ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

Cardbox for 1 L, 2.5 L and 5 L

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

ZERMEX 1 mg/ml Oral Solution for Sheep
MOXIGRO 1 mg/ml Oral Solution for Sheep
Moxidectin

2. STATEMENT OF ACTIVE AND OTHER SUBSTANCES

Each ml contains:

Active substance	
Moxidectin	1 mg
Excipients	
Benzyl Alcohol	40 mg
Butylated Hydroxytoluene	2.5 mg
Disodium edetate E 385	0.27 mg

3. PHARMACEUTICAL FORM

Oral Solution

4. PACKAGE SIZE

5 L
2.5 L
1 L

5. TARGET SPECIES

Sheep

6. INDICATION(S)

Infections of sheep with parasites sensitive to moxidectin.

For the treatment and prevention of infections caused by:

- Adult and immature gastro-intestinal nematodes
  .*Haemonchus contortus* (including inhibited larvae)
  .*Ostertagia circumcincta* (including inhibited larvae)
  .*Ostertagia trifurcata*
  .*Trichostrongylus axei* (including inhibited larvae)

.*Trichostrongylus colubriformis*
.*Trichostrongylus vitrinus*
.*Nematodirus battus*
.*Nematodirus spathiger*
.*Nematodirus filicolis* (adults only)
.*Strongyloides papillosus* (larval stages only)
.*Cooperia curticei* (adults only)
.*Cooperia oncoaphora*
.*Oesophagostomum columbianum*
.*Oesophagostomum venulosym* (adults only)
.*Chabertia ovina*
.*Trichuris ovis* (adults only)

- Adult respiratory tract nematode
.*Dictyocaulus filaria*

The product has a persistent effect in preventing reinfection:
.for 5 weeks *by Ostertagia* circumcincta and *Haemonchus contortus*
.for 4 weeks *by Oesophagostomum columbianum*

Clinical trials, after experimental and natural infection, have shown that the product is effective against certain benzimidazole resistant strains of:
.*Haemonchus contortus*
.*Ostertagia circumcincta*
.*Trichostrongylus colubriformis*
.*Cooperia curticei*

7. METHOD AND ROUTE(S) OF ADMINISTRATION

For oral use.
200 µg moxidectin/kg live body (equivalent to 1ml/5 kg live bodyweight) as a single oral drench using any standard drenching equipment.
To ensure administration of a correct dosage, body weight should be determined as accurately as possible; accuracy of the dosing should be checked. Do not mix with other products.

8. WITHDRAWAL PERIOD

Meat and offal: 14 days.
Milk: 5 days.

9. SPECIAL WARNING(S), IF NECESSARY

Special precautions to be taken by the person administering the medicinal products to animals

- Avoid direct contact with skin and eyes.
- Wash hands after use.
- Do not smoke or eat when using this product.
- Wear impermeable rubber gloves during use.

Read package leaflet before use.

10. EXPIRY DATE

EXP {month/year} DD/MMM/YY
Shelf life after first opening the immediate packaging: 6 months.
Once opened, use by: …/…/…"

11. SPECIAL STORAGE CONDITIONS

Do not store above 25ºC. Protect from light.

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

DANGEROUS to fish and aquatic life.
Do not contaminate ponds, waterways or ditches with the product or used containers.
Any unused veterinary medicinal product or waste material derived from such veterinary medicinal product should be disposed of in accordance with local requirements.

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 REACH AND SIGHT OF CHILDREN"

Keep out of the reach and sight of children.

15. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

To be completed nationally.

16. MARKETING AUTHORISATION NUMBER(S)

To be completed nationally.

17. MANUFACTURER'S BATCH NUMBER

Batch{number}:

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

Marketing authorisation holder:
To be completed nationally.

19. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED

To be completed nationally.

20. OTHER INFORMATION

PARTICULARS TO APPEAR ON IMMEDIATE PACKAGING

LABEL 1 L, 2.5 L, 5 L container

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

ZERMEX 1 mg/ml Oral Solution for Sheep
MOXIGRO 1 mg/ml Oral Solution for Sheep
Moxidectin

2. STATEMENT OF ACTIVE AND OTHER SUBSTANCES

Each ml contains:

Active substance

Moxidectin	1 mg

Excipients

Benzyl Alcohol	40 mg
Butylated Hydroxytoluene	2.5 mg
Disodium edetate E 385	0.27 mg

3. PHARMACEUTICAL FORM

Oral Solution

4. PACKAGE SIZE

5 L
2.5 L
1 L

5. TARGET SPECIES

Sheep

6. INDICATION(S)

Infections of sheep with parasites sensitive to moxidectin.

