ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Cydectin 1% w/v Solution for Injection for cattle

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active substance:
Moxidectin: 10 mg

Excipients:

Qualitative composition of excipients and other constituents	**Quantitative composition if that information is essential for proper administration of the veterinary medicinal product**
Benzyl Alcohol (E1519)	40.00 mg
Butylated Hydroxytoluene (E321)	2.50 mg
Disodium Edetate (E385)	0.27 mg
Polysorbate 80	
Propylene glycol	
Sodium phosphate dibasic	
Sodium phosphate monobasic	
Phosphoric acid and/or Sodium hydroxide	
Water for injection	

Yellow to pale yellow solution, free from suspended matter.

3. CLINICAL INFORMATION

3.1 Target species

Cattle.

3.2 Indications for use for each target species

Moxidectin is an endectocide with activity against a wide range of internal and external parasites of cattle.

Cattle
Moxidectin is indicated for treatment and prevention of infections caused by:

– Adult and immature gastro-intestinal nematodes:
- *Haemonchus placei*
- *Haemonchus contortus*
- *Ostertagia ostertagi* (including inhibited larvae)
- *Trichostrongylus axei*
- *Trichostrongylus colubriformis*
- *Nematodirus helvetianus* (adults only)
- *Nematodirus spathiger*

- *Cooperia surnabada*
- *Cooperia oncophora*
- *Cooperia pectinata*
- *Cooperia punctata*
- *Oesophagostomum radiatum*
- *Bunostomum phlebotomum* (adults only)
- *Chabertia ovina* (adults only)
- *Trichuris* spp. (adults only)

– Adult and immature respiratory tract nematode
- *Dictyocaulus viviparus*

– Warble grubs (migrating larvae)
- *Hypoderma bovis*
- *Hypoderma lineatum*

– Lice
- *Linognathus vituli*
- *Haematopinus eurysternus*
- *Solenopotes capillatus*
- Aid in the control of *Damalinia bovis*

– Mange mites
- *Sarcoptes scabiei*
- *Psoroptes ovis*
- Aid in the control of *Chorioptes bovis*

Moxidectin has a persistent effect against *Ostertagia* for 5 weeks and against *Dictyocaulus* for 6 weeks.

3.3 Contraindications

Do not use in lactating animals producing milk for human consumption.
Do not use in pregnant animals which are intended to produce milk for human consumption within 60 days of expected parturition.
Do not use in horses.
Do not use in dogs.

3.4 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 due to underestimation of body weight, misadministration of the veterinary medicinal 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.

3.5 Special precautions for use

Special precautions for safe use in the target species:

Because of the particular susceptibility, it is not recommended to treat calves of less than 8 weeks. To avoid possible incidence of secondary reactions by the death of *Hypoderma* larvae in the spine or the oesophagus of animals, it is recommended to administer Cydectin 1% injectable after the end of fly activity and before the larvae reach their resting sites. The veterinary surgeon should give advice on the correct timing of treatment.

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

Avoid direct contact with skin and eyes.
Wash hands after use.
Do not smoke, drink or eat while handling the veterinary medicinal product.
Take care to avoid self-injection.
Advice to Medical Practitioners in case of accidental self-injection: Treat any specific signs symptomatically.

Special precautions for the protection of the environment

Moxidectin fulfils the criteria for a (very) persistent, bioaccumulative and toxic (PBT) substance; therefore, exposure of the environment to moxidectin must be limited to the extent possible. Treatments should be administered only when necessary and should be based on faecal egg counts or evaluation of the risk of infestation at the animal and/or herd level.

Like other macrocyclic lactones, moxidectin has the potential to adversely affect non-target organisms:

- Faeces containing moxidectin excreted onto pasture by treated animals may temporarily reduce the abundance of dung feeding organisms. Following treatment of cattle with the veterinary medicinal product, levels of moxidectin that are potentially toxic to dung fly species may be excreted over a period more than 4 weeks and may decrease dung fly abundance during that period. It has been established in laboratory tests that moxidectin may temporarily affect dung beetle reproduction; however, field studies indicate no long-term effects. Nevertheless, in case of repeated treatments with moxidectin (as with veterinary medicinal products of the same anthelmintic class) it is advisable not to treat animals every time on the same pasture to allow dung fauna populations to recover.
- Moxidectin is inherently toxic to aquatic organisms including fish. The veterinary medicinal product should be used only according to the label instructions. Based on the excretion profile of moxidectin when administered as the injectable formulation, treated animals should not have access to watercourses during the 10 days after treatment.

3.6 Adverse events

Cattle

Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Hypersensitivity reaction[1] Weakness Lethargy, apathy, depression, drowsiness

[1] A symptomatic treatment is required.

