

**ANNEX I**

**SUMMARY OF PRODUCT CHARACTERISTICS**

## 1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Orbeseal Dry Cow 2.6 g intramammary suspension for cattle [AT, BE, BG, HR, CY, DE, FI, EL, IT, LU, NL, NO, PT, RO, SI, ES, SE, United Kingdom (NI)]

Orbesealer Vet – 2.6 g intramammary suspension for cattle [DK]

Boviseal Dry cow intramammary suspension for cattle [IE]

Orbeseal Dry cow intramammary suspension for cattle [FR]

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 4 g intramammary syringe contains:

### Active substance:

Bismuth subnitrate, heavy 2.6 g  
(equivalent to Bismuth, heavy 1.858 g)

### Excipients:

Qualitative composition of excipients and other constituents
Liquid paraffin
Aluminium Di Tri Stearate
Silica, Colloidal Anhydrous

Greyish white, smooth, unctuous intramammary suspension.

## 3. CLINICAL INFORMATION

### 3.1 Target species

Cattle (dairy cow at drying-off).

### 3.2 Indications for use for each target species

Prevention of new intramammary infections throughout the dry period.

In cows considered likely to be free of sub-clinical mastitis, the veterinary medicinal product can be used on its own in dry cow management and mastitis control.

### 3.3 Contraindications

See section 3.7 “Use during pregnancy, lactation or lay”. Do not use the veterinary medicinal product alone in cows with sub-clinical mastitis at drying off. Do not use in cows with clinical mastitis at drying off.

Do not use in cases of hypersensitivity to the active substance or to any of the excipients.

### 3.4 Special warnings

Selection of cows for treatment with the veterinary medicinal product should be based on veterinary clinical judgement. Selection criteria may be based on the mastitis and cell count history of individual cows or recognised tests for the detection of subclinical mastitis or bacteriology sampling.

### 3.5 Special precautions for use

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

It is good practice to observe dry cows regularly for signs of clinical mastitis.  
If a sealed quarter develops clinical mastitis, the affected quarter should be stripped out manually before appropriate therapy is instituted.  
To reduce the risk of contamination, do not immerse the syringe in water.  
Use the syringe only once.

Since the veterinary medicinal product does not have antimicrobial activity, in order to minimize the risk of acute mastitis due to poor infusion technique and lack of hygiene (see section 3.6 “Adverse events”), it is crucial to follow the aseptic technique of administration described in section 3.9 “Administration routes and dosage”.

Do not administer any other intramammary product following administration of the veterinary medicinal product. In cows that may have sub-clinical mastitis, the veterinary medicinal product may be used following administration of a suitable dry cow antibiotic treatment to the infected quarter.

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

This veterinary medicinal product may cause skin and eye irritation.  
Avoid contact with skin or eyes.  
Should skin or eye contact occur, wash the affected area thoroughly with water.  
If irritation persists, seek medical advice and show this label to the physician.  
People with known hypersensitivity to bismuth salts should avoid contact with the veterinary medicinal product.  
Wash hands after use.

#### Special precautions for the protection of the environment:

Not applicable.

### 3.6 Adverse events

Cattle (dairy cow at drying-off).

Very rare ( $<1$ animal / 10,000 animals treated, including isolated reports):	Acute mastitis <sup>1</sup> .
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<sup>1</sup>Primarily due to poor infusion technique and lack of hygiene. Please refer to sections 3.5 “Special precautions for use” and 3.9 “Administration routes and dosage” regarding the importance of aseptic technique.

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 its local representative or the national competent authority via the national reporting system. See also ‘Contact details’ section of the package leaflet.

### 3.7 Use during pregnancy, lactation or lay

#### Pregnancy:

The veterinary medicinal product is not absorbed following intramammary infusion.

Can be used in pregnancy. At calving, the seal may be ingested by the calf. Ingestion of the veterinary medicinal product by the calf is safe and produces no adverse effects.

#### Lactation:

Do not use during lactation. If accidentally used in a lactating cow, a small (up to 2-fold) transient rise in somatic cell count may be observed. In such an event, strip out the seal manually, no additional precautions are necessary.

