SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Norbonex 5mg/ml Pour-On Solution for Beef and Dairy Cattle

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1ml of solution contains:

Active Substance:
Eprinomectin 5mg

Excipients:
Butylated Hydroxytoluene (E321) 0.1mg

For a full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Pour-on solution
A Clear to Very Light Yellow Solution.

4. CLINICAL PARTICULARS

4.1 Target species

Cattle (beef and dairy cattle)

4.2 Indications for use, specifying the target species

Indicated for the treatment and control of infections of the following parasites

Gastrointestinal Roundworms (adults and fourth stage larvae):
Ostertagia spp., *Ostertagia lyrata* (adult), *Ostertagia ostertagi* (including inhibited L_4), *Cooperia* spp. (including inhibited L_4), *Cooperia oncophora, Cooperia pectinata, Cooperia punctata, Cooperia surnabada, Haemonchus placei, Trichostrongylus* spp., *Trichostrongylus axei, Trichostrongylus colubriformis, Bunostomum phlebotomum, Nematodirus helvetianus, Oesophagostomum* spp. (adult), *Oesophagostomum radiatum, Trichuris* spp (adult).

Lungworms (adults and fourth stage larvae):
Dictyocaulus viviparus

Warbles (parasitic stages):
Hypoderma bovis, H. lineatum

Mange Mites:
Chorioptes bovis, Sarcoptes scabiei

Lice:
Damalinia (Bovicola) bovis (biting lice), *Linognathus vituli* (sucking lice), *Haematopinus eurysternus* (sucking lice), *Solenopotes capillatus* (sucking lice).

Horn Flies:
Haematobia irritans.

While mite and louse numbers decline rapidly following treatment, due to the feeding habits of the parasites, in some cases several weeks may be required for complete eradication.

Prolonged Activity

Applied as recommended, the product controls reinfections with:

Parasite *	**Prolonged Activity**
Dictyocaulus viviparus	up to 28 days
Ostertagia spp	up to 28 days
Oesophagostomum radiatum	up to 28 days
Cooperia spp	up to 21 days
Trichostrongylus spp	up to 21 days
Haemonchus placei	up to 14 days
Nematodirus helvetianus	up to 14 days

*The following parasite species are included within each of the relevant genera: *Ostertagi ostertagi, O. lyrata, Cooperia oncophora, C. punctata, C. surnabada, Trichostronglus axei, T. colubroformis*.

For best results use as part of a program to control both internal and external parasites of cattle based on the epidemiology of these parasites.

4.3 Contraindications

This product is formulated only for topical application to beef and dairy cattle, including lactating dairy cattle. Do not use in other animal species. Do not administer orally or by injection.
Do not use in animals with known hypersensitivity to the active ingredient or any of the excipients.

4.4 Special Warnings for each target species

The details provided in section 4.10 apply.

If there is a risk for re- infection, the advice of a veterinarian should be sought regarding the need for and frequency of repeat administration.

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 (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.

To date no resistance to eprinomectin (a macrocyclic lactone) has been reported within the EU. However resistance to other macrocyclic lactones has been reported in parasite species in cattle within the EU. Therefore, use of this product should be based on local (regional, farm) epidemiological information about susceptibility of nematodes and recommendations on how to limit further selection for resistance to anthelmintics.

For effective use, the product should not be applied to areas of the backline covered with mud or manure. The product should be applied only on healthy skin.

4.5 Special precautions for use

i) Special precautions for use in animals

Not to be used in other species; avermectins can cause fatalities in dogs, especially Collies, Old English Sheepdogs and related breeds and crosses, and also in turtles/tortoises.

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 and may cause hypersensitivity.
Avoid skin and eye contact with the product during treatment and when handling recently treated animals.
Users should wear rubber gloves, boots and a waterproof coat when applying the product.
Should clothing become contaminated, remove as soon as possible and launder before re-use.
If accidental skin contact occurs, wash the affected area immediately with soap and water.

If accidental eye exposure occurs, flush eyes immediately with water.
This product may be toxic after accidental ingestion.
Avoid accidental ingestion of the product by hand to mouth contact.
Do not smoke, eat or drink while handling the product.
In the event of ingestion, wash out mouth with water and seek medical advice.
Wash hands after use.
This product is flammable. Keep away from sources of ignition.
Inhalation of the product may cause irritation.
Use only in well ventilated areas or outdoors.

iii) Other precautions

Eprinomectin is very toxic to aquatic organisms, is persistent in soils and may accumulate in sediments.

The risk to aquatic ecosystems and dung fauna can be reduced by avoiding too frequent and repeated use of eprinomectin (and products of the same anthelmintic class) in cattle.

The risk to aquatic ecosystems will be further reduced by keeping treated cattle away from water bodies for two to five weeks after treatment.

4.6 Adverse reactions (frequency and seriousness)

No undesirable effects have been identified when the product is used at the recommended dose rate.

