

IRISH MEDICINES BOARD ACT 1995, as amended

European Communities (Animal Remedies) (No. 2) Regulations 2007

VPA: **10277/027/001**
Case No: 7007417

The Irish Medicines Board in exercise of the powers conferred on it by Animal Remedies (No. 2) Regulations (S.I. No. 786 of 2007) hereby grants to:

Schering Plough Limited

Shire Park, Welwyn Garden City, Hertfordshire AL7 1TW, United Kingdom

an authorisation, subject to the provisions of the said Regulations and the general conditions of the attached authorisation, in respect of the Veterinary Medicinal Product:

Nilzan Drench Plus

The particulars of which are set out in the attached Schedule. The authorisation is also subject to any special conditions as may be specified in the Schedule.

The authorisation,unless revoked, shall continue in force from **29/06/2010**.

Signed on behalf of the Irish Medicines Board

A person authorised in that behalf by the said Board.

(NOTE: This authorisation replaces any previous authorisation in respect of this product which is now null and void.)

Part II

Summary of Product Characteristics

1 NAME OF THE VETERINARY MEDICINAL PRODUCT

Nilzan Drench Plus

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active Substances

Levamisole	15	mg
Oxyclozanide	30	mg

Excipients

Sodium metabisulphite (E223)	1	mg
Sodium Propyl Parahydroxybenzoate (E217)	0.23	mg
Tartrazine (E102)	0.2	mg

For a full list of excipients see section 6.1.

3 PHARMACEUTICAL FORM

Oral suspension.

Bright yellow, smooth and uniform suspension.

4 CLINICAL PARTICULARS

4.1 Target Species

Cattle and sheep

4.2 Indications for use, specifying the target species

Indications : For the treatment and control of gastro-intestinal and pulmonary nematode infections and as an adulticide in the treatment of fascioliasis in cattle and sheep. It also removes tapeworm segments (*Moniezia*) from sheep. It removes mature and developing immature stages of a range of nematode species.

The product is effective against the following :

In the abomasum : *Haemonchus*, *Ostertagia** and *Trichostrongylus* spp.

In the intestines : *Trichostrongylus*, *Cooperia*, *Nematodirus*, *Oesphagostomum*, *Chabertia* and *Bunostomum* spp.

In the lungs : *Dictyocaulus* spp.

It removes practically all adult flukes (*Fasciola* spp.) present in the bile ducts of the liver.

*Effective against developing immature and adult *Ostertagia* and in the treatment of Type II ostertagiasis in cattle: however it is not effective against inhibited *Ostertagia* larvae (pre-type II Ostertagiasis) in cattle and a later treatment be necessary.

Contains cobalt as a nutritional supplement to aid in the prevention and treatment of cobalt deficiency and to improve performance of animals on cobalt deficient diets.

4.3 Contraindications

Do not treat cattle within a period of 14 days before or after treatment with organophosphorus compounds. However, cattle may be treated simultaneously with organophosphorus warble fly dressings but, only if they contain one of the following active ingredients : phosmet, fenthion, metriphionate.

Do not use in animals with known hypersensitivity to the active ingredients.

Do not use in animals producing milk for human consumption.

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.

4.5 Special precautions for use

Special precaution(s) for use in animals

Care must be taken when dosing animals to avoid damage with the dosing gun and subsequent pharyngitis.

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

When using do not eat, drink or smoke.

Wash splashes immediately from eyes and skin immediately.

Take off any contaminated clothing immediately.

Wash hands and exposed skin before meals and after work.

Levamisole can cause idiosyncratic reactions and serious blood disorders in a very small number of people. If symptoms such as dizziness, nausea, vomiting or abdominal discomfort are experienced when using the product, or sore mouth/throat or fever occur shortly afterwards, then medical advice should be sought immediately.

4.6 Adverse reactions (frequency and seriousness)

At normal levamisole dose levels animals rarely show any side effects. The effects of levamisole overdosage are transient and include head shaking, salivation and slight muscle tremors, they are more likely to be observed in cattle than sheep.

At normal oxcylozanide dose levels, cattle may show slight softening of the faeces with the occasional animal showing increased frequency of defaecation and transient inappetence.

4.7 Use during pregnancy, lactation or lay

The product may be given to pregnant and lactating animals not producing milk for human consumption. Due regard must always be given to physical condition, particularly of any animals in advanced pregnancy, and/or under stress from adverse weather conditions, poor nutrition, penning, handling etc.

4.8 Interaction with other medicinal products and other forms of interaction

Cattle must not be treated within a period of 14 days before of after treatment with organophosphorus compounds (see contraindications).

