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Veterinary Medicines Division

Committee for Veterinary Medicinal Products (CVMP)

CVMP assessment report for a grouped variation requiring assessment for Suvaxyn PRRS MLV (EMEA/V/C/004276/VRA/0011/G)

Vaccine common name: Porcine respiratory and reproductive syndrome virus vaccine (live)

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

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Table of contents

1. Introduction

1.1. Submission of the variation application

In accordance with Article 64 of Regulation (EU) 2019/6, the marketing authorisation holder, Zoetis Belgium (the applicant), submitted to the European Medicines Agency (the Agency) on 2 February 2024 an application for a group of variations requiring assessment for Suvaxyn PRRS MLV.

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.
G.I.18	One-off alignment of the product information with version 9.0 of the QRD templates i.e. major update of the QRD templates in accordance with Regulation (EU) 2019/6, for veterinary medicinal products placed on the market in accordance with Directive 2001/82/EC or Regulation (EC) No 726/2004.

To change the product information related to the use in lactating sows and consequential adverse events in this subcategory of animals, together with alignment of the product information with version 9.0 of the QRD template.

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 and Part 3.

1.4. Scientific advice

Not applicable.

1.5. Limited market status

Not applicable.

2. Scientific Overview

With this grouped variation procedure, the applicant proposes to align the product information with version 9.0 of the QRD template and to change the product information regarding the use in lactating sows.

For the alignment of the product information with the QRD version 9.0 template, the applicant amended the product information satisfactorily upon request.

For the change of the product information regarding the use in lactating sows, two validation reports and two field studies have been provided to support the safe use of Suvaxyn PRRS MLV in this subcategory of animals.

A validated internal method for the detection and quantification of Porcine Respiratory and Reproductive Syndrome virus (PRRSV) in biological samples was originally provided and assessed for the marketing authorisation of Suvaxyn PRRS MLV in 2016. This report validated the RT-qPCR (internal method) of PRRSV in a variety of samples, including serum, oral and nasal swabs and cell culture. It was provided again in this submission for convenience only, as it was further optimized for the detection and quantification of PRRSV in milk samples (see below).

A validation report was provided for the detection and quantification of PRRSV in milk samples. This optimized internal method was concluded to be valid for its purpose and has been used for the milk sample analysis in the two field studies provided with this grouped variation procedure.

Two Good Clinical Practice (GCP) compliant field studies were provided to support the safety of Suvaxyn PRRS MLV in lactating sows. The safety variables assessed were: general health observations, clinical signs at one-hour post vaccination, injection site reactions, rectal temperature and lactating performance (body weight gain and average body weight gain of offspring). Furthermore, the serological status of the sows and the presence of PRRSV in milk samples was investigated.

One study was performed at a commercial farm in the Netherlands. Twenty-four seropositive sows (50% seropositive, measured by ELISA) after farrowing, including 336 piglets born to these sows, were enrolled in this study. Twelve sows were allocated to each of two groups: T01 as a control group received 0.9 % Saline and T02 group was vaccinated intramuscularly with Suvaxyn PRRS MLV in the right side of the neck 1 - 5 days after farrowing. Low appetite was observed after vaccination in three sows from group T02 and in one sow of the control group that lasted a maximum of 3 days. One hour (±30 minutes) after vaccination no clinical signs or adverse events were observed in any sow. Injection site reactions were present in 16.7% of animals of the control group (T01 group) and in 41.7% of the vaccinated animals (T02 group). All these animals showed only mild reactions (score 1), and these resolved by day 3 with a mean duration of 0.17 days (T01, vaccinated) and 0.42 days (T02, control). For rectal temperatures two acceptance criteria were defined. First, mean rectal temperature should not exceed a maximum temperature increase of 1.5 °C in each group in comparison to mean pre-vaccination rectal temperature. Second, individual maximum rectal temperature in sows should not exceed 2.0 °C compared to the same rectal temperature before vaccination. Both criteria were fulfilled. The highest individual maximum rectal temperature observed was 40.1 °C on day 3 after vaccination (sow #048 of T02 group, vaccinated). The maximum increase in mean rectal temperature compared to baseline was observed on day 3 after application: 0.5 °C in the control group (T01) and 0.4 °C in the vaccinated group (T02). For lactation performance, the live weight of the litter was measured on day -1, day 14 and at day 21 (end of the study). No differences were observed in body weight gain between groups. The average daily weight gain from day -1 to day 21 (whole study period) was 0.24 kg/day for the control group (T01) and 0.23 kg/day for the vaccinated group (T02). Furthermore, no PRRSV was detectable in milk samples from any sow taken on days -1, 7 and 14 of the study.

The second study was performed at a commercial farm in Portugal. Twenty-four PRRS seropositive sows (92% to 100% seropositive, measured by ELISA) were included. After farrowing, 313 piglets born to these sows were enrolled in this study. Twelve sows were allocated to each of two groups: T01 as a control group received 0.9 % Saline and T02 group were vaccinated intramuscularly in the right side of the neck with Suvaxyn PRRS MLV at 2 - 5 days after farrowing. No clinical signs or adverse events were observed 1 hour (±30 minutes) after vaccination in any sow vaccinated. Local reactions were observed in 1 out of 12 animals (8.3%) in both groups in the first three days after vaccination: sow #2738 (T01, control group) showed a moderate reaction (score 2) with a dimension of ≥ 4.5 cm and sow #3342 (T02, vaccinated group) showed a severe reaction (score 3) with a dimension of 11 cm which had resolved by day 4 without treatment. For rectal temperatures the first acceptance criterion (mean rectal temperature of all vaccinated sows should not exceed 1.5 °C compared to mean baseline pre-vaccination) was fulfilled in both groups. However, the second acceptance criterion (individual mean rectal temperature should not exceed 2 °C compared to individual mean baseline pre-vaccination) was not met. One sow of the T02 group (#2236, vaccinated group) showed a rectal temperature of 40.4 °C on day 0 (four hours after vaccination; baseline 38.4 °C) and another sow had a rectal temperature of 40.8 °C on day 3 and 40.7 °C on day 4 (#3253, baseline 38.6 °C) but returned to normal temperature the following day. Individual maximum rectal temperature increase compared to baseline was 1.6 °C vs. 2.2 °C in the control compared to the vaccinated group (T01 vs T02). For lactation performance, the litters were weighted on days -1, 14 and -21 (end of the study). No differences were observed in body weight gain between groups. The average daily weight gain (ADG) during the period from day -1 to day 21 (whole study period) was 0.21 for the control group (T01) and 0.20 kg/day for the vaccinated group (T02). Furthermore, no PRRSV was detectable in milk samples from all sows obtained from days -1, 7 and 14.