### **3.8 Interaction with other medicinal products and other forms of interaction**

In clinical trials, the compatibility of the veterinary medicinal product has only been shown with a cloxacillin-containing dry cow preparation.

See also section 3.5 “Special precautions for safe use in the target species”.

### **3.9 Administration routes and dosage**

Intramammary use only.

Infuse the contents of one intramammary syringe of the veterinary medicinal product into each udder quarter immediately after the last milking of the lactation (at drying off.). Do not massage the teat or udder after infusion of the veterinary medicinal product.

Care must be taken not to introduce pathogens into the teat in order to reduce the risk of post-infusion mastitis.

It is essential that the teat is thoroughly cleaned and disinfected, with surgical spirit or alcohol-impregnated wipes. The teats should be wiped until the wipes are no longer visibly dirty. Teats should be allowed to dry prior to infusion. Infuse aseptically and take care to avoid contamination of the syringe nozzle. Following infusion it is advisable to use an appropriate teat dip or spray.

Under cold conditions the veterinary medicinal product may be warmed to room temperature in a warm environment, to aid syringeability.

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

Twice the recommended dose has been administered to cows with no clinical adverse effects.

### **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**

Not applicable.

### **3.12 Withdrawal periods**

Meat and offal: Zero days.

Milk: Zero hours.

## **4. PHARMACOLOGICAL INFORMATION**

### **4.1 ATCvet code: QG52X**

## **4.2 Pharmacodynamics**

Infusion of the veterinary medicinal product into each udder quarter produces a physical barrier against the entry of bacteria there by reducing the incidence of new intramammary infections during the dry period.

## **4.3 Pharmacokinetics**

Bismuth subnitrate is not absorbed from the mammary gland, but resides as a seal in the teat until physically removed (shown in cows with a dry period up to 100 days).

# **5. PHARMACEUTICAL PARTICULARS**

## **5.1 Major incompatibilities**

None known.

## **5.2 Shelf life**

Shelf-life of the veterinary medicinal product as packaged for sale: 5 years.

## **5.3 Special precautions for storage**

This veterinary medicinal product does not require any special storage conditions.

## **5.4 Nature and composition of immediate packaging**

A 4 g single dose low-density polyethylene intramammary syringe with a smooth, tapered hermetically sealed nozzle.

Available in cardboard boxes of 24, 60 and plastic bucket of 120 or 144 syringes.  
Not all pack sizes may be marketed.

## **5.5 Special precautions for the disposal of unused veterinary medicinal product 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**

*To be completed nationally*

# **7. MARKETING AUTHORISATION NUMBER(S)**

*To be completed nationally*

# **8. DATE OF FIRST AUTHORISATION**

Date of first authorisation: 25 June 2002.

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

*To be completed nationally*

**10. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCTS**

*To be completed nationally*

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

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

## **A. LABELLING**



## **PARTICULARS TO APPEAR ON THE OUTER PACKAGE**

**CARDBOARD BOX (24, 60 Syringes) and PLASTIC BUCKET (120 or 144 syringes)**

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

Orbeseal dry cow 2.6 g intramammary suspension [AT, BE, BG, HR, CY, DE, FI, EL, IT, LU, NL, NO, PT, RO, SI, ES, SE, United Kingdom (NI)]

Orbesealer Vet – Dry Cow 2.6 g intramammary suspension [DK]

Boviseal Dry cow intramammary suspension [IE]

Orbeseal Dry cow intramammary suspension [FR]

### **2. STATEMENT OF ACTIVE SUBSTANCES**

Each intramammary syringe contains 4 g intramammary suspension containing 2.6 g Bismuth subnitrate, heavy.

### **3. PACKAGE SIZE**

24 intramammary syringes

60 intramammary syringes

120 intramammary syringes

144 intramammary syringes

### **4. TARGET SPECIES**

Cattle (dairy cow at drying-off)

### **5. INDICATIONS**

### **6. ROUTES OF ADMINISTRATION**

Intramammary use only.

