SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

NEOPRINIL POUR-ON 5 mg/ml pour-on solution for cattle

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1 ml of solution contains:

Active substance:	
Eprinomectin	5.00 mg
Excipient:	
Butylhydroxytoluene (E321)	0.10 mg
All-rac-alpha-tocopherol (E307)	0.06 mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Pour-on solution.
Slightly yellowish, clear oily solution.

4. CLINICAL PARTICULARS

4.1 Target species

Cattle.

4.2 Indications for use

In beef and dairy cattle :

Treatment of infestations by the following parasites sensitive to eprinomectin:

Gastrointestinal roundworms (adults and L4 larvae): *Ostertagia ostertagi* (including inhibited L4 larvae), *Ostertagia lyrata* (only adults), *Haemonchus placei*, *Trichostrongylus axei*, *Trichostrongylus colubriformis, Cooperia sp.* (including inhibited L4), *Cooperia oncophora*, *Cooperia punctata*, *Cooperia pectinata*, *Cooperia surnabada*, *Bunostomum phlebotomum*, *Nematodirus helvetianus*, *Oesophagostomum radiatum*, *Oesophagostomum* sp. (only adults), *Trichuris discolor* (only adults);
Lungworms: *Dictyocaulus viviparus* (adults and L4);
Warbles (parasitic stages): *Hypoderma bovis*, *Hypoderma lineatum;*
Mange mites: *Chorioptes bovis*, *Sarcoptes scabiei* var. *Bovis;*
Sucking lice: *Linognathus vituli*, *Haematopinus eurysternus*, *Solenopotes capillatus*;
Biting lice: *Damalinia bovis*;
Flies: *Haematobia irritans.*

The product protects the animals against reinfestations with:
- *Nematodirus helvetianus* for 14 days.
- *Trichostrongylus axei* and *Haemonchus placei* for 21 days.
- *Dictyocaulus viviparus,,Cooperia oncophora, Cooperia punctata, Cooperia surnabada, Oesophagostomum radiatum* and *Ostertagia ostertagi* for 28 days.

4.3 Contraindications

Do not use in animal species other than those listed in section 4.1 and 4.2.
Do not administer orally or by injection.
Do not use in animals with known hypersensitivity to the active ingredient or to any of the excipients.
Avermectins may not be well tolerated in non-target species (including dogs, cats and horses). Cases of mortality are reported in dogs, especially Collies, bobtail and related breeds and 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 (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 in cattle 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.

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.

For the best results the product should be part of a planned programme to control both internal and external parasites of cattle based on the epidemiology of these parasites.

4.5 Special precautions for use

i) Special precautions for use in animals

For external use only.
To avoid adverse reactions due to the death of warble larvae in the oesophagus or backbone, it is recommended to administer the product after the end of the swarming [illegible] before the larvae reach their sites in the body; consult a veterinary [illegible]e appropriate treatment period.

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.

ii) Special precautions to be taken by the person administering the veterinary medicinal product to animals

This product may be irritating to the skin and eyes and may cause hypersensitivity (allergic reactions).
Avoid direct contact with the skin or eyes during treatment and when handling recently treated animals.
People with known hypersensitivity to eprinomectin should avoid contact with the product.
Wear rubber gloves, boots and a waterproof coat when applying the product.
If accidental skin contact occurs, wash the affected area immediately with soap and water. If accidental eye exposure occurs, flush eyes immediately with water.
Should clothing become contaminated, remove as soon as possible and launder before re-use. This product may affect the central nervous system if accidentally ingested. Avoid accidental ingestion of the product, including by hand to mouth contact. If ingestion does occur, wash the mouth out with water and seek medical advice.
Do not smoke, eat or drink while handling the product.
Wash hands after use

iii) Other precautions

Eprinomectin is very toxic to aquatic organisms, is persistent in soils and may accumulate in sediments. Faeces containing eprinomectin excreted onto pasture by treated animals may temporarily reduce the abundance of dung feeding organisms. Following treatment of cattle with the product, levels of eprinomectin that are potentially toxic to dung fly species may be excreted over a period of more than 4 weeks and may decrease dung fly abundance during that period. In case of repeated treatments with eprinomectin ((as with products of the same anthelmintic class) it is advisable not to treat animals every time on the same pasture to allow dung fauna populations to recover.
Eprinomectin is inherently toxic to aquatic organisms. The product should be used only according to the label instructions. Based on the excretion profile of eprinomectin when administered as the pour-on formulation, treated animals should not have access to watercourses during the first 7 days after treatment.

