ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE AND IMMEDIATE PACK
250 ml vial
Individual Cardboard box for 50 ml, 100 ml and 250 ml vial
Cardboard box of 12 x 50 ml, 12 x 100 ml and 6 x 250 ml

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Trymox LA 150 mg/ml Suspension for Injection for Cattle, Sheep, Pigs, Dogs, Cats
Amoxicillin (as amoxicillin trihydrate)

2. STATEMENT OF ACTIVE SUBSTANCES

Each ml contains:
Amoxicillin 150 mg
(equivalent to amoxicillin trihydrate 172 mg)

3. PHARMACEUTICAL FORM

Suspension for injection

4. PACKAGE SIZE

50 ml
100 ml
250 ml
12 x 50 ml
12 x 100 ml
6 x 250 ml

5. TARGET SPECIES

Cattle, Sheep, Pigs, Dogs, Cats

6. INDICATION(S)

7. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.

Cattle, sheep and pigs – By intramuscular injection only.

Dogs and cats - subcutaneous or intramuscular use.

To be shortened or omitted for multilingual packs in case of space restriction

The recommended dosage rate is 15 mg per kg bodyweight, equivalent to 1 ml per 10 kg bodyweight to be repeated once after 48 hours.

Shake the vial vigorously to achieve full resuspension before use.
This product does not contain an antimicrobial preservative.
Swab the septum before removing each dose. Use a dry sterile needle and syringe.

To ensure the correct dosage, bodyweight should be determined as accurately as possible to avoid underdosing.

Animal	Weight (kg)	Dosage volume (ml)
Cattle	450 kg	45.0 ml
Sheep	65 kg	6.5 ml
Pigs	150 kg	15.0 ml
Dogs	20 kg	2.0 ml
Cats	5 kg	0.5 ml

Dose volume is equivalent to 1 ml per 10 kg body weight. If dose volume exceeds 15 ml in cattle and 4 ml in sheep and pigs, it should be divided and injected into two or more sites

The stopper should not be punctured more than 40 times.

8. WITHDRAWAL PERIOD(S)

Withdrawal period

Cattle:
Meat and offal: 39 days
Milk: 108 hours (4.5 days)

Pigs:
Meat and offal: 42 days

Sheep:
Meat and offal: 29 days

Milk: Not authorised for use in sheep producing milk for human consumption.

9. SPECIAL WARNING(S), IF NECESSARY

Penicillins may occasionally cause severe allergic reactions

Read the package leaflet before use.

10. EXPIRY DATE

EXP {month/year}
Shelf life after first opening the container: 28 days
Once opened, use by _____

11. SPECIAL STORAGE CONDITIONS

Do not store above 25 °C.
Protect from light.

12. SPECIAL 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

Univet Limited
Tullyvin
Cootehill
County Cavan
H16 T183
Ireland

16. MARKETING AUTHORISATION NUMBER(S)

Vm 05150/5003

17. MANUFACTURER'S BATCH NUMBER

<Batch> <Lot> <BN> {number}

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

50 ml and 100ml vial

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Trymox LA 150 mg/ml Suspension for Injection for Cattle, Sheep, Pigs, Dogs, Cats
Amoxicillin (as amoxicillin trihydrate)

2. QUANTITY OF THE ACTIVE SUBSTANCE(S)

Amoxicillin (as Amoxicillin trihydrate) 150 mg/ml

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

50 ml
100 ml

4. ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.

Cattle, sheep and pigs – By intramuscular injection only

Dogs and cats - subcutaneous or intramuscular use

5. WITHDRAWAL PERIOD(S)

Cattle:
Meat and offal: 39 days
Milk: 108 hours (4.5 days)

Pigs:
Meat and offal: 42 days

Sheep:
Meat and offal: 29 days

Milk: Not authorised for use in sheep producing milk for human consumption.

6. BATCH NUMBER

<Batch> <Lot> <BN> {number}

7. EXPIRY DATE

EXP {month/year}

8. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only.

