FRENCH AGENCY FOR VETERINARY MEDICINAL PRODUCTS
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" DECENTRALISED" PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

MODULE 1

PRODUCT SUMMARY

EU Procedure number	FR/V/0451/001/DC
Name and pharmaceutical form	Cevac Duoparvo Emulsion and suspension for emulsion for injection
Applicant	FILAVIE
Active substance(s)	Live attenuated Derzsy's Disease virus, Hoekstra strain : $10^{3.7}$ - $10^{5.0}$ TCID50* Inactivated Muscovy Duck ParvoVirus (MDPV), OLM2017 strain : ≥ $10^{7.2}$ genomic copies *TCID50: 50% tissue culture infectious dose
ATC Vetcode	QI01BH01
Target species	Muscovy ducks
Indication for use	For the active immunisation of Muscovy ducks from 1 day of age onwards to reduce mortality and clinical signs of Muscovy duck parvovirosis and Derzsy's disease. To reduce the excretion of field parvovirus from the ducklings. Onset of immunity : 4 days after vaccination. Duration of immunity : 5 weeks. The duration of immunity protects the birds during the period when they are most susceptible to Muscovy duck parvovirosis and Derzsy's disease

MODULE 2

The Summary of Product Characteristics (SPC) for this product is available on the website http://www.anmv.anses.fr/

MODULE 3

PUBLIC ASSESSMENT REPORT

Legal basis of original application	Decentralised application in accordance with Article 12 of Directive 2001/82/EC as amended.
Date of completion of the original decentralised procedure	27/07/2022
Concerned Member States for original procedure	HU

I. SCIENTIFIC OVERVIEW

***For public assessment reports for the first authorisation in a range**:*

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; no adverse events are observed after vaccination.
The product has been classified as intended for Minor Use/Minor Market and therefore the available data are conforming to the specific guideline for such type of products.
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 risk/benefit analysis is in favour of granting a marketing authorisation.

II. QUALITY ASPECTS

A. Composition

The product contains :

- between $10^{3.7}$ and $10^{5.0}$ $TCID_{50}$ (50% tissue culture infectious dose) of live attenuated Derszy's disease virus, Hoekstra strain

- at least $10^{7.2}$ genomic copies of inactivated Muscovy duck parvovirus, OLM2017 strain

- light paraffin oil as adjuvant

- and excipients : macrogol cetostearyl ether, macrogol stearate, sorbitan trioleate, polysorbate, sodium disulfite, thiomersal and water for injections.

The product is constituted of two vials, one containing the live attenuated Derszy's disease virus in a suspension and one containing the inactivated Muscovy duck parvovirus and the adjuvant in an emulsion.

The container/closure systems are made of type I glass vials and polypropylene vials, both sealed with rubber stopper and aluminium cap. The particulars of the containers and controls performed are provided and conform to the regulation.

The choices of the adjuvant, vaccine strain, formulation, inactivating agent and presence of preservative are justified.

The inactivation process for the Muscovy duck parvovirus and the detection limit of the control of inactivation are correctly validated.

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 from a licensed manufacturing site and in accordance with the European Pharmacopoeia and relevant European guidelines.

C. Control of Starting Materials

Starting materials of non-biological origin used in production comply with European pharmacopoeia monographs or in-house specifications.

Biological starting materials used are in compliance with the relevant Ph. Eur. Monographs and guidelines and are appropriately screened for the absence of extraneous agents according to the Ph. Eur and other European Guidelines; 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 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.

E. Control tests during production

The tests performed during production are described and the results of 2 consecutive runs, conforming to the specifications, are provided.

F. Control Tests on the Finished Product

The tests performed on the final product conform to the relevant requirements; any deviation from these requirements is justified. The tests include in particular
- for the Muscovy duck parvovirus emulsion : appearance, pH, volume, viscosity; density, emulsion, free formaldehyde, bacterial and fungal sterility, identity and purity , quantification of the MDPV strain (by PCR)
- for the Derzsy's disease virus suspension : appearance, pH, volume, bacterial and fungal sterility, identity and purity , virus titration , mycoplasma sterility .

The demonstration of the batch to batch consistency is based on the results of 2 batches produced according to the method described in the dossier. Other supportive data provided confirm the consistency of the production process.

