B. PACKAGE LEAFLET

PACKAGE LEAFLET

1. Name of the veterinary medicinal product

Closamectin 5 mg/ml + 200 mg/ml Pour-On Solution for Cattle

2. Composition

Each ml contains:

Active substances:

Ivermectin	5 mg
Closantel	200 mg
(as closantel sodium dihydrate217.5 mg)	

Excipients:

Brilliant Blue FCF (E133)	0.1 mg

A clear blue/green solution.

3. Target species

Cattle.

4. Indications for use

For the treatment of mixed trematode (fluke) and nematode or arthropod infestations due to roundworms, lungworms, eyeworms, warbles, mite and lice of cattle.

Trematodes (adult and late immatures)
Fasciola gigantica
Fasciola hepatica
Treatment of fluke at 12 weeks (mature) >95% efficacy.
Treatment of fluke at 7 weeks (late immature) >95% efficacy.

Gastrointestinal roundworms (adults and fourth stage larvae)
Ostertagia ostertagi (including inhibited *O. ostertagi*), *Haemonchus placei*, *Trichostrongylus axei*, *Trichostrongylus colubriformis*, *Cooperia* spp*, Oesophagostomum radiatum, Nematodirus helvetianus* (adult), *Strongyloides papillosus* (adult).

Lungworms (adult and fourth stage larvae)
Dictyocaulus viviparus

Eyeworms (adult)
Thelazia spp
Cattle grubs (parasitic stages)
Hypoderma bovis, Hypoderma lineatum

Lice
Linognathus vituli, Haematopinus eurysternus, Damalinia bovis

Mange Mites
Chorioptes bovis, Sarcoptes scabiei var *bovis*

5. Contraindications

Do not use on areas of skin which have mange, scabs or other lesions or to areas contaminated with mud or manure.

Do not use in cases of hypersensitivity to the active substances or to any of the excipients.

Do not use the product between December and March in those countries in which *Hypoderma* spp have not been eradicated as killed larvae may cause hypersensitivity reactions.

6. Special warnings

Special warnings:

The presence of liver fluke or *Haemonchus* infestation should be confirmed before this combination product is used.

If treatment against liver fluke infestation only is required, a single active substance product should be used.

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.

The effect of rain on the absorption of the pour-on formulation at the time of and after application has not been investigated. For maximum effect animals should be kept indoors or undercover for up to 48 hours following treatment, when there is rain or an imminent risk of rain.

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 (an avermectin) has been reported in *Cooperia oncophora* in cattle within the EU. Therefore the use of this product should be based on local (regional and farm) epidemiological information about susceptibility of the gastrointestinal nematodes and recommendations on how to limit further selection for resistance to anthelmintics.

Special precautions for safe use in the target species:

Due to the significant likelihood of cross-contamination of non-treated animals with this product due to grooming (licking), all animals in a group should be treated at the same time and treated animals should be kept separately from non-treated animals throughout the withdrawal period. Non-compliance with this recommendation may lead to residues violations (see section 10) or in very rare cases, it can lead to adverse events (see section 7) in non-treated animals.

Care should be taken to ensure animals are not overdosed by the application volume, accidental spillage or oral ingestion, as overdosage may result in signs of toxicity such as inco-ordination and blindness. It is recommended that animals are not clipped prior to treatment to reduce the risk of increased drug absorption and hence bioavailability, or oral ingestion through mutual grooming.

Care should be taken when treating animals which may be of low nutritional status as this may increase susceptibility of adverse events occurring.

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 or cause hypersensitivity. Avoid skin and/or eye contact with the product during treatment, when handling recently treated animals or when cleaning the used equipment. Personal protective equipment consisting of nitrile rubber gloves and boots with a waterproof coat should be worn when applying the product. Protective clothing should be washed after use. If accidental skin contact occurs, wash the affected area immediately with soap and water.

If accidental eye exposure occurs, flush the eyes immediately with water and get medical attention.

This product may be toxic after accidental ingestion. Avoid ingestion by hand-to-mouth contact. Do not eat, drink or smoke whilst handling the product. In case of accidental ingestion, seek medical advice immediately and show the package leaflet to the physician. Wash hands after use.

Accidental spillage or ingestion could be detrimental or even fatal therefore care should be taken when handling and storing the product.

This product is flammable. Keep away from sources of ignition. Use only in well ventilated areas or outdoors.

Special precautions for the protection of the environment:

The product is very toxic to aquatic organisms and dung insects.

Treated cattle should not have direct access to ponds, streams or ditches for 14 days after treatment.

Long term effects on dung insects caused by continuous or repeated use cannot be excluded therefore repeat treatments on a pasture within a season should only be given on the advice of a veterinarian.

Other precautions:

Avermectins may not be well tolerated in non-target species (cases of intolerance with fatal outcome are reported in dogs – especially Collies, Old English Sheepdogs and related breeds or crosses, and also in turtles/tortoises).

Pregnancy:

Can be used during pregnancy.

Lactation:

Can be used during lactation provided that the milk is not intended for human consumption.

