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 substances:
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

Excipients:

Qualitative composition of excipients and other constituents
Lyophilisate:
Hydrolysed gelatine
Pancreatic digest of casein
Sorbitol
Disodium phosphate dihydrate
Solvent:
Disodium phosphate dihydrate
Potassium dihydrogen phosphate
Water for injections

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

3. CLINICAL INFORMATION

3.1 Target species

Rabbits.

3.2 Indications for use for each 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.

3.3 Contraindications

None.

3.4 Special warnings

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.

3.5 Special precautions for use

Special precautions for safe use in the target species:
Not applicable.

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

Special precautions for the protection of the environment:
Not applicable.

3.6 Adverse events

Rabbits:

Common (1 to 10 animals / 100 animals treated):	Hyperthermia[1]. Injection site swelling[2].
Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Injection site necrosis[3], injection site scab[3], injection site crust[3], injection site hair loss[3]. Hypersensitivity reaction[4]. Myxomatosis[5]. Anorexia, lethargy.

[1] Transient temperature increase of 1 – 2 °C
[2] A small, non-painful swelling (maximum 2 cm diameter) within the first two weeks after vaccination. The swelling will resolve completely by 3 weeks after vaccination.
[3] In pet rabbits.
[4] Sometimes fatal.
[5] Mild clinical signs of myxomatosis may occur within 3 weeks of vaccination.

Reporting adverse events is important. It allows continuous safety monitoring of a veterinary medicinal product. Reports should be sent, preferably via a veterinarian, to either the marketing authorisation holder or the national competent authority via the national reporting system. See the package leaflet for respective contact details.

3.7 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.

3.8 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.

3.9 Administration routes and dosage

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.

3.10 Symptoms of overdose (and where applicable, emergency procedures and antidotes)

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.

3.11 Special restrictions for use and special conditions for use, including restrictions on the use of antimicrobial and antiparasitic veterinary medicinal products in order to limit the risk of development of resistance

Any person intending to manufacture, import, possess, distribute, 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.

3.12 Withdrawal periods

Zero days.

4. IMMUNOLOGICAL INFORMATION

4.1 ATCvet 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.
Recent or latent infection with field myxoma virus seems to play a role in the development of the mild clinical signs of myxomatosis that may occur within 3 weeks after vaccination.

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities

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

5.2 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.

5.3 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.

5.4 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.

Pack sizes:
- 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.

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

Medicines should not be disposed of via wastewater or household waste.

Use take-back schemes for the disposal of any unused veterinary medicinal product or waste materials derived thereof in accordance with local requirements and with any national collection systems applicable to the veterinary medicinal product concerned.

6. NAME OF THE MARKETING AUTHORISATION HOLDER

Intervet International B.V.

7. MARKETING AUTHORISATION NUMBER(S)

EU/2/19/244/001-003

8. DATE OF FIRST AUTHORISATION

Date of first authorisation: 19/11/2019.

9. DATE OF THE LAST REVISION OF THE SUMMARY OF THE PRODUCT CHARACTERISTICS

{MM/YYYY}

10. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCTS

Veterinary medicinal product subject to prescription.

Detailed information on this veterinary medicinal product is available in the Union Product Database (https://medicines.health.europa.eu/veterinary).

ANNEX II

OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

None

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

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. PACKAGE SIZE

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

4. TARGET SPECIES

Rabbits

5. INDICATIONS

6. ROUTES OF ADMINISTRATION

Subcutaneous use.

7. WITHDRAWAL PERIODS

Withdrawal period: Zero days.

8. EXPIRY DATE

Exp. {mm/yyyy}
Once reconstituted use within 4 hours.

9. SPECIAL STORAGE PRECAUTIONS

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

10. THE WORDS "READ THE PACKAGE LEAFLET BEFORE USE"

Read the package leaflet before use.

11. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only.

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

Keep out of the sight and reach of children.

13. NAME OF THE MARKETING AUTHORISATION HOLDER

Intervet International B.V.

14. MARKETING AUTHORISATION NUMBERS

EU/2/19/244/001 (5 x 1 dose; 5 x 0.5 ml)
EU/2/19/244/002 (25 x 1 dose; 25 x 0.5 ml)
EU/2/19/244/003 (10 x 50 doses)

15. 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. PACKAGE SIZE

10 x 10 ml

4. TARGET SPECIES

Rabbits

5. INDICATIONS

6. ROUTES OF ADMINISTRATION

Subcutaneous use.

7. WITHDRAWAL PERIODS

8. EXPIRY DATE

Exp. {mm/yyyy}

9. SPECIAL STORAGE PRECAUTIONS

10. THE WORDS "READ THE PACKAGE LEAFLET BEFORE USE"

Read the package leaflet before use.

11. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only.

12. THE WORDS “KEEP OUT OF THE SIGHT AND REACH OF CHILDREN”

Keep out of the sight and reach of children.

13. NAME OF THE MARKETING AUTHORISATION HOLDER

Intervet International B.V.

