SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Bravoxin suspension for injection for cattle and sheep
Tribovax vet. suspension for injection for cattle and sheep (DK, FI, IS, NO, SE)
Tribovax 10 suspension for injection for cattle and sheep (IE)
Polibascol suspension for injection for cattle and sheep (ES)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 1 ml contains:

Active substances:

C. perfringens type A (α) toxoid	≥ 0.5 IU[#]
C. perfringens type B & C (β) toxoid	≥ 20.5 IU*
C. perfringens type D (ε) toxoid	≥ 5.9 IU*
C. chauvoei whole culture, inactivated	≥ 90% protection**
C. novyi toxoid	≥ 3.8 IU*
C. septicum toxoid	≥ 3.3 IU*
C. tetani toxoid	≥ 4.5 IU*
C. sordellii toxoid	≥ 4.4 U[1]
C. haemolyticum toxoid	≥ 25.0 U[#]

* ELISA According to Ph.Eur.
[1] In house ELISA
** Guinea pig challenge test according to Ph.Eur.
[#] *In vitro* toxin neutralisation test based on haemolysis of sheep erythrocytes.

Adjuvant:

Aluminium[1]	3.026 – 4.094 mg

[1] from aluminium potassium sulphate (alum)

Excipients:

Qualitative composition of excipients and other constituents	**Quantitative composition if that information is essential for proper administration of the veterinary medicinal product**
Thiomersal	0.05 – 0.18 mg
Sodium chloride	
Formaldehyde	
Water for injections / purified water	

Light brown aqueous suspension that settles on storage.

3. CLINICAL INFORMATION

3.1 Target species

Cattle and sheep.

3.2 Indications for use for each target species

For the active immunisation of sheep and cattle against disease associated with infections caused by *Clostridium perfringens* type A, *C. perfringens* type B, *C. perfringens* type C, *C. perfringens* type D, *Clostridium chauvoei*, *Clostridium novyi* type B, *Clostridium septicum*, *Clostridium sordellii* and *Clostridium haemolyticum* and against tetanus caused by *Clostridium tetani*.

For the passive immunisation of lambs and calves against infections caused by the above mentioned clostridial species (except *C. haemolyticum* in sheep).

Onset of immunity:
Sheep and Cattle: 2 weeks after the basic vaccination course (as demonstrated by serology only).

Duration of active immunity:
As demonstrated by serology only:
Sheep: 1 year against *C. perfringens* type A, B, C and D, *C. novyi* type B, *C. sordellii, C. Tetani*;
< 6 months against *C. septicum*, *C. haemolyticum, C. chauvoei*;
Cattle: 1 year against *C. tetani* and *C. perfringens* type D;
< 1 year against *C. perfringens* type A, B and C;
< 6 months against *C. novyi* type B, *C. septicum, C. sordellii*, *C. haemolyticum, C. chauvoei*.

An anamnestic humoral immune response (immunological memory) to all components was demonstrated 1 year following the basic course of vaccination.

Duration of passive immunity:
As demonstrated by serology only:
Lambs: At least 2 weeks for *C. septicum* and *C. chauvoei*;
At least 8 weeks for *C. perfringens* type B and *C. perfringens* type C;
At least 12 weeks for *C. perfringens* type A, *C. perfringens* type D, *C. novyi* type B, *C. tetani* and *C. sordellii*;
No passive immunity was observed for *C. haemolyticum*.
Calves: At least 2 weeks for *C. sordellii* and *C. haemolyticum*;
At least 8 weeks for *C. septicum* and *C. chauvoei*;
At least 12 weeks for *C. perfringens* type A, *C. perfringens* type B, *C. perfringens* type C, *C. perfringens* type D, *C. novyi* type B, and *C. tetani*.

3.3 Contraindications

Do not use in sick or immunodeficient animals.

3.4 Special warnings

Vaccinate healthy animals only.

The effectiveness of the vaccine in providing passive immunity to young lambs and calves depends on these animals ingesting adequate amounts of colostrum on the first day of life.

