Summary of Product Characteristics

1 NAME OF THE VETERINARY MEDICINAL PRODUCT

Topimec Injection 10 mg/ml solution for injection

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Active Substances:
Ivermectin 10 mg/ml

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for injection.
Clear, colourless to slightly yellow solution.

4 CLINICAL PARTICULARS

4.1 Target Species

Cattle, Sheep and Pigs.

4.2 Indications for use, specifying the target species

The product is indicated for the treatment of the following parasites of cattle,pigs and sheep:
Cattle:
Gastro-intestinal roundworms (adult and fourth stage larvae):
Ostertagia spp. (including inhibited *O. ostertagi*),
Haemonchus placei,
Trichostrongylus axei,
Trichostrongylus colubriformis,
Cooperia spp,
Oesophagostomum radiatum,
Strongyloides papillosus (adult)
Nematodirus helvetianus (adult),
N. spathiger (adult)

Toxocara vitulorum,
Trichuris spp. (adult).

Lungworms (adult and fourth stage larvae) :
Dictyocaulus viviparus.

Eye worms (adult) :
Thelazia spp.

Warbles (parasitic stages) :
Hypoderma bovis and *H. lineatum*.

Mange mites :
Psoroptes communis var. bovis,
Sarcoptes scabiei var. *bovis*.

Sucking lice :
Linognathus vituli,
Haematopinus eurysternus

May also be used as an aid in the reduction of infestation of the mange mite *Chorioptes bovis* but complete elimination may not occur.

Pigs:
Gastrointestinal worms (adult and fourth stage larvae):
Ascaris suum,
Hyostrongylus rubidus,
Oesophagostomum spp,
Strongyloides ransomi (adult stages)

Lungworms:
Metastrongylus spp. (adult)

Lice:
Haematopinus suis

Mange mites:
Sarcoptes scabiei var. *suis*

Sheep:
Gastrointestinal roundworms (adult and fourth-stage larvae):
Teladorsagia circumcincta including inhibited larvae
T. trifurcata
Haemonchus contortus including inhibited larvae
Trichostrongylus axei (adults)
T. colubriformis and T. vitrinus (adults)
Cooperia curticei
Oesophagostomum columbianum
O. venulosum (adults)
Nematodirus filicollis
Chabertia ovina
Trichuris ovis (adults)

Lungworms:
Dictyocaulus filaria (adult and fourth-stage larvae)
Protostrongylus rufescens (adults)

Nasal bots (all larval stages) :
Oestrus ovis.

Mange mites:
Psoroptes ovis

4.3 Contraindications

Do not use in cases of known hypersensitivity to the active substance. Do not administer by the intravenous or intramuscular route.
Do not use in dogs and cats (see section 4.5.i).

4.4 Special warnings for each target species

In sheep treatment of psoroptic mange (sheep scab) with one injection is not recommended because, although a clinical improvement may be seen, elimination of all mites may not occur.
Sheep scab (*Psoroptes ovis*) is an extremely contagious external parasite of sheep. To ensure complete control great care must be taken to avoid re–infestation, as mites may be viable for up to 15 days off the sheep. It is important that all sheep which have been in contact with infected sheep are treated. Contact between treated, infected and untreated flocks must be avoided until at least seven days after treatment.

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.

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.

Resistance to ivermectin has been reported in *Ostertagia ostertagi* and *Cooperia* spp. in cattle and *Teladorsagia circumcincta* in sheep. Resistance has also been reported in *Haemonchus contortus* in cattle outside the EU.

4.5 Special precautions for use

4.5.i Special precautions for use in animals
Ivermectins may not be well tolerated in non-target species. Cases of intolerance with fatal results are reported in dogs especially Collies, Old English Sheepdogs and related breeds and crosses, and also in turtles/tortoises. In addition, care should be taken to avoid ingestion of spilled product or access to used containers by these other species
Since ivermectin is highly bound to plasma proteins, special care should be taken in cases of sick animals or in nutritional conditions associated with low plasma protein levels.
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. Consult your veterinarian on the correct timing of treatment.