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, lactation and fertility:
Moxidectin has been shown to be safe for use in pregnant and lactating animals and breeding bulls. However, note section 3.3. Contraindications.

3.8 Interaction with other medicinal products and other forms of interaction

The effects of GABA agonists are increased by moxidectin.

3.9 Administration routes and dosage

Subcutaneous use.
1 ml/50 kg live bodyweight, equivalent to 0.2 mg moxidectin/kg live bodyweight given subcutaneously in front of or behind the shoulder using a 16-18 gauge (1.5 - 1.2 mm) 1/2 inch. (1.5 cm) needle.

The use of a multidose equipment with a draw off needle is recommended for 200 ml and 500 ml packaging.

To ensure a correct dosage, body weight should be determined as accurately as possible; accuracy of the dosing should be checked.

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

Symptoms of overdoses are consistent with the mode of action of moxidectin and generally do not occur at less than 3 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.

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

Meat and offal: 65 days.

Milk: Not authorised for use in cattle producing milk for human consumption.
Do not use in pregnant animals which are intended to produce milk for human consumption within 60 days of expected parturition.

4. PHARMACOLOGICAL INFORMATION

4.1 ATCvet code:

QP 54 AB 02

4.2 Pharmacodynamics

Moxidectin is an endectocide active against a wide range of internal and external parasites and is a second generation macrocyclic lactone of the milbemycin family. 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 result in flaccid paralysis and eventual death of parasites exposed to the veterinary medicinal product.

There is no evidence that moxidectin has any other pharmacological effect on any mammalian organ or tissue. The only toxic effects seen in toxicology or use animal safety tests are entirely consistent with its neuromuscular transmission mode of action.

4.3 Pharmacokinetics

Moxidectin is rapidly and completely absorbed following subcutaneous injection with maximum blood concentrations being achieved 8-12 hours post injection. The veterinary medicinal product is distributed throughout the body tissues but due to its lipophilicity the target tissue is fat where concentrations are 10 - 20 times those of in other tissues. The depletion half-life in fat is 23-28 days.

Moxidectin undergoes limited biotransformation by hydroxylation in the body. The only significant route of excretion is the faeces.

Environmental properties

Moxidectin fulfils the criteria for a (very) persistent, bioaccumulative and toxic (PBT) substance. In particular, in acute and chronic toxicity studies with algae, crustaceans and fish, moxidectin showed toxicity to these organisms, yielding the following endpoints:

Organism		**EC50**	**NOEC**
Algae	*S. capricornutum*	>86.9 µg/l	86.9 µg/l
Crustaceans (Water fleas)	*Daphnia magna* (acute)	0.0302 µg/l	0.011 µg/l
	Daphnia magna (reproduction)	0.0031 µg/l	0.010 µg/l
Fish	*O. mykiss*	0.160 µg/l	Not determined
	L. macrochirus	0.620 µg/l	0.52 µg/l
	P. promelas (early life stages)	Not applicable	0.0032 µg/l
	Cyprinus carpio	0.11 µg/l	Not determined

EC_{50}: the concentration which results in 50% of the test species individuals being adversely affected, i.e. both mortality and sub-lethal effects.
NOEC: the concentration in the study at which no effects are observed.

This implies that when allowing moxidectin to enter water bodies, this may have a severe and lasting impact on aquatic life. To mitigate this risk, all precautions for use and disposal must be adhered to.

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities

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

5.2 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 36 months

Shelf life after first opening the immediate packaging: 6 months.

5.3 Special precautions for storage

Do not tore above 25°C. Keep the vial in the outer carton in order to protect from light.

5.4 Nature and composition of immediate packaging

High density polyethylene containers of 50, 200 and 500 ml content sealed with bromobutyl stoppers. 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.

The veterinary medicinal product should not enter water courses as moxidectin may be dangerous for fish and other aquatic organisms.

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

To be completed nationally

7. MARKETING AUTHORISATION NUMBER(S)

To be completed nationally

8. DATE OF FIRST AUTHORISATION

To be completed nationally

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

To be completed nationally

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 III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

Box of 500 ml, 200 ml, 50 ml

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Cydectin 1% w/v Solution for Injection.

2. STATEMENT OF ACTIVE SUBSTANCES

Each ml contains:

Moxidectin	10 mg

3. PACKAGE SIZE

50 ml
200 ml
500 ml

4. TARGET SPECIES

Cattle.

5. INDICATIONS

6. ROUTES OF ADMINISTRATION

Subcutaneous injection.

7. WITHDRAWAL PERIODS

Meat and offal: 65 days.

