FRENCH AGENCY FOR VETERINARY MEDICINAL PRODUCTS
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NATIONAL PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

FILAVAC MYX L JF613 concentrate and solvent for suspension for injection for rabbits

MODULE 1

PRODUCT SUMMARY

Name, strength and pharmaceutical form	FILAVAC MYX L JF613 concentrate and solvent for suspension for injection for rabbits 50 doses / 200 doses
Applicant	FILAVIE 20, LA CORBIERE - ROUSSAY 49450 SEVREMOINE FRANCE
Active substances	Attenuated myxomatosis virus, strain JF613 $10^{3.5}$ – 10^{5} $TCID_{50}$* * 50% tissue culture infectious dose
ATC Vetcode	QI08AD02
Target species	Rabbits
Indication for use	For active immunisation of rabbits from 35 days of age onwards to reduce mortality and clinical signs of myxomatosis. Onset of immunity: 3 weeks. Duration of immunity: 4 months.

MODULE 2

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

MODULE 3

PUBLIC ASSESSMENT REPORT

Legal basis of original application	Application in accordance with Article 12 (3) of Directive 2001/82/EC as amended.
Date of completion of the original procedure	2018
Date product first authorised in the Reference Member State (MRP only)	
Concerned Member States for original procedure	

I. SCIENTIFIC OVERVIEW

The vaccine FILAVAC MYX L JF613 is considered as a MUMS product and therefore the Guideline on Data requirements for Immunological veterinary medicinal products intended for minor use or minor species/limited markets (EMA/CVMP/IWP/123243/2006-Rev.2) was taken into consideration for the assessment of the quality, safety and efficacy parts of the dossier.

The vaccine is a monovalent attenuated viral vaccine which is indicated for the immunisation of rabbits from 35 days of age, to reduce mortality and clinical signs of myxomatosis.
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 reactions observed are indicated in the SPC (Summary of Product Characteristics).
The product is safe for the user 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. Composition

One dose of vaccine contains:

Live attenuated myxomatosis virus, strain JF613 10^3-$10^{5.5}$ $TCID_{50}$*

(*) 50% tissue culture infectious dose

The vaccine is filled in glass type I vials, closed with siliconised rubber stoppers and sealed with an aluminium cap. The particulars of the containers and controls performed are provided and conform to the regulation.

The choice of the vaccine strain is justified.

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 practices in a licensed manufacturing site.

Process validation data on the product have been presented in accordance with the relevant European guidelines.

C. Control of Starting Materials

Starting materials of non-biological origin used in production comply with European pharmacopoeia monographs where these exist, 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 “Table of extraneous agents to be tested for in relation to the general and species-specific guidelines on production and control of mammalian veterinary vaccines” (Note for Guidance III/3427/93, 7Blm10a).

Seed lots have been produced 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 data of production of 2 vaccine batches, conforming to the specifications, are provided.

F. Control Tests on the Finished Product

The tests performed on the final product are in line with the relevant requirements; any deviation from these requirements is justified. The tests performed are as follows:

Suspension
- appearance
- pH
- volume
- lactose assay
- identification
- virus titration
- purity test (absence of RHDV)
- absence of mycoplasma
- sterility: according to Ph. Eur. 2.6.1

Diluent
- appearance
- volume
- sterility: according to Ph. Eur. 2.6.1

The demonstration of the batch to batch consistency is based on the results of 2 batches of vaccine (200 doses) produced according to the method described in the dossier.

G. Stability

Stability data on the finished product have been provided in accordance with applicable European guidelines, demonstrating the stability of the product throughout its shelf life (24 months) when stored under the approved conditions (at 2-8° C).

The vaccine must be used maximum 2 hours after dilution.