4.6 Adverse reactions (frequency and seriousness)

Very rare transient licking reactions, skin tremor at the administration site, minor local reactions such as the occurrence of dandruff and skin scales at the administration site have been observed.

The frequency of adverse reactions is defined using the following convention:

- Very common (more than 1 in 10 animals treated displaying adverse reaction(s))
- Common (more than 1 but less than 10 animals in 100 animals treated)
- Uncommon (more than 1 but less than 10 animals in 1,000 animals treated)
- Rare (more than 1 but less than 10 animals in 10,000 animals treated)
- Very rare (less than 1 animal in 10,000 animals treated, including isolated reports

4.7 Use during pregnancy, lactation or lay

Laboratory studies (rat, rabbit) have not produced any evidence of a teratogenic or embryotoxic effects due to the use of eprinomectin at therapeutic doses. The safety of the veterinary medicinal product in cattle has been established during pregnancy and lactation and in reproductive bulls. Can be used during pregnancy and lactation as well as in reproductive bulls.

4.8 Interaction with other medicinal products and other forms of interaction

Since eprinomectin binds strongly to plasmatic proteins, this should be taken into account if it is used in association with other molecules having the same characteristics.

4.9 Amounts to be administered and administration route

For external use.
Pour-on use.
To be administered topically in one single treatment at the dose rate of 500 µg eprinomectin per kg bodyweight equivalent to 1 ml per 10 kg bodyweight.
Apply the pour-on solution along the mid-line of the back in a narrow strip between the withers and tail head.
To ensure administration of a correct dose, bodyweight should be determined as accurately as possible and 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- and overdosing.

All the animals belonging to the same group should be treated at the same time.

Squeeze-Measure Pour-on system (1 litre bottle)
1 and 2. Remove the protective aluminium seal from the bottle.
3 and 4. Screw the dosing cup to the bottle.
Set the dose by turning the top section of the cup to align the correct bodyweight with the pointer.
When body weight is between marking, use the higher setting.
5. Hold the bottle upright and squeeze it to deliver a slight excess of the required dose as indicated by the calibration lines.
6 and 7. By releasing the pressure, the dose automatically adjusts to the correct level
Take the dosing cup off the bottle after use and screw the cap on the bottle.

Can (2.5 litre and 5 litre can)

Connect an appropriate dosing gun and draw-off tubing to the back-pack as follows.

1 and 2. Remove the protective aluminium seal from the bottle.

