B. PACKAGE LEAFLET

PACKAGE LEAFLET

1. Name of the veterinary medicinal product

EVOCTIN 10 mg/ml solution for injection for cattle, sheep, pigs

2. Composition

Each ml contains:

Active substance:
Ivermectin 10 mg

Clear, colourless solution without any visible particles.

3. Target species

Cattle, sheep, pigs.

4. Indications for use

The veterinary medicinal product is recommended for the treatment of infestation with the following parasites in cattle, sheep and pigs.

Cattle

Gastrointestinal roundworms:
Ostertagia ostertagi (adults, L3, L4, including the inhibited larvae)
Ostertagia lyrata (adults)
Haemonchus placei (adults, L3, L4)
Trichostrongylus axei (adults, L4)
Cooperia oncophora (adults, L4)
Cooperia punctata (adults, L4)
Cooperia pectinata (adults, L4)
Oesophagostomum radiatum (adults, L3, L4)
Bunostomum phlebotomum (adults, L3, L4)
Nematodirus helvetianus (adults)
Nematodirus spathiger (adults)
Strongyloides papillosus (adults)
Toxocara vitulorum (adults)
Trichuris spp. (adults)

Lungworms:
Dictyocaulus viviparus (adults, L4 including inhibited larvae)

Eye helminths:
Thelazia spp. (adults)

Warbles (all parasitic stages):
Hypoderma bovis
Hypoderma lineatum

Mange mites:
Psoroptes bovis

Sarcoptes scabiei var. *bovis*

Lice:
Linognathus vituli
Haematopinus eurysternus
Solenopotes capillatus

The veterinary medicinal product may also be used as complementary treatment to control infestation with *Chorioptes bovis* mange mites, although treatment may not eliminate them completely.

Persistence of efficacy in cattle
This veterinary medicinal product administered at the recommended dosage controls reinfections with:

- *Haemonchus placei* and *Cooperia* spp. for 14 days after treatment.
- *Ostertagia ostertagi* and *Oesophagostomum radiatum* for 21 days after treatment
- *Dictyocaulus viviparus* for 28 days after treatment

Sheep

Gastrointestinal roundworms:
Haemonchus contortus (adults, L3, L4)
Teladorsagia circumcincta (adults, L3, L4)
Trichostrongylus axei (adults)
Trichostrongylus colubriformis (adults, L3, L4)
Trichostrongylus vitrinus (adults)
Nematodirus filicollis (adults, L4)
Nematodirus spathiger (L3, L4)
Cooperia curticei (adults, L4)
Oesophagostomum columbianum (adults, L3, L4)
Oesophagostomum venulosum (adults)
Chabertia ovina (adults, L3, L4)
Trichuris ovis (adults)
Strongyloides papillosus (L3, L4)
Gaigeria pachyscelis (adults, L3, L4)

Lungworms:
Dictyocaulus filaria (adults, L3, L4)
Protostrongylus rufescens (adults)

Nasal bots (all larval stages):
Oestrus ovis

Mange mites:
Psoroptes communis var. *ovis**
Sarcoptes scabiei
Psorobia ovis (formerly *Psorergates ovis*)

* When treated against psoroptes, the injection should be administered twice at 7 days interval. One application can only reduce the number of mites that may appear to be eradicated.

Pigs

Gastrointestinal roundworms:
Ascaris suum (adults and L4)
Hyostrongylus rubidus (adults and L4)
Oesophagostomum spp. (adults and L4)
Strongyloides ransomi (adults and somatic larvae)*

* The veterinary medicinal product administered to pregnant sows 7-14 days prior to parturition effectively prevents the transmission of *Strongyloides ransomi* via milk to piglets.

Lungworms:
Metastrongylus spp. (adults)

Kidney roundworms:
Stephanurus dentatus (adults and L4)

Lice:
Haematopinus suis

The active substance does not affect lice eggs, which take 21 days to develop. Therefore, their elimination may require repeated treatment.

Mange mites:
Sarcoptes scabiei var. *suis*

5. Contraindications

Do not inject intramuscularly or intravenously.
Do not use in other animal species. Fatal intolerances have been reported in dogs and turtles.
Do not use in cases of hypersensitivity to the active substance, or to any of the excipients.

6. Special warnings

Special warnings:

Unnecessary use of antiparasitics or use deviating from the instructions given in the package leaflet may increase the resistance selection pressure and lead to reduced efficacy. The decision to use the product should be based on confirmation of the parasitic species and burden, or of the risk of infestation based on its epidemiological features, for each individual animal/ herd.

