PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGE
Base vial label text

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Closamectin 5 mg/ml/125 mg/ml Solution for Injection for Sheep

Ivermectin/Closantel

2. STATEMENT OF ACTIVE SUBSTANCES

One ml of the product contains:
Active Substances

Ivermectin	5 mg
Closantel (as closantel sodium dihydrate)	125 mg

(equivalent to 135,9 mg of closantel sodium dihydrate)

3. PHARMACEUTICAL FORM

Solution for Injection

4. PACKAGE SIZE

100ml, 250ml and 500ml

5. TARGET SPECIES

Sheep.

6. INDICATION(S)

7. METHOD AND ROUTE(S) OF ADMINISTRATION

For subcutaneous Use
Read the expanding label before use.

8. WITHDRAWAL PERIOD(S)

Withdrawal period(s):
Meat and offal: 28 days.
Milk: Not authorised for use in ewes producing milk for human consumption including during the dry period. Do not use within 1 year prior to the first lambing in ewes intended to produce milk for human consumption.

9. SPECIAL WARNING(S), IF NECESSARY

IMPORTANT – READ EXPANDING LABEL BEFORE USE.

10. EXPIRY DATE

EXP [month/year]

Discard 28 days after first removing a dose.

Discard by: _____/_____/_____

11. SPECIAL STORAGE CONDITIONS

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

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

Disposal: Read Expanding Label.

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

(EU)
Norbrook Laboratories (Ireland) Ltd.
Rossmore Industrial Estate
Monaghan
Ireland

(UK)
Norbrook Laboratories Limited
Station Works
Camlough Road
Newry
Co. Down
BT35 6JP
United Kingdom

16. MARKETING AUTHORISATION NUMBER(S)

Vm 02000/4262

17. MANUFACTURER'S BATCH NUMBER

XXXX-XX

PARTICULARS TO APPEAR ON THE OUTER PACKAGE
Expanding vial label text – Page 1

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Closamectin 5 mg/ml/125 mg/ml Solution for Injection for Sheep

Ivermectin/Closantel

2. STATEMENT OF ACTIVE SUBSTANCES

One ml of the product contains:
Active Substances

Ivermectin	5 mg
Closantel (as closantel sodium dihydrate)	125 mg

(equivalent to 135,9 mg of closantel sodium dihydrate)

3. PHARMACEUTICAL FORM

Solution for Injection

4. PACKAGE SIZE

100ml, 250ml and 500ml

5. TARGET SPECIES

Sheep.

6. INDICATION(S)

7. METHOD AND ROUTE(S) OF ADMINISTRATION

For subcutaneous Use
Read the expanding label before use

8. WITHDRAWAL PERIOD (S)

Withdrawal period(s):

Meat and offal: 28 days.
Milk: Not authorised for use in ewes producing milk for human consumption including during the dry period. Do not use within 1 year prior to the first lambing in ewes intended to produce milk for human consumption.

9. SPECIAL WARNING(S), IF NECESSARY

IMPORTANT – READ EXPANDING LABEL BEFORE USE.

10. EXPIRY DATE

EXP [month/year]

Discard 28 days after first removing a dose.

Discard by: _____/_____/_____

11. SPECIAL STORAGE CONDITIONS

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

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

Disposal: Read Expanding Label

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

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Norbrook Laboratories (Ireland) Ltd.
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Norbrook Laboratories Limited
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Co. Down
BT35 6JP
United Kingdom

16. MARKETING AUTHORISATION NUMBER(S)

Vm 02000/4262

17. MANUFACTURER'S BATCH NUMBER

XXXX-XX

PACKAGE LEAFLET
Expanding vial label text – Pages 2 to 5
Closamectin 5 mg/ml/125 mg/ml Solution for Injection 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:
(EU) Norbrook Laboratories (Ireland) Limited
Rossmore Industrial Estate
Monaghan
Ireland

(UK) Norbrook Laboratories Limited
Station Works
Camlough Road
Newry
Co. Down
BT35 6JP
United Kingdom

Manufacturer responsible for batch release:
(EU) Norbrook Manufacturing Ltd.
Rossmore Industrial Estate
Monaghan Town
Co. Monaghan
Ireland

(UK) Norbrook Laboratories Limited
Station Works
Camlough Road
Newry
Co. Down
BT35 6JP
United Kingdom

Patent No:
EP1478372B

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

Closamectin 5 mg/ml/125 mg/ml Solution for Injection for Sheep

Ivermectin/Closantel

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

One ml of the product contains:

Active Substances

Ivermectin	5 mg
Closantel (as closantel sodium dihydrate)	125 mg
(equivalent to 135,9 mg of closantel sodium dihydrate)	

Excipients

Sodium Formaldehyde Sulphoxylate	5 mg

Solution for Injection
A clear amber solution.