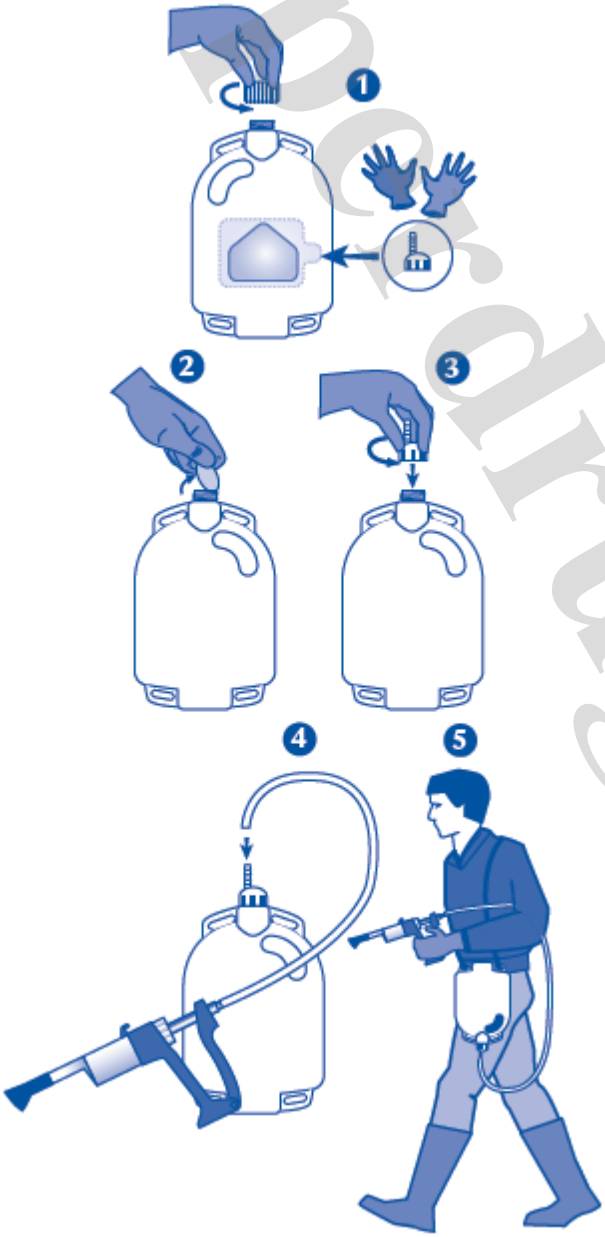
3. Replace the shipping cap with the cap having the draw-off tubing. Tighten the draw-off cap.

4. Connect one side of the tube to the draw-off cap and the other side to the dosing gun.

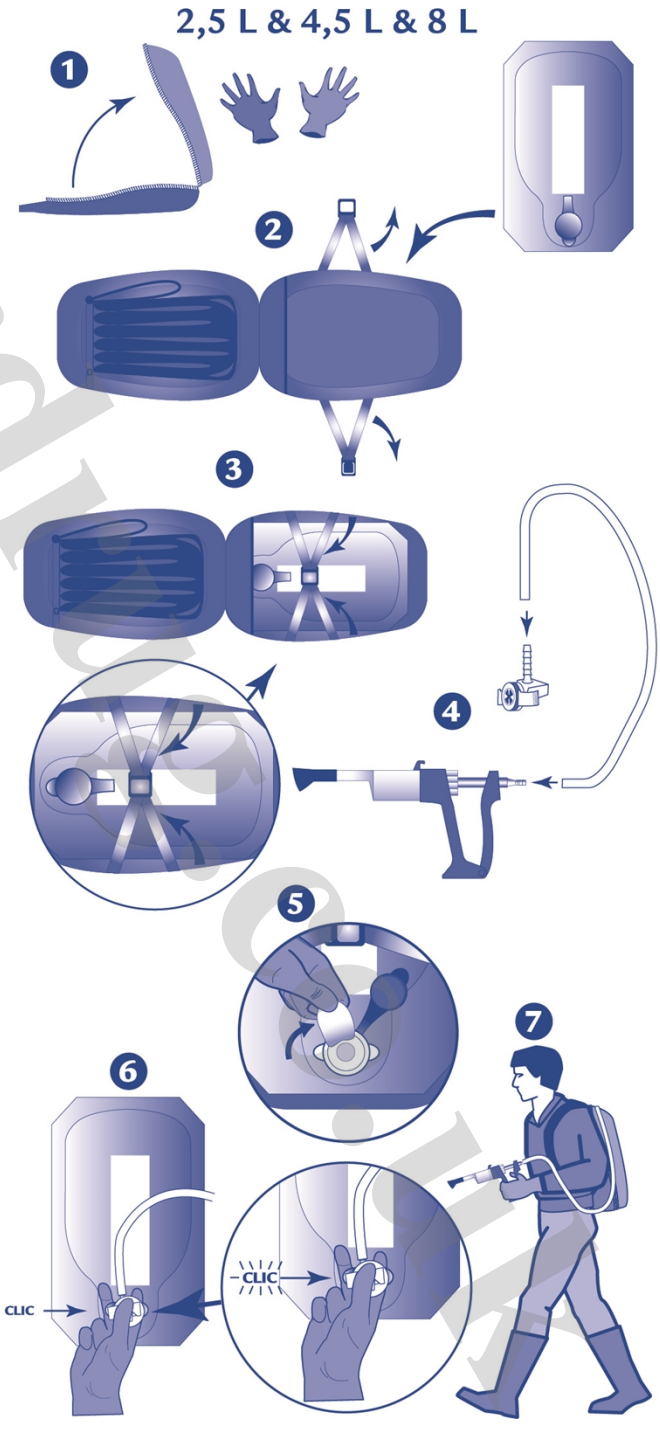
5. Gently prime the dosing gun, checking before use that all connections are tight.

