ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Nobivac Myxo-RHD PLUS lyophilisate and solvent for suspension for injection for rabbits

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each dose (0.2 ml or 0.5 ml) of reconstituted vaccine contains:

Active substance:
Live myxoma vectored RHD virus strain 009: $10^{3.0}$ - $10^{5.8}$ FFU*
Live myxoma vectored RHD virus strain MK1899: $10^{3.0}$ - $10^{5.8}$ FFU*

*Focus Forming Units

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Lyophilisate and solvent for suspension for injection.

Lyophilisate: off-white or cream-coloured pellet.
Solvent: clear colourless solution.

4. CLINICAL PARTICULARS

4.1 Target species

Rabbits.

4.2 Indications for use, specifying the target species

For active immunisation of rabbits from 5 weeks of age onwards to reduce mortality and clinical signs of myxomatosis and rabbit haemorrhagic disease (RHD) caused by classical RHD virus (RHDV1) and RHD type 2 virus (RHDV2).

Onset of immunity: 3 weeks.
Duration of immunity: 1 year.

4.3 Contraindications

None.

4.4 Special warnings for each target species

Vaccinate healthy animals only.

High levels of maternally derived antibodies against myxoma virus and/or RHD virus can potentially reduce the efficacy of the product. To ensure the full duration of immunity, vaccination from 7 weeks of age is advised in this case.

Rabbits that have been vaccinated previously with another myxomatosis vaccine, or that have experienced natural myxomatosis infection in the field, may not develop an adequate immune response against rabbit haemorrhagic disease following vaccination.

4.5 Special precautions for use

Special precautions for use in animals
Not applicable.

Special precautions to be taken by the person administering the veterinary medicinal product to animals
Not applicable.

4.6 Adverse reactions (frequency and seriousness)

A transient temperature increase of 1 – 2 °C can commonly occur. A small, non-painful swelling (maximum 2 cm diameter) at the injection site is commonly observed within the first two weeks after vaccination. The swelling will resolve completely by 3 weeks after vaccination. In pet rabbits, local reactions at the injection site such as necrosis, scabs, crusts or hair loss may occur in very rare cases. Serious hypersensitivity reactions, which may be fatal, may occur after vaccination in very rare cases. The appearance of mild clinical signs of myxomatosis may occur within 3 weeks of vaccination in very rare cases. Recent or latent infection with field myxoma virus seems to play a role in this to a certain extent.

The frequency of adverse reactions is defined using the following convention:
- very common (more than 1 in 10 animals treated displaying adverse reaction(s))
- common (more than 1 but less than 10 animals in 100 animals treated)
- uncommon (more than 1 but less than 10 animals in 1,000 animals treated)
- rare (more than 1 but less than 10 animals in 10,000 animals treated)
- very rare (less than 1 animal in 10,000 animals treated, including isolated reports).

4.7 Use during pregnancy, lactation or lay

Pregnancy:
Can be used during pregnancy.

Fertility:
No safety study on the reproductive performance has been conducted in male rabbits (bucks). Therefore, the vaccination of breeding bucks is not recommended.

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.

4.9 Amounts to be administered and administration route

Subcutaneous use.

Primary vaccination:
Administer one dose to rabbits from 5 weeks of age onwards.

Revaccination:
Revaccinate annually.

Ensure that the lyophilisate is completely reconstituted before use.
Reconstituted product: off-pink or pink coloured suspension.

Single dose vial

Reconstitute a single dose vial containing lyophilisate with 0.5 ml of the supplied solvent. Administer the total contents of the vial.

Multi-dose vial (50 doses)
Reconstitute a multi-dose vial containing lyophilisate with 10 ml of the supplied solvent. Administer 0.2 ml per animal.

For proper reconstitution of the multi-dose vial, use the following procedure:

1. Add 1 - 2 ml of solvent to the 50-dose vaccine vial and ensure that the lyophilisate is fully dissolved.
2. Withdraw the reconstituted vaccine concentrate from the vial and inject it back into the solvent vial.
3. Ensure that the resulting vaccine suspension in the solvent vial is properly mixed.
4. Use the vaccine suspension within 4 hours of reconstitution. Any reconstituted vaccine remaining at the end of this time should be discarded.