#### **Dosage:**

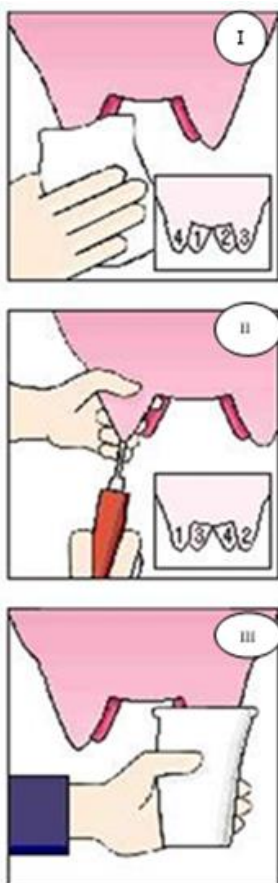
One intramammary syringe into each udder quarter immediately after the last milking of the lactation (at drying off). Do not massage the teat or udder after infusion.

#### **Administration:**

Aseptic intramammary infusion must be employed when administering this veterinary medicinal product.

Under cold conditions the veterinary medicinal product may be warmed to room temperature in a warm environment, to aid syringeability.

See images for correct administration.



## 7. WITHDRAWAL PERIODS

Withdrawal periods:  
Meat and offal: zero days.  
Milk: zero hours.

## 8. EXPIRY DATE

Exp. {month/year}

## 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.

<b>12. THE WORDS “KEEP OUT OF THE SIGHT AND REACH OF CHILDREN”</b>
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Keep out of the sight and reach of children.

<b>13. NAME OF THE MARKETING AUTHORISATION HOLDER</b>
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*To be completed nationally*

<b>14. MARKETING AUTHORISATION NUMBERS</b>
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*To be completed nationally*

<b>15. BATCH NUMBER</b>
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Lot {number}

<b>MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS</b> <b>SYRINGE LABEL</b>
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<b>1. NAME OF THE VETERINARY MEDICINAL PRODUCT</b>
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Orbeseal dry cow 2.6 g [AT, BE, BG, HR, CY, DE, FI, EL, IT, LU, NL, NO, PT, RO, SI, ES, SE, United Kingdom (NI)]  
Orbesealer Vet – Dry Cow 2.6 g [DK]  
Boviseal Dry cow [IE]  
Orbeseal Dry cow [FR]

<b>2. QUANTITATIVE PARTICULARS OF THE ACTIVE SUBSTANCES</b>
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2.6 g Bismuth subnitrate, heavy

<b>3. BATCH NUMBER</b>
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Lot {number}

<b>4. EXPIRY DATE</b>
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Exp. {mm/yyyy}

## **B. PACKAGE LEAFLET**

## PACKAGE LEAFLET

### 1. Name of the veterinary medicinal product

Orbeseal Dry cow 2.6 g intramammary suspension for cattle [AT, BE, BG, HR, CY, DE, FI, EL, IT, LU, NL, NO, PT, RO, SI, ES, SE, United Kingdom (NI)]

Orbesealer Vet – Dry Cow 2.6 g intramammary suspension for cattle [DK]

Boviseal Dry cow intramammary suspension for cattle [IE]

Orbeseal Dry cow intramammary suspension for cattle [FR]

### 2. Composition

Each 4 g intramammary syringe contains:

#### Active substance:

Bismuth subnitrate, heavy 2.6 g  
(equivalent to Bismuth, heavy 1.858 g)

#### Excipients:

Liquid paraffin

Aluminium Di Tri stearate

Silica, colloidal anhydrous

Greyish white, smooth, unctuous intramammary suspension.

### 3. Target species

Cattle (dairy cow at drying-off).

### 4. Indications for use

The veterinary medicinal product is indicated for the prevention of new intramammary infections throughout the dry period.

The veterinary medicinal product prevents new intramammary infections by producing a physical barrier against the entry of bacteria.

In cows considered likely to be free of subclinical mastitis, the veterinary medicinal product can be used on its own in dry cow management and mastitis control.

### 5. Contraindications

Do not use alone in cows with subclinical mastitis at drying off.