4.5. ii Special Precautions to be taken by the Person Administering the Product to Animals:
Do not eat, drink or smoke whilst handling the product.
Wash hands after use.
Direct contact with the skin should be avoided.
Take care to avoid self-injection: the product may cause local irritation and/or pain at the site of injection.
In case of accidental self injection, seek medical advice and show the label to the physician

4.5. iii Other precautions
The product is very toxic to aquatic organisms and dung insects. Treated cattle should not have direct access to ponds, streams or ditches for 14 days after treatment. Long term effects on dung insects caused by continuous or repeated use cannot be excluded. Therefore repeated treatment of animals on a pasture with an ivermectin-containing product within a season should only be given in the absence of alternative treatments or approaches to maintain animal/flock health, as advised by a veterinarian.

4.6 Adverse reactions (frequency and seriousness)

Cattle
Transitory discomfort has been observed in some cattle following subcutaneous administration. A low incidence of soft tissue swelling at the injection site has been observed. These reactions have disappeared without treatment.

Pigs
Mild and transient pain reactions may be seen in some pigs following subcutaneous injection. All these reactions disappeared without treatment.

Sheep
Immediately following subcutaneous injection, activity suggesting pain, sometimes intense but usually transient, has been observed in some sheep.

4.7 Use during pregnancy, lactation or lay

The product can be administered during pregnancy in cows and ewes at any stage of pregnancy or lactation provided that the milk is not intended for human consumption.. Do not use in non lactating dairy cows, including pregnant heifers within 60 days of calving. In pigs, the product can be used in breeding sows and boars. Do not administer the product in pigs during the first 40 days of pregnancy. The fertility of males is not affected by administration of the product.

4.8 Interaction with other medicinal products and other forms of interactions

Do not combine treatment with vaccination against lungworms. If vaccinated animals are to be treated, treatment should not be carried out within a period of 28 days before or after vaccination.

4.9 Amounts to be administered and administration route

For subcutaneous use only.
Each ml contains 10 mg of ivermectin sufficient to treat 50 kg of bodyweight of cattle and sheep, and 33 kg of bodyweight of pigs. The injection may be given with any standard automatic on single-dose or hypodermic syringe. Use of 17 gauge x ½ inch (1.25cm) needle is suggested.

Cattle
The recommended dose is 0.2 mg ivermectin per kg bodyweight (corresponding to 1 ml of the product per 50 kg bw) by subcutaneous injection under the loose skin in front of, or behind, the shoulder.
The volume administered per injection site should not exceed 10ml.

Pigs
The recommended dose is 0.3 mg ivermectin per kg bodyweight (corresponding to 1 ml of the product per 33 kg bw) by subcutaneous injection into the neck.
The volume administered per injection site should not exceed 5ml.

In young pigs, especially those below 16 kg for which less than 0.5 ml of the product is indicated, dosing accurately is important. The use of a syringe that can accurately deliver as little as 0.1 ml is recommended.

Sheep
The recommended dose is 0.2 mg ivermectin per kg bodyweight (corresponding to 1 ml of the product per 50 kg bw) by subcutaneous injection over the neck.
The volume administered per injection site should not exceed 1ml.

For the treatment and control of sheep scab (*Psoroptes ovis*), two injections with a seven-day interval are required to treat clinical signs of scab and to eliminate mites.
In young lambs weighing less than 25 kg give 0.1 ml of the product per 5 kg. The use of a syringe that can deliver as little as 0.1 ml is recommended.

This product does not contain any antimicrobial preservative. Swab septum before removing each dose.
The timing for treatment should be based on epidemiological factors and should be customised for each individual farm. A dosing programme should be established by the veterinary surgeon.

To ensure administration of a correct dose, body weight 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- or over-dosing.

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

Cattle
Single dose of 4.0 mg ivermectin per kg (20 x the use level) given subcutaneously resulted in ataxia and depression.