G. Stability

The shelf life of 18 months of the product is supported by data.
The in-use shelf-life of the reconstituted vaccine, 4 hours, is supported by the data provided.

III. SAFETY ASSESSMENT

The vaccine batches used for safety trials were manufactured in compliance with the manufacturing process and when relevant the maximum titre was used.

All laboratory studies were performed in GLP compliant facility and according to the GLP.

Laboratory trials

The safety of the administration of one dose, an overdose and the repeated administration of one dose in the target animal is demonstrated in safety laboratory studies (comparing thirty-six vaccinated animals to thirty seven unvaccinated animals) and also during the efficacy studies (involving in total eighty nine one-day old animals and seventy five older animals). These safety studies were performed in day-old ducklings and monitored the clinical conditions, the growth and the local reactions of the vaccinated animals. The investigation was performed according to the recommendations of Directive 2001/82/EC as amended and the relevant guidelines. The studies did confirm the general safety of the vaccine but vaccinated animals did show local reactions as described in the SPC when receiving an overdose.

No investigation of effect on reproductive performance was conducted because the vaccine is not intended to be used in animals during reproduction neither in animals in lay.

There are no data investigating the effects on immunological functions.

The Muscovy duck parvovirus strain is inactivated and thus the specific tests to be performed for live vaccines are not applicable.

For the Derzsy's disease virus strain, specific studies were carried out to investigate the spread, dissemination, reversion to virulence, biological properties, recombination or genetic reassortment of the vaccine strain(s). Studies are showing that the vaccine strain may be shed and spread by vaccinated animals for at least 3 weeks. Therefore the vaccinated animals should not be put in contact with animals that are not vaccinated during this period.

The adjuvant and excipients used are formaldehyde, sodium disulfite, polysorbate 80, macrogol stearate, macrogol cetostearyl, sorbitan oleate, light liquid paraffin and thiomersal for which no MRL are required according to regulation EC 37/2010. Thiomersal concentration complies with EC37/2010 other provisions. A zero day withdrawal period is stated in the SPC accordingly.

No specific assessment of the interaction of this product with other medicinal product was made. Therefore, an appropriate warning in the SPC is included.

Field studies

As the product is under the MUMS status, no field study is available.

Ecotoxicity

The applicant provided a first phase environmental risk assessment in compliance with the relevant guideline which showed that no further assessment is required. The assessment concluded that no warnings are therefore required.

IV. CLINICAL ASSESSMENT (EFFICACY)

IV.B Clinical Studies

Laboratory Trials

The efficacy of the product has been demonstrated in laboratory studies in accordance with the relevant requirements and using batches containing the relevant quantities of active substances.

For the Derszy's disease virus strain :
The onset of immunity was demonstrated in a challenge study involving thirteen vaccinated ducklings and ten control ducklings challenged four days after administration of a single dose and followed for clinical signs including mortality and detection of the parvovirus DNA in cloacal swabs and spleen. Outcome of the study was supportive of the SPC claim.
The antigen composition was investigated in a challenge study involving five control animals, seven ducklings receiving the vaccine (both strains), six ducklings receiving the Muscovy duck parvovirus strain alone and seven ducklings receiving the Derszy's disease virus strain alone, all challenged four days after the vaccination and followed for clinical signs including mortality and detection of the parvovirus DNA in spleen. The study was an additional support to the outcome of the onset of immunity study.

The duration of immunity was demonstrated in a challenge study in which 166 seronegative free animal were either vaccinated at one day of age or kept as control. They were challenged either at 3 or 4 or 5 weeks of age and followed for clinical signs including mortality and detection of the parvovirus DNA in cloacal swabs and spleen. Outcome of the study was supportive of the SPC claim.

The antigen composition was investigated in a challenge study involving five control animals, seven ducklings receiving the vaccine (both strains), six ducklings receiving the Muscovy duck parvovirus strain alone and seven ducklings receiving the Derszy's disease virus strain alone, all challenged four days after the vaccination and followed for clinical signs including mortality and detection of the parvovirus DNA in spleen. The study was an additional support to the outcome of the onset of immunity study.

