ASSURING THE SAFETY, QUALITY AND EFFICACY OF VETERINARY MEDICINES

United Kingdom
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MUTUAL RECOGNITION PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Mypravac Suis Suspension for Injection

PuAR correct as of 18/05/2018 when RMS was transferred to ES. Please contact the RMS for future updates.

MODULE 1

PRODUCT SUMMARY

EU Procedure number	UK/V/0176/001/00
Name, strength and pharmaceutical form	Mypravac Suis Suspension for Injection
Applicant	LABORATORIOS HIPRA, S.A. Avda. La Selva, 135 17170 - AMER (Girona) Spain
Active substance	Inactivated *Mycoplasma hyopneumoniae* strain J 1.0 guinea pig-ED^{80}
ATC Vetcode	QI09AB13
Target species	Pigs
Indication for use	Fattening pigs: For active immunisation of healthy susceptible piglets between 7 and 10 days of age to reduce lung lesion scores and weight loss associated with *Mycoplasma hyopneumoniae* infection. Duration of immunity of 70 days after the first vaccination has been shown by experimental infection. Onset and longer duration of immunity have not been investigated in laboratory trials. But, under field conditions, improved weight gain and feed conversion rate over the growth period (6 months) have been demonstrated.

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	Full application in accordance with Article < > of Directive 2001/82/EC as amended.
Date of completion of the original mutual recognition procedure	20th March 2003
Date product first authorised in the Reference Member State (MRP only)	8th February 2002
Concerned Member States involved in the original MRP procedure	Austria, Belgium, Denmark, Germany, Greece, Hungary, Ireland. Italy, The Netherlands, Portugal, Spain, Sweden

I. SCIENTIFIC OVERVIEW

The product is for use in pigs, and is an inactivated, adjuvanted vaccine against enzootic pneumonia. The active substance is inactivated *Mycoplasma hyopneumoniae* (strain J). It is indicated for use at a dose of 2 ml per pig at the age of 7 -10 days, with a repeat dose being administered after 21 days. Deep intramuscular injection is given into the neck muscles, at the cervical-lateral area behind the ear, with the second dose preferably given on the other side of the neck. The product was first authorised in the UK in February 2002, via the Mutual Recognition procedure in March 2003, and then underwent a Repeat Use procedure in October 2005, and finally, a Renewal procedure in May 2008.

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, the consumer of foodstuffs from treated animals and for the environment, when used as recommended. Suitable warnings and precautions are indicated in the SPC.[1] 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.

[1] SPC – Summary of Product Characteristics.

II. QUALITY ASPECTS

A. Composition

The product contains inactivated *Mycoplasma hyopneumoniae* (strain J), adjuvants levamisole (as hydrochloride) and carbomer, and excipients methyl parahydroxybenzoate, sodium hydroxide, sodium chloride, sodium bisulphite and water for injections. The container/closure system consists of 20 ml (10 doses) Type I coloured glass vials (Ph. Eur.) 100 ml (50 doses) Type II coloured glass vials (Ph. Eur.) 250 ml (125 doses) and 500 ml (250 doses) high density polyethylene plastic bottles (Ph. Eur.), Type II rubber stoppers (Ph. Eur.) and aluminium caps.

Package sizes:
- Cardboard box with one glass vial of 10 doses with a rubber stopper and aluminium cap.
- Cardboard box with one glass vial of 50 doses with a rubber stopper and aluminium cap.
- Cardboard box with 10 glass vials of 10 doses with a rubber stopper and aluminium cap.
- Cardboard box with 12 plastic bottles of 125 doses with a rubber stopper and aluminium cap.
- Cardboard box with 12 plastic bottles of 250 doses with a rubber stopper and aluminium cap.

The particulars of the containers and controls performed are provided and conform to the regulation. The choice of the adjuvant, vaccine strain inactivating agent and the presence of preservative are justified. The inactivation process and the detection limit of the control of inactivation are correctly validated. The product's 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 substance is manufactured in accordance with the principles of good manufacturing practice, and does not have a European Pharmacopoeial (Ph. Eu) monograph. Starting materials of non-biological origin used in production comply with the appropriate monographs 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 according to relevant Guidelines. 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

Suitable documentation were 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 suitable assays, 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 appearance, stability, pH, analysis of active substance, concentration of excipients, packaging and volume control.

The demonstration of the batch to batch consistency is based on the results of 3 consecutive 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 substance have been 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

Shelf-life of the veterinary medicinal product as packaged for sale (glass bottles): 24 months. Shelf-life of the veterinary medicinal product as packaged for sale (HDPE bottles): 9 months. Shelf-life after first opening the immediate packaging: Use immediately after first opening.

Store and transport at 2ºC - 8ºC. Do not freeze.

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 was demonstrated in appropriate studies. The investigations were performed according to the recommendations of Directive 2001/82/EC as amended and the relevant guidelines. Information regarding any adverse effects due to use of the product are cited on the SPC.

No investigation of effect on reproductive performance was conducted because the vaccine is not intended for this category of animals.

The vaccine is inactivated and thus the specific tests to be performed for live vaccines are not applicable.

A withdrawal period was proposed based on relevant data. This was established as being 2 days for meat.

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

Three field studies were submitted, which provided data for both the Safety and Efficacy sections of the dossier. The studies were GCP-compliant assessments of the innocuousness and activity of the inactivated monovalent vaccine. A suitable number of young animals were inoculated with either vaccine or placebo, and second dose given 21 days later. The animals were examined at various time points throughout the trials. No seriously adverse reactions were observed.

Ecotoxicity

The applicant provided a first phase environmental risk assessment in compliance with the relevant guideline which showed that no further assessment was required. The assessment concluded that the low doses given should induce no anthelmintic resistance; the period in which levamisole could have a resistance-causing effect on nematodes within vaccinated pigs or in the environment is short. 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 which showed that the *Mycoplasma*

hyopneumoniae strains 3067, 3371 were pathogenic for pigs and were suitable for use in challenge studies for the efficacy of the proposed vaccine, that the vaccine when containing 10^8 ccu/dose provided the highest degree of protection against virulent challenge. This was established as the minimum effective dose. It was also seen that a serological test in guinea pigs provided a valid method for determining batch potency. Further studies, which analysed the effect of the vaccine grown in different media, including relevant controls, determined that the product was efficacious in reducing lung lesions associated with enzootic pneumonia, when associated with a specific growth medium.

Field Trials

Results of three trials were submitted. In all three trials, large numbers of pigs from a variety of sites were inoculated with vaccine or placebo, followed a second dose approximately 21 days later. Lung lesions were lower in vaccinates, although there were some deaths from pneumonia in both vaccinate and non-vaccinate groups. Deaths were lower in vaccinate groups. The efficacy of the vaccines was indicated by significantly higher weight gain and lower feed conversions for vaccinates as compared to controls. The SPC carries appropriate information.

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.

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