Persistent activity

The product has a persistent effect in preventing reinfection:

.for 5 weeks *by Ostertagia* circumcincta and *Haemonchus contortus*
.for 4 weeks *by Oesophagostomum columbianum*

Resistance

Clinical trials, after experimental and natural infection, have shown that the product is effective against certain benzimidazole resistant strains of:

.*Haemonchus contortus*
.*Ostertagia circumcincta*
.*Trichostrongylus colubriformis*
.*Cooperia curticei*

Read the package leaflet before use.

7. METHOD AND ROUTE(S) OF ADMINISTRATION

200 µg moxidectin/kg live body (equivalent to 1ml/5 kg live bodyweight) as a single oral drench using any standard drenching equipment.
To ensure administration of a correct dosage, body weight should be determined as accurately as possible; accuracy of the dosing should be checked. Do not mix with other products.

8. WITHDRAWAL PERIOD

Meat and offal: 14 days.
Milk: 5 days.

9. SPECIAL WARNING(S), IF NECESSARY

User warnings

- Avoid direct contact with skin and eyes.
- Wash hands after use.
- Do not smoke or eat when using this product.
- Wear impermeable rubber gloves during use.

Read package leaflet before use.

10. EXPIRY DATE

EXP {month/year} DD/MMM/YY
Shelf life after first opening the immediate packaging: 6 months.
Once opened, use by: …/…/…"

11. SPECIAL STORAGE CONDITIONS

Do not store above 25ºC. Protect from light.

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

DANGEROUS to fish and aquatic life.
Do not contaminate ponds, waterways or ditches with the product or used containers.
Any unused veterinary medicinal product or waste material derived from such veterinary medicinal product should be disposed of in accordance with local requirements.

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 REACH AND SIGHT OF CHILDREN"

Keep out of the reach and sight of children.

15. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

To be completed nationally.

16. MARKETING AUTHORISATION NUMBER(S)

To be completed nationally.

17. MANUFACTURER'S BATCH NUMBER

Batch {number}:

B. PACKAGE LEAFLET

PACKAGE LEAFLET

Zermex 1 mg/ml Oral Solution for Sheep
MOXIGRO 1 mg/ml Oral Solution for 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:
<Zoetis subsidiaries in the EU member states>

Manufacturer for the batch release:
Zoetis Manufacturing & Research Spain S.L.
Carretera Camprodon s/n – La Riba
17813 – Vall de Bianya
Gerona, Spain

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

Zermex 1 mg/ml Oral Solution for Sheep
Moxidectin

3. STATEMENT OF THE ACTIVE SUBSTANCES AND OTHER INGREDIENTS

Oral solution.
Pale yellow solution.

Each ml contains:
Active substance
Moxidectin 1 mg

Excipients

Benzyl Alcohol (E1519)	40 mg
Butylated Hydroxytoluene	2.5 mg
Disodium Edetate	0.27 mg

4. INDICATION(S)

For the treatment and prevention of infections caused by:

- Adult and immature gastro-intestinal nematodes:
.*Haemonchus contortus* (including inhibited larvae)
.*Ostertagia circumcincta* (including inhibited larvae)
.*Ostertagia trifurcata*
.*Trichostrongylus axei* (including inhibited larvae)
.*Trichostrongylus colubriformis*
.*Trichostrongylus vitrinus*
.*Nematodirus battus*
.*Nematodirus spathiger*
.*Nematodirus filicolis* (adults only)
.*Strongyloides papillosus* (larval stages only)
.*Cooperia curticei* (adults only)
.*Cooperia oncophora*

.*Oesophagostomum columbianum*
.*Oesophagostomum venulosum* (adults only)
.*Chabertia ovina*
.*Trichuris ovis* (adults only)

- Adult respiratory tract nematode:
.*Dictyocaulus filaria*

Persistent activity:
The product has a persistent effect in preventing reinfection:
.for 5 weeks *by Ostertagia circumcincta* and *Haemonchus contortus*
.for 4 weeks *by Oesophagostomum columbianum*

Resistance:
Clinical trials, after experimental and natural infection, have shown that the product is effective against certain benzimidazole resistant strains of:
.*Haemonchus contortus*
.*Ostertagia circumcincta*
.*Trichostrongylus colubriformis*
.*Cooperia curticei*

5. CONTRAINDICATIONS

None

6. ADVERSE REACTIONS

None known.
If you notice any serious effects or other effects not mentioned in this package leaflet, please inform your veterinary surgeon

7. TARGET SPECIES

Sheep

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

For oral use.
The product should be given as a single oral drench of 1 ml/5 kg live bodyweight, equivalent to 200 µg moxidectin/kg live bodyweight, using any standard drenching equipment.