Efficacy at various vaccination ages was also investigated in a challenge study involving seven fifteen days old control animals, seven fifteen days old ducklings receiving the vaccine, seven day old control animals and fifteen days old ducklings receiving the vaccine, all challenged seven days after the vaccination and followed for clinical signs including mortality. Study showed no difference between both ages for vaccination with respect to the followed parameters.
Influence of the maternal derived antibodies was investigated in a challenge study involving nine groups of twelve birds: three groups of unvaccinated birds, three groups of birds vaccinated with the product and three groups of birds vaccinated with a vaccine with a different formulation (higher quantity of adjuvant and different quantities of active substances).
In each of the three categories, vaccination was performed at one day of age or 8 days of age or 15 days of age and the challenge was performed one week later. Animals were followed for clinical signs. Outcome of the study did not allow to conclude of the absence of influence of the maternal derived antibodies.

For the Muscovy duck parvovirus strain :

The onset of immunity was demonstrated in a challenge study involving thirteen vaccinated ducklings and nine control ducklings challenged four days after administration of a single dose and followed for clinical signs including mortality and detection of the parvovirus DNA in cloacal swabs and spleen. Outcome of the study was supportive of the SPC claim.

The duration of immunity was demonstrated in a challenge study in which 49 seronegative free animal were either vaccinated at one day of age or kept as control. They were challenged either at 1 or 3 or 5 weeks of age and followed for clinical signs including mortality and detection of the parvovirus DNA in cloacal swabs and spleen. Outcome of the study was supportive of the SPC claim.

The antigen composition was investigated in a challenge study involving 12 control animals, 13 ducklings receiving the vaccine (both strains), 13 ducklings receiving the Muscovy duck parvovirus strain alone and 12 ducklings receiving the Derszy's disease virus strain alone, all challenged 7 days after the vaccination and followed for clinical signs including mortality and detection of the parvovirus DNA in spleen. The study was an additional support to the outcome of the onset of immunity study and proved that efficacy against Muscovy duck parvovirus strain requires a complete vaccination with the reconstituted vaccine.

Efficacy at various vaccination ages was also investigated in a challenge study involving four 15-day-old control animals, eleven 15-day-old ducklings receiving the vaccine, four 8-day-old control animals, nine 8-day-old ducklings receiving the vaccine and fourteen 1-day-old ducklings receiving the vaccine, all challenged 7 days after the vaccination and followed for clinical signs including mortality. Study suggested no difference between both ages for vaccination with respect to the followed parameters despite some limitations due to the design of the study.

Influence of the maternal derived antibodies was investigated in a challenge study involving nine groups of twelve birds : three groups of unvaccinated birds, three groups of birds vaccinated with the product and three groups of birds vaccinated with a vaccine with a different formulation (higher quantity of adjuvant and different quantities of active substances).

In each of the three categories, vaccinated was performed at one day of age or 8 days of age or 15 days of age and the challenge was performed one week later. Animals were followed for clinical signs. Outcome of the study did not allow to conclude of the absence of influence of the maternal derived antibodies.

Other information :

One study involving 12 vaccinated ducklings with the product and 12 control ducklings vaccinated with a reference product vaccine (commercial vaccine containing inactivated Muscovy duck parvovirus strain and inactivated Derszy's disease virus) was provided. Animals were followed for the level of antibodies during 10 weeks. The outcome of the study showed that there were no detectable levels of antibodies in both groups during the 5 first weeks after vaccination.

One another study was a challenge study involving

- two groups of 10 day old control ducklings
- two groups of 11 day old ducklings vaccinated with the product
- two groups of 10 day old ducklings vaccinated with the reference product

In each category, one of the group was challenged 21 days later with a GPV strain and one other with a MDPV strain. The animals were followed for clinical signs. Outcome of the study was not statistically significant and did not support any duration of immunity due to limitations of the study (including the limited number of animals).

Field Trials

As the product is under the MUMS status, no field study is available.

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 risk benefit 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 veterinary Heads of Agencies 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.

Safety/efficacy changes

Summary of change **(Type; application number)**	**Section updated**	**Approval date**
Change to the onset and duration of immunity FR/V/0451/001/A/001	IV	11/03/2024