SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

EpriMole 5mg/ml pour-on solution for cattle

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active substance:
Eprinomectin 5.0 mg
……

Excipients:
Butylhydroxytoluene (E321) 0.1 mg
……

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Pour-on solution
Clear slightly yellow solution

4. CLINICAL PARTICULARS

4.1 Target species

Cattle (beef and dairy cattle).

4.2 Indications for use, specifying the target species

Treatment of infestation by the following parasites sensitive to eprinomectin:

PARASITE	ADULT	L4	Inhibited L4
Gastrointestinal Roundworms:			
Ostertagla spp.	◆	◆	
O. lyrata	◆		
O. ostertagi	◆	◆	◆
Cooperia spp.	◆	◆	◆
C. oncophora	◆	◆	
C. pectinata	◆	◆	
C. punctata	◆	◆	
C. surnabada	◆	◆	
Haemonchus placei	◆	◆	
Trichostrongylus spp.	◆	◆	
T. axei	◆	◆	
T. colubriformis	◆	◆	
Bunostomum phlebotomum	◆	◆	

Nematodirus helvetianus	◆	◆
Oesophagostomum spp.	◆	
O. radiatum	◆	◆
Trichuris spp.	◆	
Lungworm:		
Dictyocaulus viviparus	◆	◆

Warbles (parasitic stages)
Hypoderma bovis
Hypoderma lineatum

Mange mites
Chorioptes bovis
Sarcoptes scabiei var. *bovis*

Lice
Linognathus vituli
Damalinia bovis
Haematopinus eurysternus
Solenopotes capillatus

PROLONGED ACTIVITY
Applied as recommended, the product controls reinfections with:

Parasite	**Prolonged Activity**
Dictyocaulus viviparus	Up to 28 days
Ostertagia ostertagi	Up to 28 days
Ostertagia lyrata	Up to 28 days
Oesophagostomum radiatum	Up to 28 days
Cooperia oncophora	Up to 21 days
Cooperia surnabada	Up to 21 days
Cooperia punctata	Up to 21 days
Trichostrongylus axei	Up to 21 days
Trichostrongylus colubriformis	Up to 21 days
Haemonchus placei	Up to 14 days
Nematodirus helvetianus	Up to 14 days

For best results the veterinary medicinal product should be part of a programme 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 cases of hypersensitivity to the active substance or to any of the excipients.

4.4 Special warnings for each target species

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.
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.

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.

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.

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.

4.5 Special precautions for use

Special precautions for use in animals
For external use only.
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.

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

- This product may be irritating to skin and eyes and may cause hypersensitivity.
- Avoid skin and eye contact with the product during treatment and when handling recently treated animals.
- Individuals with known hypersensitivity to the active substance or to any of the excipients should avoid contact with the product.
- Users should wear rubber gloves, boots and a waterproof coat when applying the product.
- If accidental eye exposure occurs, flush eyes immediately with water and seek medical advice if irritation persists.

- If accidental skin contact occurs, wash the affected area immediately with soap and water.
- Should clothing become contaminated, remove as soon as possible and launder before re-use.
- 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.

Other precautions
Eprinomectin is very toxic to dung fauna and 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)

Pruritus and alopecia have been observed in very rare cases, after the use of the veterinary medicinal product.

The frequency of adverse reactions is defined using the following convention:
- very common (more than 1 in 10 animals treated displaying adverse reactions)
- 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

Pregnancy:
Can be used during pregnancy.
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.

Lactation:
May be used in dairy cattle during all stages of lactation.

4.8 Interaction with other medicinal products and other forms of interaction

None known.

4.9 Amounts to be administered and administration route

Pour-on use. For single administration only.

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

Administer only by topical application at the dose rate of 0.5 mg eprinomectin per kg bodyweight, corresponding to the recommended dose rate of 1 ml per 10 kg bodyweight. The product should be applied topically by pouring along the backline in a narrow strip extending from the withers to the tailhead.

Method of administration
For 250 ml and 1 liter bottles:

- Attach the dose dispenser to the bottle.
- Set the dose by turning the top section of the dose dispenser to align the correct bodyweight with the pointer inside the dose dispenser. When bodyweight is between markings, use the higher setting.
- Hold the bottle upright and squeeze it to deliver a slight excess of the required dose as indicated by the calibration lines.
- By releasing the pressure, the dose automatically adjusts to the correct level. Tilt the bottle to deliver the dose. For the 1 litre bottle: when a 10 ml or 15 ml dose is required, turn the pointer to “STOP” before delivering the dose. The off (STOP) position will close the system between dosing.
- The dose dispenser should not be stored attached to the bottle when not in use. Remove the dose dispenser after each use and replace with the bottle cap.

For 2.5 and 5 litre back-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.

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 the treatment.
No antidote has been identified.

4.11 Withdrawal period(s)

Meat and offal: 15 days
Milk: Zero hours

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Antiparasitic products, Insecticides and Repellents. Endectocides, Macrocyclic Lactones, Avermectins, eprinomectin.
ATCvet code: QP54AA04

5.1 Pharmacodynamic properties

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 particulars

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} ($\geq$ 90%) and B_{1b} ($\leq$ 10%) which differ by a methylene unit. 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.

Environmental properties
See section 4.5 (other precautions).
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

Butylhydroxytoluene (E321)
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: see expiry date.

6.4 Special precautions for storage

Keep the container in the outer carton in order to protect from light.
This veterinary medicinal product does not require any special temperature storage conditions.

6.5 Nature and composition of immediate packaging

250 ml and 1L HDPE bottle
2.5 and 5L HDPE back pack
Sealed foil and tamper evident HDPE screw cap with polypropylene liner

250 ml bottle with dose dispenser of 25 ml
1L bottle with dose dispenser of 60 ml
2.5L back-pack with a high density polyethylene polypropylene co-polymer dispensing cap
5L back-pack with a high density polyethylene polypropylene co-polymer dispensing cap

One bottle or one back-pack per cardboard box.
The 2.5 litre and 5 litre back-packs are designed for use with a suitable automatic dispensing gun.
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 lakes or waterways with the product or used containers. Any unused veterinary medicinal product or waste material derived from such veterinary medicinal product should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Boehringer Ingelheim Animal Health UK Limited
Ellesfield Avenue
Bracknell
Berkshire
RG12 8YS
United Kingdom

8. MARKETING AUTHORISATION NUMBER

Vm 08327/4281

9. DATE OF FIRST AUTHORISATION

10 October 2016

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