SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

EPRINEX Pour-On for Beef and Dairy Cattle
(eprinomectin)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active substance
Eprinomectin 5 mg

Excipients
For the full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Pour-on solution.

4. CLINICAL PARTICULARS

4.1 Target species

Beef and dairy cattle.

4.2 Indications for use, specifying the target species

Indicated for treatment and control of the following parasites:

Gastronintestinal Roundworms	Adult	L4	Inhibited L4
Ostertagia spp.	◆	◆	
Ostertagia lyrata	◆		
Ostertagia ostertagi	◆	◆	◆
Cooperia spp.	◆	◆	◆
Cooperia oncophora	◆	◆	
Cooperia pectinata	◆	◆	
Cooperia punctata	◆	◆	
Cooperia surnabada	◆	◆	
Haemonchus placei	◆	◆	
Trichostrongylus spp.	◆	◆	
Trichostrongylus axei	◆	◆	
Trichostrongylus colubriformis	◆	◆	
Bunostomum phlebotomum	◆	◆	
Nematodirus helvetianus	◆	◆	
Oesophagostomum spp.	◆		
Oesophagostomum radiatum	◆	◆	

Trichuris spp	◆	
Lungworms		
Dictyocaulus viviparus	◆	◆
Warbles (parasitic stages)		
Hypoderma bovis		
H. lineatum		
Mange Mites		
Chorioptes bovis		
Sarcoptes scabiei		
Lice		
Damalinia bovis (biting lice)		
Linognathus vituli (sucking lice)		
Haematopinus eurysternus (sucking lice)		
Solenopotes capillatus (sucking lice)		

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:
Ostertagia ostertagi, O. lyrata, Cooperia oncophora, C. punctata, C. surnabada, Trichostrongylus axei, T. colubriformis.

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 Contra-indications

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 apply to areas of the backline covered with mud or manure.
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.

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.

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.

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

Operators should wear rubber gloves 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.
Do not smoke, eat or drink while handling the product.
Wash hands after use.
Should clothing become contaminated, remove as soon as possible and launder before re-use. In the event of ingestion, wash out mouth with water and seek medical advice.

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

Administer only by topical application at the dose rate of 1 ml per 10 kg of body weight, corresponding to the recommended dose rate of 0.5 mg eprinomectin per kg b.w. The product should be applied topically by pouring along the backline in a narrow strip extending from the withers to the tailhead. The following dosing packs are available:

Dosing cup with Measure-Squeeze-Pour System (250 ml and 1 litre bottles)

The 250 ml pack contains one 25 ml dosing cup and one dip tube.
The 1 litre pack contains one 60 ml dosing cup and one dip tube.

Insert the dip tube into base of the dosing cup. Leave the “slotted end” of the dip tube exposed in the bottom of the bottle. Unscrew the bottle cap from the top of the bottle. Screw the dosing cup onto the top of the bottle.

Measure: To select the correct dose rate, rotate the adjuster cap at the top of the cup in either direction to position the dose indicator to the weight of the animal you want to treat. When body weight is between markings, use the higher setting.

Squeeze the bottle gently to fill the dosing cup to the required dose. Release your grip and any excess will return to the bottle.

Pour: Apply the full dose by tipping and pouring along the backline of the animal until the dosing cup is empty.

The dosing cup should not remain attached to the bottle when not in use. Detach the dosing cup after each use and replace the bottle cap.

Back-pack (2.5 and 5 litre packs)
Connect the dosing gun and draw-off tubing to the back-pack as follows.
Attach the open end of the draw-off tubing to an appropriate dosing gun.
Attach draw-off tubing to the cap with the stem that is included in the pack. Replace shipping cap with the cap having the draw-off tubing. Tighten the draw-off cap.
Gently prime the dosing gun, checking for leaks.

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

Rainfall at anytime before or after treatment will not affect the efficacy of the product.
The product is intended for use on cattle only. Do not use in other species.

To ensure administration of a correct dose, bodyweight should be determined as accurately as possible; accuracy of the dosing device should be checked.

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

No signs of toxicity appeared when 8-week old calves were treated at up to 5x the therapeutic dose (2.5 mg eprinomectin/kg b.w.) 3 times at 7-day intervals.

One calf treated once at 10x the therapeutic dose (5 mg/kg b.w.) in the tolerance study showed transient mydriasis. There were no other adverse reactions to treatment.

No antidote has been identified.

4.11 Withdrawal periods

Meat may only be taken for human consumption from 15 days after the last treatment.

