SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Eprecis 5 mg/ml pour-on solution for cattle, sheep and goats

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active substance:
Eprinomectin 5.0 mg

Excipients:
Butylhydroxytoluene (E321) 0.10 mg
all-rac-α-tocopherol (E307) 0.06 mg

For the full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Pour-on solution.
Pale yellow to yellow clear solution.

4. CLINICAL PARTICULARS

4.1 Target species

Cattle (beef and dairy cattle)
Sheep
Goats

4.2 Indications for use, specifying the target species

Treatment of infections by the following endo- and ectoparasites sensitive to eprinomectin:

Cattle:

	Adult	L4	Inhibited L4
Gastrointestinal roundworms			
Ostertagia ostertagi	●	●	●
Ostertagia lyrata	●		
Ostertagia spp.	●	●	
Cooperia oncophora	●	●	
Cooperia pectinata	●	●	
Cooperia surnabada	●	●	
Cooperia punctata	●	●	
Cooperia spp.	●	●	●
Haemonchus placei	●	●	
Trichostrongylus axei	●	●	
Trichostrongylus	●	●	

colubriformis			
Trichostrongylus spp.	●	●	
Bunostomum phlebotomum	●	●	
Nematodirus helvetianus	●	●	
Oesophagostomum radiatum	●	●	
Oesophagostomum spp.	●		
Trichuris spp.	●		
Lungworms			
Dictyocaulus viviparus	●	●	

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 (Bovicola) bovis*;
Flies: *Haematobia irritans.*

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

For best results, this 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.

Sheep:
Gastrointestinal roundworms (adults)
Teladorsagia circumcincta (pinnata/trifurcata)
Haemonchus contortus
Trichostrongylus axei
Trichostrongylus colubriformis
Nematodirus battus
Cooperia curticei
Chabertia ovina
Oesophagostomum venulosum

Lungworm (adult)
Dictyocaulus filaria

Goats:
Gastrointestinal roundworms (adult)
Teladorsagia circumcincta (pinnata/trifurcata)
Haemonchus contortus
Trichostrongylus axei
Trichostrongylus colubriformis
Nematodirus battus
Cooperia curticei

Oesophagostomum venulosum

Lungworm (adult)
Dictyocaulus filaria

4.3 Contraindications

This veterinary medical product is formulated only for topical application for cattle, sheep and goats, including lactating animals.
Do not administer orally or by injection.
Do not use in other animal species.
Do not use in known cases of hypersensitivity to the active substance or to any of the excipient(s).

4.4 Special warnings for each target species

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

In order to limit cross-transfer of eprinomectin, treated animals may be separated from untreated animals. Non-compliance with this recommendation may lead to residue violations in untreated animals.

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 body weight, misadministration of the veterinary medicinal 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 while resistance to eprinomectin has been reported in sheep and goats within the EU. However resistance to other macrocyclic lactones has been reported in nematode populations in cattle, sheep and goats within the EU, which may be associated with side-resistance to eprinomectin. Therefore, use of this veterinary medicinal 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 some mites, 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.
The veterinary medicinal product should be applied only on healthy skin.
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.
The death of warble fly larvae in the oesophagus or spinal cord canal may lead to secondary reactions. In order to avoid secondary reactions due to the death of Hypoderma larvae in the oesophagus or the spine, it is recommended to administer the veterinary medicinal product at the end of the period of fly activity and before the larvae reach their resting site.
The details provided in overdose section apply.

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

This veterinary medicinal product may be irritating to the skin and eyes. Avoid contact with eyes and skin.
Operators should wear rubber gloves, boots and waterproof coat when applying the veterinary medicinal 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 irritation persist, seek medical advice.
Do not smoke, eat or drink while handling the veterinary medicinal product.
Wash hands after use. Should clothing become contaminated, remove as soon as possible and launder before re-use.
Do not ingest.
In the event of ingestion, wash out mouth with water and seek medical advice and show the package leaflet or the label to the physician.
People with known hypersensitivity to the active substance or to any of the excipients should avoid contact with the veterinary medicinal product.
Eprinomectin can be transferred to breast milk. Therefore, breast-feeding users should handle the product with great care.

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, sheep and goats.
The risk to aquatic ecosystems will be further reduced by keeping treated animals away from water bodies for two to five weeks after treatment.

4.6 Adverse reactions (frequency and seriousness)

In very rare cases, pruritus and alopecia have been observed 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 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. Laboratory studies in cattle have not produced any evidence of a teratogenic or foetotoxic effect at the recommended therapeutic dose. Can be used in dairy cattle during pregnancy and lactation.

The safety of eprinomectin during pregnancy in sheep and goats has not been tested. Use only according to the benefit/risk assessment of the responsible veterinarian in these species.

4.8 Interaction with other medicinal products and other forms of interaction

Since eprinomectin binds strongly to plasma 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

Pour-on use. For single application 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 overdosing.

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

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

Sheep and goats:
Administer only by topical application at the dose rate of 1.0 mg eprinomectin per kg b.w., corresponding to the recommended dose rate of 2 ml of the veterinary medicinal product per 10 kg b.w.. When administering the veterinary medicinal product along the backline, part the fleece/coat and place applicator nozzle or bottle spout against the skin.

