# Summary of Product Characteristics

## 1 NAME OF THE VETERINARY MEDICINAL PRODUCT

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

## 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

**Active Ingredient(s)**

| | | |
|---|---|---|
| Ivermectin | 5 | mg/ml |
| Closantel (as closantel sodium) | 200 | mg/ml |

**Excipients**

| | | |
|---|---|---|
| Brilliant Blue FCF (E133) | 0.1 | mg/ml |

For the full list of excipients see section 6.1.

## 3 PHARMACEUTICAL FORM

Pour-On solution.
A clear blue/green solution.

## 4 CLINICAL PARTICULARS

### 4.1 Target Species

Cattle.

### 4.2 Indications for use, specifying the target species

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

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*

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.

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*

**4.3 Contraindications**

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

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

**4.4 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.

The effect of rain on 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 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 has been reported in *Ostertagia ostertagi* and *Cooperia* spp in cattle. Therefore the use of this product should be based on local (regional, farm) epidemiological information about the susceptibility of these species and recommendations on how to limit further selection for resistance to anthelmintics.

**4.5 Special precautions for use**

**i. Special precautions for use in animals**

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 4.11) or in very rare cases, it can lead to adverse events (see section 4.6) in non-treated animals.

It is not advisable to administer the product when *Hypoderma lineatum* larvae are localised in the periaesophagic region, or when *Hypoderma bovis* larvae are situated in the spinal canal. Seek professional veterinary advice to determine the best period of use.

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.

**ii. 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. Operators should wear nitrile

rubber gloves and boots with a waterproof coat 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. If accidental ingestion occurs, get medical attention and show the package leaflet to the physician. Wash hands after use. This product is flammable. Keep away from sources of ignition. Use only in well ventilated areas or outdoors.

**iii. Other Precautions Regarding 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.

**4.6 Adverse reactions (frequency and seriousness)**

In very rare cases (less than 1 animal in 10,000 animals, including isolated reports), neurological signs such as blindness, ataxia, and recumbency may occur after administration of the product. These cases may also be associated with gastrointestinal signs such as anorexia, diarrhoea and in extreme cases signs may persist and may result in death of the animal.

Even though the overall incidence of adverse events is very rare, it has been noted that, when there is an adverse event in a herd, several animals may be affected. Therefore, should neurological signs be observed in one animal, it is recommended to reinforce surveillance, at the herd level, of all treated animals.

**4.7 Use during pregnancy, lactation or lay**

Closamectin Pour-On can be administered to cattle (including dairy, beef/suckler cattle) at any stage of pregnancy or lactation provided that the milk is not intended for human consumption. See Section 4.11.

**4.8 Interaction with other medicinal products and other forms of interactions**

None known.

**4.9 Amounts to be administered and administration route**

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).

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

Assess bodyweight carefully prior to administration.

The timing for treatment should be based on epidemiological factors and should be customised for each individual farm. A dosing programme should be established by a veterinary professional.

| 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 |
| 100kg* | 10ml | 25 | 50 | 100 | 250 | 500 |
| 150kg | 15ml | 16 | 33 | 66 | 166 | 333 |
| 200kg | 20ml | 12 | 25 | 50 | 125 | 250 |
| 250kg | 25ml | 10 | 20 | 40 | 100 | 200 |
| 300kg | 30ml | 8 | 16 | 33 | 83 | 166 |
| 350kg | 35ml | 7 | 14 | 28 | 71 | 142 |
| 400kg | 40ml | 6 | 12 | 25 | 62 | 125 |
| 450kg | 45ml | 5 | 11 | 22 | 55 | 111 |
| 500kg | 50ml | 5 | 10 | 20 | 50 | 100 |
| 550kg | 55ml | 4 | 9 | 18 | 45 | 90 |
| 600kg | 60ml | 4 | 8 | 16 | 41 | 83 |

* Dose rate 1 ml per 10 kg bodyweight

Avoid introduction of contamination.
If stored at temperatures below 0°C, Closamectin Pour-On Solution for Cattle may appear cloudy. Allowing to warm at room temperature will restore the normal appearance without affecting efficacy.