Milk: Not permitted for use in cattle producing milk for human consumption or industrial purposes or within 60 days before parturition.

8. EXPIRY DATE

Exp. {mm/yyyy}
Shelf life after first opening the immediate packaging: 6 months.
Once opened, use by: "…/…/…"

9. SPECIAL STORAGE PRECAUTIONS

Do not store above 25ºC. Keep the vial in the outer carton in order to 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

To be completed nationally

14. MARKETING AUTHORISATION NUMBERS

To be completed nationally

15. BATCH NUMBER

Lot {number}

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGE

LABEL 200 ml, 500 ml vial

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Cydectin 1% w/v Solution for Injection.

2. STATEMENT OF ACTIVE SUBSTANCES

Each ml contains:

Moxidectin 10 mg

200 ml
500 ml

3. TARGET SPECIES

Cattle.

4. ROUTES OF ADMINISTRATION

Subcutaneous injection.

Read the package leaflet before use

5. WITHDRAWAL PERIODS

Meat and offal: 65 days.
Milk: Not permitted for use in cattle producing milk for human consumption or industrial purposes or within 60 days before parturition.

6. EXPIRY DATE

Exp. {mm/yyyy}:
After first opening, use the product within 6 months. Once opened, use by: "…/…/…"

7. SPECIAL STORAGE PRECAUTIONS

Do not store above 25ºC. Keep the vial in the outer carton in order to 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

LABEL 50 ml vial

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Cydectin 1% w/v Solution for Injection

2. QUANTITATIVE PARTICULARS OF THE ACTIVE SUBSTANCES

Each ml contains:

Moxidectin 10 mg

50 ml

3. BATCH NUMBER

Lot {number}

4. EXPIRY DATE

Exp. {mm/yyyy}
Once opened, use by: "…/…/…"

B. PACKAGE LEAFLET

PACKAGE LEAFLET

1. Name of the veterinary medicinal product

Cydectin 1% w/v Solution for Injection for cattle

2. Composition

Each ml contains:

Active substance:

Moxidectin	10 mg

Excipients:

Benzyl Alcohol (E1519)	40 mg
Butylated Hydroxytoluene (E321)	2.5 mg
Disodium edetate (E385)	0.27 mg

Yellow to pale yellow solution for injection, free from suspended matter.

3. Target species

Cattle

4. Indications for use

Moxidectin is an endectocide with activity against a wide range of internal and external parasites of cattle. Moxidectin is indicated for treatment and prevention of infections caused by:

– Adult and immature gastro-intestinal nematodes:
- *Haemonchus placei*
- *Haemonchus contortus*
- *Ostertagia ostertagi* (including inhibited larvae)
- *Trichostrongylus axei*
- *Trichostrongylus colubriformis*
- *Nematodirus helvetianus* (adults only)
- *Nematodirus spathiger*
- *Cooperia surnabada*
- *Cooperia oncophora*
- *Cooperia pectinata*
- *Cooperia punctata*
- *Oesophagostomum radiatum*
- *Bunostomum phlebotomum* (adults only)
- *Chabertia ovina* (adults only)
- *Trichuris* spp. (adults only)

– Adult and immature respiratory tract nematode
- *Dictyocaulus viviparus*

– Warble grubs (migrating larvae)
- *Hypoderma bovis*
- *Hypoderma lineatum*

– Lice
  - *Linognathus vituli*
  - *Haematopinus eurysternus*
  - *Solenopotes capillatus*
  - Aid in the control of *Damalinia bovis*

– Mange mites
  - *Sarcoptes scabiei*
  - *Psoroptes ovis*
  - Aid in the control of *Chorioptes bovis*

Moxidectin has a persistent effect against *Ostertagia* for 5 weeks and against *Dictyocaulus* for 6 weeks.

5. Contraindications

Do not use in lactating animals producing milk for human consumption.
Do not use in pregnant animals which are intended to produce milk for human consumption within 60 days of expected parturition.

Do not use in horses.
Do not use in dogs.

6. Special warnings

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 due to underestimation of body weight, misadministration of the veterinary medicinal 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.

Special precautions for safe use in the target species:
Because of the particular susceptibility, it is not recommended to treat calves of less than 8 weeks. To avoid possible incidence of secondary reactions by the death of *Hypoderma* larvae in the spine or the oesophagus of animals, it is recommended to administer Cydectin 1% injectable after the end of fly activity and before the larvae reach their resting sites. The veterinary surgeon should give advice on the correct timing of treatment.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
Avoid direct contact with skin and eyes.
Wash hands after use.
Do not smoke, drink or eat while handling the veterinary medicinal product.
Take care to avoid self-injection.
Advice to Medical Practitioners in case of accidental self injection: Treat any specific signs symptomatically.

