1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Enovex 10 mg/ml Solution for Injection for cattle, sheep and pigs

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active substance:

Ivermectin 10 mg

Excipients:

Qualitative composition of excipients and other constituents
Glycerol formal
Polyethylene glycol 200

A clear, colourless solution.

3. CLINICAL INFORMATON

3.1 Target Species

Cattle, sheep and pigs.

3.2 Indications for use for each target species

Cattle
Treatment of infections by the following parasites:

Gastrointestinal roundworms (adults and fourth stage larvae):
*Ostertagia ostertagi (*including inhibited *O. ostertagi), Ostertagia lyrata, Haemonchus placei, Trichostrongylus axei, Trichostrongylus colubriformis, Cooperia oncophora, Cooperia punctata, Cooperia pectinata, Bunostomum phlebotomum, Oesophagostomum radiatum, Nematodirus helvetianus (adult).*

Lungworms (adult and fourth stage larvae):
Dictyocaulus viviparous

Warbles (parasitic stages):
Hypoderma bovis, Hypoderma lineatum

Sucking Lice:
Linognathus vituli, Haematopinus eurysternus

Mange Mites:
Psoroptes communis var *bovis, Sarcoptes scabiei* var *bovis*

The veterinary medicinal product may also be used to reduce infection of the mange mite *Chorioptes bovis*, but complete elimination may not occur.

Sheep

The veterinary medicinal product is indicated for the effective treatment and control of the following:

Gastrointestinal roundworms (adults and fourth stage larvae):
Ostertagia circumcincta (including inhibited larvae*), O. trifurcata, Haemonchus contortus* (including inhibited larvae), *Trichostrongylus axei* (adults*),Trichostrongylus colubriformis* (adults), *Trichostrongylus vitrinus* (adults*), Cooperia curticei, Oesophagostomum venulosum* (adults), *Oesophagostomum columbianum, Nematodirus filicollis, Chabertia ovina, Trichuris ovis* (adults). Inhibited larval stages and benzimidazole resistant strains of *Haemonchus contortus* and *Ostertagia circumcincta* are also controlled.

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

Nasal Bots:
Oestrus ovis (all larval stages)

Mange Mites:
*Psoroptes ovis**
*For the treatment and control of sheep scab, two injections with a seven day interval are required to treat clinical signs of scabs to eliminate the mites.

Pigs
Treatment of infections by the following parasites:

Gastrointestinal roundworms:
Ascaris suum (adults and fourth-stage larvae)
Hyostrongylus rubidus (adults and fourth-stage larvae)
Oesophagostomum spp (adults and fourth-stage larvae)
Strongyloides ransomi (adults)

Lungworms:
Metastrongylus spp (adults)

Lice:
Haematopinus suis

Mange mites:
Sarcoptes scabiei var *suis*

3.3 Contraindications

Do not administer by the intravenous or intramuscular route.
Do not use in dogs or cats as severe adverse reactions may occur.
Do not use in cases of hypersensitivity to the active substance or to any of the excipients.

3.4 Special warnings

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.

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 tests 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* in cattle. Therefore, the use of this product should be based on local (regional, farm) epidemiological information about susceptibility of this helminth species and recommendations on how to limit further selection for resistance to anthelmintics.

In cattle, 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.

Treatment of psoroptic mange (sheep scab) with one injection is not recommended, because although clinical improvement may be seen elimination of all mites may not occur.

Sheep scab (*Psoroptes ovis*) is an extremely contagious external parasite of sheep. Following treatment of infected sheep 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 to ensure all sheep which have been in contact with infected sheep are treated. Contact between treated, infected and nontreated, non-infected flocks must be avoided until at least 7 days after the last treatment.

3.5 Special precautions for safe use in the target species

Special precautions for safe use in the target 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.

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

Do not smoke or eat while handling the product.
Direct contact of the product with the skin should be kept to a minimum. Wash hands after use.
Take care to avoid self-injection. Inadvertent self-injection may result in local irritation and/or pain at the injection site. In case of accidental self-injection, seek medical advice immediately and show the package leaflet or the label to the physician.

Other precautions:

Avermectins may not be well tolerated in all non-target species (cases of intolerance with fatal outcome are reported in dogs - especially Collies, Old English Sheepdogs and related breeds and crosses, and also in turtles/tortoises).

3.6 Adverse events

Cattle.

Common (1 to 10 animals / 100 animals treated):	Injection site swelling[1]
Very rare	Discomfort[2]

(<1 animal / 10,000 animals treated, including isolated reports):	

[1] These soft tissue swellings disappear without treatment.
[2] Following subcutaneous administration.

Sheep.

Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Pain[1]

[1] Immediately following subcutaneous injection. Sometimes intense, but usually transient.

Pigs.

Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Pain[1] Injection site swelling[1]

[1] Mild and transient - following subcutaneous injection. All reactions disappear without treatment.

Reporting adverse events is important. It allows continuous safety monitoring of a veterinary medicinal product. Reports should be sent, preferably via a veterinarian, to either the marketing authorisation holder or the national competent authority via the national reporting system. See the package leaflet for respective contact details.

