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

Stellamune Once

PuAR correct as of 17/05/2018 when RMS was transferred to DE.
Please contact the RMS for future updates.

MODULE 1

PRODUCT SUMMARY

EU Procedure number	UK/V/0157//001
Name, strength and pharmaceutical form	Stellamune Once
Applicant	Elanco Animal Health Eli Lilly & Company Limited Lilly House Priestley Road Basingstoke Hampshire RG24 9NL
Active substance(s)	Inactivated *Mycoplasma hyopneumoniae,* strain NL1042, between 4.5 and 5.2 $\log_{10}$ units*. *ELISA Relative Potency Units by comparison with a reference vaccine. (per 2 ml dose).
ATC Vet code	Q109AB13
Target species	Pigs
Indication for use	For active immunisation of piglets from 7 days of age to reduce lung lesions related to infection by *Mycoplasma hyopneumoniae* in fattening animals. The onset of immunity is within 2 weeks after vaccination. A duration of immunity of at least 25 weeks has been demonstrated. In more detailed studies in piglets from 3 weeks of age, vaccination has also been shown to reduce coughing and losses in weight gain related to infection by *Mycoplasma hyopneumoniae* in fattening animals. In these studies onset of immunity 3 weeks after vaccination and a duration of immunity of at least 23 weeks were demonstrated; periods shorter than 3 weeks or longer than 23 weeks were not tested.

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 (3) of Directive 2001/82/EC as amended.
Date of completion of the original mutual recognition procedure	06 September 2002.
Date product first authorised in the Reference Member State (MRP only)	10 September 2001.
Concerned Member States for original procedure	Austria, Belgium, Bulgaria, Denmark, France, Germany, Greece, Iceland, Ireland, Italy, Luxembourg, The Netherlands, Norway, Portugal, Romania, Spain, Sweden

I. SCIENTIFIC OVERVIEW

The product is an inactivated oil-adjuvanted emulsion for injection vaccine recommended for intramuscular administration to pigs for active immunisation of piglets from 7 days of age to reduce lung lesions related to infection by *Mycoplasma hyopneumoniae* in fattening animals. The onset of immunity is within 2 weeks after vaccination; and a duration of immunity of at least 25 weeks was demonstrated. In piglets from 3 weeks of age, vaccination was also shown to reduce coughing and weight gain losses associated with the disease in fattening animals. Here, the onset of immunity is 3 weeks post-vaccination and the duration of immunity is at least 23 weeks.

The product is produced and controlled using validated methods 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[1]. The product is safe for the user, for the consumer of foodstuffs derived from treated animals, 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.

[1] SPC – Summary of Product Characteristics.

II. QUALITY ASPECTS

A. Composition

The product contains inactivated *Mycoplasma hyopneumoniae,* strain NL1042, between 4.5 and 5.2 $\log_{10}$ units[2] adjuvanted with mineral oil. The excipients are thiomersal and water for injections.

The particulars of the containers and controls performed are provided and conform to the regulation. The choice of the adjuvant, vaccine strain and the presence of preservative are justified. The inactivation process and the detection limit of the control of inactivation are correctly validated.

The product is of an established pharmaceutical form and its development is adequately described in accordance with the relevant European guidelines. The product is presented in high density polyethylene vials containing 10, 50 or 125 doses of vaccine, respectively 20, 100 or 250 ml. The vials are sealed with chlorobutyl rubber closures and are packaged as boxes of 10 vials of 10 doses, 10 vials of 50 doses or 4 vials of 125 doses. Not all pack sizes may be marketed.

B. Method of Preparation of the Product

The product is manufactured fully in accordance with the principles of Good Manufacturing Practice at appropriately authorised manufacturing sites. Process validation data on the product have been presented in accordance with the relevant European guidelines. Working seed is inoculated after thawing into appropriate flasks, and passaging is performed, with pH of the product and cell density being regularly monitored.

C. Control of Starting Materials

The active substance, inactivated *Mycoplasma hyopneumoniae*, strain NL1042, is manufactured in accordance with the principles of Good Manufacturing Practice. Starting materials used in the production of the product comply with appropriate control data. 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 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.

[2] ELISA Relative Potency Units by comparison with a reference vaccine

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. Tests during production include those for purity, infectious titre, control of inactivation, sterility and test for residual sodium thiosulfate.

F. Control Tests on the Finished Product

The tests performed on the final product conform to the relevant requirements. Tests include those for appearance, identification of the active substance, sterility, complete inactivation, potency, extractable volume, stability of the emulsion, viscosity, pH and quantity of thiomersal.

G. Stability

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

H. Genetically Modified Organisms

Not applicable.

J. Other Information

Store and transport refrigerated (2° □C – 8° □C).
Protect from light.
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. The investigation was performed according to the recommendations of Directive 2001/82/EC as amended, and to relevant guidelines.

Effects on reproductive performance were not examined. The product is not to be used during pregnancy or lactation. An appropriate warning in the SPC is included. The product is not recommended to be used in conjunction with other products; a decision to use the vaccine before or after any other medication must be taken on a case by case basis.

The safety of the product administered at a single and double dose as given to the target species, was demonstrated in a GLP[3] study. The single dose was given as a 5.22 $\log_{10}$ RU/dose, and a negative control was included in the study,

[3] GLP – Good laboratory practice.

consisting of saline. Minor adverse reactions were observed, these are cited in the current SPC.

Field studies

GCP[4]-compliant studies were performed on a suitable number of *M. hyopneumoniae* seronegative and seropositive pigs, using the same maximum potency batch as used for the laboratory trial. The animals were observed for any adverse reaction, and no serious reactions were observed.

Ecotoxicity

The applicant provided an appropriate Phase I risk assessment in compliance with the relevant guideline. Warnings and precautions as listed on the product literature are adequate to ensure safety to the environment when the product is used as directed. No live vaccine enters the environment as the active substance is inactivated, and the mineral oil adjuvant also has no impact on the environment because the product is parenterally administered.

IV CLINICAL ASSESSMENT (EFFICACY)

Clinical Studies

A review of the causes of enzootic pneumonia of pigs was provided. The causes may be multifactorial in nature, with management of the disease significantly affected by environmental factors such as overcrowding, extremes of temperature, mixing of livestock and poor ventilation. *M. hyopneumoniae* is considered to be the primary agent of the pathogenesis of pneumonia, although other micro-organisms may be involved.

Laboratory Trials

Laboratory trials were performed in pigs of the minimum age recommended for vaccination in order to ascertain the minimum immunising dose of a single dose of the product. The serological status of pigs from *M. hyopneumoniae* positive and negative herds was confirmed where appropriate, and antibody titres of animals enrolled in the trial reflected those that might be seen in the field. The animals were challenged after approximately 2 weeks post-vaccination with a virulent heterologous *M. hyopneumoniae* strain and scored for lung lesions according to Ph. Eur. 2448. Statistical analysis demonstrated that serological status had no influence on the positive results obtained. Data in relation to the time to onset of immunity, and in support of the designated administration of the minimum dose were obtained. Similar studies were conducted in order to demonstrate a duration of immunity of not less than 25 weeks post-vaccination. The SPC carries the current specification for age of vaccination, onset and duration of immunity.

[4] GCP – Good clinical practice.

Field Trials

A number of commercial pig-rearing sites were used to test the vaccine in two tests. The animals were young pigs, either seropositive or seronegative for the disease. Results, where lung lesions were analysed, confirmed the efficacy of the product.

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)