To ensure a correct dosage, body weight should be determined as accurately as possible; accuracy of the dosing device should be checked. If animals are to be treated collectively rather than individually, they should be grouped according to their body weight and dosed accordingly, in order to avoid under- or overdosing. Do not mix with other products.

9. ADVICE ON CORRECT ADMINISTRATION

None.

10. WITHDRAWAL PERIOD

Meat and offal: 14 days.
Milk: 5 days.

11. SPECIAL STORAGE PRECAUTIONS

Do not store above 25°C.
Protect from light.
Keep out of the reach and sight of children.
Do not use after the expiry date stated on the carton and label after "EXP".
Shelf-life after first opening the container: 6 months
When the container is broached (opened) for the first time, using the in-use shelf-life which is specified on this package insert, the date on which any product remaining in the container should be discarded should be worked out. This discard date should be written in the space provided on the label.

12. SPECIAL WARNINGS

- Care should be taken to avoid the following practices because they increase the risk of development of resistance and could ultimately result in ineffective therapy:
  - Too frequent and repeated use of anthelmintics from the same class, over an extended period of time.
  - Underdosing, which may be due to underestimation of body weight, misadministration of the product, or lack of calibration of the dosing device (if any).

    - Suspected clinical cases of resistance to anthelmintics should be further investigated using appropriate tests (e.g. Faecal Egg Count Reduction Test). Where the results of the test(s) strongly suggest resistance to a particular anthelmintic, an anthelmintic belonging to another pharmacological class and having a different mode of action should be used.

- Resistance to macrocyclic lactones has been reported in *Teladorsagia* in sheep in a number of countries. In 2008, throughout Europe, moxidectin resistance is very rare; it has been reported in a single case involving a levamisole-, benzimidazole and ivermectin-resistant strain of *Teladorsagia circumcincta*. Therefore the use of this product should be based on local (regional, farm) epidemiological information about susceptibility of parasites, local history of treatments and recommendations on how to use the product under sustainable conditions to limit further selection for resistance to antiparasitic compounds. These precautions are especially important when moxidectin is being used to control resistant strains.

- Symptoms of overdose generally do not occur at less than 5 times the recommended dose. They are manifested as transient salivation, depression, drowsiness and ataxia 8 to 12 hours post-treatment. Treatment is not generally necessary and recovery is generally complete within 24 to 48 hours. There is no specific antidote.

User warning:
Avoid direct contact with skin and eyes.
Wash hands after use.
Do not smoke, drink or eat when using this product.
Wear impermeable rubber gloves during use.

The effects of GABA agonists are increased by moxidectin
Not to be mixed with other Veterinary Medicinal Products before administration.

The product has been shown to be safe for use in pregnant, lactating and breeding animals.

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

DANGEROUS to fish and aquatic life.
Do not contaminate ponds, waterways or ditches with the product or used containers.
Any unused product or waster material should be disposed of in accordance with national requirements.

14. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED

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15. OTHER INFORMATION

Pharmacodynamic properties
Moxidectin is a parasiticide active against a wide range of economically important internal and external parasites and is a second generation macrocyclic lactone of the milbemycin family. Its principal mode of action is interfering with neuromuscular transmission of the GABA (gamma amino butyric acid)-gated or glutamate-gated chloride channels.
Moxidectin stimulates the release of GABA and increases its binding to the postsynaptic receptors. The net effect is to open the chloride channels on the postsynaptic junction to allow the inflow of chloride ions and induce an irreversible resting state. This results in flaccid paralysis and eventual death of parasites exposed to the drug

Pharmacokinetic properties
22% of an oral dose of moxidectin is absorbed with maximum blood concentrations being achieved 9 hours post treatment. The drug is distributed throughout the body tissues but due to its lipophilicity the target tissue is fat where concentrations are 10 to 20 times higher than those found in other tissues. The depletion half life in fat is 23-28 days.
Moxidectin undergoes limited biotransformation by hydroxylation. The only significant route of excretion is the faeces.

1 litre HDPE jerrycan with white polypropylene cap (screw fit)
2.5 and 5.0 litre LDPE flexipacks with green polypropylene cap (screw fit)
Secondary pack: fibreboard carton containing 1 x 1 litre, 1 x 2.5 litre and 1 x 5 litre.
Not all pack sizes may be marketed.