SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Premadex 0.8mg/ml Oral Solution for Sheep

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active substance:
Each ml contains:

Ivermectin	0.8mg

Excipient(s):

Benzyl Alcohol (E1519)	28.6mg
Butylhydroxyanisole (E320)	0.10 mg
Propyl Gallate (E310)	0.10 mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Oral Solution.
A transparent, yellow coloured solution.

4. CLINICAL PARTICULARS

4.1 Target species

Sheep

4.2 Indications for use, specifying the target species

For the treatment of infections with the following parasites:

Nematodes
Gastrointestinal roundworms (adult and fourth larval stage)
Haemonchus contortus
Teladorsagia circumcincta
Trichostrongylus spp.
Cooperia spp.
Nematodirus spp.
Including *N. battus*
Strongyloides papillosus
Chabertia ovina

Lungworms (adult and fourth larval stage)
Dictyocaulus filaria

Arthropods

Nasal bot (all larval stages)
Oestrus ovis

4.3 Contraindications

Do not use in animals with known hypersensitivity to the active ingredient or 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 body weight or misadministration of the product.

Resistance to ivermectin (an avermectin) has been reported in *Teladorsagia* in sheep and goats within the EU and it is common in *Haemonchus* in sheep outside the EU. Therefore the use of this product should be based on local (regional, farm) epidemiological information about susceptibility of nematode and recommendations on how to limit further selection for resistance to anthelmintics.

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.
There is cross-resistance with other avermectins and with milbemycins

4.5 Special precautions for use

(i) Special precautions for use in animals

The timing of 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.
Veterinary advice should be sought on appropriate dosing programmes and stock management to achieve adequate parasite control, and to reduce the likelihood of anthelmintic resistance developing. Veterinary advice should also be sought if the product does not achieve the desired clinical effect, as other diseases, nutritional disturbances or anthelmintic resistance might be involved'.

Avermectins may not be well tolerated in non-target species. Cases of intolerance resulting in fatalities have been reported in dogs, especially Collies, Old English Sheep Dogs and related breeds or crosses, and also in turtles/tortoises.

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

Wash hands after use. Avoid contact with skin and eyes.
Do not eat, drink or smoke while handling the product.

Wear impervious gloves when handling or administering the product.
As absorption through skin can occur, in the event of accidental skin contact, wash the affected area immediately with soap and water.
If accidental eye exposure occurs, flush the eyes immediately with water.

(iii) Other precautions

None known.

4.6 Adverse reactions (frequency and seriousness)

Some sheep may cough immediately after treatment. This passing response is of no consequence.

4.7 Use during pregnancy, lactation or lay

The veterinary medicinal product can be administered to ewes at any stage of pregnancy or lactation.
See Section 4.11

4.8 Interaction with other medicinal products and other forms of interaction

None known.

4.9 Amounts to be administered and administration route

For oral administration only.
The recommended dose rate is 0.2 mg ivermectin per kg bodyweight (corresponding to 2.5 ml per 10 kg bodyweight)

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

At doses up to 4 mg ivermectin per kg administered by stomach tube (20x the recommended dose level) undesirable toxic reactions occurred. Acute symptoms (ataxia, staggering gait, incoordination, depression) were observed at the dose rate of 8 mg/kg (40x the recommended dose level) during a study carried out on 4 animals. Twenty-four hours later, the animals showed only mild incoordination and depression.
Three days post dose all the animals were nearly normal. It is possible that the signs of toxaemia were due to the propylene glycol.
No antidote has been identified. Symptomatic treatment may be beneficial.

4.11 Withdrawal period(s)

Meat and offal: 10 days.
Milk: Do not use in lactating sheep producing milk for human consumption.
Sheep must not be treated within 60 days prior to the commencement of lactation, if milk is to be used for human consumption.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Endectocides, avermectins
ATCvet code: QP54AA01

5.1 Pharmacodynamic properties

Ivermectin belongs to the avermectin family, which are a macrocyclic lactone group of endectocides. Compounds of the 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 grated 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 Pharmocokinetic particulars

The maximum plasma concentration is reached in 12 hours after oral administration and ranges from 6.3 to 17.9 ng/ml at the dose rate of 0.2 mg ivermectin per kg bodyweight. This concentration gradually decreases to range from 1.31 to 10.55 ng/ml 2 days post dose with a terminal half-life of 42.4 hours.

Ivermectin binds extensively to plasma proteins. Due to its high lipophilic nature, Ivermectin is extensively distributed. It tends to

accumulate in fat tissue, which acts as a drug reservoir and the highest levels of Ivermectin are found in liver and fat. Ivermectin is only partially metabolized. Ivermectin is mainly eliminated in the faeces as unaltered drug and faecal excretion accounts for 90% of the dose administered with <2% of the dose excreted in urine. Ivermectin is also excreted by the mammary gland.

Environmental Properties

None known.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Butylhydroxyanisole (E320)
Propyl Gallate (E310)
Benzyl Alcohol (E1519)
Propylene Glycol
Disodium Edetate
Polysorbate 80
Disodium Hydrogen Phosphate Dihydrate
Sodium Dihydrogen Phosphate Monohydrate
Purified Water

6.2 Incompatibilities

None known.

6.3 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 3 years.
Shelf life after first opening the container: 18 months.

6.4 Special precautions for storage

Do not store above 30ºC.

6.5 Nature and composition of immediate packaging

White flat-bottomed flexi packs (1L, 2.5L, 5L and 6L (5L + 1L)) composed of high density polyethylene container, with a 38 mm tamper evident polypropylene cap.
Standard containers (jerri-cans) (1L, 2.5L, 5 L and 10L) composed of high density polyethylene container, with tamper evident polyethylene cap.
Pack sizes (flexi pack): 1, 2.5 , 5L and 6L (5L+1L)
Pack sizes (jerri-cans): 1, 2.5, 5L and 10 Litre
Not all pack sizes may be marketed.

6.6 Special precautions for the disposal of unused veterinary medicinal products or waste materials

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 Pharmaceutical Manufacturing Limited
Loughrea
Co. Galway
Ireland

8. MARKETING AUTHORISATION NUMBER

Vm 08749/4029

9. DATE OF FIRST AUTHORISATION

23 March 2010

10. DATE OF REVISION OF THE TEXT

June 2018

Approved: 21 June 2018