4. INDICATION(S)

For the treatment of mixed trematode (fluke) and nematode or arthropod infestations due to gastrointestinal roundworms, trematodes, lungworms, nasal bots and mites of sheep.

Gastrointestinal roundworms
Teladorsagia circumcincta (including inhibited L4), *Teladorsagia trifurcata* (adult and L4), *Haemonchus contortus* (including inhibited L4), *Trichostrongylus axei* (adult), *Trichostrongylus colubriformis* (adult and L4), *T. vitrinus* (adult) *Cooperia curticei* (adult and L4), *Oesophagostomum columbianum* (adult and L4), *O. venulosum* (adult) *Chabertia ovina* (adult and L4) *Nematodirus filicollis* (adult and L4), *Trichuris ovis* (adult).

[L4 = fourth stage larvae]

Lungworms
Dictyocaulus filaria (adult and 4th stage larvae)
Protostrongylus rufescens (adult)

Liver Fluke (Adults and 7 weeks immature)
Fasciola gigantica, Fasciola hepatica

Nasal Bots
Oestrus ovis

Mange Mites
Psoroptes ovis (Treatment require a second injection of an ivermectin-only product 7 days later. See section dosage for each species, routes and method of administration and special warnings.)

Benzimidazole – resistant strains of *Haemonchus contortus* and *Teladorsagia circumcincta* are also controlled.

5. CONTRAINDICATIONS

Do not use in intramuscular or intravenous route.

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

Avermectins may not be well tolerated in all non-target species (cases of intolerance with fatal outcome are reported in dogs – especially Collies, Bobtails, Old English Sheepdogs and related breeds or crosses, and also in turtles/tortoises).
Do not administer concomitantly with chlorinated compounds. The effect of GABA agonists are increased by ivermectin.

6. ADVERSE REACTIONS

Transitory swelling has rarely been observed in sheep at the injection site and occasionally this swelling is accompanied by pain and discomfort. This swelling resolves completely within 14 days following treatment.

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

Sheep.

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

Bodyweight and dosage should be accurately determined prior to treatment to avoid underdosing; accuracy of the dosing device should be checked.

The product should be administered at a dosage rate of 200 mcg ivermectin per kg and 5 mg closantel per kg bodyweight (1ml per 25kg). A sterile 16-gauge, one-inch needle is recommended.
It should only be injected subcutaneously into the neck.

For the treatment and control of sheep scab an injection of the product may be administered but must be followed with a second injection of an ivermectin only product seven days after the initial injection to treat clinical signs of scab and to eliminate mites. This injection should be administered at the other side of the neck.

Swab septum before removing each dose. Use a dry sterile needle and syringe. For 250 ml and 500 ml pack sizes, use of a multiple dose syringe is recommended.

Bodyweight (Kg)	Dose Volume (ml)
Up to 12.5	0.5
13.5 - 25	1.0
26 - 37.5	1.5
38.5 - 50	2.0
51 - 62.5	2.5
63.5 - 75	3.0

Over 75 Kg bodyweight give 0.5 ml per 12.5 kg of bodyweight.

9. ADVICE ON CORRECT ADMINISTRATION

To refill the syringe, use of a draw-off needle is recommended to avoid excessive broaching of the stopper.

If more than 40 broachings are required, use of a draw off needle is recommended.

The timing for treatment should be based on epidemiological factors and should be customised for each individual farm.

Professional veterinary advice should be sought on appropriate dosing programmes and stock management to achieve adequate parasite control and reduce the likelihood of resistance developing.

If animals are to be treated collectively rather than individually they should be grouped according to their bodyweight and dosed accordingly, in order to avoid under- or overdosing.

10. WITHDRAWAL PERIOD(S)

Meat and offal: 28 days.
Milk: Not authorised for use in ewes producing milk for human consumption including during the dry period. Do not use within 1 year prior to the first lambing in ewes intended to produce milk for human consumption.

