

**ANNEX III**  
**LABELLING AND PACKAGE LEAFLET**

## **A. LABELLING**

**PARTICULARS TO APPEAR ON THE OUTER PACKAGE**

**CARDBOARD BOX**

1 x 10 doses freeze-dried pellet and 1 x 20 ml diluent  
1 x 50 doses freeze-dried pellet and 1 x 100 ml diluent

**1. NAME OF THE VETERINARY MEDICINAL PRODUCT**

Rispoval IBR-Marker Live lyophilisate and diluent for suspension for injection.

**2. STATEMENT OF ACTIVE SUBSTANCES**

Each 2 ml dose contains:

BoHV-1, strain Difivac (gE-negative), live attenuated  $10^{5.0} - 10^{7.0}$  CCID<sub>50</sub>

**3. PACKAGE SIZE**

1 x 10 doses freeze-dried pellet and 1 x 20 ml diluent.  
1 x 50 doses freeze-dried pellet and 1 x 100 ml diluent.

**4. TARGET SPECIES**

Cattle.

**5. INDICATIONS**

**6. ROUTES OF ADMINISTRATION**

Intranasal use.  
Intramuscular use.

**7. WITHDRAWAL PERIODS**

Withdrawal period: Zero days.

**8. EXPIRY DATE**

Exp. {mm/yyyy}  
Once reconstituted use within 8 hours.

**9. SPECIAL STORAGE PRECAUTIONS**

Store in a refrigerator.  
Do not freeze.  
Protect from light.  
After reconstitution keep the vaccine refrigerated.

**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**

Zoetis UK Limited

**14. MARKETING AUTHORISATION NUMBER**

Vm 42058/3015

**15. BATCH NUMBER**

Lot {number}

**MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS**

**LABEL ON GLASS VIAL - FREEZE-DRIED PELLETS**  
(10 doses)  
(50 doses)

**1. NAME OF THE VETERINARY MEDICINAL PRODUCT**

Rispoval IBR-Marker Live

**2. QUANTITATIVE PARTICULARS OF THE ACTIVE SUBSTANCES**

BoHV-1

10 doses

50 doses

**3. BATCH NUMBER**

Lot {number}

**4. EXPIRY DATE**

Exp. {mm/yyyy}

Once reconstituted use within 8 hours.

**MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS**

**LABEL ON GLASS VIAL - DILUENT**

20 ml

100 ml

**1. NAME OF THE VETERINARY MEDICINAL PRODUCT**

Rispoval IBR-Marker Live diluent

**2. QUANTITATIVE PARTICULARS OF THE ACTIVE SUBSTANCES**

Water for injections

20 ml

100 ml

**3. BATCH NUMBER**

Lot {number}

**4. EXPIRY DATE**

Exp. {mm/yyyy}

Once reconstituted use within 8 hours.

## **B. PACKAGE LEAFLET**

## **PACKAGE LEAFLET**

### **1. Name of the veterinary medicinal product**

Rispoval IBR-Marker Live lyophilisate and diluent for suspension for injection for cattle

### **2. Composition**

Each 2 ml dose contains:

#### **Active substance:**

#### **Freeze-dried pellet:**

Bovine Herpes Virus type 1 (BoHV-1), strain Difivac (gE-negative),  
modified live (attenuated) virus

min.  $10^{5.0}$  CCID<sub>50</sub>\*  
max.  $10^{7.0}$  CCID<sub>50</sub>\*

\* CCID<sub>50</sub> = Cell culture infective dose 50%.

#### **Excipient:**

#### **Diluent:**

Water for injections 2 ml

Lyophilisate: slightly coloured freeze-dried pellet.

Diluent: clear, colourless solution.

### **3. Target species**

Cattle.

### **4. Indications for use**

For active immunisation of cattle against Infectious Bovine Rhinotracheitis (IBR), to reduce virus shedding and clinical signs including, in female cattle, abortions associated with BoHV-1 infection. A reduction of abortion associated with BoHV-1 infections has been demonstrated during the second trimester of gestation upon challenge 28 days after vaccination. Vaccinated cattle can be differentiated from field virus infected animals due to the marker deletion, unless the cattle were previously vaccinated with a conventional vaccine or infected with field virus.

Onset of immunity: 7 days following a single intranasal administration.

21 days following a single intramuscular administration.

