EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Veterinary Medicines Division

Committee for Veterinary Medicinal Products (CVMP)

CVMP assessment report for a worksharing variation requiring assessment for Porcilis PCV ID (EMEA/V/C/WS2294)

Vaccine 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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1. Introduction

1.1. Submission of the variation application

In accordance with Article 62 of Regulation (EU) 2019/6, the marketing authorisation holder, Intervet International B.V. (the applicant), submitted to the European Medicines Agency (the Agency) on 22 July 2022 an application for a variation requiring assessment for Porcilis PCV ID and other related nationally authorised products, following a worksharing procedure.

1.2. Scope of the variation

Variation(s) requested	
G.I.4	Change(s) in the Summary of Product Characteristics, Labelling or Package Leaflet due to new quality, preclinical, clinical or pharmacovigilance data.

To update the product information of Porcilis PCV ID, Porcilis Lawsonia ID, Porcilis M Hyo ID ONCE and Porcilis PRRS to include new associated use combinations of these four products.

1.3. Changes to the dossier held by the European Medicines Agency

This application relates to the following sections of the current dossier held by the Agency:

Part 1, Part 3 and Part 4

1.4. Scientific advice

Not applicable.

1.5. Limited market status

Not applicable.

2. Scientific Overview

Porcilis PCV ID (PCV ID), Porcilis Lawsonia ID (LID) Porcilis M Hyo ID ONCE (M1 ID) and Porcilis PRRS (PRRS) are registered porcine vaccines indicated to induce protection against porcine circovirus (PCV) type 2, *Lawsonia intracellularis*, *Mycoplasma hyopneumoniae* and Porcine Respiratory and Reproductive Syndrome Virus (PRRSV), respectively. As all four vaccines can administered intradermally to piglets around 3 weeks of age, from a convenience and animal welfare point of view, it is beneficial to administer two, three or all four of these vaccines at the same time. Some associated uses are already registered, namely the associated non-mixed use of PCV ID and M1 ID as well as the mixed use of PCV ID and LID.

To support the safety of the proposed associated uses, one field safety study in 3-week-old pigs was performed. The study was appropriately designed and conducted to an acceptable standard (GCP). The application of the 4-way combination in this study provided a worst-case scenario for the different possible associated uses and is acceptable also in support of the other 2- and 3-way combinations proposed.

After vaccination, local soft or hard non-painful swellings were apparent in almost all animals. Swellings occurred in a biphasic pattern, sometimes with redness and scabs. This is largely similar to what has been recorded for the individual vaccines. However, the 4-way concurrent administration gave rise to a slight increase in the size, duration and severity (redness, crusts) of local reactions, while still remaining within an acceptable range. Additional warnings have been included in section 4.8 of the SPC's.

General health observations that possibly relate to vaccination were observed in two vaccinated pigs, at +4 hours (and in one pig also at day 1 p.v.), this consisted of reluctance to move. Reluctance to move was also observed in control pigs, however this was not associated with the time of vaccination and was mostly clearly related to lameness. A warning sentence has been included in the SPC of all vaccines for the associated use.

At 4 hours post vaccination, a slight increase (mean 0.3°C, max. +1.2°C) in rectal temperatures was seen in the vaccinates, compared to baseline. The magnitude of the temperature increase is considered acceptable. An appropriate warning for increased temperatures after vaccination is included in the SPC for all four vaccines.

No negative effects on growth, mortality or medication use were observed during the study. The results of the field safety study generally support the safety of associated use of the four products.

Efficacy of the 4-way associated use was investigated in 7 laboratory studies. These vaccination-challenge studies were generally appropriately designed. Standard doses were used and for PRRS the maximum dose except when testing efficacy of the PRRS vaccine when a minimum dose was applied. The challenges induced disease symptoms in the control animals that enabled to support all or most efficacy claims.

No evidence of serious interference was observed after a PCV2 challenge either at 2 or 26 weeks post-vaccination, thus supporting the absence of interference for Porcilis PCV ID.

