

ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Eprizero 5 mg/ml Pour-On Solution for Beef and Dairy Cattle [IE, AT, CZ, FR, DE, HU, IT, BG, EE, EL, LV, LT, PT, RO, SK, SL, ES, UK]

Eprizero 5 mg/ml pour-on solution for cattle [PL]

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1 ml of solution contains:

Active substance:

Eprinomectin 5 mg

Excipients:

Qualitative composition of excipients and other constituents	Quantitative composition if that information is essential for proper administration of the veterinary medicinal product
Butylated Hydroxytoluene (E321)	0.1 mg
Cetearyl Ethylhexanoate and Isopropyl Myristate	
Propylene Glycol Dicaprylocaprate	
Denatonium Benzoate	
Isopropyl Alcohol	

A clear to very light yellow solution.

3. CLINICAL INFORMATION

3.1 Target species

Cattle (beef and dairy cattle).

3.2 Indications for use for each target species

Indicated for the treatment and prevention of the following parasites:

Gastrointestinal Roundworms (adults and fourth stage larvae):

Ostertagia spp.,

Ostertagia lyrata (adult),

Ostertagia ostertagi (including inhibited *O. ostertagi*),
Cooperia spp. (including inhibited *Cooperia* spp),
Cooperia oncophora,
Cooperia pectinata,
Cooperia punctata,
Cooperia surnabada,
Haemonchus placei,
Trichostrongylus spp.,
Trichostrongylus axei,
Trichostrongylus colubriformis,
Bunostomum phlebotomum,
Nematodirus helvetianus,
Oesophagostomum spp. (adult),
Oesophagostomum radiatum,
Trichuris spp (adult).

Lungworms (adults and fourth stage larvae):

Dictyocaulus viviparus

Warbles (parasitic stages):

Hypoderma bovis, *H. lineatum*

Mange Mites:

Chorioptes bovis, *Sarcoptes scabiei* var *bovis*

Lice:

Damalinia (Bovicola) bovis (biting lice), *Linognathus vituli* (sucking lice), *Haematopinus euryesternus* (sucking lice), *Solenopotes capillatus* (sucking lice).

Horn Flies:

Haematobia irritans.

Prolonged Activity

Applied as recommended, the product prevents reinfections with:

Parasite *	Prolonged Activity
<i>Dictyocaulus viviparus</i>	up to 28 days
<i>Ostertagia</i> spp	up to 28 days
<i>Oesophagostomum radiatum</i>	up to 28 days
<i>Cooperia</i> spp	up to 21 days
<i>Trichostrongylus</i> spp	up to 21 days
<i>Haemonchus placei</i>	up to 14 days
<i>Nematodirus helvetianus</i>	up to 14 days

*The following parasite species are included within each of the relevant genera: *Ostertagia ostertagi*, *O. lyrata*, *Cooperia oncophora*, *C. punctata*, *C. surnabada*, *Trichostrongylus axei*, *T. colubroformis*.

3.3 Contraindications

This product is formulated only for topical application to beef and dairy cattle, including lactating dairy cattle. Do not use in other animal species. Do not administer orally or by injection. Do not use in cases of hypersensitivity to the active substance(s) or to any of the excipient(s).

3.4 Special warnings

If there is a risk for re-infestation, the advice of a veterinarian should be sought regarding the need for and frequency of repeat administration.

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 bodyweight, 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.

To date no resistance to eprinomectin (a macrocyclic lactone) has been reported within the EU. However resistance to other macrocyclic lactones has been reported in parasite species in cattle within the EU. Therefore, use of this product should be based on local (regional, farm) epidemiological information about susceptibility of nematodes and recommendations on how to limit further selection for resistance to anthelmintics.

While mite and louse numbers decline rapidly following treatment, due to the feeding habits of the parasites, in some cases several weeks may be required for complete eradication.

For effective use, the product should not be applied to areas of the backline covered with mud or manure.

For the best results the product should be part of a program to control both internal and external parasites of cattle based on the epidemiology of these parasites.

