IPAR

Publicly Available Assessment Report for a
Veterinary Medicinal Product

Porcilis APP suspension for injection

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PRODUCT SUMMARY

EU Procedure number	IE/V/0327/001/MR
Name, strength and pharmaceutical form	Porcilis APP suspension for injection
Active substance(s)	Inactivated toxoids of ApxI, ApxII, ApxIII and an outer membrane protein (OMP) of *Actinobacillus pleuropneumoniae*
Applicant	Intervet International B.V. Wim de Körverstraat 35 5831 AN Boxmeer The Netherlands
Legal basis of application	MRP application in accordance with Article 12(3) of Directive 2001/82/EC as amended.
Date of completion of procedure	16th December 2013
Target species	Pigs
Indication for use	For the active immunization of weaned piglets to reduce mortality, clinical signs and lesions of pleuropneumonia caused by *Actinobacillus pleuropneumoniae*.
ATCvet code	QI09AB07
Concerned Member States	UK

PUBLIC ASSESSMENT REPORT

The public assessment report reflects the scientific conclusion reached by the HPRA at the end of the evaluation process and provides a summary of the grounds for approval of the marketing authorisation for the specific veterinary medicinal product. It is made available by the HPRA for information to the public, after the deletion of commercially confidential information. The legal basis for its creation and availability is contained in Article 25.4 of EC Directive 2001/82/EC as amended by Directive 2004/28/EC for veterinary medicinal products. It is a concise document which highlights the main parts of the documentation submitted by the applicant and the scientific evaluation carried out by the HPRA leading to the approval of the product for marketing in Ireland.

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Characteristics (SPC) for this product is available on the HPRA's website.

I. SCIENTIFIC OVERVIEW

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.

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.Qualitative and Quantitative Particulars

The product contains as active ingredient an antigen concentrate of 600 mg / 2 ml dose containing 50 units of each of the following *Actinobacillus pleuropneumoniae* antigens: outer membrane protein (OMP) and detoxified antigens (toxoids) of the ApxI, ApxII and ApxIII toxins. The unit of activity for each antigen is measured relative to an internal standard determined to be efficacious in pigs.

The vaccine includes dl-α-tocopherol(150 mg / 2 ml dose) as adjuvant and 0.02% w/v formaldehyde as preservative. Polysorbate 80, simethicone, sodium chloride and water for injection are also included.

The container/closure system consists of Type I glass (Ph. Eur. 3.2.1) or polyethylene terephthalate (PET) (Ph. Eur. 3.2.2.) containers closed with a halogenated rubber stopper (Ph. Eur. 3.2.9) and sealed with a colour coded aluminium cap.

The choice of the adjuvant, vaccine antigens, formulation, inactivating agent and the preservative are justified.
Prior to release each vaccine batch is tested according to the Ph. Eur. 1360 'Porcine actinobacillosis vaccine (inactivated)' residual toxicity test. In addition, the vaccine has been safely used to date for over 15 years, therefore the inactivation processes and the detection limit of the control of inactivation are considered adequate.

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 at a licensed manufacturing site.

Sufficient batch to batch consistency data are presented demonstrating that the manufacturing process is in accordance with the relevant European guidelines.

C.Control of Starting Materials

Starting materials of non-biological origin used in the vaccine blending process comply with the European pharmacopoeia monographs.

Biological starting materials used in the manufacturing processes are not considered to pose a risk of extraneous agent contamination.

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

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.

D.Control Tests During Production

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

E.Control Tests on the Finished Product

The finished product specification controls the relevant parameters for the pharmaceutical form. The tests in the specification, and their limits, have been justified and are considered appropriate to adequately control the quality of the product.

Satisfactory validation data for the analytical methods has been provided.
Batch analytical data from the proposed production site has been provided demonstrating compliance with the specification.

F.Stability

Data supporting the proposed shelf life of the antigens has been provided.

Stability data on the finished product has been provided in accordance with applicable European guidelines, demonstrating the stability of the product throughout its shelf life when stored under the approved conditions.

The 10 hours in-use shelf-life of the broached vaccine is justified.

G.Other Information

Not applicable.

