LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

CARDBOARD BOX – for 1 x 20 ml, 1 x 50 ml, or 1 x 100 ml bottles

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Bravoxin suspension for injection for cattle and sheep

2. STATEMENT OF ACTIVE SUBSTANCES

Each 1 ml of vaccine contains:

C. perfringens type A (α) toxoid	≥ 0.5 IU
C. perfringens type B & C (β) toxoid	≥ 18.2 IU
C. perfringens type D (ε) toxoid	≥ 5.3 IU
C. chauvoei whole culture, inac	≥ 90% protection
C. novyi toxoid	≥ 3.8 IU
C. septicum toxoid	≥ 4.6 IU
C. tetani toxoid	≥ 4.9 IU
C. sordellii toxoid	≥ 4.4 U
C. haemolyticum toxoid	≥ 17.4 U

3. PHARMACEUTICAL FORM

Suspension for injection

4. PACKAGE SIZE

20 ml
50 ml
100 ml

5. TARGET SPECIES

Cattle and sheep

6. INDICATION(S)

7. METHOD AND ROUTE(S) OF ADMINISTRATION

Subcutaneous use.
Shake well before use.
Read the package leaflet before use.

8. WITHDRAWAL PERIOD(S)

Withdrawal period: zero days.

9. SPECIAL WARNING(S), IF NECESSARY

Read the package leaflet before use.

10. EXPIRY DATE

EXP {month/year}
Once broached use within 8 hours.

11. SPECIAL STORAGE CONDITIONS

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

12. SPECIFIC PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCTS OR WASTE MATERIALS, IF ANY

Disposal: read package leaflet.

13. THE WORDS "FOR ANIMAL TREATMENT ONLY" AND CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE, IF APPLICABLE

For animal treatment only. To be supplied only on veterinary prescription.

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

Keep out of the sight and reach of children.

15. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

MSD Animal Health UK Ltd.
Walton Manor
Walton
Milton Keynes
MK7 7AJ

16. MARKETING AUTHORISATION NUMBER(S)

Vm 01708/4649

17. MANUFACTURER'S 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 for cattle and sheep

2. STATEMENT OF ACTIVE SUBSTANCES

Each 1 ml of vaccine contains

C. perfringens type A (α) toxoid	≥ 0.5 IU
C. perfringens type B & C (β) toxoid	≥ 18.2 IU
C. perfringens type D (ε) toxoid	≥ 5.3 IU
C. chauvoei whole culture, inac	≥ 90% protection
C. novyi toxoid	≥ 3.8 IU
C. septicum toxoid	≥ 4.6 IU
C. tetani toxoid	≥ 4.9 IU
C. sordellii toxoid	≥ 4.4 U
C. haemolyticum toxoid	≥ 17.4 U

3. PHARMACEUTICAL FORM

Suspension for injection

4. PACKAGE SIZE

100 ml

5. TARGET SPECIES

Cattle and sheep

6. INDICATION(S)

7. METHOD AND ROUTE(S) OF ADMINISTRATION

SC
Read the package leaflet before use.

8. WITHDRAWAL PERIOD(S)

Withdrawal period: zero days.

9. SPECIAL WARNING(S), IF NECESSARY

Shake well before use.
Read the package leaflet before use.

10. EXPIRY DATE

EXP {month/year}
Once broached use within 8 hours.

11. SPECIAL STORAGE CONDITIONS

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

12. SPECIFIC PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCTS OR WASTE MATERIALS, IF ANY

13. THE WORDS "FOR ANIMAL TREATMENT ONLY" AND CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE, IF APPLICABLE

For animal treatment only. To be supplied only on veterinary prescription.

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

15. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

MSD Animal Health UK Ltd.
Walton Manor
Walton
Milton Keynes
MK7 7AJ

16. MARKETING AUTHORISATION NUMBER(S)

Vm 01708/4649

17. MANUFACTURER'S BATCH NUMBER

Lot {number}

MINIUMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

BOTTLE LABEL – 20 ml, 50 ml

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Bravoxin suspension for injection

2. QUANTITY OF THE ACTIVE SUBSTANCE(S)

Clostridial cells and toxoids; see package leaflet.

3. CONTENTS BY WEIGHT, BY VOLUME OR BY NUMBER OF DOSES

20 ml
50 ml

4. ROUTE(S) OF ADMINISTRATION

SC

5. WITHDRAWAL PERIOD(S)

Withdrawal period: zero days.