III. SAFETY ASSESSMENT

Laboratory trials

The safety of the subcutaneous administration of one dose of vaccine in the target species is demonstrated in a laboratory study. Safety was assessed in Specific Pathogen Free (SPF) rabbits 35 days old (10 vaccinates) receiving 10 doses of vaccine and 1 additional dose 3 weeks later. Rabbits were observed during 4 weeks after the 2nd administration of vaccine. A control group of non-vaccinated animals was included in the study.
The investigation was performed according to the recommendations of Directive 2001/82/EC as amended and the relevant guidelines.

Overall, the vaccine proved to be well tolerated in the target species. The local and systemic reactions observed are described in the SPC (Summary of Product Characteristics) and package leaflet under “adverse reactions”.

Data show that the vaccine strain does not spread between animals (no spread to susceptible control rabbits in contact of vaccinated rabbits under laboratory conditions after a 50-day contact period).
No reversion to virulence is evidenced after performance of 5 passages in animals.

Effects on reproductive performance were examined in a field trial. As the vaccine proved to be safe in pregnant rabbits, the vaccine can be used during pregnancy. A corresponding note is included in the SPC and package leaflet.

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

Details are given in the Summary of Product Characteristics (SPC) as follows:

4.6 Adverse reactions (frequency and seriousness)

Very common: A swollen redness (maximum diameter 2 cm) is observed at the injection site within the 2 weeks after vaccination. This swelling completely resolves within 4 weeks. Some small crusts (maximum diameter 0.5 cm) can be observed during the skin-healing process.

Common: Small papules (maximum diameter 0.4 cm) can be observed on the eyelids of animals one week after vaccination. This lesion completely disappears within 2 weeks after onset.

The frequency of adverse reactions is defined using the following convention:

-very common (more than 1 in 10 animals occurring adverse reactions during the course of one treatment);
-common (more than 1 but less than 10 animals in 100 animals);
-uncommon (more than 1 but less than 10 animals in 1,000 animals);
-rare (more than 1 but less than 10 animals in 10,000 animals);
-very rare (less than 1 animal in 10,000 animals, including isolated reports).

4.7 Use during pregnancy, lactation or lay

Pregnancy:
In field conditions, data have not shown any effect on pregnancy and offspring in pregnant animals vaccinated on the 21nd day of pregnancy. Use only according to the benefit-risk assessment by the responsible veterinarian.

" Fertility:
The influence of the vaccination on the fertility of rabbits has not been investigated.

4.8 Interaction with other medicinal products and other forms of interaction

No information is available on the safety and efficacy of this vaccine when used with any other veterinary medicinal product. A decision to use this vaccine before or after any other veterinary medicinal product therefore needs to be made on a case by case basis.

4.10 Overdose (symptoms, emergency procedures, antidotes), if necessary

No adverse reactions other than those referenced in section 4.6 have been observed after administration of 10 doses of vaccine.

Field studies

One field study was performed to assess the safety of the vaccine. 50 conventional pregnant females of a rabbit breeding farm in France were vaccinated according to the vaccination scheme at the 21th days of pregnancy. All animals were observed for local or systemic reactions during the study. The zootechnical performances were also followed. The field study demonstrates the safety of the vaccine in rabbit's industrial breeding farm in pregnant animals for the animals and for the offspring.
Overall, the vaccine proved to be well tolerated in the target species. The results confirm the observations made in the laboratory studies. The local and systemic

reactions observed are described in the SPC and package leaflet under “adverse reactions”.

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 the risk to the environment from the use of the vaccine is minimal. No warnings in regards to environmental exposure from the use of the vaccine are therefore required.

Warnings and precautions as listed on the product literature for its disposal are adequate to ensure safety to the environment when the product is used as directed.

IV. CLINICAL ASSESSMENT (EFFICACY)

Laboratory Trials

The efficacy of the product has been demonstrated in laboratory studies in accordance with the Ph. Eur. monograph 1943 “myxomatosis vaccine live for rabbits”.

2 studies were performed in laboratory conditions with the vaccine FILAVAC MYX L JF613.
The efficacy was demonstrated in controlled laboratory challenge studies by infection with a virulent myxomatosis virus strain.
All the animals tested were SPF rabbits without antibodies against myxomatosis virus.

