# ANNEX I

# SUMMARY OF PRODUCT CHARACTERISTICS

## 1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Bovilis Cryptium emulsion for injection for cattle

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each dose (2 ml) contains:

**Active substance:**
*Cryptosporidium parvum* Gp40[1]: At least 1.0 U[2]

[1] Gp40: Glycoprotein 40
[2] ELISA unit as measured in potency test

**Adjuvants:**
Montanide ISA70VG: 1140 - 1260 mg
Aluminium hydroxide: 2.45 - 3.32 mg

**Excipients:**

| **Qualitative composition of excipients and other constituents** | **Quantitative composition if that information is essential for proper administration of the veterinary medicinal product** |
|---|---|
| HEPES | |
| Sodium chloride | |
| Thiomersal | 0.032 - 0.069 mg |
| Water for injections | |

Off-white emulsion.

## 3. CLINICAL INFORMATION

### 3.1 Target species

Cattle (pregnant heifers and cows).

### 3.2 Indications for use for each target species

For active immunisation of pregnant heifers and cows to raise antibodies in their colostrum against Gp40 of *Cryptosporidium parvum*, intended for passive immunisation of calves to reduce clinical signs (i.e. diarrhoea) caused by *C. parvum*.

Newborn calves:
Onset of immunity: Passive immunity commences from the start of colostrum feeding.
Duration of immunity: In calves that receive colostrum and transition milk as indicated and which were challenged at birth, passive immunity has been demonstrated until 2 weeks of age.

### 3.3 Contraindications

None.

### 3.4 Special warnings

Vaccinate healthy animals only.

Feeding of calves
The protection of calves depends on adequate ingestion of colostrum and transition milk from vaccinated cows. It is recommended that all calves are fed colostrum and subsequent transition milk during the first 5 days of life. At least 3 litres of colostrum should be fed within the first 6 hours after birth.

To achieve optimum results a whole herd vaccination policy should be adopted.
Farm management should aim at reduction of exposure to *C. parvum*.

### 3.5 Special precautions for use

Special precautions for safe use in the target species:
Administration in the ischiorectal fossa has resulted in local painful chronic granulomatous reactions up to 15 cm in diameter and in abscess formation (multiple small abscesses up to 1 cm in diameter at post mortem 15 weeks after the first vaccination and 11 weeks after second vaccination) in one out of two necropsied cows (the study included 9 cows).
Administration in the dewlap can give rise to extensive chronic inflammatory reactions up to 30 cm in diameter which can lead to painful local reactions with possible persistent impact on cow welfare.

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

To the user:
This veterinary medicinal product contains mineral oil. Accidental injection/self-injection may result in severe pain and swelling, particularly if injected into a joint or finger, and in rare cases could result in the loss of the affected finger if prompt medical attention is not given. If you are accidentally injected with this veterinary medicinal product, seek prompt medical advice even if only a very small amount is injected and take the package leaflet with you. If pain persists for more than 12 hours after medical examination, seek medical advice again.

To the physician:
This veterinary medicinal product contains mineral oil. Even if small amounts have been injected, accidental injection with this product can cause intense swelling, which may, for example, result in ischaemic necrosis and even the loss of a digit. Expert, PROMPT, surgical attention is required and may necessitate early incision and irrigation of the injected area, especially where there is involvement of finger pulp or tendon.

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

### 3.6 Adverse events

Cattle (pregnant heifers and cows):

| | |
|---|---|
| Very common<br>(>1 animal / 10 animals treated): | Injection site swelling[1], injection site pain, injection site warmth, injection site granuloma. Elevated temperature[2]. |
| Uncommon<br>(1 to 10 animals / 1,000 animals treated): | Muscle inflammation[3].<br>Injection site abscess[4]. |

[1] Mean size up to 14 cm, maximum size up to 40 cm, swellings reduce in size over time, but may persist as chronic granulomatous inflammation extending from the injection site for at least 125 days.

[2] Mean increase up to 1 °C with a maximum of 1.8 °C, returning to normal on ultimately the 2nd day after vaccination.
[3] Granulomatous haemorrhagic inflammatory reaction in dermal and subdermal tissues with inflammation extending into the underlying muscular tissue.
[4] An abscess up to 1 cm in diameter detected in the neck after the 3rd 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 and lactation:
This veterinary medicinal product is intended for use in the third trimester of pregnancy.