Pigs

A dose of 30 mg ivermectin per kg (100 x the recommended dose of 0.3 mg per kg) injected subcutaneously to pigs caused lethargy, ataxia, bilateral mydriasis, intermittent tremors, laboured breathing and lateral recumbency.

Cattle and Pigs
No systemic or local signs of toxic effects were reported at 3 times the recommended dose in both species, cattle and pigs.

Sheep
At dose levels up to 4 mg ivermectin per kg (20 x the use level) given subcutaneously resulted in ataxia and depression.

No antidote has been identified; however, symptomatic therapy may be beneficial.

4.11 Withdrawal period(s)

Cattle
Meat and offal: 49 days
Do not use in lactating dairy cows producing milk for human consumption.
Do not use in non-lactating dairy cows, including pregnant dairy heifers within 60 days of calving.

Pigs
Meat and offal: 28 days.

Sheep
Meat and offal: 25 days
Do not use in lactating sheep producing milk for human consumption.
Do not use in sheep within 60 days of lambing where milk is to be used for human consumption.

5 PHARMACOLOGICAL or IMMUNOLOGICAL PROPERTIES

Pharmacotherapeutic Group: Endectocides
ATCvet code: QP54AA01

5.1 Pharmacodynamic properties

Ivermectin 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 and 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

Maximum plasma concentration
Cattle
At a dose level of 0.2 mg ivermectin per kg a Cmax of 30 ng/ml is reached at a Tmax of 131 hours with an elimination half-life of 5.9 days. It is also established that ivermectin is carried mainly in the plasma (80%). This distribution between plasma and blood cells remains relatively constant.

Pigs
At a dose level of 0.3 mg ivermectin per kg bodyweight, a mean C_{max} of 6.94 ng/ml was reached at a mean T_{max} of 86.75 hours, and the mean elimination half life was 133.56 hours.

Sheep
At a dose level of 0.2 mg ivermectin per kg bodyweight, a mean C_{max} of 10.976 $\pm$ 8.24 ng/ml was reached at a mean T_{max} of 59.6 $\pm$ 50.5 hours, and the mean elimination half life was 83.1 $\pm$ 29.3 hours. An average peak of 16 ng/ml is reached one day after injection.

Excretion: length of time and route
Cattle
Only about 1 - 2% is excreted in the urine, the remainder is excreted in the faeces approximately 60% of which is excreted as unaltered drug. The remainder is excreted as metabolites or degradation products.

Pigs
Biliary excretion is also the major route of ivermectin excretion in pigs.

Sheep:
Radioactive ivermectin was administered to sheep at a dose rate of 0.3 mg per kg. Analyses of the faeces showed that about 99% of the drug and its metabolites are excreted in the faeces, +/- 1% being excreted in the urine.

Environmental properties
Like other macrocyclic lactones, Ivermectin has the potential to adversely affect non-target organisms. Following treatment, excretion of potentially toxic levels of Ivermectin may take place over a period of several weeks. Faeces containing Ivermectin 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

Glycerol
Glycerol formal

6.2 Major incompatibilities

In the absence of compatibility studies this veterinary medicinal product should not be mixed with other veterinary medicinal products.

6.3 Shelf-life

Shelf-life of the veterinary medicinal product aas packaged: 3 years
Shelf-life after first opening the immediate packageing: 28 days.

6.4 Special precautions for storage

This veterinary medicinal product does not require any special storage precautions.

6.5 Nature and composition of immediate packaging

Multidose polyethylene bottles of 50 ml, 250 ml and 500 ml sealed with bromobutyl seals and aluminium overseals.
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 surface waters or ditches with product or used container. 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

Chanelle Pharmaceuticals Manufacturing Limited
Loughrea
Co. Galway
Ireland

8 MARKETING AUTHORISATION NUMBER(S)

VPA10987/157/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 04 February 2005
Date of last renewal: 26 July 2010

10 DATE OF REVISION OF THE TEXT

June 2021