The onset of immunity was established based on the results of 1 study in which seronegative rabbits 35 days old were vaccinated once by intradermal route. Control groups of rabbits were included. All the rabbits were challenged with virulent myxomatosis virus strain 21 days after the vaccination.
Following the challenge, the mortality in both groups was compared. 100 % of the controls developed severe signs of myxomatosis and were ethically euthanised while 100% of vaccinated animals did not display signs of myxomatosis generalization.

The duration of immunity was established based on the results of one trial in which 50 SPF rabbits 35 days old were vaccinated and 38 of them received a booster vaccination after 4.5 months. Control groups of rabbits were included. The vaccinated rabbits (one dose or 1 dose and one booster) were challenged with virulent myxomatosis virus strain 4 months after each vaccination.

Following the challenges, all controls developed severe signs of myxomatosis and died or were ethically euthanised while more than 90% of vaccinated animals did not display signs of myxomatosis generalisation.

Summary of the efficacy studies

Study	Animals	Vaccine	Challenge Time- strain used	Results (severe signs of myxomatosis)	Conclusion
1	19 SPF rabbits 35 days old G1 : 11 V G2 : 8 C	Filavac myx L JF613	Day 21 post-vaccination	G1 : 0% G2 : 100%	Protection myxomatosis in compliance with Ph. Eur. 1943
2	78 SPF rabbits 35 days old G1 : 12 V G1bis : 38 V including booster at 4.5 months G2 : 28 C	Filavac myx L JF613	4 months after each vaccination 10-12 vaccinates & 5-8 controls	G2 : 100% G1 : 100% G1bis : 90%	Duration of immunity of 4 months established

C: control animals
V: vaccinates
SPF: Specific Pathogen Free rabbit

Field Trials

No specific efficacy field trial was provided (a trial investigated safety in pregnant rabbits is presented in safety part). As the vaccine FILAVAC MYX L JF613 is a MUMS product the absence of efficacy study in field conditions is acceptable.
The following conclusions can be drawn from the results of the studies concerning onset and duration of immunity, indications for use and immunisation scheme:

4.2. Indications for use, specifying the target species

For active immunisation of rabbits from 35 days of age onwards to reduce mortality and clinical signs of myxomatosis.

Onset of immunity: 3 weeks.
Duration of immunity: 4 months.

4.4 Special warnings

No information is available on the use of the vaccine in 35-day old animals with maternally derived antibodies.
No information is available on the safety and efficacy in pet rabbits.

Vaccinate healthy animals only (and not infected).

4.9 Amounts to be administered and administration route

One dose per intradermal injection at the ear to each animal with a volume of:
- 0.2 ml for the 0.2 ml/dose after reconstitution presentation
- 0.1 ml for the 0.1 ml/dose after reconstitution presentation

First vaccination from 35 days of age.
Booster-vaccination every 4 months.
Dilution of the vaccine:
Apply usual aseptic conditions.
Take the vaccine in a sterile syringe with a sterile needle and inject the vaccine into the vial of diluent.
For 0.2 ml/dose after reconstitution presentation:
50-dose: inject the vaccine (2.5 ml) in the diluent vial (7.5 ml)
200-dose: inject the vaccine (10 ml) in the diluent vial (30 ml)
For 0.1 ml/dose after reconstitution presentation:
50-dose: inject the vaccine (2.5 ml) in the diluent vial (2.5 ml)
200-dose: inject the vaccine (10 ml) in the diluent vial (10 ml)

Shake gently before and occasionally during administration to maintain a homogeneous suspension.
If an injector is used for injection to the animal, the user must ensure that the injector delivers the required volume.

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.

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 (http://www.hma.eu/vmriproductindex.html).

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.

Date	Variation
07/2020	Extension of the approved stability from 12 months to 24 months.
07/2021	Addition of a volume of administration of 0.1 mL