EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Veterinary Medicines Division

Committee for Medicinal Products for Veterinary Use

CVMP assessment report for Ingelvac PCV FLEX (EMEA/V/C/004645/0000)

Common name: porcine circovirus vaccine (inactivated)

Assessment report as adopted by the CVMP with all information of a commercially confidential nature deleted.

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Introduction

On 18 November 2016 the applicant Boehringer Ingelheim Vetmedica GmbH submitted an application for a marketing authorisation to the European Medicines Agency (the Agency) for Ingelvac PCV FLEX, through the centralised procedure. This application is submitted as a duplicate of Ingelvac CircoFLEX authorised on 15 February 2008 in accordance with Article 82(1) of Regulation (EC) No 726/2004.

The eligibility to the centralised procedure was agreed upon by the CVMP on 8 September 2016. Ingelvac PCV FLEX is a duplicate application of Ingelvac CircoFLEX which has been authorised in the Community since 13 February 2008.

The rapporteur appointed was B. Urbain and the co-rapporteur P. Pasquali.

The applicant applied for the following indication: For active immunisation of pigs with no porcine circovirus type 2 (PCV2) maternally derived antibodies from the age of 2 weeks against PCV2. Under experimental challenge conditions in which only seronegative animals were included, it was demonstrated that vaccination reduces mortality, clinical signs and lesions in lymphoid tissues associated with PCV2 related disease (PCVD). In addition, vaccination has been shown to reduce PCV2 nasal shedding, viral load in blood and lymphoid tissues, and duration of viraemia.

Onset of immunity: 2 weeks post vaccination.

Duration of immunity: at least 17 weeks.

Ingelvac PCV FLEX is suspension for injection containing PCV2 ORF2 protein: RP* 1.0–3.75. * Relative potency (ELISA test) by comparison with a reference vaccine. It is presented in packs sizes of one or 12 bottles of 10 ml (10 doses), 50 ml (50 doses), 100 ml (100 doses) or 250 ml (250 doses).

The dossier has been submitted in line with the requirements for submissions under Article 13c of Directive 2001/82/EC – informed consent application.

On 16 March 2017 the CVMP adopted an opinion and CVMP assessment report.

On 24 May 2017 the European Commission adopted a Commission Decision granting the marketing authorisation for Ingelvac PCV FLEX.

Scientific advice

Not applicable.

MUMS limited market status

Not applicable.

Part 1 - Administrative particulars

Detailed description of the pharmacovigilance system

A detailed description of the pharmacovigilance system has been provided (dated November 2012) which fulfils the requirements of Directive 2001/82/EC, as amended. Based on the information provided the applicant has the services of a qualified person responsible for pharmacovigilance and the necessary means for the notification of any adverse reaction occurring either in the Community or in a third country.

Manufacturing authorisations and inspection status

The manufacture of the active substance takes place outside the EEA. The manufacturer is Boehringer Ingelheim Vetmedica Inc., St. Joseph, Missouri, USA. A Good Manufacturing Practice (GMP) certificate of compliance was issued on 23/05/2016 by the German competent authority. The latest inspection was conducted on 03-12/06/2015.

There are three sites for secondary packaging:

- Secondary Packaging Site No. 1 is outside the EEA: Boehringer Ingelheim Vetmedica Inc., St Joseph, USA. A GMP certificate of compliance was issued on 23/05/2016 by the German competent authority. The latest inspection was conducted on 05-09/03/2015.
- The two other sites are within the EEA:
    - Secondary Packaging Site No. 2: Boehringer Ingelheim Animal Health, Weesp, the Netherlands. A GMP certificate of compliance was issued on 20/01/2015 by the Dutch competent authority;
    - Secondary Packaging Site No. 3: Globopharm, Wien, Austria. A GMP certificate has been provided. The latest inspection was conducted on 21/10/2015.

There are two sites for quality testing:

- Testing site No.1: Labor Dr. Merk & Kollegen GmbH, Ochsenhausen, Germany. A GMP certificate of compliance was issued on 20/10/2015 by the German competent authority. The latest inspection was conducted on 17/10/2015.
- Testing site No. 2: Boehringer Ingelheim Animal Health, Weesp, the Netherlands. A GMP certificate of compliance was issued on 20/01/2015 by the Dutch competent authority.

Batch release is done at two sites:

- Boehringer Ingelheim Animal Health, Weesp, the Netherlands. A GMP certificate of compliance was issued on 20/01/2015 by the Dutch competent authority.
- Boehringer Ingelheim Vetmedica GmbH, Ingelheim, Germany. A GMP certificate of compliance was issued on 31/05/2016 by the German competent authority.

All manufacturing sites (secondary packaging, QC testing and batch release) are appropriately authorised/certified as complying with GMP requirements.

Overall conclusions on administrative particulars

The detailed description of the pharmacovigilance system and the GMP certification of the manufacturing sites were considered in line with legal requirements.

Part 2 - Quality Composition

This application is an informed consent of Ingelvac CircoFLEX, the quality data in support of the application for Ingelvac PCV FLEX are identical to the up-to-date quality data of the Ingelvac CircoFLEX dossier, which has been assessed and approved (including all post-marketing procedures).

Therefore, no quality data have been submitted. This is acceptable.

Part 3 – Safety

This application is an informed consent of Ingelvac CircoFLEX, the quality data in support of the application for Ingelvac PCV FLEX are identical to the up-to-date quality data of the Ingelvac CircoFLEX dossier, which has been assessed and approved (including all post-marketing procedures).

Therefore, no safety data have been submitted. This is acceptable.