Do not use in cows with clinical mastitis at drying off.

Do not use in cases of hypersensitivity to the active substance or to any of the excipients

See section “Special warnings”; “Pregnancy” and “Lactation”.

### 6. Special warnings

#### Special warnings:

Selection of cows for treatment with the veterinary medicinal product should be based on veterinary clinical judgement. Selection criteria may be based on the mastitis and cell count history of individual cows or recognised tests for the detection of subclinical mastitis or bacteriology sampling.

Special precautions for safe use in the target species:

In cows that may have subclinical mastitis, the veterinary medicinal product may be used following administration of a suitable dry cow antibiotic treatment to the infected quarter. As with all dry cow intramammary treatments, it is good practice to observe dry cows regularly for signs of clinical mastitis. If a sealed quarter develops clinical mastitis the affected quarter should be stripped out manually before appropriate antibiotic therapy is instituted.

To reduce the risk of contamination, do not immerse syringes in water.

Use syringe only once.

Since the veterinary medicinal product does not have antimicrobial activity, in order to minimize the risk of acute mastitis due to poor infusion technique and lack of hygiene (see section “Adverse events”), it is crucial to follow the aseptic technique of administration described in section “Dosage for each species, routes and method of administration”.

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

This veterinary medicinal product may cause skin and eye irritation.

Avoid contact with skin or eyes.

Should skin or eye contact occur, wash the affected area thoroughly with water.

If irritation persists, seek medical advice and show this label to the doctor.

People with known hypersensitivity to bismuth salts should avoid contact with the veterinary medicinal product.

Wash hands after use.

Pregnancy:

The veterinary medicinal product is not absorbed following intramammary infusion.

Can be used during pregnancy. At calving, the seal may be ingested by the calf. Ingestion of the veterinary medicinal product by the calf is safe and produces no adverse effects.

Lactation:

Do not use during lactation. If accidentally used in a lactating cow, a small (up to 2-fold) transient rise in somatic cell count may be observed. In such an event, strip out the seal manually, no additional precautions are necessary.

Interaction with other medicinal products and other forms of interaction:

In clinical trials, the compatibility of the veterinary medicinal product has only been shown with a cloxacillin-containing dry cow preparation.

Do not administer any other intramammary product following the administration of the veterinary medicinal product.

Overdose:

Twice the recommended dose has been administered to cows with no clinical adverse effects.

## **7. Adverse events**

Cattle (dairy cow at drying-off).

Very rare ( $<1$ animal / 10,000 animals treated, including isolated reports):	Acute mastitis <sup>1</sup> .
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<sup>1</sup>Primarily due to poor infusion technique and lack of hygiene. Please refer to sections “Dosage for each species, routes and method of administration” and “Special warnings” regarding the importance of aseptic technique.

Reporting adverse events is important. It allows continuous safety monitoring of a veterinary medicinal 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

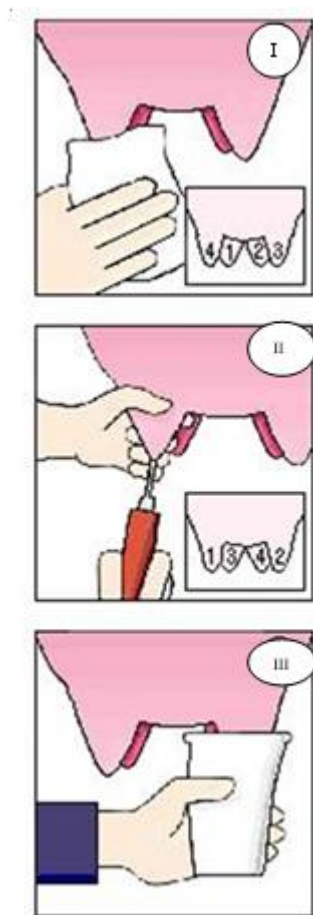
Intramammary use only.

### Dosage:

One intramammary syringe into each udder quarter immediately after the last milking of the lactation (at drying off). Do not massage the teat or udder after infusion.