III. SAFETY ASSESSMENT

Laboratory Trials

The safety studies included in the dossier demonstrate that the administration of one dose, a 2x overdose, and the repeated administration of a dose can be considered to be safe, when used in accordance with the recommended vaccination schedule.
Adverse reactions following recommended use consist of transient temperature increases (up to 2 °C), anorexia, decreased activity/depression, lower appetite, increases in respiration rate with a change towards abdominal breathing and dyspnea. These reactions are transient and resolve within 24 hours after vaccination. More severe reactions such as anaphylaxis may occasionally occur.
In addition, mild to moderate injection site reactions may occur in some animals, these resolve within 5 days post-vaccination.
The nature of the clinical signs observed after the administration of a 2x overdose were similar but were more severe.
The adverse reactions that were observed in the laboratory and field studies are adequately reflected in the SPC.

Study of residues

The excipients and adjuvant included in the composition of this vaccine are listed in Commission Regulation (EU) No. 37/2010 in Annex I (Allowed substances) for which no MRL is required, or are included in the list of substances considered as not falling within the scope of Regulation (EU) No 470/2009.
Ph. Eur. 0062 (Vaccines for veterinary use) recommends that the content of free formaldehyde is not greater than 0.5g/L unless a higher amount has been shown to be safe. Formaldehyde is included in the vaccine at a concentration below the limit specified by Ph. Eur. 0062.

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Consequently, there is no need to perform residue studies for the vaccine and a withdrawal period of zero days is considered acceptable.

User Safety

The active ingredients (detoxified toxins and OMP produced from different serotypes of A. pleuropneumoniae), the excipients and adjuvant (dl-α-tocopherol) are not considered to present an unacceptable risk to the user. Furthermore, in the most recent PSUR for the product covering a three year period, no reports of human exposure were received. The main risk to the user would relate to accidental self-injection and an appropriate warning is included in the SPC.
It is accepted that use of the vaccine does not pose an unacceptable risk to the user. Advice is included in the SPC to seek medical advice in case of accidental self-injection or ingestion, and in case of accidental spillage on the skin to wash with soap and water.

Interactions

The compatibility of the use of Porcilis APP with another veterinary medicinal product has not been established. Therefore the standard warning when no information is available concerning the use of this product with any other veterinary medicinal product is included in the SPC.

Field Studies

One combined safety and efficacy multicentric, placebo-controlled field trial was performed, which was conducted in an EU Member State in pig farms known to be affected by A. pleuropneumoniae infections within the year prior to the conduct of the trial. A total number of 3336 pigs were included, approximately half of which were vaccinated with a placebo injection (saline) and half of which were vaccinated with Porcilis APP. The adverse reaction profile observed in the field study reflected that described in the laboratory studies with the exception of vomiting which was not previously observed.
The adverse reactions that were observed in the laboratory and field studies are adequately reflected in the SPC.

Environmental Risk Assessment

Given the nature of the product, an inactivated vaccine which will be administered parenterally, no risks to the environment following use of the product are anticipated. The standard disposal statement for inactivated immunologicals is included in the SPC.

IV. CLINICAL ASSESSMENT

IV.AGeneral requirements

The choice of antigenic components with respect to the epidemiological situation in the EU has been justified by the applicant. Detailed information concerning the development of the vaccine which was carried out to ensure that the subunit vaccine would contain sufficient antigenic components/cross-protection against the heterologous subtypes of *A. pleuropneumoniae* was provided.

IV.B Clinical Studies Laboratory Trials

The claims for the vaccine for a reduction in mortality, clinical signs and lesions of pleuropneumonia are considered to be supported by a number of laboratory studies. The conduct of different studies with challenges with five different serotypes were carefully selected in order to cover the range of *A. pleuropneumoniae* serotypes known at time of original authorisation of the vaccine in the RMS, with cross-protection for non-tested serotypes considered likely on the basis of toxin expression/pattern for non-tested serotypes.

The onset of immunity of 2 weeks is adequately supported as is the duration of immunity of 11 weeks.

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As the vaccine is indicated for use in pigs from six weeks of age, the impact of the presence of maternally derived antibodies on the response to vaccination was investigated in two studies. While the studies are now rather old (and therefore not strictly in accordance with current guidance), the studies demonstrated that vaccination afforded protection from challenge in pigs with maternally derived antibodies in accordance with the authorised indications. Therefore, no warnings were considered necessary on the SPC regarding possible interference on the response to vaccination in the presence of MDAs.

Field Trials

No efficacy data were generated during the combined safety and efficacy field trial as a clinical outbreak of pleuropneumonia did not occur.However, it should be noted that the level of reports of suspected lack of efficacy in the field since authorisation have not raised concern.

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.

VI. 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 HPRA website.

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.

Changes:
None.

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