3.7 Use during pregnancy, lactation or lay

Pregnancy and lactation:
The product can be used during pregnancy and lactation in ewes and in cattle provided that the milk is not intended for human consumption. The product can be used during pregnancy and lactation in sows. See also Section 3.12.

3.8 Interaction with other medicinal products and other forms of interaction

The effects of GABA agonists are increased by ivermectin.

3.9 Administration routes and dosage

For single administration only.
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.

Cattle
Ivermectin should be administered at a dosage rate of 200 micrograms per kg bodyweight (1 ml/50 kg). It should be injected subcutaneously in front of or behind the shoulder using aseptic technique. A sterile 17-gauge, 12.7 mm needle (equivalent to half inch needle) is recommended. Use of a draw-off needle is recommended to avoid excess broaching of the stopper.

Sheep
Ivermectin should be administered at a dosage rate of 0.5 ml per 25 kg bodyweight (based on a recommended level of 200 micrograms per kg bodyweight). For the treatment of gastrointestinal

roundworms, lungworms and nasal bots, inject once subcutaneously in the neck using aseptic precautions; a sterile 17 gauge, 12.7 mm needle (equivalent to half inch needle) is recommended. For the treatment of *Psoroptes ovis* (sheep scab), two injections with a 7 day interval are required to treat clinical signs of scab and to eliminate living mites.

Pigs
Ivermectin should be administered at a dosage rate of 300 micrograms per kg bodyweight (1 ml/33 kg). It should be injected subcutaneously into the neck using aseptic technique. A sterile 17-gauge, 12.7 mm needle (equivalent to half inch needle) is recommended. Exact dosing is important especially in pigs with low bodyweight, therefore a syringe capable of dosing in 0.1 ml steps should be used.

For all species, the treatment schedule should be based on the local epidemiological situation. The advice of a veterinarian should be sought regarding appropriate dosing programmes and stock management to achieve adequate parasite control.

3.10 Symptoms of overdose (and where applicable, emergency procedures and antidotes)

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

Sheep
Clinical symptoms of ivermectin toxicity include 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.

No antidote has been identified. In case of overdose, symptomatic treatment should be given.

3.11 Special restrictions for use and special conditions for use, including restrictions on the use of antimicrobial and antiparasitic veterinary medicinal products in order to limit the risk of development of resistance.

Not applicable.

3.12 Withdrawal periods

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

Sheep
Meat and offal: 42 days
Not authorised for use in animals producing milk for human consumption. Do not use in non-lactating dairy ewes including pregnant dairy ewes within 60 days of lambing.

Pigs
Meat and Offal: 18 days.

4. PHARMACOLOGICAL INFORMATION

4.1 ATCvet code: QP54AA01

4.2 Pharmacodynamics

Ivermectin is a macrocyclic lactone derivative and acts by inhibiting nerve impulses. It binds selectively 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 hyperpolarisation of the nerve or muscle cell, resulting in the paralysis and death of the relevant parasites.

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.

4.3 Pharmacokinetics

Following the subcutaneous administration of the product to sheep at a dose of 200 microg ivermectin/kg, the maximum concentration in plasma (C_{max} = ~ 14 ng/ml) was reached within 1-5 days. After subcutaneous administration of the recommended dose of the product to cattle (200 microg/kg) the following parameters were observed. C_{max} of 37 ng/ml and AUC of 7558 ng/ml.h. After subcutaneous administration of the recommended dose of the product to pigs (300 microg/kg), the following parameters were observed: C_{max} of 14 ng/ml, and AUC of 1887 ng/ml.h. Ivermectin is only partially metabolised. In 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. Biliary excretion, followed by elimination in faeces is probably the major route of ivermectin excretion.

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities

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

5.2 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 2 years.
Shelf life after first opening the immediate packaging: 28 days.

5.3 Special precautions for storage

Store below 25°C.
Protect from direct sunlight.

5.4 Nature and composition of immediate packaging

The product will be supplied in 50ml, 100ml, 250ml, 500ml and 1L volumes, presented in high density polyethene vials with bromobutyl bungs and aluminium caps.

Not all pack sizes may be marketed.

5.5 Special precautions for the disposal of unused veterinary medicinal products or waste materials derived from the use of such products.

Medicines should not be disposed of via wastewater or household waste.

Use take-back schemes for the disposal of any unused veterinary medicinal product or waste materials derived thereof in accordance with local requirements and with any national collection systems applicable to the veterinary medicinal product concerned.

Ivermectin is extremely dangerous to fish and aquatic life. Do not contaminate surface water or ditches with the product or used containers.

6. NAME OF THE MARKETING AUTHORISATION HOLDER

Norbrook Laboratories (Ireland) Limited

7. MARKETING AUTHORISATION NUMBER(S)

VPA 22664/055/001

8. DATE OF FIRST AUTHORISATION

29 October 1999

9. DATE OF THE LAST REVISION OF THE SUMMARY OF THE PRODUCT CHARACTERISTICS

04 July 2024

10. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCTS

Veterinary medicinal product subject to prescription.

Detailed information on this veterinary medicinal product is available in the Union Product Database (https://medicines.health.europa.eu/veterinary).