B. PACKAGE LEAFLET

PACKAGE LEAFLET:

TRYMOX LA 150 mg/ml Suspension for Injection for Cattle, Sheep, Pigs, Dogs, Cats

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

Marketing authorisation holder and manufacturer responsible for batch release:

Univet Limited

Tullyvin

Cootehill

County Cavan

H16 T183
Ireland

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

Trymox LA 150 mg/ml Suspension for Injection for Cattle, Sheep, Pigs, Dogs, Cats
Amoxicillin (as amoxicillin trihydrate).

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

Each ml contains:

Active substance:

Amoxicillin	150 mg
(equivalent to amoxicillin trihydrate	172 mg)

A white to off-white oily suspension

4. INDICATION(S)

For the treatment of infections of the alimentary tract, respiratory tract, urogenital tract, skin and soft tissue caused by bacteria susceptible to amoxicillin.

5. CONTRAINDICATIONS

Do not administer via the intravenous or intrathecal routes

Do not administer to rabbits, hamsters, gerbils or guinea pigs.

Do not use in known cases of hypersensitivity to penicillins, cephalosporins or any of the excipients.

6. ADVERSE REACTIONS

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.

In very rare cases, allergic reactions may occur, varying in severity from a light skin reaction such as urticaria to anaphylactic shock.
In the case of allergic reactions, treatment should be discontinued and a symptomatic treatment should be initiated.
In rare cases local irritation may occur due to the injection of amoxicillin. The frequency of this adverse reaction may be decreased by reducing the volume of injection per injection site. The irritation is typically of low intensity and recedes spontaneously and quickly.

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).

7. TARGET SPECIES

Cattle, Sheep, Pigs, Dogs, Cats

8. DOSAGE FOR EACH SPECIES, ROUTE(S) AND METHOD OF ADMINISTRATION

Shake the vial vigorously to achieve full resuspension before use.
.
This product does not contain an antimicrobial preservative.

Swab the septum before removing each dose. Use a dry sterile needle and syringe.

To ensure the correct dosage, bodyweight should be determined as accurately as possible to avoid underdosing.

Cattle, sheep and pigs – By intramuscular injection only.

Dogs and cats - subcutaneous or intramuscular use.

The recommended dosage rate is 15 mg per kg bodyweight, equivalent to 1 ml per 10 kg bodyweight to be repeated once after 48 hours.

Dose volume is equivalent to 1 ml per 10 kg body weight. If dose volume exceeds 15 ml in cattle and 4 ml in sheep and pigs, it should be divided and injected into two or more sites.

Animal	Weight (kg)	Dosage volume (ml)
Cattle	450 kg	45.0 ml
Sheep	65 kg	6.5 ml
Pigs	150 kg	15.0 ml
Dogs	20 kg	2.0 ml
Cats	5 kg	0.5 ml

9. ADVICE ON CORRECT ADMINISTRATION

As with other injectable preparations normal aseptic precautions should be observed. An appropriately graduated syringe must be used to allow accurate administration of the required dose volume. This is particularly important when injecting small volumes. The stopper should not be punctured more than 40 times.

10. WITHDRAWAL PERIOD(S)

Cattle:
Meat and offal: 39 days
Milk: 108 hours (4.5 days)

Pigs:
Meat and offal: 42 days

Sheep:
Meat and offal: 29 days

Milk: Not authorised for use in sheep producing milk for human consumption.

11. SPECIAL STORAGE PRECAUTIONS

Keep out of the sight and reach of children.

Do not store above 25 °C.
Protect from light.

Do not use this veterinary medicinal product after the expiry date which is stated on the label and carton after 'EXP'.
Shelf life after first opening the immediate packaging: 4 weeks

12. SPECIAL WARNING(S)

Special warnings for each target species:
The product is not effective against beta-lactamase producing organisms.
Complete cross-resistance has been shown between amoxicillin and other penicillins, in particular amino-penicillins.

Use of the product/amoxicillin should be carefully considered when antimicrobial susceptibility testing has shown resistance to penicillins because its effectiveness may be reduced.

Special precautions for use in animals:
Use of the product should be based on susceptibility testing of the bacteria isolated from the animal. If this is not possible, therapy should be based on local (regional, farm level) epidemiological information about susceptibility of the target bacteria.