4.9 Amounts to be administered and administration route

Give as an oral drench.

The contents should be thoroughly shaken before use.

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 underdosing.

Dose according to bodyweight at the rate of 7.5 mg levamisole hydrochloride, 15 mg oxyclozanide and 0.4 mg cobalt per kg bodyweight as follows : -

Cattle : 5 ml per 10 kg bodyweight ;

For example : -

Bodyweight	Dose
50 kg (approx 1 cwt)	25 ml
100 kg (approx 2 cwt)	50 ml
150 kg (approx 3 cwt)	75 ml
200 kg (approx 4 cwt)	100 ml
250 kg (approx 5 cwt)	125 ml
300 kg and over	
(approx 6 cwt and over)	150 ml

Sheep: 1 ml per 2 kg bodyweight

For example : -

Bodyweight	Dose
10 kg (approx 22 lb)	5 ml
20 kg (approx 44 lb)	10 ml
30 kg (approx 66 lb)	15 ml
40 kg (approx 88 lb)	20 ml
50 kg (approx 110lb)	25 ml
60 kg (approx 132 lb)	30 ml

Sheep over 60 kg should be given a further 1 ml for each additional 2 kg bodyweight.

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

The effects of levamisole overdosage are transient and include head shaking, salivation and slight muscle tremors, and are more likely to be observed in cattle than in sheep.

The effects of oxyclozanide overdosage are dullness and some loosening of faeces in sheep and possible diarrhoea, inappetence and loss of weight in cattle. These effects are occasionally enhanced in animals with severe liver damage and/or dehydration at the time of dosing.

4.11 Withdrawal Period(s)

Cattle (meat and offal): 28 days

Sheep (meat and offal): 28 days

Do not use in animals producing milk for human consumption.

5 PHARMACOLOGICAL or IMMUNOLOGICAL PROPERTIES

Pharmacotherapeutic group: Anthelmintics; Levamisole, combinations.

ATCvet code: QP52 AE51

5.1 Pharmacodynamic properties

Levamisole is the laevo-enantiomer of tetramisole and is an anthelmintic imidazothiazole. It is effective upon oral, intramuscular and subcutaneous administration against various species of nematodes. It's anthelmintic action is characterised by paralysis of the worm through a neuromuscular inhibition of the depolarising type, leading to passive elimination of the worm.

Oxyclozanide is an anthelmintic of the salicylanilide group. It is effective against *Fasciola* species, acting as an uncoupler of oxidative phosphorylation. It may act at more than one site to decrease levels of ATP leading to metabolic malfunction and death of the parasite.

5.2 Pharmacokinetic properties

Levamisole is very rapidly absorbed and peak plasma concentrations are attained on average 2 to 4 hours after oral dosing. Levamisole is rapidly distributed to all tissues, where levels are several times higher than the corresponding plasma levels. Elimination from plasma and tissues is also very rapid, the main elimination routes being the urine (up to 50% of the dose within 24 hours) and the bile (30% of the dose). The fraction of the unchanged parent drug in the urine and bile is low as metabolism is extensive.

Oxyclozanide is slowly absorbed after oral administration with peak plasma levels 24 hours after dosing. Excretion is predominantly faecal, biliary excretion being the most important route of elimination (cattle studies only).

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Cobalt sulphate heptahydrate
Polysorbate 80
Sodium metabisulphite (E223)
Light kaolin
Xanthan gum
Citric acid monohydrate
Sodium citrate
Sodium propyl parahydroxybenzoate (E217)
Tartrazine (E102)
Purified water

6.2 Incompatibilities

None known.

6.3 Shelf-life

Shelf-life of the veterinary medicinal product as packaged for sale: 4 years.

6.4 Special precautions for storage

Store below 25°C.
Protect from light.
Do not freeze.

6.5 Nature and composition of immediate packaging

(i) 1, 2.5, 5 and 10 litre high density polyethylene flexi-packs with screw cap.

(ii) 1, 2.5 and 5 litre high density polyethylene back-packs with screw cap.

Not all pack sizes may be marketed.

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

Unused product or waste material should be disposed of in accordance with current practice for pharmaceutical waste under national waste disposal regulations.

7 MARKETING AUTHORISATION HOLDER

Schering Plough Ltd.
Shire Park
Welwyn Garden City
Hertfordshire
AL7 1TW
England

8 MARKETING AUTHORISATION NUMBER(S)

VPA 10277/027/001

9 DATE OF THE FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

30th September 2009

10 DATE OF REVISION OF THE TEXT

29th June 2010