### 3.8 Interactions with other medicinal products and other forms of interaction

Safety and efficacy data are available which demonstrate that this vaccine can be administered on the same day but not mixed with Bovilis Rotavec Corona. The vaccines should be given at different sites. The product literature of Bovilis Rotavec Corona should be consulted before administration. Different routes of administration should be respected.
No information is available on the safety and efficacy of this vaccine when used with any other veterinary medicinal product except the product mentioned above. 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.
Administer the vaccine in the side of the neck.

Allow the vaccine to reach room temperature before use.
Shake well before and occasionally during use to ensure homogeneity of the vaccine prior to administration.
Common aseptic procedures should be used during vaccination.
Only sterile syringes and needles should be used.
Use of a multidose applicator is recommended when vaccinating multiple animals.

One dose: 2 ml

Primary vaccination consists of 2 doses, 4 to 5 weeks apart, in the third trimester of pregnancy. To be completed at least 3 weeks before calving. These subsequent doses are preferably administered at different sides of the animal.
Revaccination consists of 1 dose in the third trimester of each next pregnancy. To be completed at least 3 weeks before calving.

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

Following the administration of an overdose, no adverse reactions other than those mentioned in section 3.6 occur.

### 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

Zero days.

## 4. IMMUNOLOGICAL INFORMATION

### 4.1 ATCvet code: QI02AO02.

The vaccine contains purified *Cryptosporidium parvum* glycoprotein 40 adjuvanted with mineral oil and aluminium hydroxide.
The vaccine is intended to stimulate active immunity of the vaccinated dam in order to provide passive immunity against *Cryptosporidium parvum* to the progeny.

## 5. PHARMACEUTICAL PARTICULARS

### 5.1 Major incompatibilities

Do not mix with any other veterinary medicinal product.

### 5.2 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 2 years.
Shelf life after first opening the immediate packaging: 28 days.

### 5.3 Special precautions for storage

Store in a refrigerator (2 °C – 8 °C).
Do not freeze.
Protect from light.
After broaching and first use, store upright and refrigerated (2 °C – 8 °C) until the next use.

### 5.4 Nature and composition of immediate packaging

Type I glass vial containing 2 ml or 10 ml, closed with a rubber stopper and an aluminium cap.
PET (polyethylene terephthalate) vial containing 10 ml, 40 ml, or 100 ml, closed with a rubber stopper and an aluminium cap.

Pack sizes:
Cardboard box with 10 x 2 ml (10 x 1 dose).
Cardboard box with 1 x 10 ml (5 doses).
Cardboard box with 1 x 40 ml (20 doses).
Cardboard box with 1 x 100 ml (50 doses).

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

Intervet International B.V.

## 7. MARKETING AUTHORISATION NUMBER(S)

EU/2/23/303/001-005

## 8. DATE OF FIRST AUTHORISATION

Date of first authorisation: {DD/MM/YYYY}.

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

## 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**

**SPECIFIC PHARMACOVIGILANCE REQUIREMENTS:**
The MAH shall record in the pharmacovigilance database all results and outcomes of the signal management process, including a conclusion on the benefit-risk balance, according to the following frequency: annually.

**ANNEX III**

**LABELLING AND PACKAGE LEAFLET**

# A. LABELLING

**PARTICULARS TO APPEAR ON THE OUTER PACKAGE**

**CARDBOARD BOX**

## 1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Bovilis Cryptium emulsion for injection

## 2. STATEMENT OF ACTIVE SUBSTANCES

Each dose (2 ml) contains:
*Cryptosporidium parvum* Gp40: ≥ 1.0 U

## 3. PACKAGE SIZE

10 x 2 ml (10 x 1 dose)
10 ml (5 doses)
40 ml (20 doses)
100 ml (50 doses)

## 4. TARGET SPECIES

Cattle

## 5. INDICATIONS

## 6. ROUTES OF ADMINISTRATION

Subcutaneous use.

## 7. WITHDRAWAL PERIODS

Withdrawal period: Zero days.