To ensure comprehensive adverse event surveillance, it is recommended the applicant synchronises the periodic safety update report (PSUR) submissions for the duplicate products, Ingelvac PCV FLEX and Ingelvac CircoFLEX.

Part 4 – Efficacy

This application is an informed consent of Ingelvac CircoFLEX, the quality data in support of the application for Ingelvac PCV FLEX are identical to the up-to-date quality data of the Ingelvac CircoFLEX dossier, which has been assessed and approved (including all post-marketing procedures).

Therefore, no efficacy data have been submitted. This is acceptable.

Part 5 – Benefit-risk assessment

Introduction

Ingelvac PCV FLEX is a biotechnology derived inactivated immunological veterinary medicinal product intended to be used for active immunisation of pigs with no PCV2 maternally derived antibodies from the age of 2 weeks against PCV2 to reduce mortality, clinical signs and lesions in lymphoid tissues associated with PCVD. The antigen is the PCV2 ORF2 protein. The application is submitted as a duplicate of Ingelvac CircoFLEX authorised on 13 February 2008 in accordance with Article 82(1) of Regulation (EC) No 726/2004.

The application has been submitted in line with the requirements for submissions under Article 13c of Directive 2001/82/EC (informed consent application).

Benefit assessment

As this application is an informed consent of Ingelvac CircoFLEX no new quality, safety and efficacy data has been submitted.

Direct therapeutic benefit

Ingelvac PVC FLEX administered once via the intramuscular route to seronegative pigs from two weeks of age is capable of reducing mortality, clinical signs and lesions in lymphoid tissues associated with PCVD in addition to a reduction of PCV2 nasal shedding, viral load in blood and lymphoid tissues, and duration of viraemia. The onset of protection is 2 weeks post vaccination and the duration of protection is at least 17 weeks.

Additional benefits

Safety and efficacy data are available which demonstrate that this vaccine can be mixed with Ingelvac MycoFLEX and administered at one injection site.

Risk assessment

Main potential risks have been identified as follows:

Quality:

The formulation and manufacture of Ingelvac PCV FLEX is well described and specifications set will ensure that product of consistent quality will be produced.

The transmissible spongiform encephalopathy (TSE) risk for this product can be regarded as negligible.

Safety:

Risks for the target animal:

All safety studies were conducted with a vaccine batch formulated to contain the maximum relative potency. Following the administration of one dose, a transient increase of body temperature was always recorded in field studies 4 hours after vaccination, but the increase in body temperature lasted no longer than 24 hours.

With an overdose administration of vaccine to seronegative piglets approximately two weeks of age compared to control animals, mild clinical signs described as depression, anorexia, and in case of one vaccinated animal, vomiting, were recorded (in both groups) starting generally, 4 hours after vaccination. Local tolerance was acceptable.

Concerning the repeated administration of one dose, results were comparable with those obtained in the one dose safety study.

With regard to reproductive performance safety data have been generated in sows/gilts in the 1st, 2nd or 3rd trimester of pregnancy or in lactation to support the use during pregnancy and lactation. However, in the absence of safety data obtained with the use of Ingelvac MycoFlex at maximum potency and because Ingelvac MycoFlex is not intended for pregnant and lactating animals, Ingelvac PCV FLEX will not be used in combination with Ingelvac MycoFLEX in these categories of animals.

The safety of the vaccine was further assessed in three Good Clinical Practice (GCP) field trials conducted under swine farm management and breeding conditions typical of the European pig industry. In these field trials, the safety profile of the vaccine was clearly demonstrated and the SPC adequately reflects the major outcome of a potential increase in body temperature observed after a few hours following vaccination.

Risk for the user:

The CVMP concluded that user safety for this product is acceptable when used as recommended and taking into account the safety advice in the SPC.

Risk for the environment:

The product is not expected to pose any risk to the environment when used as recommended.

Risk for the consumer:

Due to the nature of the product, no residue depletion study has been carried out. While carrying out field trials the presence of any residue of the vaccine at the injection site was investigated and in none of the animals submitted to necropsy could any residue of the vaccine be observed at the injection site. A withdrawal period of zero days is justified.

Risk management or mitigation measures

Appropriate information has been included in the SPC to inform on the potential risks of this product relevant to the target animal, user, environment and consumer to provide advice on how to prevent or reduce these risks.

Evaluation of the benefit-risk balance

This application is a duplicate application of Ingelvac CircoFLEX by informed consent. The quality, safety and efficacy data in support of the application for Ingelvac CircoFLEX are therefore considered identical to the up-to-date data contained on the dossier for Ingelvac CircoFLEX at the time of submission of the application for Ingelvac PCV FLEX. The product has been shown to be efficacious for the indication for active immunisation of seronegative pigs from the age of 2 weeks PCVD2 to reduce mortality, clinical signs and lesions in lymphoid tissues associated with PCVD.

Information on development, manufacture and control of the active substance and finished product has been presented and lead to the conclusion that the product should have a satisfactory and uniform performance in clinical use. It is well tolerated by the target animals and presents an acceptable risk for users, the environment and consumers when used as recommended.

Conclusion on benefit-risk balance

The overall benefit-risk evaluation is deemed positive with a sufficiently clear and complete SPC and product literature.

Conclusion

Based on the original data presented on quality, safety and efficacy the Committee for Medicinal Products for Veterinary Use (CVMP) concluded that the application for Ingelvac PCV FLEX is approvable since these data satisfy the requirements for an authorisation set out in the legislation (Regulation (EC) No 726/2004 in conjunction with Directive 2001/82/EC).

The CVMP considers that the benefit-risk balance is positive and, therefore, recommends the granting of the marketing authorisation for Ingelvac PCV FLEX.