Duration of immunity following vaccination before 3 months of age: after intranasal vaccination of calves aged 2 weeks or older without maternally derived antibodies, immunity lasts until at least 3 months of age, when the animals should be revaccinated via intramuscular injection. A proportion of young calves may have maternally derived

antibodies to BoHV-1, which may affect the immune response to vaccination. Consequently, the protection afforded by the vaccine may not be complete until the revaccination at 3 months of age.

Duration of immunity following vaccination at or after 3 months of age: 6 months.

### **Additional information on protection from abortion afforded by combined vaccination of Rispoval IBR-Marker Vivum with Rispoval IBR-Marker Inactivatum\*:**

prevention of abortion has been demonstrated during the third trimester of gestation upon BoHV-1 challenge applied 86 days after a single dose booster vaccination using Rispoval IBR-Marker Inactivatum\*, which was administered 6 months after a single dose primary vaccination by the intramuscular route using Rispoval IBR-Marker Vivum.

\* Where this veterinary medicinal product is authorised.

## **5. Contraindications**

None.

## **6. Special warnings**

### Special warnings:

The presence of maternal antibodies can influence the efficacy of the vaccination. Therefore it is recommended to ascertain the immune status of calves before vaccination is started.

Vaccinate healthy animals only.

### Special precautions for safe use in the target species:

In some cases, the vaccine virus may be excreted after intranasal administration from vaccinated animals. After intranasal administration of a 10-fold overdose, the vaccine virus was detected for up to 9 days after vaccination. In very young calves and in rare cases, vaccine virus was excreted until day 18 post intramuscular vaccination with a 10-fold overdose.

Exceptional transmission of the virus from intranasally-vaccinated animals to non-vaccinated in-contact animals may occur due to the nature of the vaccine even though no verified data available would indicate that spreading of the vaccine virus occurs in a group of animals.

It is recommended to vaccinate all the cattle in the herd.

### Special precautions to be taken by the person administering the veterinary medicinal product to animals:

In case of accidental self-injection, seek medical advice immediately and show the package leaflet or the label to the physician.

Pregnancy and lactation:

Can be used during pregnancy and lactation.

Interaction with other medicinal products and other forms of interaction:

Immunosuppressive substances, i.e. corticosteroids or Bovine Virus Diarrhoea modified live vaccines, should be avoided in a period of 7 days prior to and after vaccination as this may impair the development of the immunity.

Interferon sensitive veterinary medicinal products should not be applied intranasally following 5 days after intranasal vaccination.

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 decided on a case by case basis.

Overdose:

After intranasal administration of a 10-fold overdose, a transient hyperthermia (> 39.5°C) was observed in some calves for up to 3 consecutive days.

After intramuscular administration of a 10-fold overdose, a transient hyperthermia (> 39.5°C) was observed in some calves for up to 4 consecutive days. In another study, a transient (one day) slight serous ocular discharge was observed in some calves after intramuscular administration of a 10-fold overdose.

Otherwise, adverse events after administration of an overdose of the vaccine are not different from those observed after the single dose.

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 diluent supplied for use with the veterinary medicinal product.

## 7. Adverse events

Cattle:

Rare (1 to 10 animals / 10,000 animals treated):	Nasal discharge <sup>1</sup>
Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Injection site swelling <sup>2</sup> , Hypersensitivity reaction <sup>3</sup>

<sup>1</sup>Slight transient, serous discharge may occur for up to 7 days following intranasal inoculation.

<sup>2</sup>Transient swelling up to 3 cm which generally subsides within 7 days; when injected intramuscularly.

<sup>3</sup>Vaccinated animals should be observed for approximately 30 minutes following immunisation. If such reactions occur, antiallergics should be administered.

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 <or the local representative of 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

Dose: 2 ml reconstituted vaccine.

Route of administration: intranasal and/or intramuscular inoculation.

### Vaccination programme:

The vaccination scheme consists of basic immunisation and booster vaccinations.

### Basic immunisation:

#### *Calves of 2 weeks to 3 months of age at first vaccination*

The first vaccination should be applied intranasally, followed by a second vaccination intramuscularly at 3 months of age. A proportion of young calves may have maternally derived antibodies to BoHV-1, which may affect the immune response to vaccination.

Consequently, the protection afforded by the vaccine may not be complete until the revaccination at 3 months of age. As an extra precaution in situations of high challenge with BoHV-1, maternal antibody positive animals that have been initially vaccinated at around 2 weeks of age may be given an additional vaccination between the first vaccination and vaccination at 3 months of age. This additional vaccination may be given via either intranasal or intramuscular administration and may be given from 3 weeks after the first vaccination.