14. MARKETING AUTHORISATION NUMBERS

EU/2/19/244/003

15. 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. QUANTITATIVE PARTICULARS OF THE ACTIVE SUBSTANCES

Live myxoma vectored RHD viruses
1 dose
50 doses

3. BATCH NUMBER

Lot {number}

4. EXPIRY DATE

Exp. {mm/yyyy}

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

SOLVENT LABEL
0.5 ml and 10 ml glass vial

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Solvent for Nobivac Myxo-RHD PLUS

2. QUANTITATIVE PARTICULARS OF THE ACTIVE SUBSTANCES

0.5 ml
10 ml

3. BATCH NUMBER

Lot {number}

4. EXPIRY DATE

Exp. {mm/yyyy}

B. PACKAGE LEAFLET

PACKAGE LEAFLET

1. Name of the veterinary medicinal product

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

2. Composition

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

Active substances:
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.

3. Target species

Rabbits.

4. Indications for use

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. Special warnings

Special warnings:
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.

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:
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.

Special restrictions for use and special conditions for use:
Any person intending to manufacture, import, possess, distribute, 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.

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

7. Adverse events

Rabbits:

Common (1 to 10 animals / 100 animals treated):	Hyperthermia[1]. Injection site swelling[2].
Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Injection site necrosis[3], injection site scab[3], injection site crust[3], injection site hair loss[3]. Hypersensitivity reaction[4]. Myxomatosis[5]. Anorexia, lethargy.

[1] Transient temperature increase of 1 – 2 °C
[2] A small, non-painful swelling (maximum 2 cm diameter) within the first two weeks after vaccination. The swelling will resolve completely by 3 weeks after vaccination.
[3] In pet rabbits.
[4] Sometimes fatal.
[5] Mild clinical signs of myxomatosis may occur within 3 weeks of vaccination.

Reporting adverse events is important. It allows continuous safety monitoring of a product. 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 contact, in the first instance, your veterinarian. You can also report any adverse events to the marketing authorisation holder using the contact details at the end of this leaflet, or via your national reporting system: {national system details}.

8. Dosage for each species, routes 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 periods

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. The expiry date refers to the last day of that month.

Shelf life after reconstitution according to directions: 4 hours.

12. Special precautions for disposal

Medicines should not be disposed of via wastewater or household waste.

Use take-back schemes for the disposal of any unused veterinary medicinal product or waste materials derived thereof in accordance with local requirements and with any applicable national collection systems. These measures should help to protect the environment.

Ask your veterinary surgeon or pharmacist how to dispose of medicines no longer required.

13. Classification of veterinary medicinal products

Veterinary medicinal product subject to prescription.

14. Marketing authorisation numbers and pack sizes

EU/2/19/244/001-003

Pack sizes:
- 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.

15. Date on which the package leaflet was last revised

{MM/YYYY}

Detailed information on this veterinary medicinal product is available in the Union Product Database (https://medicines.health.europa.eu/veterinary).

16. Contact details

Marketing authorisation holder and manufacturer responsible for batch release and contact details to report suspected adverse reactions:
Intervet International B.V., Wim de Körverstraat 35, 5831 AN Boxmeer, The Netherlands

België/Belgique/Belgien
Tél/Tel: + 32 (0)2 370 94 01

Република България
Тел: + 359 28193749

Česká republika
Tel: + 420 233 010 242

Danmark
Tlf: + 45 44 82 42 00

Deutschland
Tel: + 49 (0)8945614100

Eesti
Tel: + 37052196111

Lietuva
Tel: + 37052196111

Luxembourg/Luxemburg
Tél/Tel: + 32 (0)2 370 94 01

Magyarország
Tel.: + 36 1 439 4597

Malta
Tel: + 39 02 516861

Nederland
Tel: + 32 (0)2 370 94 01

Norge
Tlf: + 47 55 54 37 35

Ελλάδα
Τηλ: + 30 210 989 7452

España
Tel: + 34 923 19 03 45

France
Tél: + 33 (0)241228383

Hrvatska
Tel: + 385 1 6611339

Ireland
Tel: + 353 (0) 1 2970220

Ísland
Sími: + 354 535 7000

Italia
Tel: + 39 02 516861

Κύπρος
Τηλ: + 30 210 989 7452

Latvija
Tel: + 37052196111

Österreich
Tel: + 43 (1) 256 87 87

Polska
Tel.: + 48 22 18 32 200

Portugal
Tel: + 351 214 465 700

România
Tel: + 40 21 311 83 11

Slovenija
Tel: + 385 1 6611339

Slovenská republika
Tel: + 420 233 010 242

Suomi/Finland
Puh/Tel: + 358 10 2310 750

Sverige
Tel: + 46 (0)8 522 216 60

United Kingdom (Northern Ireland)
Tel: + 353 (0) 1 2970220

17. 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.
Recent or latent infection with field myxoma virus seems to play a role in the development of the mild clinical signs of myxomatosis that may occur within 3 weeks after vaccination.