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

In addition to the adverse reactions observed after single dose vaccination, a mild swelling of the local lymph nodes may be observed within the first 3 days after administration of a ten-fold overdose.

4.11 Withdrawal period(s)

Zero days.

5. IMMUNOLOGICAL PROPERTIES

Pharmacotherapeutic group: Immunologicals for Leporidae, live viral vaccine for rabbits
ATC-vet code: QI08AD

The vaccine is intended to stimulate immunity against myxoma virus and rabbit haemorrhagic disease viruses in rabbits.

The vaccine strains are myxoma viruses expressing the capsid protein gene of classical or type 2 RHD viruses. As a consequence, rabbits are immunised against myxoma virus and both classical and type 2 RHD viruses.

After infection with virulent field myxoma virus some vaccinated animals may develop a few very small swellings, especially on hairless places of the body, which quickly form scabs. These scabs usually disappear within 2 weeks. The scabs are only observed in animals with active immunity and have no influence on the general health, appetite or behaviour of the rabbit.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lyophilisate:
Hydrolysed gelatine
Pancreatic digest of casein
Sorbitol
Disodium phosphate dihydrate

Solvent:
Disodium phosphate dihydrate
Potassium dihydrogen phosphate

Water for injections

6.2 Major incompatibilities

Do not mix with any other veterinary medicinal product, except solvent supplied for use with the veterinary medicinal product.

6.3 Shelf life

Shelf life of the veterinary medicinal product (lyophilisate) as packaged for sale: 2 years.
Shelf life of the solvent as packaged for sale: 4 years.
Shelf life after reconstitution according to directions: 4 hours.

6.4 Special precautions for storage

Lyophilisate:
Store in a refrigerator (2°C – 8°C).
Do not freeze.
Protect from light.

Solvent:
No special precautions for storage.

6.5 Nature and composition of immediate packaging

Lyophilisate:
Type I clear glass vial of 1 or 50 doses closed with a chlorobutyl rubber stopper and aluminium cap.

Solvent:
Type I clear glass vial of 0.5 ml or 10 ml closed with a bromobutyl rubber stopper and aluminium cap.

Packaging:
- Plastic box with 5 x 1 dose vial of vaccine and 5 vials containing 0.5 ml of solvent.
- Plastic box with 25 x 1 dose vial of vaccine and 25 vials containing 0.5 ml of solvent.
- Cardboard box with 10 x 50 dose vials of vaccine; and cardboard box with 10 x 10 ml vials of solvent.

Not all pack sizes may be marketed.

6.6 Special precautions for the disposal of unused veterinary medicinal product or waste materials derived from the use of such products

Any unused veterinary medicinal product or waste materials derived from such medicinal product should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Intervet International B.V.
Wim de Körverstraat 35
5831 AN Boxmeer
The Netherlands

8. MARKETING AUTHORISATION NUMBER(S)

EU/2/19/244/001-003

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 19/11/2019

10. DATE OF REVISION OF THE TEXT

{MM/YYYY}

Detailed information on this veterinary medicinal product is available on the website of the European Medicines Agency http://www.ema.europa.eu/.

PROHIBITION OF SALE, SUPPLY AND/OR USE

Any person intending to manufacture, import, possess, sell, supply and use this veterinary medicinal product must first consult the relevant Member State's competent authority on the current vaccination policies, as these activities may be prohibited in a Member State on the whole or part of its territory pursuant to national legislation.

ANNEX II

A. MANUFACTURERS OF THE BIOLOGICAL ACTIVE SUBSTANCE AND MANUFACTURER RESPONSIBLE FOR BATCH RELEASE

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

C. STATEMENT OF THE MRLs

A. MANUFACTURERS OF THE BIOLOGICAL ACTIVE SUBSTANCE AND MANUFACTURER RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer of the biological active substances
Intervet International B.V.
Wim de Körverstraat 35
5831 AN Boxmeer
The Netherlands

Name and address of the manufacturer responsible for batch release
Intervet International B.V.
Wim de Körverstraat 35
5831 AN Boxmeer
The Netherlands

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Veterinary medicinal product subject to prescription.