Clinical trials have demonstrated that the presence of maternal derived antibodies (MDA), particularly against *C. tetani*, *C. novyi* type B, *C. perfringens* type A (calves only), *C. chauvoei* (lambs only) and *C. perfringens* type D may reduce the antibody response to vaccination in young lambs and calves. Therefore, to ensure an optimal response in young animals with high levels of MDA, the basic vaccination should be delayed until the levels wane (which is after about 8-12 weeks of age, see section 3.2).

3.5 Special precautions for use

Special precautions for safe use in the target species:

It is good practice to observe animals regularly for adverse reactions at the injection site following vaccination. It is recommended to seek medical advice from a veterinarian in case of a severe injection site reaction.

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.

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

3.6 Adverse events

Cattle and sheep:

Very common (>1 animal / 10 animals treated):	Injection site swelling[1].
Common (1 to 10 animals / 100 animals treated):	Injection site abscess, injection site skin discolouration[2]. Hyperthermia[3].
Uncommon (1 to 10 animals / 1,000 animals treated):	Injection site pain[4].
Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Anaphylactic type reaction[5].

[1] Up to a mean value of 6 cm in sheep and 15 cm diameter in cattle; sometimes reactions of up to 25 cm diameter may be seen in cattle. Most local reactions resolve within 3-6 weeks in sheep and in less than 10 weeks in cattle. In a minority of animals they may persist longer.
[2] Returns to normal as the local reaction resolves.
[3] Mild.
[4] For 1-2 days post first vaccination.
[5] In such cases appropriate treatment such as adrenaline should be administered without delay.

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 the package leaflet for respective contact details.
{< > to be adjusted nationally}

3.7 Use during pregnancy, lactation or lay

Pregnancy:
No side effects other than those described under section 3.6 were seen when the vaccine was used in sheep and cattle between 8 and 2 weeks prior to parturition. In the absence of specific data, the use of the vaccine is not recommended during the first or second third of pregnancy.
Avoid stress in pregnant ewes and cows.

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.

Dose:

- Sheep: 1 ml – from 2 weeks of age
- Cattle: 2 ml – from 2 weeks of age

Administration:
By subcutaneous injection preferably in the loose skin on the side of the neck, observing aseptic precautions.
Shake the bottle thoroughly before use.
Syringes and needles should be sterile before use and the injection should be made through an area of clean, dry skin taking precautions against contamination.

Basic vaccination: Two doses should be administered, 4-6 weeks apart (see section 3.2 and 3.4).
Re-vaccination: A single dose should be administered at 6 to 12 month intervals after the basic vaccination (see section 3.2.)

Use in pregnancy:
To provide passive protection of the offspring, via the colostrum, a single re-vaccination should be administered between 8 and 2 weeks before parturition, provided that animals have received a full basic vaccination course before pregnancy.

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

In calves and lambs, local reactions may increase slightly if twice the recommended dose is administered (see section 3.6).

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.
{to be completed nationally}

3.12 Withdrawal periods

Zero days.

4. IMMUNOLOGICAL INFORMATION

4.1 ATCvet code: QI02AB01, QI04AB01.

Inactivated clostridium vaccine. To stimulate active immunity in sheep and cattle against *C. chauvoei* and the toxins of *Clostridium perfringens* type A, *C. perfringens* type B, *C. perfringens* type C, *C. perfringens* type D, *C. novyi, C. septicum, C. tetani, C. sordellii*, and *C. haemolyticum* contained in the vaccine.
To provide passive immunity via the colostrum against the above mentioned clostridial infections in young lambs and calves.

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: 30 months.
Shelf life after first opening the immediate packaging: 8 hours.

5.3 Special precautions for storage

Store and transport refrigerated (2 °C – 8 °C). Do not freeze.
Protect from light.

5.4 Nature and composition of immediate packaging

Flexible low density polyethylene (LDPE) bottle with 50 ml or 100 ml, closed with a bromobutyl rubber stopper and held in place with an aluminium cap.