No evidence of serious interference was observed after a *Lawsonia intracellularis* challenge at either 4 or 17 weeks post-vaccination, thus supporting the absence of interference for Porcilis Lawsonia ID.

To investigate interference for *M. hyopneumoniae* two studies were performed, in one study pigs were challenged at 3 weeks post-vaccination, in the second study at 22 weeks post-vaccination, coinciding with the registered OOI and DOI. Neither of the two studies included a M1 ID single vaccine group for comparison. Statistically significant reduction of lung lesion scores was achieved with the 4-way vaccination (50-65%). The applicant clarified that this result falls within the range of reductions historically achieved in studies with the single M1 ID vaccine (28-88% reduction in LLS). It can be concluded that no evidence of serious interference was observed for M1 ID vaccine.

One study was performed to investigate interference for PRRS. Challenge was performed at 4 weeks post-vaccination and no significant differences were found between groups vaccinated with the single vaccine or the 4-way combination. Since the live PRRS vaccine generally provides improved immunity at DOI compared to OOI and there is no obvious mechanism for the associated use to affect the efficacy of this live vaccine at 24 weeks post-vaccination when the immunity at 4 weeks post-vaccination is not negatively affected, it is accepted that no evidence of serious interference was observed for PRRS.

3. Benefit-risk assessment of the proposed change

Porcilis PCV ID is an emulsion for injection authorised for the active immunisation of pigs to reduce viraemia, virus load in lungs and lymphoid tissues and virus shedding caused by PCV2 infection. It is also authorised to reduce loss of daily weight gain and mortality associated with PCV2 infection.

While safety and efficacy data already supported some claim for associated use, with this variation the applicant wishes to update the product information of Porcilis PCV ID, Porcilis Lawsonia ID, Porcilis M Hyo ID ONCE and Porcilis PRRS to include new associated use combinations of these four products.

3.1. Benefit assessment

Direct therapeutic benefit

Well-designed laboratory studies have demonstrated that there is no serious interference when the four products are used concurrently.

Additional benefits

The variation provides the possibility to treat animals with the four products at the same time. This is beneficial from a welfare perspective since it reduces animal handling and it increases convenience for the user.

3.2. Risk assessment

Quality

Quality remains unaffected by this variation.

Safety

Safety for the user, consumer and environment remains unaffected by this variation.

With respect to safety for the target animal, administration of the four vaccinates simultaneously, in accordance with SPC recommendations, is generally well tolerated. The main reported adverse reactions include local reactions and transient general reactions (temperature increase, reluctance to move), largely similar to what is observed after application of the single vaccines but in some cases slightly increased.

3.3. Risk management or mitigation measures

Since adverse reactions may be slightly increased after associated use compared to the single use, appropriate warnings have been included in the SPC.

3.4. Evaluation of the benefit-risk balance

The benefit-risk balance of the associated use of the products is considered to be positive.

4. Conclusion

Based on the original data presented on safety and efficacy the Committee for Veterinary Medicinal Products (CVMP) concluded that the application for variation to the terms of the marketing authorisation

for Porcilis PCV ID, Porcilis Lawsonia ID, Porcilis M Hyo ID ONCE and Porcilis PRRS can be approved, since the data satisfy the requirements as set out in the legislation (Regulation (EU) 2019/6), as follows:

To administer two, three or all four of the vaccines Porcilis PCV ID, Porcilis Lawsonia ID, Porcilis M Hyo ID ONCE and Porcilis PRRS at the same time.

The CVMP considers that the benefit-risk balance remains positive and, therefore, recommends the approval of the variation to the terms of the marketing authorisation for the above mentioned medicinal product

Changes are required in the following Annexes to the Community marketing authorisation.

I and IIIB

Please refer to the separate product information showing the tracked changes.

As a consequence of this variation section 3.8 or 4.8 of the SPC's are updated. The corresponding sections of the Package Leaflets are updated accordingly.