In conclusion, vaccination with Suvaxyn PRRS MLV has shown to be safe in lactating sows (1 - 5 days post farrowing - including seropositive sows) in two field trials provided with the documentation for this grouped variation procedure. Vaccination did not induce any systemic reactions 1 hour (± 30 minutes) after vaccination. In the field study performed in the Netherlands only reduced appetite was observed between day 1 and day 3 post-vaccination in 3 out of 12 vaccinated sows for up to 3 days. Mild local reactions (score 1) were observed 1 to 3 days post-vaccination in the field study performed in the Netherlands. In the field trial performed in Portugal 2 out of 12 sows showed moderate (score 2) to severe (score 3) local reactions, respectively, between day 1 and 3 which had resolved by day 4 without treatment. Furthermore, mean rectal temperatures were below 1.5 °C compared to baseline (first acceptance criterion) in both studies. The second acceptance criterion for individual rectal temperature which should stay below 2 °C compared to the mean baseline pre-vaccination was only met in the field trial performed in the Netherlands. In the field trial performed in Portugal this acceptance criterion was however not met, as one sow showed a rectal temperature of 40.4 °C on day 0 (baseline 38.4 °C) and another for another sow a rectal temperature of 40.7 °C and 40.8 °C was observed on day 3 and day 4 (#3253 baseline 38.6 °C) post vaccination. This elevated rectal temperature returned to normal the following day. These results are adequately reflected in section 3.6 "Adverse events" for lactating sows as follows:

Very common (>1 animal / 10 animals treated):	Elevated temperature[1] Decreased appetite[2] Injection site swelling[3]

[1] Up to 2.2 ºC. Observed 2 days post vaccination; resolves spontaneously within 4 days without treatment.

[2] Observed 1 - 4 days post vaccination and resolves spontaneously within 3 days without treatment.

[3] Up to 11 cm in diameter. Resolves spontaneously within 3 days without treatment.

In summary, the safety of vaccination with Suvaxyn PRRS MLV in lactating sows has been adequately demonstrated. Adverse events described in section 3.6 of the SPC reflect the results of the two field trials adequately.

3. Benefit-risk assessment of the proposed change

Suvaxyn PRRS MLV is authorised for the active immunisation of clinically healthy pigs (pigs for fattening, gilts and sows) from 1 day of age in a PRRSV-contaminated environment, to reduce viraemia and nasal shedding caused by infection with European strains of PRRS virus (genotype 1). The withdrawal period is zero days.

The onset of immunity is 3 weeks after immunisation of one dose and the duration of immunity is 26 weeks. Gilts and sows should be vaccinated prior to introduction into the sow herd and approximately 4 weeks prior to breeding. A single booster dose should be administered every 6 months.

The proposed variation is to change the product information related to the use in lactating sows and consequential adverse events in this subcategory of animals, together with alignment of the product information with version 9.0 of the QRD template.

3.1. Benefit assessment

Direct therapeutic benefit

The benefits of the product remain unaffected by this variation.

Additional benefits

Suvaxyn PRRS MLV can be used during lactation in sows, which enables the user to apply booster vaccinations every 6 months as recommended independently of the production phase of the sows. The addition of this subcategory of animals supports that vaccination achieves a homogenous immunity against PRRSV in the target population at farm level.

3.2. Risk assessment

Quality:

Quality remains unaffected by this variation.

Safety:

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

Risks for the target animal:

The safety of Porcine respiratory and reproductive syndrome virus vaccine (live) in lactating sows was confirmed in two field studies.

Administration of Porcine respiratory and reproductive syndrome virus vaccine (live) to lactating sows in accordance with SPC recommendations is generally well tolerated.

The main reported adverse reactions include elevated temperature, reduced appetite and injection site swelling which were observed very commonly.

3.3. Risk management or mitigation measures

Risk management or mitigation measures remain unaffected by this variation.

3.4. Evaluation of the benefit-risk balance

No change to the impact of the product is envisaged on the following aspects: quality, user safety, environmental safety, consumer safety, efficacy.

The product is well tolerated by the lactating sows and presents an acceptable risk for users, the environment and consumers, when used as recommended.

The benefit-risk balance remains unchanged.

4. Conclusion

Based on the original and complementary data presented on safety the Committee for Veterinary Medicinal Products (CVMP) concluded that the application for this grouped variation to the terms of the marketing authorisation for Suvaxyn PRRS MLV can be approved, since the data satisfy the requirements as set out in the legislation (Regulation (EU). 2019/6), as follows:

- Use in lactating sows and consequential adverse events.
- Alignment of the product information with version 9.0 of the QRD template.

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 Union marketing authorisation:

I, II, IIIA and IIIB.

As a consequence of these variations, several sections of the SPC are updated. The corresponding sections of the Package Leaflet are updated accordingly.