Follow the gun manufacturer's instructions for adjusting the dose and proper use and maintenance of the dosing gun and draw-off tubing.

When body weight is between marking, use the higher setting.



FlexiBag (2.5 litre, 4.5 litre and 8 litre flexible pouch)
Connect an appropriate dosing gun to the FlexiBag as follows.
1 to 4. Connect one side of the tube to the coupling E-lock system draw-off and the other side to the dosing gun.
5 and 6. Plug the E-lock coupling system to the FlexiBag.
7. Gently prime the dosing gun, checking before use that all connections are tight.
Follow the gun manufacturer's instructions for adjusting the dose and proper use and maintenance of the dosing gun.
When body weight is between marking, use the higher setting.



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

No signs of toxicity have been observed after administration of up to 5 times the recommended dose. No specific antidote has been identified.

4.11 Withdrawal period(s)

Meat and offal : 15 days.
Milk : zero hours.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: endectocides, macrocyclic lactones, avermectins.
ATCvet code: QP54AA04.

5.1 Pharmacodynamic properties

Eprinomectin is a molecule with an endectocidal activity belonging to the macrocyclic lactone class. Compounds of the class bind with high affinity to glutamate-gated chloride ion channels which occur in invertebrate nerve or muscle cells. These compounds bind selectively to these channels, which 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).

5.2 Pharmacokinetic particulars

The bioavailability of topically applied eprinomectin in cattle is about 30% with most absorption occurring within 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} ($\geq$ 90%) and B_{1b} ($\leq$ 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.
Eprinomectin is strongly bound to plasma proteins (99%). Faeces is the major route of elimination.

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 and may accumulate in sediments. Eprinomectin is persistent in soils.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Butylhydroxytoluene (E321)
All-rac-alpha-tocopherol (E307)
Propylene glycol dicaprylocaprate

6.2 Major 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: 3 years.
Shelf-life after first opening the immediate packaging (bottles and cans): 1 year.
Shelf-life after first opening the immediate packaging (pouches): 2 years.

6.4 Special precautions for storage

This veterinary medicinal product does not require any special storage conditions.

6.5 Nature and composition of immediate packaging

- 1 litre white opaque HDPE bottles with a removable aluminium seal, a HDPE cap and a PP dosing device equipped with a delivering cap graduated each 5 ml up to 60 ml;
- 2.5 and 5 litres white opaque HDPE cans with a removable aluminium seal, a PP cap and a PP coupling vented cap;
- 2.5 litres, 4.5 litres and 8 litres multi-layer PET/aluminium/PA/PE flexible pouches with a PP cap and its specific coupling POM “E-lock”.

Not all pack 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

Extremely dangerous to fish and aquatic life. Do not contaminate ponds, waterways or ditches with the product or empty container. Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal products should be disposed of in accordance with local requirements.

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8. MARKETING AUTHORISATION NUMBER

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9. DATE OF FIRST AUTHORISATION

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10. DATE OF REVISION OF THE TEXT

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