SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Norofas Solution for Injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active Substance(s)

Ivermectin	0.5% w/v
Closantel (as closantel sodium dihydrate)	12.5% w/v

Excipients

Sodium Formaldehyde Sulphoxylate	0.5% w/v

For a full list of excipients see Section 6.1

3. PHARMACEUTICAL FORM

Solution for injection.

A clear amber 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 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 at 9 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*

Norofas Injection 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 in cattle
When cattle have to graze on pasture contaminated with infective larvae of cattle nematodes, treatment with Norofas Injection 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 28 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

4.3 Contraindications:

Norofas Injection 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 cattle producing milk for human consumption.

Do not use in non-lactating dairy cows including pregnant heifers within 60 days of calving.

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 body weight, 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. 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 susceptibility of the Cooperia spp 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

None.

(ii) 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.
Direct contact of the product with the skin should be kept to a minimum. 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.

4.6 Adverse Reactions (Frequency and Seriousness):

Transitory discomfort has been observed in some cattle following subcutaneous administration. Tissue swellings at the injection site have been observed. These reactions resolve without treatment.

4.7 Use During Pregnancy, Lactation or Lay:

Norofas Injection can be administered to cattle at any stage of pregnancy or lactation provided that the milk is not intended for human consumption.

4.8 Interactions with Other Medicaments and Other Forms of Interaction:

None identified.

4.9 Amounts to be Administered and Administration Route:

Norofas Injection 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.

To ensure administration of a correct dose, 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.

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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.

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 Suitably Qualified Person.

4.10 Overdose (Symptoms, Emergency Procedures and Antidotes) (if necessary):

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.

4.11 Withdrawal Period:

Cattle must not be treated within 49 days of slaughter for human consumption.

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.

Do not use any closantel-containing products during the 49 day withdrawal period. If an ivermectin-only product is used during this period, the withdrawal periods for all products must be observed.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Anthelmintic

ATC Vet Code: QP54AA51

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

5.2 Pharmacokinetic Properties:

After subcutaneous administration of Norofas Injection to cattle at a dose rate of 200ug ivermectin per kg and 5mg closantel per kg the following parameters were observed: Ivermectin Cmax of 57.3ng/ml and AUC of 7106ng.hr/ml; Closantel Cmax of 63.4ug/ml and AUC of 21996ug.hr/ml. Ivermectin is only partially metabolised. In cattle, 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 in cattle.

6. PHARMACEUTICAL PARTICULARS

6.1 List of Excipients:

Sodium Formaldehyde Sulphoxylate
Povidone K12
Polyethylene Glycol
Glycerol Formal

6.2 Incompatibilities:

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

6.3 Shelf-Life:

Shelf-life of the veterinary medicinal product as packaged for sale: 1 year

Shelf-life after first opening the immediate packaging: 28 days

6.4 Special Precautions for Storage:

Do not store above 25°C.
Protect from light.
After first use, discard the vial within 28 days. Discard unused material. Avoid introduction of contamination.

6.5 Nature and Composition of Immediate Packaging:

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

Not all pack sizes maybe marketed.

6.6 Special Precautions for the Disposal of Unused Veterinary Medicinal Product or Waste Materials Derived from the Use of Such Products, if appropriate:

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 products should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Norbrook Laboratories Limited
Station Works
Camlough Road
Newry
Co Down, BT35 6JP
Northern Ireland

8 MARKETING AUTHORISATION NUMBER

Vm 02000/4273

9. DATE OF RENEWAL OF THE AUTHORISATION

23 August 2012

10. DATE OF REVISION OF THE TEXT

June 2013

APPROVED T. NASH **20/06/13**