## 8. EXPIRY DATE

Exp. {mm/yyyy}

Once broached use within 28 days.

## 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/2/23/303/001 (10 x 1 dose)
EU/2/23/303/002 (5 doses - glass)
EU/2/23/303/003 (20 doses)
EU/2/23/303/004 (50 doses)
EU/2/23/303/005 (5 doses - PET)

## 15. BATCH NUMBER

Lot {number}

**PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGE**

**PET VIAL containing 100 ml**

## 1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Bovilis Cryptium emulsion for injection

## 2. STATEMENT OF ACTIVE SUBSTANCES

50 doses

Each dose (2 ml) contains :
*Cryptosporidium parvum* Gp40 : ≥ 1.0 U

## 3. TARGET SPECIES

Cattle

## 4. ROUTES OF ADMINISTRATION

Subcutaneous use.
Read the package leaflet before use.

## 5. WITHDRAWAL PERIODS

Withdrawal period: Zero days.

## 6. EXPIRY DATE

Exp. {mm/yyyy}

Once broached use within 28 days.

## 7. SPECIAL STORAGE PRECAUTIONS

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

## 8. NAME OF THE MARKETING AUTHORISATION HOLDER

Intervet International B.V.

## 9. BATCH NUMBER

Lot {number}

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

**GLASS (2 or 10 ml), PET (10 or 40 ml) VIAL containing 2, 10 or 40 ml**

## 1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Bovilis Cryptium

## 2. QUANTITATIVE PARTICULARS OF THE ACTIVE SUBSTANCES

1 dose
5 doses
20 doses

*C. parvum* Gp40: ≥ 1.0 U per dose (2 ml)

## 3. BATCH NUMBER

Lot {number}

## 4. EXPIRY DATE

Exp. {mm/yyyy}

Once broached use within 28 days.

# B. PACKAGE LEAFLET

# PACKAGE LEAFLET

## 1. Name of the veterinary medicinal product

Bovilis Cryptium emulsion for injection for cattle

## 2. Composition

Each dose (2 ml) contains:

**Active substance:**
*Cryptosporidium parvum* Gp40[1]: ≥ 1.0 U[2]

[1] Gp40: Glycoprotein 40
[2] ELISA unit as measured in potency test

**Adjuvants :**
Montanide ISA70VG: 1140 – 1260 mg
Aluminium hydroxide: 2.45 – 3.32 mg

**Excipients:**
Thiomersal: 0.032 – 0.069 mg

Off-white emulsion.

## 3. Target species

Cattle (pregnant heifers and cows).

## 4. Indications for use

For active immunisation of pregnant heifers and cows to raise antibodies in their colostrum against Gp40 of *Cryptosporidium parvum*, intended for passive immunisation of calves to reduce clinical signs (i.e. diarrhoea) caused by *C. parvum*.

Newborn calves:
Onset of immunity: Passive immunisation commences from the start of colostrum feeding.
Duration of immunity: In calves that receive colostrum and transition milk as indicated and which were challenged at birth, passive immunity has been demonstrated until 2 weeks of age.

## 5. Contraindications

None.

## 6. Special warnings

Special warnings:
Vaccinate healthy animals only.

Feeding of calves

The protection of calves depends on adequate ingestion of colostrum and transition milk from vaccinated cows. It is recommended that all calves are fed colostrum and subsequent transition milk during the first 5 days of life. At least 3 litres of colostrum should be fed within the first 6 hours after birth.

To achieve optimum results a whole herd vaccination policy should be adopted.
Farm management should aim at reduction of exposure to *C. parvum*.

Special precautions for safe use in the target species:
Administration in the ischiorectal fossa has resulted in local painful chronic granulomatous reactions up to 15 cm in diameter and in abscess formation (multiple small abscesses up to 1 cm in diameter at post mortem 15 weeks after the first vaccination and 11 weeks after second vaccination) in one out of two necropsied cows (the study included 9 cows).
Administration in the dewlap can give rise to extensive chronic inflammatory reactions up to 30 cm in diameter which can lead to painful local reactions with possible persistent impact on cow welfare.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
To the user:
This veterinary medicinal product contains mineral oil. Accidental injection/self-injection may result in severe pain and swelling, particularly if injected into a joint or finger, and in rare cases could result in the loss of the affected finger if prompt medical attention is not given. If you are accidentally injected with this veterinary medicinal product, seek prompt medical advice even if only a very small amount is injected and take the package leaflet with you. If pain persists for more than 12 hours after medical examination, seek medical advice again.