4.7 Use during pregnancy, lactation or lay

May be used in dairy cattle during all stages of lactation.
Studies have demonstrated a wide safety margin. Studies conducted at three times the recommended use level of 0.5 mg eprinomectin/kg b.w. had no adverse effect on breeding performance of cows or bulls.

4.8 Interaction with other medicinal products and other forms of interaction

No interactions with other medicaments and no other forms of interactions are known.

4.9 Amounts to be administered and administration route

Pour-On use

For single topical application.

To ensure administration of a correct dose, bodyweight should be determined as accurately as possible; accuracy of the dosing device should be checked. The recommended dose rate is 0.5 mg eprinomectin per kg body weight (equivalent to 1 ml/ 10 kg body weight). The product should be applied topically by pouring along the backline in a narrow strip extending from the withers to the tailhead.

To avoid secondary reactions due to the death of Hypoderma larvae in the oesophagus or in the spine, it is recommended to administer the product at the end of warble fly activity and before the larvae reach their resting sites. Consult a veterinary surgeon to determine the appropriate time for treatment

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- and overdosing.

Rainfall before or after treatment will not affect the efficacy of the product. The influence of extreme weather conditions on long term effect of the product is unknown.

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

In adult cattle, after administration of 5 times the recommended dose (2.5 mg eprinomectin/kg body weight), mild hair loss was observed. No other signs of toxicity were seen.

No antidote has been identified.

4.11 Withdrawal period(s)

Cattle (meat & offal): 10 days
Cattle (milk): zero hours.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Antiparasitic products, Avermectins

ATC Vet Code: QP54AA04

5.1 Pharmacodynamic properties

Mode of action

Eprinomectin is a member of the macrocyclic lactone class of endectocides which have a unique mode of action. Compounds of the class bind selectively and with high affinity to glutamate-gated chloride ion channels which occur in invertebrate nerve or 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 parasite.

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 macrocyclic lactones have a low affinity for other mammalian ligand-gated chloride channels, and they do not readily cross the blood-brain barrier.

5.2 Pharmacokinetic properties

The bioavailability of topically applied eprinomectin in cattle is about 30% with most absorption occurring by about 10 days after treatment. Eprinomectin is not extensively metabolized in cattle following topical administration. In all biological matrices, the B1a component of eprinomectin is the single most abundant residue.

Eprinomectin consists of the components B_{1a} (≥ 90%) and B_{1b} (≤ 10%) which differ by a methylene unit and is not extensively metabolized in cattle. Metabolites amount to approximately 10% of the total residues in plasma, milk, edible tissues and faeces.

The metabolism profile is nearly identical, qualitatively and quantitatively, in the above biological matrices and does not change significantly with time after administration of eprinomectin. The percent contribution of B_{1a} and B_{1b} to the overall metabolite profile remains constant. The ratio of the two drug components in the biological matrices is identical to that in the formulation demonstrating that the two eprinomectin components are metabolized with nearly equal rate constants. Since the metabolism and the tissue distribution of the two components are quite similar, the pharmacokinetics of the two components would be also similar.

Since the two components of the closely related avermectin and ivermectin were found to be equally efficacious, it may be concluded that this also applies to the two eprinomectin components.

5.3 Environmental properties

Like other macrocyclic lactones, eprinomectin has the potential to adversely affect non-target organisms. Following treatment, excretion of potentially toxic levels of eprinomectin may take place over a period of several weeks. Faeces containing eprinomectin excreted onto pasture by treated animals may reduce the abundance of dung feeding organisms which may impact on the dung degradation.

Eprinomectin is very toxic to aquatic organisms, is persistent in soils and may accumulate in sediments.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Butylated Hydroxytoluene (E321)
Cetearyl Ethylhexanoate and Isopropyl Myristate
Propylene Glycol Dicaprylocaprate
Denatonium Benzoate
Isopropyl Alcohol

6.2 Major Incompatibilities

None known.

6.3 Shelf life

Shelf-life of the veterinary medicinal product as packaged for sale: 24 months.
Shelf-life after first opening the immediate packaging: 3 months

6.4 Special precautions for storage

Do not store above 30°C. Keep container in the outer carton. Protect from light.

6.5 Nature and composition of immediate packaging

Translucent 250 mL and 1L HDPE containers with integral squeeze measure pour system and white HDPE caps.
White 1L, 2.5L and 5L HDPE backpacks for use with a dosing gun delivery system and white polypropylene screw caps.

Not all packs sizes may be marketed.

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

Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal products should be disposed of in accordance with local requirements.

Extremely dangerous to fish and aquatic life. Do not contaminate ponds, waterways or ditches with the product or empty container.

7. MARKETING AUTHORISATION HOLDER

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

8. MARKETING AUTHORISATION NUMBER

Vm 02000/4342

9. DATE OF FIRST AUTHORISATION

11 June 2014

10. DATE OF REVISION OF THE TEXT

March 2018

Approved 01 March 2018