6. BATCH NUMBER

Lot {number}

7. EXPIRY DATE

EXP {month/year}
Once broached use within 8 hours.

7. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only.

B. PACKAGE LEAFLET

PACKAGE LEAFLET:
Bravoxin suspension for injection for cattle and sheep

1. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER AND OF THE MANUFACTURING AUTHORISATION HOLDER RESPONSIBLE FOR BATCH RELEASE, IF DIFFERENT

Marketing authorisation holder:
MSD Animal Health UK Ltd.
Walton Manor
Walton
Milton Keynes
Buckinghamshire
MK7 7AJ

Manufacturer responsible for batch release:
Intervet International B.V.
Wim de Körverstraat 35
5831 AN Boxmeer
The Netherlands.

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

Bravoxin suspension for injection for cattle and sheep

3. STATEMENT OF THE ACTIVE SUBSTANCE(S) AND OTHER INGREDIENTS

Each 1 ml of vaccine contains:

Active substances

C. perfringens type A (α) toxoid	≥ 0.5 IU#
C. perfringens type B & C (β) toxoid	≥ 18.2 IU*
C. perfringens type D (ε) toxoid	≥ 5.3 IU*
C. chauvoei whole culture, inactivated	≥ 90% protection**.
C. novyi toxoid	≥ 3.8 IU*
C. septicum toxoid	≥ 4.6 IU*
C. tetani toxoid	≥ 4.9 IU*
C. sordellii toxoid	≥ 4.4 U[1]
C. haemolyticum toxoid	≥ 17.4 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 – 0.18mg

Light brown aqueous suspension that settles on storage.

4. INDICATION(S)

For the active immunisation of sheep and cattle against diseases 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*, *C. haemolyticum* and against tetanus caused by *C. tetani*. For the passive immunisation of lambs and calves against infection caused by the above mentioned clostridial species (except *C. haemolyticum* in sheep).

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

Duration of active immunity:
As demonstrated by serology only:
Sheep: 12 months 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: 12 months against *C. tetani* and *C. perfringens* type D
< 12 months 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 12 months 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. ADVERSE REACTIONS

Swelling at the injection site was observed very commonly in clinical studies. This may reach 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.

An abscess may develop commonly.

Skin discolouration at the injection site (which returns to normal as the local reaction resolves) may occur commonly.

Mild hyperthermia may occur commonly.

Localised pain at the injection site for 1-2 days post first vaccination may occur uncommonly.

Anaphylactic reactions were observed in very rare cases in spontaneous pharmacovigilance reports. In such cases appropriate treatment such as adrenaline should be administered without delay.

The frequency of adverse reactions is defined using the following convention:
- very common (more than 1 in 10 animals treated displaying adverse reaction(s))
- common (more than 1 but less than 10 animals in 100 animals treated)
- uncommon (more than 1 but less than 10 animals in 1,000 animals treated)
- rare (more than 1 but less than 10 animals in 10,000 animals treated)
- very rare (less than 1 animal in 10,000 animals treated, including isolated reports).

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 inform your veterinary surgeon.

7. TARGET SPECIES

Cattle and sheep.

8. DOSAGE FOR EACH SPECIES, ROUTE(S) 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" and "Special Warnings").
Re-vaccination: A single dose should be administered at 6 to 12 month intervals after the basic vaccination (see section "Indications").

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 PERIOD(S)

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.

Shelf-life after first opening the container: 8 hours.

12. SPECIAL WARNING(S)

Special warnings for each target species:
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").

Special precautions for use in animals
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 Reactions" 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 (symptoms, emergency procedures, antidotes):
In calves and lambs, local reactions may increase slightly if twice the recommended dose is administered (see section "Adverse Reactions").

Incompatibilities:
Do not mix with any other veterinary medicinal product.

13. SPECIFIC PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCT OR WASTE MATERIALS, IF ANY

Medicines should not be disposed of via wastewater or household waste. Ask your veterinary surgeon how to dispose of medicines no longer required. These measures should help to protect the environment.

14. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED

April 2021

15. OTHER INFORMATION

Pack sizes:
Cardboard box with one bottle of 20 ml (20 doses of 1 ml or 10 doses of 2 ml).

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.

Approved: 28/04/21