To the physician:
This veterinary medicinal product contains mineral oil. Even if small amounts have been injected, accidental injection with this product can cause intense swelling, which may, for example, result in ischaemic necrosis and even the loss of a digit. Expert, PROMPT, surgical attention is required and may necessitate early incision and irrigation of the injected area, especially where there is involvement of finger pulp or tendon.

Pregnancy and lactation:
This veterinary medicinal product is intended for use in the third trimester of pregnancy.

Interactions with other medicinal products and other forms of interaction:
Safety and efficacy data are available which demonstrate that this vaccine can be administered on the same day but not mixed with Bovilis Rotavec Corona. The vaccines should be given at different sites. The product literature of Bovilis Rotavec Corona should be consulted before administration. Different routes of administration should be respected.
No information is available on the safety and efficacy of this vaccine when used with any other veterinary medicinal product except the product mentioned above. 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:
Following the administration of an overdose, no adverse reactions other than those mentioned in the section 'Adverse events' occur.

Major incompatibilities:
Do not mix with any other veterinary medicinal product.

## 7. Adverse events

Cattle (pregnant heifers and cows):

| | |
|---|---|
| Very common<br>(>1 animal / 10 animals treated): | Injection site swelling[1], injection site pain, injection site warmth, injection site granuloma. Elevated temperature[2]. |
| Uncommon<br>(1 to 10 animals / 1,000 animals treated): | Muscle inflammation[3].<br>Injection site abscess[4]. |

[1] Mean size up to 14 cm, maximum size up to 40 cm, swellings reduce in size over time, but may persist as chronic granulomatous inflammation extending from the injection site for at least 125 days.
[2] Mean increase up to 1 °C, with a maximum of 1.8 °C, returning to normal on ultimately the 2nd day after vaccination.
[3] Granulomatous haemorrhagic inflammatory reaction in dermal and subdermal tissues with inflammation extending into the underlying muscular tissue.
[4] An abscess up to 1 cm in diameter detected in the neck after the 3rd 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.

One dose: 2 ml

Primary vaccination consists of 2 doses, 4 to 5 weeks apart, in the third trimester of pregnancy. To be completed at least 3 weeks before calving. These subsequent doses are preferably administered at different sides of the animal.
Revaccination consists of 1 dose in the third trimester of each next pregnancy. To be completed at least 3 weeks before calving.

## 9. Advice on correct administration

Allow the vaccine to reach room temperature before use.
Shake well before and occasionally during use to ensure homogeneity of the vaccine prior to administration.
Common aseptic procedures should be used during vaccination.
Only sterile syringes and needles should be used.
Use of a multidose applicator is recommended when vaccinating multiple animals.
Administer the vaccine in the side of the neck.

## 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.
After broaching and first use, store upright and refrigerated (2 °C – 8 °C) until the next use.

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 first opening the immediate packaging: 28 days.

## 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/2/23/303/001-005

Pack sizes:
Cardboard box with 10 x 2 ml (10 x 1 dose), 1 x 10 ml (5 doses), 1 x 40 ml (20 doses) or 1 x 100 ml (50 doses).

Not all pack sizes may be marketed.

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

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

**Lietuva**
Tel: + 37052196111

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

**Magyarország**
Tel.: + 36 1 439 4597

**Danmark**
Tlf: + 45 44 82 42 00

**Deutschland**
Tel: + 49 (0)8945614100

**Eesti**
Tel: + 37052196111

**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

**Malta**
Tel: + 39 02 516861

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

**Norge**
Tlf: + 47 55 54 37 35

**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 contains purified *Cryptosporidium parvum* glycoprotein 40 adjuvanted with mineral oil and aluminium hydroxide.
The vaccine is intended to stimulate active immunity of the vaccinated dam in order to provide passive immunity against *Cryptosporidium parvum* to the progeny.