*Cattle at 3 months of age or older at first vaccination*

Animals should be given one intramuscular or intranasal vaccination.

Beef cattle and fattening bulls are vaccinated preferably just prior to housing (crowding) or at transfer to new groups, while taking into account the interval needed for the onset of protection following the basic vaccination scheme.

*For female cattle for protection against abortion*

To prevent abortions associated with BoHV-1, female cattle require a primary course of two intramuscular doses of Rispoval IBR-Marker Vivum 3-5 weeks apart or alternatively a primary course of a single intramuscular dose of Rispoval IBR-Marker Vivum followed 6 months later by a single dose booster using Rispoval IBR-Marker Inactivatum\*. In order to cover the main abortion risk period, it is recommended that the second dose of the primary course of two intramuscular doses of Rispoval IBR-Marker Vivum or the single dose booster using Rispoval IBR-Marker Inactivatum\* is administered no later than by the start of the second trimester of each pregnancy.

*Cattle at immediate risk of IBR*

In the case of known high BoHV-1 infection pressure, the first dose in cattle (including pregnant females) should be administered intranasally in order to stimulate local immunity, followed 3 – 5 weeks later by the second dose administered intramuscularly to complete the primary vaccination course.

Booster vaccinations:

Animals should be given a single dose booster vaccination 6 months after their initial vaccination course. Animals initially vaccinated with Rispoval IBR-Marker Vivum may be given a single dose booster vaccination with either Rispoval IBR-Marker Vivum to provide 6 months of protection or Rispoval IBR-Marker Inactivatum\* to provide a duration of immunity of 12 months of protection.

Thereafter, single dose booster vaccinations should be administered every 6 months (if using Rispoval IBR-Marker Vivum) or every 12 months (if using Rispoval IBR-Marker Inactivatum\*).

Vaccination schemes summary:

**From 2 weeks to 3 months of age**

<b>Risposal IBR-Marker vaccine used</b>			
<b>Primary Vaccination</b>		<b>Revaccination Intervals</b>	
<b>First dose (vaccine, route of administration)</b>	<b>Second dose (vaccine, route of administration)</b>	<b>Interval to next booster vaccination (vaccine, route of administration)</b>	<b>All subsequent booster vaccinations (vaccine, route of administration)</b>
2 weeks (Vivum, intranasal)	3 months (Vivum, intramuscular)	6 months (Vivum, intramuscular)	6 months (Vivum, intramuscular)
2 weeks (Vivum, intranasal)	3 months (Vivum, intramuscular)	6 months (Inactivatum*, subcutaneous)	12 months (Inactivatum*, subcutaneous)

**From 3 months of age**

<b>Risposal IBR-Marker vaccine used</b>		
<b>Primary Vaccination (number of doses, route of administration)</b>	<b>Revaccination Intervals</b>	
	<b>Interval to first booster vaccination (vaccine, route of administration)</b>	<b>All subsequent booster vaccinations (vaccine, route of administration)</b>
Vivum (one dose, intramuscular or intranasal)	6 months (Vivum, intramuscular)	6 months (Vivum, intramuscular)
Vivum (one dose, intramuscular)	6 months (Inactivatum*, subcutaneous)	12 months (Inactivatum*, subcutaneous)
Inactivatum* (two doses, subcutaneous, with 3-5 week interval)	6 months (Inactivatum*, subcutaneous)	6 months (Inactivatum*, subcutaneous)

**For female cattle for protection against abortion:**

Rispoval IBR-Marker vaccine used	
Primary Vaccination (number of doses, route of administration) recommended to be applied no later than by the start of second trimester of pregnancy	Revaccination
Vivum (two doses, intramuscular, with 3-5 weeks interval)	Inactivatum* (one dose, subcutaneous) recommended to be applied no later than by the start of the second trimester of each pregnancy
Vivum (one dose, intramuscular) followed by Inactivatum* (one dose, subcutaneous), with 6 months interval	
Inactivatum* (two doses, subcutaneous, with 3-5 week interval)	

**For vaccination in known high BoHV-1 infection pressure:**

Rispoval IBR-Marker vaccine used		
Primary Vaccination (number of doses, route of administration)	Revaccination Intervals	
	Interval to first booster vaccination (vaccine, route of administration)	All subsequent booster vaccinations (vaccine, route of administration)
Vivum (one dose, intranasal), followed by Vivum (one dose, intramuscular) with 3-5 weeks interval	6 months (Vivum, intramuscular, OR Inactivatum*, subcutaneous)	6 months (Vivum, intramuscular) OR 12 months (Inactivatum*, subcutaneous)

\* Where this veterinary medicinal product is authorised.