C. STATEMENT OF THE MRLs

The active substances being a principle of biological origin intended to produce active immunity is not within the scope of Regulation (EC) No 470/2009.

The excipients listed in section 6.1 of the SPC are either allowed substances for which table 1 of the annex to Commission Regulation (EU) No 37/2010 indicates that no MRLs are required or are considered as not falling within the scope of Regulation (EC) No 470/2009 when used as in this veterinary medicinal product.

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

BOX
Plastic box with 5 x 1 dose vials of vaccine and 5 x 0.5 ml solvent vials (glass)
Plastic box with 25 x 1 dose vials of vaccine and 25 x 0.5 ml solvent vials (glass)
Cardboard box with 10 x 50 doses of vaccine

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Nobivac Myxo-RHD PLUS lyophilisate and solvent for suspension for injection for rabbits

2. STATEMENT OF ACTIVE SUBSTANCES

Live myxoma vectored RHD virus strain 009: $10^{3.0}$ - $10^{5.8}$ FFU/dose.
Live myxoma vectored RHD virus strain MK1899: $10^{3.0}$ - $10^{5.8}$ FFU/dose.

3. PHARMACEUTICAL FORM

Lyophilisate and solvent for suspension for injection

4. PACKAGE SIZE

5 x 1 dose of vaccine including solvent
25 x 1 dose of vaccine including solvent
10 x 50 doses of vaccine

5. TARGET SPECIES

Rabbits

6. INDICATION(S)

7. METHOD AND ROUTE(S) OF ADMINISTRATION

Subcutaneous use.
Read the package leaflet before use.

8. WITHDRAWAL PERIOD(S)

Withdrawal period: Zero days.

9. SPECIAL WARNING(S), IF NECESSARY

Read the package leaflet before use.

10. EXPIRY DATE

EXP {month/year}
Once reconstituted use within 4 hours.

11. SPECIAL STORAGE CONDITIONS

Store in a refrigerator.
Do not freeze.
Protect from light.

12. SPECIFIC PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCTS OR WASTE MATERIALS, IF ANY

Disposal: read package leaflet.

13. THE WORDS "FOR ANIMAL TREATMENT ONLY" AND CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE, IF APPLICABLE

For animal treatment only. To be supplied only on veterinary prescription.

14. THE WORDS "KEEP OUT OF THE SIGHT AND REACH OF CHILDREN"

Keep out of the sight and reach of children.

15. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Intervet International B.V.
Wim de Körverstraat 35
NL - 5831 AN Boxmeer

16. MARKETING AUTHORISATION NUMBER(S)

EU/2/19/244/001
EU/2/19/244/002
EU/2/19/244/003

17. MANUFACTURER'S BATCH NUMBER

Lot {number}

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

BOX (SOLVENT ONLY)
Cardboard box with 10 x 10 ml solvent vials (glass)

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Solvent for Nobivac Myxo-RHD PLUS

2. STATEMENT OF ACTIVE SUBSTANCES

3. PHARMACEUTICAL FORM

4. PACKAGE SIZE

10 x 10 ml

5. TARGET SPECIES

Rabbits

6. INDICATION(S)

7. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.

8. WITHDRAWAL PERIOD(S)

9. SPECIAL WARNING(S), IF NECESSARY

10. EXPIRY DATE

EXP {month/year}

11. SPECIAL STORAGE CONDITIONS

No special storage conditions.

12. SPECIFIC PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCTS OR WASTE MATERIALS, IF ANY

13. THE WORDS "FOR ANIMAL TREATMENT ONLY" AND CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE, IF APPLICABLE

For animal treatment only. To be supplied only on veterinary prescription.

14. THE WORDS "KEEP OUT OF THE SIGHT AND REACH OF CHILDREN"

Keep out of the sight and reach of children.

15. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Intervet International B.V.
Wim de Körverstraat 35
NL - 5831 AN Boxmeer

16. MARKETING AUTHORISATION NUMBER(S)

17. MANUFACTURER'S BATCH NUMBER

Lot {number}

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

VACCINE GLASS VIAL LABEL – 1 dose / 50 doses glass vial

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Nobivac Myxo-RHD PLUS

2. QUANTITY OF THE ACTIVE SUBSTANCE(S)

Live myxoma vectored RHD viruses

3. CONTENTS BY WEIGHT, BY VOLUME OR BY NUMBER OF DOSES

1 dose
50 doses

4. ROUTE(S) OF ADMINISTRATION

SC

5. WITHDRAWAL PERIODS

Withdrawal period: Zero days

6. BATCH NUMBER

Lot {number}

7. EXPIRY DATE

EXP {month/year}

8. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only.

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

SOLVENT LABEL
0.5 ml and 10 ml glass vial

1. NAME OF THE SOLVENT

Solvent for Nobivac Myxo-RHD PLUS

2. CONTENTS BY WEIGHT, BY VOLUME OR BY NUMBER OF DOSES

0.5 ml
10 ml

3. ROUTE(S) OF ADMINISTRATION

Read package leaflet before use.

4. STORAGE CONDITIONS

No special storage conditions.

5. BATCH NUMBER

Lot {number}

6. EXPIRY DATE

EXP {month/year}

7. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only.

B. PACKAGE LEAFLET

PACKAGE LEAFLET:

Nobivac Myxo-RHD PLUS
lyophilisate and solvent for suspension for injection for rabbits

1. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER AND OF THE MANUFACTURING AUTHORISATION HOLDER RESPONSIBLE FOR BATCH RELEASE, IF DIFFERENT

Marketing authorisation holder and manufacturer responsible for batch release:
Intervet International B.V.
Wim de Körverstraat 35
5831 AN Boxmeer
The Netherlands

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

Nobivac Myxo-RHD PLUS lyophilisate and solvent for suspension for injection for rabbits

3. STATEMENT OF THE ACTIVE SUBSTANCE(S) AND OTHER INGREDIENT(S)

Each dose (0.2 ml or 0.5 ml) of reconstituted vaccine contains:

Live myxoma vectored RHD virus strain 009: $10^{3.0}$ - $10^{5.8}$ FFU *
Live myxoma vectored RHD virus strain MK1899: $10^{3.0}$ - $10^{5.8}$ FFU*

*Focus Forming Units

Lyophilisate: off-white or cream-coloured pellet.
Solvent: clear colourless solution.

4. INDICATION(S)

For active immunisation of rabbits from 5 weeks of age onwards to reduce mortality and clinical signs of myxomatosis and rabbit haemorrhagic disease (RHD) caused by classical RHD virus (RHDV1) and RHD type 2 virus (RHDV2).

Onset of immunity: 3 weeks.
Duration of immunity: 1 year.

5. CONTRAINDICATIONS

None.

6. ADVERSE REACTIONS

A transient temperature increase of 1–2 °C can commonly occur. A small, non-painful swelling (maximum 2 cm diameter) at the injection site is commonly observed within the first two weeks after vaccination. The swelling will resolve completely by 3 weeks after vaccination. In pet rabbits, local reactions at the injection site such as necrosis, scabs, crusts or hair loss may occur in very rare cases. Serious hypersensitivity reactions, which may be fatal, may occur after vaccination in very rare cases.

The appearance of mild clinical signs of myxomatosis may occur within 3 weeks of vaccination in very rare cases. Recent or latent infection with field myxoma virus seems to play a role in this to a certain extent.

The frequency of adverse reactions is defined using the following convention:
- very common (more than 1 in 10 animals treated displaying adverse reaction(s))
- common (more than 1 but less than 10 animals in 100 animals treated)
- uncommon (more than 1 but less than 10 animals in 1,000 animals treated)
- rare (more than 1 but less than 10 animals in 10,000 animals treated)
- very rare (less than 1 animal in 10,000 animals treated, including isolated reports).

If you notice any side effects, even those not already listed in this package leaflet or you think that the medicine has not worked, please inform your veterinary surgeon.

7. TARGET SPECIES

Rabbits.

8. DOSAGE FOR EACH SPECIES, ROUTE(S) AND METHOD OF ADMINISTRATION

Subcutaneous use.