Pack sizes:
Cardboard box with one bottle of 50 ml (50 doses of 1 ml or 25 doses of 2 ml).
Cardboard box with one bottle of 100 ml (100 doses of 1 ml or 50 doses of 2 ml).

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>.
{< > to be adjusted nationally}

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.
{to be completed nationally}

6. NAME OF THE MARKETING AUTHORISATION HOLDER

{Name}
{to be completed nationally}

7. MARKETING AUTHORISATION NUMBER(S)

{number}
{to be completed nationally}

8. DATE OF FIRST AUTHORISATION

Date of first authorisation: {DD/MM/YYYY}. {to be completed nationally}

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

{MM/YYYY} {to be completed nationally}

10. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCTS

[AT, BE, BG, HR, CY, CZ, DE, DK, EE, FI, FR, EL, HU, IS, IT, LV, LT, LU, NL, NO, PL, PT, RO, SK, ES, SE, UK(NI)]: Veterinary medicinal product subject to prescription.

[IE]: Veterinary medicinal product not subject to prescription.

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

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

CARDBOARD BOX – for 1 x 50 ml or 1 x 100 ml bottles

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Bravoxin suspension for injection

2. STATEMENT OF ACTIVE SUBSTANCES

Each 1 ml contains:

C. perfringens type A (α) toxoid	≥ 0.5 IU
C. perfringens type B & C (β) toxoid	≥ 20.5 IU
C. perfringens type D (ε) toxoid	≥ 5.9 IU
C. chauvoei whole culture, inac	≥ 90% protection
C. novyi toxoid	≥ 3.8 IU
C. septicum toxoid	≥ 3.3 IU
C. tetani toxoid	≥ 4.5 IU
C. sordellii toxoid	≥ 4.4 U
C. haemolyticum toxoid	≥ 25.0 U

3. PACKAGE SIZE

50 ml
100 ml

4. TARGET SPECIES

Cattle and sheep

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 8 hours.

9. SPECIAL STORAGE PRECAUTIONS

Store and transport refrigerated.
Protect from light.
Do not freeze.

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

{to be completed nationally}

14. MARKETING AUTHORISATION NUMBERS

{number} {to be completed nationally}

15. BATCH NUMBER

Lot {number}

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGE

BOTTLE LABEL – 100 ml

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Bravoxin suspension for injection

2. STATEMENT OF ACTIVE SUBSTANCES

Each 1 ml contains:

C. perfringens type A (α) toxoid	≥ 0.5 IU
C. perfringens type B & C (β) toxoid	≥ 20.5 IU
C. perfringens type D (ε) toxoid	≥ 5.9 IU
C. chauvoei whole culture, inac	≥ 90% protection
C. novyi toxoid	≥ 3.8 IU
C. septicum toxoid	≥ 3.3 IU
C. tetani toxoid	≥ 4.5 IU
C. sordellii toxoid	≥ 4.4 U
C. haemolyticum toxoid	≥ 25.0 U

100 ml

3. TARGET SPECIES

Cattle and sheep

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 8 hours.

7. SPECIAL STORAGE PRECAUTIONS

Store and transport refrigerated.
Do not freeze.
Protect from light.

8. NAME OF THE MARKETING AUTHORISATION HOLDER

{to be completed nationally}

9. BATCH NUMBER

Lot {number}

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

BOTTLE LABEL – 50 ml

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Bravoxin

2. QUANTITATIVE PARTICULARS OF THE ACTIVE SUBSTANCES

Clostridial cells and toxoids; see package leaflet.

