Summary of Product Characteristics

1 NAME OF THE VETERINARY MEDICINAL PRODUCT

Zeromectin 5 mg/ml Pour-on Solution for beef and dairy cattle

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

One ml contains:
Active substance:
Eprinomectin 5 mg

Excipients:
Butylated hydroxytoluene (E321) 10 mg

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Pour-on solution.
Clear solution.

4 CLINICAL PARTICULARS

4.1 Target Species

Cattle (beef and dairy cattle)

4.2 Indications for use, specifying the target species

Treatment of infestations by the following internal and external parasites sensitive to eprinomectin:

Gastrointestinal roundworms (adults and fourth-stage larvae)
Ostertagia spp.
*Ostertagia lyrata (*adults only)
Ostertagia ostertagi (including inhibited L4)
Cooperia spp. (including inhibited L4)
Cooperia oncophora
Cooperia pectinata
Cooperia punctata
Cooperia surnabada
Haemonchus placei
Trichostrongylus spp.
Trichostrongylus axei
Trichostrongylus colubriformis
Bunostomun phlebotomum
Nematodirus helvetianus
Oesophagostomum spp. (adults only)
Oesophagostomum radiatum
Trichuris spp. (adults only)

Lungworms
Dictyocaulus viviparus (adults and L4)

Warbles (parasitic stages)
Hypoderma bovis
Hypoderma lineatum

Mange Mites
Chorioptes bovis
Sarcoptes scabiei var.*bovis*

Lice
*Damalinia (Bovicola) bovis (*biting lice)
Linognathus vituli (sucking lice)
Haematopinus eurysternus (sucking lice)
Solenopotes capillatus (sucking lice)

Horn flies
Haematobia irritans

Prevention of reinfestations:
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

The product is formulated only for topical application for 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 known cases of hypersensitivity to the active substance or to any of the excipients.

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 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 programme to control both internal and external parasites of cattle based on the epidemiology of these parasites.

4.5 Special precautions for use

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

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 warble fly activity and before the larvae reach their resting sites in the body; consult a veterinary surgeon regarding the appropriate time for treatment.
Rainfall at any time before or after treatment will not affect the efficacy of the product.

Special precautions to be taken by the person administering the veterinary medicinal product to animals
This product may be irritating to human skin and eyes and may cause hypersensitivity.
Avoid direct contact with the skin or eyes.
Wear rubber gloves and protective clothing 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 veterinary medicinal 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.
People with known hypersensitivity to the active substance or to any of the excipients should avoid contact with the veterinary medicinal product.

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 three weeks after treatment.

4.6 Adverse reactions (frequency and seriousness)

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

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 eprinomectin 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 interactions

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.

Administer only by topical application at the dose rate of 1 ml of the product 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 along the backline in a narrow strip extending from the withers to the tailhead.

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.

Method of administration:

For the 1L presentation:
The bottle is equipped with an integrated dosing system, and has two openings. One opening is connected to the body of the container and the other 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 to 25 ml doses). Squeeze the bottle to fill the dispensing chamber with the required volume of product.

For the 2.5 L, 3 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 cap. 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 should be removed and replaced by the polypropylene cap.

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 period(s)

Meat and Offal: 15 days
Milk: Zero hours

5 PHARMACOLOGICAL or IMMUNOLOGICAL PROPERTIES

Pharmacotherapeutic group: endectocides, macrocyclic lactones, avermectins
ATCvet 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

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 B1a component of eprinomectin is the single most abundant residue.
The contribution of eprinomectin B1a 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
In beef cattle treated topically with radiolabelled eprinomectin at the recommended dose of 0.5 mg/kg bodyweight, there was no distinct peak in the plasma radioactivity versus time curve, but a broad plateau occurred between 9 and 14 days after dosing. Highest concentrations of eprinomectin B1a were in the range of 7.33 - 19.74 ng/ml.
In lactating dairy cows treated topically with 0.75 mg radiolabelled eprinomectin/kg bodyweight, some animals showed a distinct peak in plasma radioactivity levels, whereas others exhibited a broad plateau. Peak levels of eprinomectin B1a were in the range of 42.7 - 134.4 ng/ml. The highest levels of plasma radioactivity occurred between one and 7 days after dosing.

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 0.25 % 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.

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, is persistent in soils and may accumulate in sediments.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Propylene glycol dicaprylocaprate
Butylated hydroxytoluene (E321)

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: 36 months.
Shelf life after first opening the immediate packaging: 6 months.

6.4 Special precautions for storage

For Squeeze pour containers (1L) : Keep the container in the outer container in order to protect from light.
For Flexi-pack containers (2.5 L, 3 L and 5L): Protect from light.

6.5 Nature and composition of immediate packaging

High density polyethylene container with a polypropylene tamper evident screw cap which consists of the following:
1L 'Squeeze pour' packs.
2.5 L, 3L and 5L 'Flexi' packs.
Pack sizes 1L, 2.5L, 3L and 5 L.
Not all pack sizes may be marketed.

6.6 Special precautions for the disposal of unused veterinary medicinal products 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

Chanelle Pharmaceuticals Manufacturing Limited
Loughrea
Co. Galway
Ireland

8 MARKETING AUTHORISATION NUMBER(S)

VPA10987/109/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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Date of last renewal: 22 May 2020

10 DATE OF REVISION OF THE TEXT

July 2020