Method of administration:
For the 250 ml presentation:
The bottle is equipped with an integrating dosing system, and has two openings. One opening is connected to the body of the container and the other one to the dispensing chamber (dosing system).
Unscrew the tamper-evident cap and remove the seal of the dispensing chamber (integrated dosing system allowing 5-ml doses and 10-ml doses).
Squeeze the bottle to fill the dispensing chamber with the required volume of veterinary medicinal product.

For the 1 L, 2.5 L and 5 L presentations:
To be used with an appropriate dosing system such as a dosing gun and coupling vented cap.
Unscrew the polypropylene (PP) simple cap. Remove the protective seal from the bottle. Screw a coupling vented cap on the bottle and make sure it is tightened. Connect the other side to a dosing gun.
Follow the gun manufacturer's instructions for adjusting the dose and proper use and maintenance of the dosing gun and vented cap.
After use, coupling vented caps should be removed and replaced by PP simple cap.

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

No clinical 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 clinical signs of toxicity were observed when 17-week old sheep were treated at doses up to 5 times the therapeutic dose (5 mg eprinomectin/kg bodyweight) 3 times at 14-day intervals.
No antidote has been identified.

4.11 Withdrawal period(s)

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

Sheep:
Meat and offal: 2 days
Milk: zero hours.

Goats:
Meat and offal: 1 day
Milk: zero hours.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: endectocides, macrocyclic lactones, avermectins
ATC vet code: QP54AA04

5.1 Pharmacodynamic properties

Eprinomectin is a member of the macrocyclic lactone class of endectocides. Compounds of this 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

Eprinomectin is strongly bound to plasma proteins (99%).

Pharmacokinetic studies have been conducted in lactating and non-lactating animals, administered topically at a single dosage of 0.5 mg/kg body weight in cattle and at 1 mg/kg bodyweight in sheep and goats.

For cattle, results from two representative studies found mean peak plasma concentrations of 9.7 and 43.8 ng/ml that were observed at 4.8 and 2.0 days post dose. The corresponding elimination half-lives in plasma were 5.2 and 2.0 days, and mean area-under-the-curve values of 124 and 241 ng.day/ml.

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. The faeces are the major route of elimination in both beef cattle and dairy cows.
For sheep, a mean peak plasma concentration (Cmax) of 6.20 ng/ml was observed following a topical dose of 1mg/kg. The elimination half-life in plasma was 6.4 days with mean area under the curve (AUClast) value of 48.8 ng.day/ml.
For goats, peak mean plasma concentrations ranging from 3 to 13.1 ng/ml were observed from day 1 to day 2 post dose. The elimination half-life in plasma ranged from less than one day to 3 days with area under the curve mean values ranging from 15.7 to 39.1 ng.day/ml.

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. In all biological matrices, the B1a component of eprinomectin is the single most abundant residue. 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.
An *in vitro* microsomal metabolism study was conducted using liver microsomes isolated from cattle, sheep and goats. It showed that the differences in pharmacokinetics observed between cattle, sheep and goats do not result from differences in the rate or extent of metabolism but suggests more complete absorption of eprinomectin by cattle.

5.3 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.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Butylhydroxytoluene (E321)
all-rac-α-tocopherol (E307)
Propylene glycol dicaprylocaprate

6.2 Major incompatibilities

Not applicable.

6.3 Shelf life

Shelf-life of the veterinary medicinal product as packaged for sale: 30 months.
Shelf-life after first opening the immediate packaging: 6 months.

6.4. Special precautions for storage

250 ml: keep the bottle in the outer carton in order to protect from light.
1 L, 2.5 L, 5 L: this veterinary medicinal product does not require any special storage conditions.

6.5 Nature and composition of immediate packaging

- Squeeze-measure pour-on system:
250 ml translucent high density polyethylene (HDPE) bottle including 10 ml dispenser graduated each 5 ml, with removable aluminium/PE seals and PE screw cap.

- Back pack:
1 L, 2.5 L or 5 L white HDPE bottles, with a removable aluminium/PE seal and a polypropylene (PP) screw cap.

1 L, 2.5 L or 5 L white HDPE bottles, with a removable aluminium/PE seal and a polypropylene (PP) screw cap included in a cardboard box.

Package sizes:
1 bottle of 1L
1 bottle of 2.5L
1 bottle of 5L
Cardboard box with 1 bottle of 250 ml.
Cardboard box with 1 bottle of 1L.
Cardboard box with 1 bottle of 2.5L.
Cardboard box with 1 bottle of 5L.

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

The veterinary medicinal product is dangerous for aquatic organisms. Do not contaminate lakes and streams with the veterinary medicinal product or with used containers.

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

7. MARKETING AUTHORISATION HOLDER

Ceva Animal Health Ltd
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Mercury Park
Wycombe Lane
Wooburn Green
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Buckinghamshire
HP10 0HH
United Kingdom

8. MARKETING AUTHORISATION NUMBER

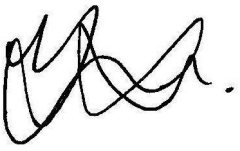
Vm 15052/4072

9. DATE OF FIRST AUTHORISATION

19 August 2015

10. DATE OF REVISION OF THE TEXT

September 2022



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