pharmaceutical form	Protivity Lyophilisate and Solvent for Suspension for Injection for Cattle
Applicant	Zoetis UK Limited, 5th Floor, 6 St. Andrew Street, London, EC4A 3AE
Active substance(s)	Mycoplasma bovis
ATC Vetcode	QI02AE05
Target species	Cattle
Indication for use	For active immunisation of calves from 1 week of age to reduce clinical signs and lung lesions caused by Mycoplasma bovis infection.

MODULE 2

The Summary of Product Characteristics (SPC) for this product is available on the Product Information Database of the Veterinary Medicines Directorate.

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

MODULE 3

PUBLIC ASSESSMENT REPORT

Legal basis of original application	Full application in accordance with Article 8 of VMRs 2013 (Schedule 1, Part 1) as amended.
Date of conclusion of the procedure	1/3/2024

I. SCIENTIFIC OVERVIEW

This is a full application for Protivity Lyophilisate and Solvent for Suspension for Injection for Cattle.

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, any reactions observed are indicated in the SPC.[1] The product is safe for the user, the consumer of foodstuffs from treated animals and for the environment, when used as recommended. Suitable warnings and precautions are indicated in the SPC. The efficacy [2] 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. QUALITATIVE AND QUANTITATIVE PARTICULARS OF THE CONSTITUENTS

II.A. Composition

The product contains live modified *Mycoplasm bovis* strain N2805-1 and the excipients lactose monohydrate, potassium dihydrogen phosphate, dipotassium hydrogen phosphate trihydrate, monopotassium L-glutamate, gelatin, casein hydrolysate, basal medium eagle, magnesium chloride hexahydrate, phenol red, sodium hydrogen carbonate and water for injections.

The container/closure system consists of type I glass vials closed with bromobutyl or chlorobutyl rubber stoppers and sealed with aluminium caps. The particulars of the containers and controls performed are provided and conform to the regulation.

The choice of the vaccine strain 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.

[1] SPC – Summary of product Characteristics.
[2] Efficacy – The production of a desired or intended result.

II.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.

II.C. Control of Starting Materials

The active substance is *Mycoplasma bovis* an established active substance. The active substance is manufactured in accordance with the principles of good manufacturing practice.

Starting materials of non-biological origin used in production comply with Ph. Eur. or in-house specifications.

Biological starting materials used are in compliance with the relevant Ph. Eur. Monographs and guidelines or in-house monographs and are appropriately screened for the absence of extraneous agents according to the Ph. Eur.

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

The packaging materials comply with the relevant monographs.

II.C.4. Substances of Biological Origin

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.

II.D. Control Tests Carried Out at Intermediate Stages of the Manufacturing Process

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

II.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 are description, viable CFU count, sterility, residual humidity and identity.

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

II.F. 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.

G. Other Information

Shelf life of the veterinary medicinal product as packaged for sale: 2 years.
Shelf life after reconstitution according to directions: use immediately.
Store and transport refrigerated (2 °C – 8 °C).
Keep the vial in the outer carton in order to protect from light.

III. SAFETY ASSESSMENT

Laboratory trials

The safety of the administration of one dose, an overdose and the repeated administration of one dose in the target animal is demonstrated in laboratory studies. The investigation was performed according to the recommendations of Schedule 1, Part 1 as amended and the relevant guidelines.

No investigation of effect on reproductive performance was conducted because the vaccine is not intended for this category of animals. The safety of the veterinary medicinal product has not been established in breeding bulls. The safety of the veterinary medicinal product has not been established during pregnancy and lactation.

The applicant has addressed the issue of immunological functions by references to established literature.

Specific studies were carried out or justification was provided to describe the spread, dissemination, reversion to virulence, biological properties, recombination or genetic reassortment of the vaccine strain.

The active ingredient does not fall in the scope of residue regulations. The vaccine does not contain adjuvant or any other excipients that fall within the scope of the MRL regulations. Based on this information, no withdrawal period is proposed.

No specific assessment of the interaction of this product with other medicinal product was made. Therefore, an appropriate warning in the SPC is included.

Field studies

Four field studies were performed to evaluate safety and efficacy.

Two field studies were conducted with the administration of two 2 ml doses with a 3-week interval to calves. Overall, 811 animals were vaccinated and 406 animals received a non-treatment control. In the first study, only one animal showed signs of lameness and no other adverse events were observed after vaccine administration. In the second trial, no adverse events of unexpected type or frequency were detected during the 120 day observation period. No *M. bovis* positive swabs were found two weeks after vaccination, confirming that the *M. bovis* vaccine strain does not shed from vaccinated animals, and no animals were lame.

Two more studies were undertaken with control groups. Data analysis demonstrated no significant differences in clinical scoring after treatment administration between treatment groups and there were no significant temperature increases following vaccination. Only one animal showed lameness. No adverse events of unexpected type or frequency were detected.

Ecotoxicity

The applicant provided a Phase 1 environmental risk assessment in compliance with the relevant guideline which showed that no further assessment is required. The assessment concluded that the product presents a negligible risk to the environment. No warnings are therefore 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)

Clinical Studies

Laboratory Trials

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

A challenge model was established to determine the onset of immunity and serology of the vaccine.

Onset of Immunity

Two doses of the vaccine were given. On day 0 and day 21, a single dose was administered to the target species and a control group was administered diluent. The challenge was given by aerosol 12 days after the second vaccination. Vaccinated animals were demonstrated to have statistically significantly reduced clinical signs and lung lesions compared to the controls when challenged. This study supports the claims of reduction in clinical signs and lung lesions with an onset of immunity of 12 days from the completion of the basic vaccination scheme.

Duration of Immunity

A serological study was carried out. Animals either received the vaccine or the control on day 0 and day 21, and all animals received the vaccine on day 119.

The vaccinated animals had statistically significant increases in antibody titre on prior to the second vaccine administration on day 21 and thereon throughout the study. The duration of immunity has not been established.

Field Trials

Field studies were performed and are the same studies mentioned above in the Safety section.

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 of the product is favourable.

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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