### Administration:

Care must be taken not to introduce pathogens into the teat. It is essential that strict aseptic techniques are used for the infusion of the veterinary medicinal product as it possesses no antimicrobial activity. Failure to follow these recommendations can lead to serious cases of post-infusion mastitis and even death.



1. All teats need to be thoroughly cleansed and disinfected prior to infusion of the veterinary medicinal product. Ensure sufficient time is allocated to treat each animal and do not combine this with other husbandry activities.

2. Ensure animals are appropriately restrained in hygienic conditions. Keep syringes clean and DO NOT immerse in water.

3. A separate pair of clean disposable gloves should be worn for the treatment of each cow.

4. Start with a visibly clean, dry teat and udder. If teats are obviously dirty then clean off dirt from teats only, with moistened disposable paper towels and dry thoroughly. Dip teats in a rapid-acting pre-dip, leave for 30 seconds, then wipe each teat completely dry with separate disposable paper towels. Strip fore milk into a strip cup and discard.

5. Thoroughly disinfect the whole surface of the teat with a disposable spirit/alcohol soaked swab. Studies indicate that the most effective means of teat cleaning involves the use of swabs freshly prepared from clean dry cotton wool soaked in surgical spirit (or the equivalent). If this is not available, then the supplied cleaningswabs can be used. Clean the teats furthest away from you first, to avoid contaminating clean teats. See image I.

6. Gently scrub each teat end with new individual, disposable, spirit/alcohol swabs, until both teat end and swab are visibly clean.

7. Remove the cap from the intramammary tube, being careful not to touch the nozzle.

8. Grip the teat base firmly between your fingers at the junction with the udder. Turn the teat to a slight angle. Infuse the contents of the syringe into the bottom portion of the teat below where you are pinching the teat avoiding contaminating the teat end. Infuse teats in the opposite order to cleaning i.e. treat the quarters closest to you first. See image II. Do not massage the veterinary medicinal product into the udder.

9. Apply a post-milking teat disinfectant and confine the treated cows to a yard where they should stand for at least 30 minutes to allow the teat canal to close. See image III.

## 9. Advice on correct administration



It is important that you read the instructions before using this veterinary medicinal product. Great care should be taken in maintaining cleanliness when administering the veterinary medicinal product in order to reduce the risk of potentially fatal post-infusion mastitis. Full advice on teat cleaning technique prior to tubing is included in the instructions and should be followed.

Under cold conditions the veterinary medicinal product may be warmed to room temperature in a warm environment, to aid syringeability.

#### **10. Withdrawal periods**

Meat and offal: zero days.

Milk: zero hours.

#### **11. Special storage precautions**

Keep out of the sight and reach of children.

This veterinary medicinal product does not require any special storage conditions.

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

#### **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**

*To be completed nationally*

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

Available in cardboard boxes of 24, 60 and plastic bucket of 120 or 144 syringes.

Not all pack sizes may be marketed.

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

To be completed at the end of the procedure.

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:

*To be completed nationally*

Manufacturers responsible for batch release:

Cross Vetpharm Group Ltd,  
Dublin 24  
IRELAND

Haupt Pharma Latina S.r.l  
Strada Statale 156 Dei Monti Lepini Km 47600  
Latina  
04100  
ITALY

<Local representatives < and contact details to report suspected adverse reactions\*>:>

*To be completed nationally (if needed\*)*

## **17. Other information**

Most of the seal comes out at the first stripping or suckling after calving, but small amounts may occasionally be seen for a few days as flecks on the filter. The veterinary medicinal product can be differentiated from mastitis by its texture.

After calving, the following steps are recommended for the effective removal of the veterinary medicinal product to minimise residual veterinary medicinal product entering the milking machine. The milking machine should not be used to remove the veterinary medicinal product from the teat.

1. Pinch the teat at the top and strip quarter 10-12 times prior to first milking.
2. Strip foremilk and check for residual veterinary medicinal product for first few milkings.
3. Inspect mastitis filters and milk sock for evidence of residual veterinary medicinal product after every milking.

<i>To be completed nationally</i>
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