50 ml

3. BATCH NUMBER

Lot {number}

4. EXPIRY DATE

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

B. PACKAGE LEAFLET

PACKAGE LEAFLET

1. Name of the veterinary medicinal product

Bravoxin suspension for injection for cattle and sheep

2. Composition

Each 1 ml contains:

Active substances:

C. perfringens type A (α) toxoid	≥ 0.5 IU[#]
C. perfringens type B & C (β) toxoid	≥ 20.5 IU*
C. perfringens type D (ε) toxoid	≥ 5.9 IU*
C. chauvoei whole culture, inactivated	≥ 90% protection**
C. novyi toxoid	≥ 3.8 IU*
C. septicum toxoid	≥ 3.3 IU*
C. tetani toxoid	≥ 4.5 IU*
C. sordellii toxoid	≥ 4.4 U[1]
C. haemolyticum toxoid	≥ 25.0 U[#]

* ELISA According to Ph.Eur.
[1] In house ELISA
** Guinea pig challenge test according to Ph.Eur.
[#] *In vitro* toxin neutralisation test based on haemolysis of sheep erythrocytes.

Adjuvant:

Aluminium[1]	3.026 – 4.094 mg

[1] from aluminium potassium sulphate (alum)

Excipient:

Thiomersal	0.05 – 0.18 mg

Light brown aqueous suspension that settles on storage.

3. Target species

Cattle and sheep.

4. Indications for use

For the active immunisation of sheep and cattle against disease caused by *Clostridium perfringens* type A, *C. perfringens* type B, *C. perfringens* type C, *C. perfringens* type D, *C. chauvoei*, *C. novyi* type B, *C. septicum*, *C. sordellii* and *C. haemolyticum* and against tetanus caused by *C. tetani*. For the passive immunisation of lambs and calves against infections caused by the above mentioned clostridial species (except *C. haemolyticum* in sheep).

Onset of immunity:
Sheep and Cattle: 2 weeks after the basic vaccination course (as demonstrated by serology only).

Duration of active immunity:
As demonstrated by serology only:

Sheep: 1 year against *C. perfringens* type A, B, C and D, *C. novyi* type B, *C. sordellii, C. Tetani*;
< 6 months against *C. septicum*, *C. haemolyticum, C. chauvoei*;
Cattle: 1 year against *C. tetani* and *C. perfringens* type D;
< 1 year against *C. perfringens* type A, B and C;
< 6 months against *C. novyi* type B, *C. septicum, C. sordellii*, *C. haemolyticum, C. chauvoei*.

An anamnestic humoral immune response (immunological memory) to all components was demonstrated 1 year following the basic course of vaccination.

Duration of passive immunity:
As demonstrated by serology only:
Lambs: At least 2 weeks for *C. septicum* and *C. chauvoei*;
At least 8 weeks for *C. perfringens* type B and *C. perfringens* type C;
At least 12 weeks for *C. perfringens* type A, *C. perfringens* type D, *C. novyi* type B, *C. tetani* and *C. sordellii*;
No passive immunity was observed for *C. haemolyticum.*
Calves: At least 2 weeks for *C. sordellii* and *C. haemolyticum*;
At least 8 weeks for *C. septicum* and *C. chauvoei*;
At least 12 weeks for *C. perfringens* type A, *C. perfringens* type B, *C. perfringens* type C, *C. perfringens* type D, *C. novyi* type B, and *C. tetani*.

5. Contraindications

Do not use in sick or immunodeficient animals.

6. Special warnings

Special warnings:
Vaccinate healthy animals only.

The effectiveness of the vaccine in providing passive immunity to young lambs and calves depends on these animals ingesting adequate amounts of colostrum on the first day of life.

Clinical trials have demonstrated that the presence of maternal derived antibodies (MDA), particularly against *C. tetani*, *C. novyi* type B, *C. perfringens* type A (calves only), *C. chauvoei* (lambs only) and *C. perfringens* type D may reduce the antibody response to vaccination in young lambs and calves. Therefore, to ensure an optimal response in young animals with high levels of MDA, the basic vaccination should be delayed until the levels wane (which is after about 8-12 weeks of age, see section "Indications for use").

Special precautions for safe use in the target species:
It is good practice to observe animals regularly for adverse reactions at the injection site following vaccination. It is recommended to seek medical advice from a veterinarian in case of a severe injection site reaction.