**4.10 Overdose (symptoms, emergency procedures, antidotes), if necessary**

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

No antidote has been identified for ivermectin or closantel overdose. 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.

**4.11 Withdrawal period(s)**

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.

**5 PHARMACOLOGICAL or IMMUNOLOGICAL PROPERTIES**

**ATC Vet Code:** QP54AA51
**Pharmacotherapeutic Group:** Ivermectin, combinations.

**5.1 Pharmacodynamic properties**

Ivermectin is an endectocide with activity against a wide range of internal and external parasites. Ivermectin is a macrocylic lactone and acts by inhibiting nerve impulses. It binds selectively and with high affinity to glutamate-gated chloride ion

channels which occur in invertebrate nerve and 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 relevant parasites. 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 macrocylic lactones have a low affinity for other mammalian ligand-gated chloride channels and they do not readily cross the blood-brain barrier.

Closantel is a member of the salicylanilide class of anthelmintics. Salicylanilides are hydrogen (proton) ionophores (referred to as oxidative phosphorylase uncouplers.)

The chemical structure of salicylanilides illustrate the possession of a detachable proton. This type of molecule is lipophilic and is known to shuttle protons across membranes, in particular the inner mitochondrial membrane. Closantel acts by uncoupling oxidative phosphorylation.

Closantel is a parasiticide with flukicide activity and efficacy against certain other helminths and arthropods.

**5.2 Pharmacokinetic particulars**

After topical administration of Closamectin Pour-On to cattle at a dose rate of 500 µg ivermectin per kg and 20 mg closantel per kg the following parameters were observed: Ivermectin – Cmax of 19.13 ng/mL and AUC of 2440 ng.hr/mL; Closantel – Cmax of 68.5 µg/mL and AUC of 35207 µg.hr/mL.

Ivermectin is only partially metabolised. In cattle, only about 1 to 2% is excreted in the urine the remainder is excreted in the faeces, approximately 60% of which is excreted as unaltered drug. The remainder is excreted as metabolites or degradation products. Salicylanilides are poorly metabolised and are excreted mainly unchanged. About 90% of closantel is excreted unchanged in the faeces and urine in cattle.

**6 PHARMACEUTICAL PARTICULARS**

**6.1 List of excipients**

Brilliant Blue FCF (E133) Dye
Anhydrous Ethanol
Macrogol
Cetearyl Ethylhexanoate
Isopropyl Myristate
Povidone
Denatonium Benzoate
Trolamine
Isopropyl alcohol

**6.2 Major incompatibilities**

None known.

**6.3 Shelf-life**

Shelf-life of the veterinary medicinal product as packaged for sale: 18 months.

**6.4 Special precautions for storage**

Do not store above 25°C.
Store upright in original container.
Protect from light.
Discard unused material.
Flammable – keep away from heat, sparks, open flame or other sources of ignition.

**6.5 Nature and composition of immediate packaging**

Translucent 250 ml, 500 ml and 1L HDPE containers with white HDPE caps and integrated measuring device, packaged in cartons and white 1L, 2.5L and 5L HDPE backpacks with white polypropylene screw caps, packaged in cartons.

A 4L combination pack is also available containing 1 x 1L container or back pack, 1 x 2.5L HDPE back pack and a 1 x 500ml HDPE container with dosing gun.

Not all packs sizes may be marketed.

**6.6 Special precautions for the disposal of unused veterinary medicinal products or waste materials derived from the use of such products**

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 material from such veterinary medicinal product should be disposed of in accordance with local requirements.

**7 MARKETING AUTHORISATION HOLDER**

Norbrook Laboratories (Ireland) Limited
Rossmore Industrial Estate
Monaghan
Ireland

**8 MARKETING AUTHORISATION NUMBER(S)**

VPA22664/088/001

**9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION**

Date of first authorisation: 07 August 2009
Date of last renewal: 07 August 2014

**10 DATE OF REVISION OF THE TEXT**

October 2021