July 2022

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Eprinex Multi 5 mg/ml pour-on solution for cattle, sheep and goats (AT, BE, BG, HR, CY, CZ, EE, , FR, EL, HU, IE, IT, LV, LT, LU, NL, PL, PT, RO, SK, SI, ES,, UK)
Eprinex vet. 5 mg/ml pour-on solution for cattle, sheep and goats (for DK, FI, NO, SE)

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)
Sheep
Goats

4.2 Indications for use, specifying the target species

Treatment of infestation by the following parasites sensitive to eprinomectin:

Cattle

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

Flies
Haematobia irritans

PROLONGED ACTIVITY
Applied as recommended, the product prevents reinfestations with:

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

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

Nasal Bots (L1, L2, L3)
Oestrus ovis

Goats

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

Lungworm (adult)
Dictyocaulus filaria

Nasal Bots (L1, L2, L3)
Oestrus ovis

Warbles (L1, L2, L3)
Przhevalskiana silenus

For best results the veterinary medicinal product should be part of a programme to control both internal and external parasites of sheep and goats based on the epidemiology of these parasites.

4.3 Contraindications

Do not use in other animal species. Avermectins can cause fatalities in dogs, especially Collies, Old English Sheepdogs and related breeds and crosses, and also in turtles/tortoises.
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.

In cattle, rainfall before, during or after the application of the product, has been shown to have no impact on its efficacy. It also has been demonstrated that haircoat length has no impact on the product's efficacy. The effect of rainfall and haircoat length on efficacy has not been evaluated in sheep and goats.

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

Unnecessary use of antiparasitics or use deviating from the instructions given in the SPC may increase the resistance selection pressure and lead to reduced efficacy. The decision to use the product should be based on confirmation of the parasitic species and burden, or of the risk of infestation based on its epidemiological features, for each herd.

Repeated use for an extended period, particularly when using the same class of substances, increases the risk of resistance development. Within a herd, maintenance of susceptible refugia is essential to reduce that risk. Systematically applied interval-based treatment and treatment of a whole herd should be avoided. Instead, if feasible, only selected individual animals or subgroups should be treated (targeted selective treatment). This should be combined with appropriate husbandry and pasture management measures. Guidance for each specific herd should be sought from the responsible veterinarian.

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 goats and sheep 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.

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 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.

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

People with known hypersensitivity to the active substance or to any of the excipients should avoid contact with the product.
This product may be irritating to skin and eyes. Avoid contact with eyes and skin.
Operators should wear rubber gloves, boots and 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.
Should accidental eye exposure occur, flush eyes immediately with plenty of clean water. Should irritation persist, seek medical advice.
Do not ingest.
In case of accidental ingestion, rinse out mouth thoroughly with water, seek medical advice immediately and show the package insert or the label to the physician.
Do not smoke, eat or drink while handling the product.
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 repeated use of eprinomectin (and products of the same anthelmintic class).
In order to reduce the risk to aquatic ecosystems, treated animals should not have direct access to 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 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. The product 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

No interactions with other medicines and no other forms of interactions are known.
Since eprinomectin binds extensively 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

Pour-on use. For single application only.

To ensure administration of a correct dose, bodyweight should be determined as accurately as possible; 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. Underdosing could result in ineffective use and may favour resistance development.

The product should be applied topically by pouring along the backline in a narrow strip extending from the withers to the tailhead.

Cattle:
Administer 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.

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

Method of administration
For 250 ml and 1 litre 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 were observed when 8-week old calves were treated at up to 5 times the therapeutic dose (2.5 mg eprinomectin/kg bodyweight.) 3 times at 7-day intervals.
One calf treated once at 10 times the therapeutic dose (5 mg/kg bodyweight.) in the tolerance study showed transient mydriasis. There were no other adverse reactions to the treatment.

No 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: Antiparasitic products, Insecticides and Repellent, Endectocides, Macrocyclic Lactones, Avermectins. eprinomectin
ATC-vet code: QP54AA04

5.1 Pharmacodynamic properties

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

Eprinomectin is bound extensively 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.

Eprinomectin is not extensively metabolized in cattle following topical administration.
Faeces was the major route of elimination of the drug in beef cattle and dairy cows.

For sheep, a mean peak plasma concentration (C_{max}) of 6.20 ng/ml was observed following a topical dose of 1mg/kg. The half-life in plasma was 6.4 days with mean area under the curve (AUC_{last}) value of 48.8 ng*day/ml.

For goats, peak mean plasma concentrations ranging from 3 to 13.1 ng/ml were observed on average from 17 hours to 2 days post dose. The mean half-life in plasma ranged from one day to up to 5 days with area under the curve mean values ranging from 15.7 to 39.1 ng*day/ml.

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.

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.
Store container upright

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 2 dose dispensers of 25 ml (1 for cattle, 1 for sheep/goat)
1L bottle with 2 dose dispensers (1 of 60 ml for cattle, 1 of 25 ml for sheep/goat)
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

To be filled nationally

8. MARKETING AUTHORISATION NUMBER(S)

To be filled nationally

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation:

Date of last renewal:

10 DATE OF REVISION OF THE TEXT

XX/XX/2022

PROHIBITION OF SALE, SUPPLY AND/OR USE

Not applicable