11. SPECIAL STORAGE PRECAUTIONS

Keep out of the sight and reach of children.
Do not store above 25°C.
Shelf life after first opening the immediate packaging: 28 days
Protect from light.
This product does not contain a preservative.
When the container is broached (opened) for the first time, using the in-use shelf-life which is specified on this package leaflet, 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.
Do not use this veterinary medicinal product after the expiry date which is stated on the label after EXP. The expiry date refers to the last day of that month.

12. SPECIAL WARNING(S)

Special warnings for each target species:
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.

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 tests 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 ivermectin and closantel has been reported in *Haemonchus contortus* in sheep. Therefore the use of this product should be based on local epidemiological information about the susceptibility of the *Haemonchus contortus* and recommendations on how to limit further selection for resistance to anthelmintics.

In sheep treatment of psoroptic mange (sheep scab) with one injection of this product will not be effective in eliminating all the mites. A suitable ivermectin–only injectable product must be administered seven days after the treatment with this product to treat clinical signs and to eliminate the mites.

Sheep scab (*Psoroptes ovis*) is an extremely contagious external parasite of sheep. To ensure complete control great care must be taken to avoid re-infestation, as mites may be viable for up to 15 days off the sheep. It is important that all sheep which have been in contact with infected sheep are treated with an appropriate product. Contact between treated, infected and untreated flocks must be avoided until at least seven days after treatment.

Other precautions:
Ivermectin is very toxic to aquatic organisms and dung insects. Long term effects on dung insects caused by continuous or repeated use cannot be excluded. Therefore repeated treatment of animals on a pasture with an ivermectin-containing product within a season should only be given in the absence of alternative treatments or approaches to maintain animal/flock health, as advised by a veterinarian.

Pregnancy and lactation:
The product can be administered to sheep at any stage of pregnancy or lactation provided that the milk is not intended for human consumption. Before use in dairy animals see section on “Withdrawal Period”.

Interaction with other medicinal products and other forms of interaction:
Do not administer concomitantly with chlorinated compounds. The effect of GABA agonists are increased by ivermectin.

Overdose (symptons, emergency procedures, antidotes)
The lethal dose (LD_{50}) of closantel in sheep, after a single intramuscular dose, was higher than 40 mg/kg. Moreover, some studies conducted in sheep reported signs of overdose with doses of around 4 times the therapeutic dose (both injectable and oral).

Dose levels approaching 4.0 mg/kg ivermectin (20 times the recommended dosage) administered subcutaneously, result in ataxia and depression in sheep.

Closantel like other salicylanilides is a potent uncoupler of oxidative phosphorylation and the safety index is not as high as is the case of many other anthelmintics. However where used as directed there are unlikely to be any untoward effects. Signs of overdosage can include loss of appetite, decreased vision, loose faeces and increased frequency of defaecation. High doses may cause blindness, hyperventilation, hyperthermia, general weakness, inco-ordination, convulsions, tachycardia and in extreme cases death.

No antidote has been identified for either ivermectin or closantel overdosage. Symptomatic treatment may be beneficial.

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

For Animal Treatment Only.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
Do not smoke, eat or drink while handling the product.
Avoid direct contact of the product with the skin. In case of spillage onto the skin rinse immediately with fresh water.

Wash hands after use.
Take care to avoid self-injection. Inadvertent self-injection may result in local irritation and/or pain at the injection site.
In case of accidental self-injection, seek medical advice immediately and show the package leaflet to the physician.

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

EXTREMELY DANGEROUS TO FISH AND AQUATIC LIFE. Do not contaminate surface waters or ditches with the product or used container. 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

January 2023

15. OTHER INFORMATION

MODE OF ACTION

Ivermectin paralyses and ultimately kills parasitic nematodes, arachnids and insects by its effect on the nervous system of these parasites. Ivermectin belongs to the avermectin class of anthelmintic endectocides. The mode of action exhibited by the avermectins is unique to this class of antiparasitic agents.

Closantel is a member of the salicylanilide class of anthelmintics. Salicylanilides are hydrogen ionophores which act as potent uncouplers of oxidative phosphorylation. The site of action of these proton ionophores is known to be selective uncoupling of oxidative phosphorylation in parasite mitochondria.

Treatment with the product when flukes are five weeks and greater has been shown to reduce subsequent reproductive capacity and egg shedding.

100ml / 250ml / 500ml multidose vials.
Not all pack sizes may be marketed.

Distributed by:

Norbrook Laboratories Limited
Carnbane Industrial Estate
Newry
BT35 6QQ
Co. Down
Northern Ireland

Approved 02 February 2023