There is no milk withdrawal period for lactating dairy cattle. Milk from cows may be used for human consumption at any time following treatment.

5. PHARMACOLOGICAL PROPERTIES

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

Metabolism

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 B_{1a} 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.

The contribution of eprinomectin B_{1a} to the total radioresidue level remained relatively constant between 7 days and 28 days after treatment - for example, between 84% and 90% in liver, the proposed principal target tissue.

Maximum plasma concentration

Pharmacokinetic studies were conducted in nongravid, nonlactating dairy cows which were dosed with eprinomectin by i.v. (25, 50, and 100 mcg/kg doses) and topical (500 mcg/kg) routes in a cross-over design. The plasma clearance was independent of i.v. dose, indicating that the plasma concentration increased

proportionally to the dose. Following topical administration, peak plasma concentrations of 22.5 ng/mL (range 17.2 - 31.9 ng/mL) were observed 2 - 5 days postdose. Bioavailability of eprinomectin by the topical route was 0.29 (range 0.21 - 0.36).
Most of the drug absorption occurred within 7 - 10 days postdose.
The mean residence time (the average time it takes the animal to clear the drug from the time of absorption) of topically administered eprinomectin was calculated to be 165 hours.

Tissue residues

The level of total residues in tissues of beef cattle and lactating dairy cows was of the same order with liver > kidney > fat > muscle.

The distribution of total residue in edible tissues differs from that seen with other macrocyclic lactones such as abamectin and ivermectin. For these compounds, residue concentrations in fat were much closer to those in liver, and fat contained significantly higher total residue concentrations than kidney, whereas the eprinomectin residue concentrations in fat were much lower than those in liver and kidney.

The half-life for depletion of total residue was about 8 days for all 4 tissues in cattle. Eprinomectin B_{1a} concentration depleted at a similar rate to that of total residue.

Milk residues

Twenty dairy cows were treated with unlabeled eprinomectin at the recommended dose of 0.5 mg/kg of body weight. The maximum concentration of eprinomectin B_{1a} in milk ranged from < 2.3 ng/ml (the limit of quantitation) to 11.36 ng/ml, with the peak occurring 2-3 days after treatment in most of the animals.

Excretion

Faeces was the major route of elimination of the drug in beef cattle and dairy cows.
In beef cattle, faeces and urine were collected from 2 steers, and the amount of drug excreted up to 28 days after dosing was determined as 15-17% and 0.35% in faeces and urine, respectively.
A further 53-56% of the dose was recovered from the skin at the application site collected from 3 animals sacrificed at 28 days after dosing.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Butylated hydroxytoluene
Propylene glycol octanoate decanoate

6.2 Incompatibilities

None known

6.3 Shelf-life

Shelf-life of the veterinary medicinal product as packaged for sale:
3 years.

6.4 Special precautions for storage

Keep the container in the outer carton. Protect from light. Store upright.
The dosing cup should not be stored attached to the bottle when not in use. Remove the cup after each use and replace with the bottle cap.

6.5 Nature and composition of immediate packaging

EPRINEX Pour-On for Beef and Dairy Cattle is available in four pack sizes - 250 ml, and 1 litre high density polyethylene bottles, and 2.5 litre and 5 litre high density polyethylene flexipacks.
The 250 ml bottle is provided with a 25 ml dosing cup (screw-on-squeeze-and-pour measuring chamber). Each bottle contains sufficient solution to treat 10 head of 250 kg cattle.
The 1 litre bottle is provided with a 60 ml dosing cup (screw-on-squeeze-and-pour measuring chamber). Each bottle contains sufficient solution to treat 40 head of 250 kg cattle.
The 2.5 litre pack is a back-pack designed for use with a suitable automatic dispensing gun. Each pack contains sufficient solution to treat 100 head of 250kg cattle.
The 5 litre pack is a back-pack designed for use with a suitable automatic dispensing gun. Each pack contains sufficient solution to treat 200 head of 250kg cattle.

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, if appropriate

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

Boehringer Ingelheim Animal Health UK Ltd
Ellesfield Avenue
Bracknell
Berkshire
RG12 8YS

8. MARKETING AUTHORISATION NUMBER

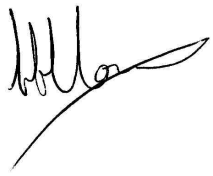
Vm 08327/4157

9. DATE OF FIRST AUTHORISATION

02 July 1997

10. DATE OF REVISION OF THE TEXT

November 2018



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