3.5 Special precautions for use

Special precautions for safe use in the target species:

To avoid secondary reactions due to the death of Hypoderma larvae in the oesophagus or in the spine, it is recommended to administer the product at the end of warble fly activity and before the larvae reach their resting sites.

Rainfall at any time before or after treatment will not affect the efficacy of the product.

The product should be applied only to healthy skin.

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

This product may be irritating to human skin and eyes and may cause hypersensitivity. Avoid skin and eye contact with the product during treatment and when handling recently treated animals.

Personal protective clothing consisting of rubber gloves, boots and a waterproof coat should be worn when applying the product.

Should clothing become contaminated, remove as soon as possible and launder before re-use.

In case of accidental spillage onto skin, seek medical advice immediately and show the package leaflet or the label to the physician.

If accidental eye exposure occurs, flush eyes immediately with water.

This product may be toxic after accidental ingestion.

Avoid accidental ingestion of the product by hand to mouth contact.

Do not smoke, eat or drink while handling the product.

In the event of ingestion, wash out mouth with water and seek medical advice.

Wash hands after use.

This product is flammable. Keep away from sources of ignition.

Inhalation of the product may cause irritation.

Use only in well ventilated areas or outdoors.

Special precautions for the protection of the environment:

Eprinomectin is very toxic to dung fauna and aquatic organisms and may accumulate in sediments.

The risk to aquatic ecosystems and dung fauna can be reduced by avoiding too frequent and repeated use of eprinomectin (and products of the same anthelmintic class) in cattle.

The risk to aquatic ecosystems will be further reduced by keeping treated cattle away from water bodies for two to four weeks after treatment.

Other precautions:

Not to be used in other species; avermectins can cause fatalities in dogs, especially Collies, Old English Sheepdogs and related breeds and crosses, and also in turtles/tortoises.

3.6 Adverse events

Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Application site reaction (e.g. Alopecia)
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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.

3.7 Use during pregnancy, lactation or lay

Pregnancy and lactation:

May be used in dairy cattle during all stages of lactation.

Studies conducted at three times the recommended use level of 0.5 mg eprinomectin/kg b.w. had no adverse effect on breeding performance of cows or bulls.

3.8 Interaction with other medicinal products and other forms of interaction

Since eprinomectin binds strongly to plasma proteins, this should be taken into account if it is used in association with other molecules having the same characteristics.

3.9 Administration routes and dosage

Pour-on use. Administer only by topical application at the dose rate of 1 ml per 10 kg of body weight, corresponding to the recommended dose rate of 0.5 mg eprinomectin per kg b.w. The

product should be applied topically by pouring along the backline in a narrow strip extending from the withers to the tailhead.

To ensure administration of a correct dose, bodyweight should be determined as accurately as possible; accuracy of the dosing device (dosing cup or dosing gun delivery system) should be checked.

For external use.

All the animals belonging to the same group should be treated at the same time.

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

In adult cattle, after administration of 5 times the recommended dose (2.5 mg eprinomectin/kg body weight), mild hair loss was observed. No other signs of toxicity were seen.

No antidote has been identified.

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 & offal: 10 days.

Milk: zero hours.

4. PHARMACOLOGICAL INFORMATION

4.1 ATCvet code:

QP54AA04

4.2 Pharmacodynamics

Mode of action

Eprinomectin is a member of the macrocyclic lactone class of endectocides. Compounds of the class bind selectively and with high affinity to glutamate-gated chloride ion channels which occur in invertebrate nerve or muscle cells. This leads to an increase in the permeability of the cell membrane to chloride ions with hyperpolarization of the nerve or muscle cell, resulting in paralysis and death of the parasite.

Compounds of this class may also interact with other ligand-gated chloride channels, such as those gated by the neurotransmitter gamma-aminobutyric acid (GABA).

The margin of safety for compounds of this class is attributable to the fact that mammals do not have glutamate-gated chloride channels; the macrocyclic lactones have a low affinity for other mammalian ligand-gated chloride channels, and they do not readily cross the blood-brain barrier.