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:
No side effects other than those already described in section "Adverse events" were seen when the vaccine was used in sheep and cattle between 8 and 2 weeks prior to parturition. In the absence of

specific data, the use of the vaccine is not recommended during the first or second third of pregnancy. Avoid stress in pregnant ewes and cows.

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 calves and lambs, local reactions may increase slightly if twice the recommended dose is administered (see section "Adverse events").

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

7. Adverse events

Cattle and sheep:

Very common (>1 animal / 10 animals treated):	Injection site swelling[1].
Common (1 to 10 animals / 100 animals treated):	Injection site abscess, injection site skin discolouration[2]. Hyperthermia (elevated temperature)[3].
Uncommon (1 to 10 animals / 1,000 animals treated):	Injection site pain[4].
Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Anaphylactic type reaction (severe allergic reaction)[5].

[1] Up to a mean value of 6 cm in sheep and 15 cm diameter in cattle; sometimes reactions of up to 25 cm diameter may be seen in cattle. Most local reactions resolve within 3-6 weeks in sheep and in less than 10 weeks in cattle. In a minority of animals they may persist longer.
[2] Returns to normal as the local reaction resolves.
[3] Mild.
[4] For 1-2 days post first vaccination.
[5] In such cases appropriate treatment such as adrenaline should be administered without delay.

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}.
{< > to be adjusted nationally}

8. Dosage for each species, routes and method of administration

Subcutaneous use.

Dose:
- Sheep: 1 ml – from 2 weeks of age
- Cattle: 2 ml – from 2 weeks of age

Administer by subcutaneous injection preferably in the loose skin on the side of the neck, observing aseptic precautions.

Basic vaccination: Two doses should be administered, 4-6 weeks apart (see section "Indications for use" and "Special Warnings").
Re-vaccination: A single dose should be administered at 6 to 12 month intervals after the basic vaccination (see section "Indications for use").

Use in pregnancy:
To provide passive protection of the offspring, via the colostrum, a single re-vaccination should be administered between 8 and 2 weeks before parturition, provided that animals have received a full basic vaccination course before pregnancy.

9. Advice on correct administration

Shake the bottle thoroughly before use.
Syringes and needles should be sterile before use and the injection should be made through an area of clean, dry skin taking precautions against contamination.

10. Withdrawal periods

Zero days.

11. Special storage precautions

Keep out of the sight and reach of children.

Store and transport refrigerated (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 and the carton. The expiry date refers to the last day of that month.

Shelf life after first opening the immediate packaging: 8 hours.

12. Special precautions for disposal

Medicines should not be disposed of via wastewater or <household waste>.
{< > to be adjusted nationally}

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

[AT, BE, BG, HR, CY, CZ, DE, DK, EE, FI, FR, EL, HU, IS, IT, LV, LT, LU, NL, NO, PL, PT, RO, SK, ES, SE, UK(NI)]: Veterinary medicinal product subject to prescription.

[IE]: Veterinary medicinal product not subject to prescription.

14. Marketing authorisation numbers and pack sizes

{number} {to be completed nationally}

Pack sizes:
Cardboard box with one bottle of 50 ml (50 doses of 1 ml or 25 doses of 2 ml).
Cardboard box with one bottle of 100 ml (100 doses of 1 ml or 50 doses of 2 ml).

Not all pack sizes may be marketed.

15. Date on which the package leaflet was last revised

{MM/YYYY} {to be completed nationally}

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>:
{< > to be adjusted nationally}

<Manufacturer responsible for batch release:> {to be adjusted nationally if included in the above}
Intervet International B.V.
Wim de Körverstraat 35
5831 AN Boxmeer
The Netherlands

<Local representatives <and contact details to report suspected adverse reactions>:>
{< > to be adjusted nationally}

<For any information about this veterinary medicinal product, please contact the local representative of the marketing authorisation holder.>
{< > to be adjusted nationally}

17. Other information

{to be completed nationally}