Primary vaccination:
Administer one dose to rabbits from 5 weeks of age onwards.

Revaccination:
Revaccinate annually.

9. ADVICE ON CORRECT ADMINISTRATION

Ensure that the lyophilisate is completely reconstituted before use.
Reconstituted product: off-pink or pink coloured suspension.

Single-dose vial
Reconstitute a single dose vial containing lyophilisate with 0.5 ml of the supplied solvent. Administer the total contents of the vial.

Multi-dose vial
Reconstitute a multi-dose vial containing lyophilisate with 10 ml of the supplied solvent. Administer 0.2 ml per animal.

For proper reconstitution of the multidose vial, use the following procedure:

1. Add 1 –2 ml of solvent to the 50-dose vaccine vial and ensure that the lyophilisate is fully dissolved.
2. Withdraw the reconstituted vaccine concentrate from the vial and inject it back into the solvent vial.
3. Ensure that the resulting vaccine suspension in the solvent vial is properly mixed.
4. Use the vaccine suspension within 4 hours of reconstitution. Any reconstituted vaccine remaining at the end of this time should be discarded.

10. WITHDRAWAL PERIOD(S)

Zero days.

11. SPECIAL STORAGE PRECAUTIONS

Keep out of the sight and reach of children.

Lyophilisate:
Store in a refrigerator (2°C – 8°C).
Do not freeze.
Protect from light.

Solvent:
No special precautions for storage.

Do not use this veterinary medicinal product after the expiry date which is stated on the label.

Shelf life after reconstitution according to directions: 4 hours.

12. SPECIAL WARNING(S)

Special warnings for each target species:
Vaccinate healthy animals only.

High levels of maternally derived antibodies against myxoma virus and/or RHD virus can potentially reduce the efficacy of the product. To ensure the full duration of immunity, vaccination from 7 weeks of age is advised in this case.

Rabbits that have been vaccinated previously with another myxomatosis vaccine, or that have experienced natural myxomatosis infection in the field, may not develop a proper immune response against rabbit haemorrhagic disease following vaccination.

Special precautions for use in animals:
Not applicable.

Pregnancy:
Can be used during pregnancy.

Fertility:
No safety study on the reproductive performance has been conducted in male rabbits (bucks). Therefore, the vaccination of breeding bucks is not recommended.

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.

Overdose (symptoms, emergency procedures, antidotes):
In addition to the signs observed after single dose vaccination, a mild swelling of the local lymph nodes may be observed within the first 3 days after the administration of a ten-fold overdose.

Incompatibilities:
Do not mix with any other veterinary medicinal product, except solvent supplied for use with the veterinary medicinal product.

13. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCT OR WASTE MATERIALS, IF ANY

Ask your veterinary surgeon how to dispose of medicines no longer required. These measures should help to protect the environment.

14. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED

Detailed information on this veterinary medicinal product is available on the website of the European Medicines Agency http://www.ema.europa.eu/.

15. OTHER INFORMATION

The vaccine is intended to stimulate immunity against myxoma virus and rabbit haemorrhagic disease viruses in rabbits.

The vaccine strains are myxoma viruses expressing the capsid protein gene of classical or type 2 RHD viruses. As a consequence rabbits are immunised against myxoma virus and both classical and type 2 RHD virus.

The vector technology used to develop the vaccine strains allows the RHD virus components to be produced *in vitro* instead of using live rabbits for cultivation.

After infection with virulent field myxoma virus some vaccinated animals may develop a few very small swellings, especially on hairless places of the body, which quickly form scabs. These scabs usually disappear within 2 weeks. The scabs are only observed in animals with active immunity and have no influence on the general health, appetite or behaviour of the rabbit.

- Plastic box with 5 x 1 dose vials of vaccine and 5 vials containing 0.5 ml of solvent.
- Plastic box with 25 x 1 dose vials of vaccine and 25 vials containing 0.5 ml of solvent.
- Cardboard box with 10 x 50 doses vials of vaccine; and cardboard box with 10 x 10 ml vials of solvent.

Not all pack sizes may be marketed.