Interaction with other medicinal products and other forms of interaction:

Do not combine ivermectin treatment with vaccination against lungworms. If vaccinated animals are to be treated, treatment should not be carried out within a period of 28 days before or after vaccination.

Overdose:

At doses of three times the recommended dose, no significant clinical signs were recorded.

Ivermectin

No antidote has been identified. Symptomatic treatment may be beneficial.

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 slight loss of appetite, loose faeces, decreased vision and increased frequency of defecation. High doses may cause blindness, hyperventilation, general weakness and inco-ordination, hyperthermia, convulsions, tachycardia and in extreme cases death. Treatment of overdosage is symptomatic as no antidote has been identified.

7. ADVERSE REACTIONS

Cattle.

Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Neurological signs[1] (e.g. Ataxia (incoordination), Blindness, Recumbency) Digestive tract disorder (e.g. Anorexia (loss of appetite), Diarrhoea) Death[2]

[1] When there is an adverse event in a herd, several animals may be affected. Should neurological signs be observed in one animal, it is recommended to reinforce surveillance, at the herd level, of all treated animals.
[2] In case of persistent digestive tract disorders.

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 event 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

Pour-on use.

For external use only.

The veterinary medicinal product should be administered topically at a dosage rate of 500 µg ivermectin per kg bodyweight and 20 mg closantel per kg bodyweight (1 mL per 10 kg).

HANDY DOSING GUIDE		ANIMALS SHOULD BE WEIGHED AND GROUPED ACCORDING TO BODYWEIGHT TO AVOID UNDER OR OVER-DOSING*				
BODYWEIGHT	DOSE VOLUME	NUMBER OF FULL DOSES PER PACK				
		250 mL	500 mL	1 litre	2.5 litre	5 litre
100 kg*	10 mL	25	50	100	250	500
150 kg	15 mL	16	33	66	166	333
200 kg	20 mL	12	25	50	125	250
250 kg	25 mL	10	20	40	100	200
300 kg	30 mL	8	16	33	83	166
350 kg	35 mL	7	14	28	71	142
400 kg	40 mL	6	12	25	62	125
450 kg	45 mL	5	11	22	55	111
500 kg	50 mL	5	10	20	50	100
550 kg	55 mL	4	9	18	45	90
600 kg	60 mL	4	8	16	41	83

* Dose rate 1 mL per 10kg bodyweight

The formulation should be applied along the midline of the back in a narrow strip between the withers and the tail head.

The timing for treatment should be based on local epidemiological factors and should be customised for each individual farm. A comprehensive parasite control programme should be established by a veterinary professional. It should be confirmed that mixed infestations are present before the product is prescribed.

The efficacy profile of the product is such that a single treatment seven weeks after housing will control infestation for the entire housed period.

The product should not be repeatedly applied (within 7 weeks) to cattle.

9. Advice on correct administration

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 bodyweight and dosed accordingly, in order to avoid under- or overdosing.

10. Withdrawal periods

Meat and offal: 58 days

Not authorised for use in cattle producing milk for human consumption including during the dry period. Do not use during the second half of pregnancy in heifers which are intended to produce milk for human consumption.

Due to the significant likelihood of cross-contamination of non-treated animals with this product due to grooming (licking), all animals in a group should be treated at the same time and treated animals should be kept separately from non-treated animals throughout the withdrawal period. Non-compliance with this recommendation may lead to residues violations in non-treated animals.

11. Special storage precautions

Keep out of the sight and reach of children.

Do not store above 25 °C.
Protect from light.
Store upright in original container.

Avoid introduction of contamination.
Replace the cap securely after use.

Flammable – keep away from heat, sparks, open flame or other sources of ignition.

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

Shelf life after first opening the immediate packaging: use immediately.

12. Special precautions for disposal

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

EXTREMELY DANGEROUS TO FISH AND AQUATIC LIFE. The veterinary medicinal product should not enter water courses as ivermectin and closantel may be dangerous for fish and other aquatic organisms. Do not contaminate surface waters or ditches with the product or used container.

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

250 ml, 500 ml and 1 lcontainers with integral squeeze measure pour system.
1 l, 2.5 l and 5 l HDPE backpacks for use with a dosing gun delivery system.

Not all pack 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*).

16. Contact details

Marketing authorisation holder:
Norbrook Laboratories (Ireland) Limited
Rossmore Industrial Estate
Monaghan
Ireland

Manufacturer responsible for batch release:
Norbrook Laboratories Limited
Station Works, Camlough Road
Newry, Co. Down, BT35 6JP
Northern Ireland

Norbrook Manufacturing Limited
Rossmore Industrial Estate
Monaghan
Ireland

Local representative and contact details to report suspected adverse reactions:

For any information about this veterinary medicinal product, please contact the local representative of the marketing authorisation holder.

17. Other information

For animal treatment only.

If stored at temperatures below 0°C, the veterinary medicinal product may appear cloudy. Allowing to warm at room temperature will restore the normal appearance without affecting efficacy.

{Supply category to be completed nationally}