SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Closamectin Solution for Injection for Cattle

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active substance(s):

Ivermectin	5mg
Closantel (as Closantel Sodium Dihydrate)	125mg
Sodium Formaldehyde Sulphoxylate	5mg

Excipient(s):

Qualitative composition of excipients and other constituents
Povidone K12
Macrogol 200
Glycerol Formal

3. CLINICAL INFORMATION

3.1 Target species

Cattle

3.2 Indications for use for each target species

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

Gastrointestinal roundworms

Ostertagia ostertagi (including inhibited larval stages), *Ostertagia lyrata* (adult), *Haemonchus placei* (adult and immature), *Trichostrongylus axei* (adult and immature), *Trichostrongylus colubriformis* (adult and immature), *Cooperia oncophora* (adult and immature), *Cooperia punctata* (adult and immature), *Cooperia pectinata* (adult and immature), *Oesophagostomum radiatum* (adult and immature), *Nematodirus helvetianus* (adult), *Nematodirus spathiger* (adult), *Strongyloides papillosus* (adult), *Bunostomum phlebotomum* (adult and immature), *Toxocara vitulorum* (adult), *Trichuris* spp.

Lungworms

Dictyocaulus viviparus (adult and 4th stage larvae)

Liver Fluke (trematodes)

Fasciola gigantica, Fasciola hepatica

Treatment of fluke at 12 weeks (mature) >99% efficacy.
Treatment of fluke from 7 weeks (late immature) >90% efficacy

Eyeworms (adult)
Thelazia spp

Cattle grubs (parasitic stages)
Hypoderma bovis, Hypoderma lineatum

Lice
Linognathus vituli, Haematopinus eurysternus, Solenopotes capillatus

Mange Mites

*Psoroptes ovis (*syn *P communis* var *bovis), Sarcoptes scabiei* var *bovis*

The veterinary medicinal product may also be used as an aid in the control of the biting louse *Damalinia bovis* and the mange mite *Chorioptes bovis*, but complete elimination may not occur.

Persistent activity

When cattle have to graze on pasture contaminated with infective larvae of cattle nematodes, treatment with the veterinary medicinal product at the recommended dose rate of 200 µg ivermectin per kg bodyweight and 5 mg closantel per kg bodyweight controls re-infection with:

	Prolonged activity
Dictyocaulus viviparus	Up to 21 days
Ostertagia ostertagi	Up to 21 days
Oesophagostomum radiatum	Up to 21 days
Cooperia spp	Up to 14 days
Trichostrongylus axei	Up to 14 days
Haemonchus placei	Up to 14 days

3.3 Contraindications

The veterinary medicinal product is not for intravenous or intramuscular use.

Avermectins may not be well tolerated in all 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).

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

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 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 has been reported in *Cooperia* spp., in cattle. Therefore the use of this product should be based on local epidemiological information about the susceptibility of the *Cooperia* spp., and recommendations on how to limit further selection for resistance to anthelmintics.

3.5 Special precautions for use

Special precautions for safe use in the target species:

Not Applicable.

Special precautions to be taken by the person administering the medical veterinary 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 or the label to the physician.

Special precautions for the protection of the environment:
Ivermectin 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 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/herd health, as advised by a veterinarian.

3.6 Adverse events

Common (1 to 10 animals / 100 animals treated):	Injection site swelling[1] Injection site pain[2]

[1]Tissue swellings at the injection site are common occurrences up to 48 hours after injection.
[2]Injection site pain is common and will resolve thereafter without treatment. Hardness on palpation may be observed up to 7 days following administration.

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 'Contact details' section of the package leaflet.

3.7 Use during pregnancy, lactation or lay

Pregnancy and lactation:
The veterinary medicinal product can be administered to cattle at any stage of pregnancy or lactation provided that the milk is not intended for human consumption.

3.8 Interaction with other medicinal products and other forms of interaction

Do not administer concomitantly with chlorinated compounds. The effects of GABA agonists are increased by ivermectin. Please refer to section 4.2 of the SPC.

3.9 Administration routes and dosage

The veterinary medicinal product should be administered at a dosage rate of 200 µg ivermectin per kg bodyweight and 5 mg closantel per kg bodyweight (1 ml per 25 kg). It should only be injected subcutaneously into the neck. A maximum dose of 10ml should be administered at any one site with any residual volume administered at another site in the neck. A sterile 16-gauge, one-inch needle is recommended.

This product does not contain an antimicrobial preservative. 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. To refill the syringe, use of a draw-off needle is recommended to avoid excessive broaching of the stopper.

Do not exceed 40 broachings per vial. 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. As with other anthelmintics, veterinary advice should be sought on appropriate dosing programmes and stock management to achieve adequate parasite control and reduce the likelihood of resistance developing.

To ensure administration of a correct dose, bodyweight 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 over-dosing.

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

Single doses of 4.0 mg/kg ivermectin (20 times the recommended dosage) administered subcutaneously, result in ataxia and depression. 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 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. Treatment of overdosage is symptomatic as no antidote has been identified.

Oral closantel doses in excess of 82.5 mg/kg in cattle may cause blindness, hyperventilation, hyperthermia, general weakness, in-coordination, convulsions, tachycardia and in extreme cases death.

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: 49 days.
Milk: Not authorised for use in cattle producing milk for human consumption including during the dry period. Do not use during the last trimester of pregnancy in heifers which are intended to produce milk for human consumption.

4. PHARMACOLOGICAL INFORMATION

4.1 ATCvet code: QP54AA51

4.2 Pharmacodynamics

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. Treatment with Closamectin when fluke are five weeks and greater has been shown to reduce subsequent reproductive capacity and egg shedding.

4.3 Pharmacokinetics

After subcutaneous administration of the veterinary medicinal product to cattle at a dose rate of 200 µg ivermectin per kg and 5 mg closantel per kg the following parameters were observed: Ivermectin Cmax of 57.3 ng/ml and AUC of 7106 ng.hr/ml; Closantel Cmax of 63.4 µg/ml and AUC of 21996 µg.hr/ml. Ivermectin is only partially metabolised. Only about 1-2% 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.

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 product as packaged for sale: 18 months.
Shelf-life after first opening of immediate packaging: 28 days.

5.3 Special precautions for storage

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

5.4 Nature and composition of immediate packaging

100 ml, 250 ml and 500 ml multidose vials and aluminium caps complete with bromobutyl bungs and aluminium seals. 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 ivermectin 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 Limited

7. MARKETING AUTHORISATION NUMBER

Vm 02000/3000

8. DATE OF THE FIRST AUTHORISATION

28 July 2006

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

August 2023

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). .

Approved: 18 August 2023