4.3 Pharmacokinetics

The bioavailability of topically applied eprinomectin in cattle is about 30% with most absorption occurring by about 10 days after treatment. Eprinomectin is not extensively metabolized in cattle following topical administration. In all biological matrices, the B_{1a} component of eprinomectin is the single most abundant residue.

Eprinomectin consists of the components B_{1a} ($\geq 90\%$) and B_{1b} ($\leq 10\%$) which differ by a methylene unit and is not extensively metabolized in cattle. Metabolites amount to approximately 10% of the total residues in plasma, milk, edible tissues and faeces.

The metabolism profile is nearly identical, qualitatively and quantitatively, in the above biological matrices and does not change significantly with time after administration of eprinomectin. The percent contribution of B_{1a} and B_{1b} to the overall metabolite profile remains constant. The ratio of the two drug components in the biological matrices is identical to that in the formulation demonstrating that the two eprinomectin components are metabolized with nearly equal rate constants. Since the metabolism and the tissue distribution of the two components are quite similar, the pharmacokinetics of the two components would be also similar.

Eprinomectin is strongly linked to plasma proteins (99%). Faeces is the major route of elimination.

Environmental properties

Like other macrocyclic lactones, eprinomectin has the potential to adversely affect non-target organisms. Following treatment, excretion of potentially toxic levels of eprinomectin may take place over a period of several weeks. Faeces containing eprinomectin excreted onto pasture by treated animals may reduce the abundance of dung feeding organisms which may impact on the dung degradation.

Eprinomectin is very toxic to aquatic organisms and may accumulate in sediments.

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities

None known.

5.2 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 2 years.

Shelf life after first opening the immediate packaging: 3 months.

5.3 Special precautions for storage

Do not store above 30 °C.

Keep container in the outer carton.

Protect from light.

5.4 Nature and composition of immediate packaging

Translucent 250 mL and 1 L HDPE containers with integral squeeze measure pour system and white HDPE screw caps.

White 1 L, 2.5 L and 5 L HDPE backpacks and white polypropylene screw caps.

Not all packs sizes may be marketed.

5.5 Special precautions for the disposal of unused veterinary medicinal product 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 eprinomectin is extremely 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

Norbrook Laboratories (Ireland) Limited.

7. MARKETING AUTHORISATION NUMBER(S)

8. DATE OF FIRST AUTHORISATION

Date of first authorisation:

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

DD/MM/YYYY

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 \(https://medicines.health.europa.eu/veterinary\)](https://medicines.health.europa.eu/veterinary).

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

250 mL, 1 L, 2.5 L, 5 L CARTON

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Eprizero 5 mg/ml Pour-On Solution

2. STATEMENT OF ACTIVE SUBSTANCES

1 ml of solution contains:

Active substance:

Eprinomectin: 5 mg

3. PACKAGE SIZE

250 mL

1 L,

2.5 L,

5 L

4. TARGET SPECIES

Cattle (beef and dairy cattle).

5. INDICATIONS**6. ROUTES OF ADMINISTRATION**

Pour-on use.

7. WITHDRAWAL PERIODS

Withdrawal period:

Meat & offal: 10 days.

Milk: zero hours.

8. EXPIRY DATE

Exp. {mm/yyyy}

Once opened use within 3 months.

9. SPECIAL STORAGE PRECAUTIONS

Do not store above 30 °C.
Keep container in the outer carton.
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

Norbrook Laboratories (Ireland) Limited.

14. MARKETING AUTHORISATION NUMBER(S)

15. BATCH NUMBER

Lot {number}

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGE**250 mL, 1 L, 2.5 L, 5 L LABEL****1. NAME OF THE VETERINARY MEDICINAL PRODUCT**

Eprizero 5 mg/ml Pour-On Solution

2. STATEMENT OF ACTIVE SUBSTANCES

1 ml of solution contains:

Active substance:

Eprinomectin: 5 mg

3. TARGET SPECIES

Cattle (beef and dairy cattle).

4. ROUTES OF ADMINISTRATION

Pour-on use.

Read the package leaflet before use.

5. WITHDRAWAL PERIODS

Withdrawal period:

Meat & offal: 10 days.

Milk: zero hours.