**9. Advice on correct administration**

Method of administration:

The freeze-dried pellet should be reconstituted aseptically just prior to use. The vaccine is prepared as follows:

For 10 and 50 dose vials approx. 4 ml of the respective diluent are transferred to the vial containing the freeze-dried pellet and then mixed.

The reconstituted virus fraction is finally transferred back into the respective remaining diluent and mixed well. The veterinary medicinal product is then ready for use.

The needles and syringes used for application of the vaccine must not be sterilised by chemical disinfectants as this may impair the efficacy of the vaccine.

The vaccine must be administered aseptically via the intramuscular route (2 ml) or sprayed into the nostrils (1 ml per nostril during aspiration) with the intranasal applicator available from Zoetis. Once resuspended the vaccine remains potent for max. 8 hours when the veterinary medicinal product is withdrawn sterile and refrigerated.

After reconstitution, the suspension should be a colourless clear liquid, which might contain a loose resuspendable sediment.

## **10. Withdrawal periods**

Zero days.

## **11. Special storage precautions**

Keep out of the sight and reach of children.

Store in a refrigerator (2 °C – 8 °C).

Do not freeze.

Protect from light.

Do not use this veterinary medicinal product after the expiry date which is stated on the label after Exp. The expiry date refers to the last day of that month.

Shelf life after reconstitution according to directions: 8 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.

## **13. Classification of veterinary medicinal products**

Veterinary medicinal product subject to prescription.

## **14. Marketing authorisation numbers and pack sizes**

Vm 42058/3015

1 box with 1 glass vial, type 1, freeze-dried pellet (10 doses) and 1 glass vial, type 1, containing 20 ml (10 doses) diluent, each closed respectively with bromobutyl and chlorobutyl rubber stopper and an aluminium flip-off cap.

1 box with 1 glass vial, type 1, freeze-dried pellet (50 doses) and 1 glass vial, type 1, containing 100 ml (50 doses) diluent, each closed respectively with bromobutyl and chlorobutyl rubber stopper and an aluminium flip-off cap.

Not all pack sizes may be marketed.

## 15. Date on which the package leaflet was last revised

November 2023

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 contact details to report suspected adverse reactions>:

Zoetis UK Limited  
1st Floor, Birchwood Building  
Springfield Drive  
Leatherhead  
Surrey  
KT22 7LP

Manufacturer responsible for batch release:

Zoetis Belgium  
Rue Laid Burniat 1  
1348 Louvain-La-Neuve  
Belgium

<Local representative <and contact details to report suspected adverse reactions>:>  
*To be completed nationally (if needed).*

## 17. Other information

Glycoprotein gE is absent in virus particles of Rispoval IBR-Marker Vivum. Therefore the vaccine virus, and the antibodies against it can be clearly differentiated from field strains, or antibodies against the latter by serological methods, unless the cattle were previously vaccinated with a conventional vaccine or infected with field virus.

The vaccine induces immunity in cattle against clinical respiratory symptoms caused by the Infectious Bovine Rhinotracheitis (IBR) virus. After a single dose vaccination, a significant reduction of virus shedding duration has been demonstrated upon challenge.

After two doses of vaccine, the intensity and duration of clinical symptoms as well as the titre and duration of virus shedding are significantly reduced following infection. As with other vaccines, vaccination may not completely prevent but does reduce risk of infection.

The veterinary medicinal product induces in vaccinated cattle antibodies, which are detected in the serum neutralisation test and in conventional ELISA tests. With specific test kits these antibodies can be differentiated - due to the lack of antibodies against gE - from those of field virus infected animals or animals vaccinated with conventional vaccines.

Vaccination of all cattle in a herd, both infected and uninfected, is recommended. Following use of Rispoval IBR-Marker Vivum the risk of infection, titre and duration of virus shedding are all reduced. The duration of a programme to achieve the status of a BoHV-1 free herd is dependent on the initial level of BoHV-1 infection in the herd and the culling of remaining BoHV-1 positive animals.

Approved 07 November 2023