Official, national and regional antimicrobial policies should be taken into account when the product is used.
Use of the product deviating from the instructions given in the package leaflet may increase the prevalence of bacteria resistant to amoxicillin and may decrease the effectiveness of treatment with other penicillins, due to the potential for cross-resistance.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
Care should be taken to avoid accidental self-injection. In the case of accidental self-injection, seek medical advice immediately.

Penicillins and cephalosporins may cause hypersensitivity (allergy) following injection, inhalation, ingestion or skin contact. Hypersensitivity to penicillins may lead to cross-reactions to cephalosporins and vice versa. Allergic reactions to these substances may occasionally be serious.

1. Do not handle this product if you know you are sensitised, or if you have been advised not to work with such preparations.

2. Handle this product with great care to avoid exposure, taking all recommended precautions.

3. If you develop symptoms following exposure such as skin rash, you should seek medical advice and show the doctor this warning. Swelling of the face, lips or eyes or difficulty with breathing, are more serious symptoms and require urgent medical attention.

Wash hands after use.

Pregnancy and lactation:
Can be used during pregnancy and lactation.

Interaction with other medicinal products and other forms of interaction
It is not generally recommended to use bactericidal and bacteriostatic antibiotics at the same time.
Beta-lactam antibiotics are known to interact with antibiotics with bacteriostatic action such as chloramphenicol, macrolides, sulfonamides and tetracyclines. There is also synergic action of penicillins with aminoglycosides.

Overdose (symptoms, emergency procedures, antidotes)

The safety of amoxicillin is typical of that of other penicillins in that intrinsic toxicity is very low. Amoxicillin has a wide safety margin.
In case of overdose, treatment is symptomatic.

Incompatibilities
In the absence of compatibility studies, this veterinary medicinal product must not be mixed with other veterinary medicinal products.

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

Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal product should be disposed of in accordance with local requirements.

14. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED

December 2020

15. OTHER INFORMATION

For animal treatment only

Pack sizes:
50 ml vial
100 ml vial
250 ml vial
12 x 50 ml
12 x 100 ml
6 x 250 ml

Not all pack sizes may be marketed.
For any information about this veterinary medicinal product, please contact the local representative of the marketing authorisation holder

Amoxicillin is a broad-spectrum antibiotic of the β-lactam family belonging to the aminopenicillin group. This substance has time-dependent bactericidal activity and acts against Gram-positive and some Gram-negative microorganisms.
The mechanism of antibacterial action of amoxicillin is the inhibition of the biochemical processes of bacterial cell wall synthesis by an irreversible and selective inhibition of various enzymes involved in these processes, mainly transpeptidases, endopeptidases and carboxypeptidases. Inadequate synthesis of the bacterial wall in susceptible species produces an osmotic imbalance that particularly affects the growth of bacteria (when the processes of bacterial wall synthesis are particularly important), eventually leading to lysis of the bacterial cell.
Species considered to be susceptible to amoxicillin include Gram-positive bacteria: *Streptococcus* spp and Gram-negative bacteria: *Pasteurellaceae* and *Enterobacteriaceae* including strains of *E. coli*.

Bacteria normally resistant to amoxicillin are Penicillinase-producing *staphylococci*, certain *Enterobacteriaceae* such as *Klebsiella* spp., *Enterobacter* spp., *Proteus* spp. and other Gram-negative bacteria such as *Pseudomonas aeruginosa*.
There are three main mechanisms of resistance to beta-lactams: beta-lactamase production, altered expression and/or modification of penicillin binding proteins (PBP), and decreased penetration of the outer membrane. One of the most important is the inactivation of penicillin by beta-lactamase enzymes produced by certain bacteria. These enzymes are capable of cleaving the beta-lactam ring of penicillins, making them inactive. The beta-lactamase could be encoded in chromosomal or plasmidic genes.
Acquired resistances are frequent for Gram-negative bacteria such as *E. coli* which produce different types of β-lactamases that remain in the periplasmic space. Cross-resistance is observed between amoxicillin and other penicillins, particularly with aminopenicillins.
The use of extended spectrum beta-lactam drugs (e.g. aminopenicillins) might lead to the selection of multi-resistant bacterial phenotypes (e.g. those producing extended spectrum beta-lactamases (ESBLs)).