6. EXPIRY DATE

Exp. {mm/yyyy}

Once opened use within 3 months.

7. SPECIAL STORAGE PRECAUTIONS

Do not store above 30 °C.

Keep container in the outer carton.

Protect from light.

8. NAME OF THE MARKETING AUTHORISATION HOLDER

Norbrook Laboratories (Ireland) Limited

9. BATCH NUMBER

Lot {number}

B. PACKAGE LEAFLET

PACKAGE LEAFLET

1. Name of the veterinary medicinal product

Eprizero 5 mg/ml Pour-On Solution for Beef and Dairy Cattle

2. Composition

1 ml of solution contains:

Active substance:

Eprinomectin	5 mg
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Excipient:

Butylated Hydroxytoluene (E321)	0.1 mg
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A clear to very light yellow solution.

3. Target species

Cattle (beef and dairy cattle).

4. Indications for use

Indicated for treatment and prevention of the following parasites

Gastrointestinal Roundworms (adults and fourth stage larvae):

Ostertagia spp.,

Ostertagia lyrata (adult),

Ostertagia ostertagi (including inhibited *O. ostertagi*),

Cooperia spp. (including inhibited *Cooperia* spp),

Cooperia oncophora,

Cooperia pectinata,

Cooperia punctata,

Cooperia surnabada,

Haemonchus placei,

Trichostrongylus spp.,

Trichostrongylus axei,

Trichostrongylus colubriformis,

Bunostomum phlebotomum,

Nematodirus helvetianus,

Oesophagostomum spp. (adult),

Oesophagostomum radiatum,
Trichuris spp (adult).

Lungworms (adults and fourth stage larvae):
Dictyocaulus viviparus

Warbles (parasitic stages):
Hypoderma bovis, *H. lineatum*

Mange Mites:
Chorioptes bovis, *Sarcoptes scabiei* var *bovis*

Lice:
Damalinia (Bovicola) bovis (biting lice), *Linognathus vituli* (sucking lice), *Haematopinus euryesternus* (sucking lice), *Solenopotes capillatus* (sucking lice).

Horn Flies:
Haematobia irritans.

Prolonged Activity

Applied as recommended, the product prevents reinfections with:

Dictyocaulus viviparus (up to 28 days)
Ostertagia spp (up to 28 days)
Oesophagostomum radiatum (up to 28 days)
Cooperia spp (up to 21 days)
Trichostrongylus spp (up to 21 days)
Haemonchus placei (up to 14 days)
Nematodirus helvetianus (up to 14 days)

The following parasite species are included within each of the relevant genera: *Ostertagia ostertagi*, *O. lyrata*, *Cooperia oncophora*, *C. punctata*, *C. surnabada*, *Trichostrongylus axei*, *T. colubroformis*.

5. Contraindications

This product is formulated only for topical application to beef and dairy cattle, including lactating dairy cattle.

Do not use in other animal species. Do not administer orally or by injection.

Do not use in cases of hypersensitivity to the active substance(s) or to any of the excipient(s).

6. Special warnings

Special warnings:

If there is a risk for re-infestation, the advice of a veterinarian should be sought regarding the need for and frequency of repeat administration.

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 bodyweight, 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.

To date no resistance to eprinomectin (a macrocyclic lactone) has been reported within the EU. However resistance to other macrocyclic lactones has been reported in parasite species in cattle within the EU. Therefore, use of this product should be based on local (regional, farm) epidemiological information about susceptibility of nematodes and recommendations on how to limit further selection for resistance to anthelmintics.

While mite and louse numbers decline rapidly following treatment, due to the feeding habits of the parasites, in some cases several weeks may be required for complete eradication.

For effective use, the product should not be applied to areas of the backline covered with mud or manure.

For the best results the product should be part of a program to control both internal and external parasites of cattle based on the epidemiology of these parasites.

Special precautions for safe use in the target species:

The product should be applied only to healthy skin.

To avoid secondary reactions due to the death of Hypoderma larvae in the oesophagus or in the spine, it is recommended to administer the product at the end of warble fly activity and before the larvae reach their resting sites.

Rainfall at any time before or after treatment will not affect the efficacy of the product.