Special precautions for the protection of the environment:
Moxidectin fulfils the criteria for a (very) persistent, bioaccumulative and toxic (PBT) substance; therefore, exposure of the environment to moxidectin must be limited to the extent possible. Treatments should be administered only when necessary and should be based on faecal egg counts or evaluation of the risk of infestation at the animal and/or herd level.

Like other macrocyclic lactones, moxidectin has the potential to adversely affect non-target organisms, in particular aquatic organisms and dung fauna.

- Faeces containing moxidectin excreted onto pasture by treated animals may temporarily reduce the abundance of dung feeding organisms. Following treatment of cattle with the veterinary medicinal product, levels of moxidectin that are potentially toxic to dung fly species may be excreted over a period of more than 4 weeks and may decrease dung fly abundance during that period. It has been established in laboratory tests that moxidectin may temporarily affect dung beetle reproduction; however, field studies indicate no long-term effects. Nevertheless, in case of repeated treatments with moxidectin (as with veterinary medicinal products of the same anthelmintic class) it is advisable not to treat animals every time on the same pasture to allow dung fauna populations to recover.
- Moxidectin is inherently toxic to aquatic organisms including fish. This implies that when allowing moxidectin to enter water bodies, this may have a severe and lasting impact on aquatic life. To mitigate this risk, the veterinary medicinal product should be used only according to the label instructions. Based on the excretion profile of moxidectin when administered as the injectable formulation, treated animals should not have access to watercourses during the first 10 days after treatment.

Pregnancy, lactation and fertility:
Moxidectin has been shown to be safe for use in pregnant and lactating animals and breeding bulls. However, note section 5. Contraindications.

Interaction with other medicinal products and other forms of interaction:
The effects of GABA agonists are increased by moxidectin.

Overdose:
Symptoms of overdoses are consistent with the mode of action of moxidectin and generally do not occur at less than 3 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.

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

7. Adverse events

Cattle

Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Hypersensitivity reaction[1] Weakness Lethargy, apathy, depression, drowsiness

[1] A symptomatic treatment is required.

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.
1 ml/50 kg live bodyweight, equivalent to 0.2 mg moxidectin/kg live bodyweight given subcutaneously in front of or behind the shoulder using a 16-18 gauge (1.5 - 1.2 mm) 1/2 inch. (1.5 cm) needle.

The use of a multidose equipment with a draw off needle is recommended for 200 ml and 500 ml packaging.

9. Advice on correct administration

None.

10. Withdrawal periods

Meat and offal: 65 days.

Milk: Not authorised for use in cattle producing milk for human consumption.
Do not use in pregnant animals which are intended to produce milk for human consumption within 60 days of expected parturition.

11. Special storage precautions

Do not store above 25°C. Keep the vial in the outer carton in order to protect from light.
Keep out of the sight and reach 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.

12. Special precautions for disposal

Medicines should not be disposed of via wastewater or household waste.

The veterinary medicinal product should not enter water courses as moxidectin may be dangerous for fish and other aquatic organisms.

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

To be completed nationally.

High density polyethylene containers of 50, 200 and 500 ml content sealed with bromobutyl stoppers.
Not all pack sizes may be marketed.

15. Date on which the package leaflet was last revised

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 contact details to report suspected adverse reactions:
To be completed nationally

Manufacturer for the batch release:
Zoetis Manufacturing & Research Spain, S.L.
Ctra. Camprodón s/n "la Riba"
17813 Vall de Bianya
Girona
SPAIN

<Local representatives <and contact details to report suspected adverse reactions:>>

To be completed nationally.

17. Other information

Moxidectin is a parasiticide active against a wide range of internal and external parasites and is a second generation macrocyclic lactone of the milbemycin family. 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 result in flaccid paralysis and eventual death of parasites exposed to the veterinary medicinal product.

There is no evidence that moxidectin has any other pharmacological effect on any mammalian organ or tissue. The only toxic effects seen in toxicology or use animal safety tests are entirely consistent with its neuromuscular transmission mode of action.

Moxidectin is rapidly and completely absorbed following subcutaneous injection with maximum blood concentrations being achieved 8-12 hours post injection. The veterinary medicinal product is distributed throughout the body tissues but due to its lipophilicity the target tissue is fat where concentrations are 10 - 20 times those of in other tissues. The depletion half life in fat is 23-28 days.

Moxidectin undergoes limited biotransformation by hydroxylation in the body. The only significant route of excretion is the faeces.

To be completed in accordance with national requirements.