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

This product may be irritating to human skin and eyes and may cause hypersensitivity.

Avoid skin and eye contact with the product during treatment and when handling recently treated animals.

Personal protective clothing consisting of rubber gloves, boots and a waterproof coat should be worn when applying the product.

Should clothing become contaminated, remove as soon as possible and launder before re-use.

In case of accidental spillage onto skin, seek medical advice immediately and show the package leaflet or the label to the physician.

If accidental eye exposure occurs, flush eyes immediately with water.

This product may be toxic after accidental ingestion.

Avoid accidental ingestion of the product by hand to mouth contact.

Do not smoke, eat or drink while handling the product.

In the event of ingestion, wash out mouth with water and seek medical advice.

Wash hands after use.

This product is flammable. Keep away from sources of ignition.

Inhalation of the product may cause irritation.

Use only in well ventilated areas or outdoors.

Special precautions for the protection of the environment:

Eprinomectin is very toxic to dung fauna and aquatic organisms and may accumulate in sediments.

The risk to aquatic ecosystems and dung fauna can be reduced by avoiding too frequent and repeated use of eprinomectin (and products of the same anthelmintic class) in cattle.

The risk to aquatic ecosystems will be further reduced by keeping treated cattle away from water bodies for two to four weeks after treatment.

Other precautions:

Not to be used in other species; avermectins can cause fatalities in dogs, especially Collies, Old English Sheepdogs and related breeds and crosses, and also in turtles/tortoises.

Pregnancy and lactation:

May be used in dairy cattle during all stages of lactation.

Studies conducted at three times the recommended use level of 0.5 mg eprinomectin/kg b.w. had no adverse effect on breeding performance of cows or bulls.

Interaction with other medicinal products and other forms of interaction

Since eprinomectin binds strongly to plasma proteins, this should be taken into account if it is used in association with other molecules having the same characteristics.

Overdose:

In adult cattle, after administration of 5 times the recommended dose (2.5 mg eprinomectin/kg body weight), mild hair loss was observed. No other signs of toxicity were seen.

No antidote has been identified.

7. Adverse events

Cattle (beef and dairy cattle).

Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Application site reaction (e.g. Alopecia (hair loss))
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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.

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

Administer only by topical application at the dose rate of 1 ml per 10 kg of body weight, corresponding to the recommended dose rate of 0.5 mg eprinomectin per kg b.w. The product should be applied topically by pouring along the backline in a narrow strip extending from the withers to the tailhead.

If there is a risk for re-infestation, the advice of a veterinarian should be sought regarding the need for and frequency of repeat administration.

For best results use as part of a program to control both internal and external parasites of cattle based on the epidemiology of these parasites.

9. Advice on correct administration

Pour-on use.

To ensure administration of a correct dose, bodyweight should be determined as accurately as possible; accuracy of the dosing device (dosing cup or dosing gun delivery system) should be checked.

For external use.

All the animals belonging to the same group should be treated at the same time.

10. Withdrawal periods

Withdrawal period:

Meat & offal: 10 days

Milk: zero hours.

11. Special storage precautions

Keep out of the sight and reach of children.

Do not store above 30 °C.

Keep container in the outer carton.

Protect from light.

Shelf life after first opening the immediate packaging: 3 months.

Do not use this veterinary medicinal product after the expiry date which is stated on the label. The expiry date refers to the last day of that month.

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 eprinomectin is extremely 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.

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

250 mL and 1 L containers and 1 L, 2.5 L and 5 L backpacks.

Not all package sizes may be marketed.

15. Date on which the package leaflet was last revised

MM/YYYY

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

(EU)

Norbrook Laboratories (Ireland) Limited

Rossmore Industrial Estate

Monaghan

Ireland

Tel: +44 (0)28 3025 4435

E-mail: phvdept@norbrook.co.uk

(UK) Norbrook Laboratories Ltd

Station Works

Newry

Co. Down

BT35 6JP

Manufacturer responsible for batch release:

Norbrook Manufacturing Ltd.

Rossmore Industrial Estate

Monaghan

Ireland

17. Other information