Repeated use for an extended period, particularly when using the same class of substances, increases the risk of resistance development. Within a herdmaintenance of susceptible refugia is essential to reduce that risk. Systematically applied interval-based treatment and treatment of a whole herd should be avoided. Instead, if feasible, only selected individual animals or subgroups should be treated (targeted selective treatment). This should be combined with appropriate husbandry and pasture management measures. Guidance for each specific herd should be sought from the responsible veterinarian.

The use of this veterinary medicinal product should take into account local information about susceptibility of the target parasites, where available.

It is recommended to further investigate cases of suspected resistance, using an appropriate diagnostic method (e.g. Faecal Egg Count Reduction Test). Where tests clearly suggest resistance to a particular anthelmintic, an anthelmintic belonging to another pharmacological class and having a different mode of action should be used.

Confirmed resistance should be reported to the marketing authorisation holder or to the competent authorities.

Resistance to anthelmintic macrocyclic lactones is a serious problem for the control of *Trichostrongylus* nematodes in sheep and goats and is becoming a problem in *Trichostrongylus* nematodes in cattle in some parts of the world.

In pigs ivermectin resistance was detected in *Oesophagostomum* species. Resistance to ivermectin was also reported within and outside Europe for *Cooperia* spp. and *Ostertagia ostertagi* in cattle and *Haemonchus contortus* and *Teladorsagia circumcincta* in sheep.

Special precautions for safe use in the target species:

To avoid secondary reactions due to the death of *Hypoderma* larvae in the oesophagus or in the spine it is recommended to administer the veterinary medicinal 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.

Do not administer through wet and dirty skin.

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

People with known hypersensitivity to ivermectin should administer the veterinary medicinal product with caution.

This product may cause skin and eye irritation. Avoid contact with skin and eyes. In case of accidental contact with skin or eyes wash the affected area immediately with plenty of water.

In case of accidental self-injection seek medical advice immediately and show the package leaflet or the label to the physician.

Do not eat, drink or smoke while handling the product.

Wash hands after use.

Since foetotoxic and teratogenic effects are described in laboratory animals after exposure to glycerol formal, pregnant women or women attempting to conceive should not administer the product.

Special precautions for the protection of the environment:

The veterinary medicinal product is very toxic to aquatic organisms, therefore treated animals should not have direct access to ponds, streams or ditches for 14 days after treatment.
The veterinary medicinal product is very toxic to dung fauna and 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/herd health, as advised by a veterinarian.

Pregnancy and lactation:

Can be used during pregnancy and lactation.

Fertility:

Use of this veterinary medicinal product does not affect fertility of bulls, rams, and boars.

Interaction with other medicinal products and other forms of interaction:

No data available.

Overdose:

Cattle
A single dose of 4.0 mg ivermectin per kg b.w. (twenty times the recommended dose) administered subcutaneously results in ataxia and depression.

Sheep
Ivermectin administered subcutaneously has demonstrated adequate safety at the recommended dose. At an oral dose of the commercial formulation for oral administration up to 4 mg ivermectin per kg b.w. (twenty times the recommended dose), given by stomach tube, ivermectin did not cause adverse toxic reactions.

Pigs
A dose of 30 mg ivermectin per kg b.w. (one hundred times the recommended dose of 0.3 mg per kg b.w.) administered subcutaneously to pigs caused lethargy, ataxia, bilateral mydriasis, intermittent tremor, laboured breathing and lateral recumbency.

No antidote has been defined; symptomatic treatment is recommended.

Major incompatibilities:

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

7. Adverse events

Cattle:

Undetermined frequency (cannot be estimated from the available data)	Injection site swelling[1]
Undetermined frequency (cannot be estimated from the available data)	Discomfort[1]

[1] These reactions disappear on their own.

Sheep:

Undetermined frequency (cannot be estimated from the available data)	Discomfort[1]

[1] These reactions disappear on their own.

Pigs:

Undetermined frequency (cannot be estimated from the available data)	Injection site swelling[1]

[1] These reactions disappear on their own.

Reporting adverse events is important. It allows continuous safety monitoring of a product. If you notice any side effects, even those not already listed in this package leaflet, or you think that the medicine has not worked, please contact, in the first instance, your veterinarian. You can also report any adverse events to the marketing authorisation holder or the local representative of the marketing authorisation holder using the contact details at the end of this leaflet, or via your national reporting system.

8. Dosage for each species, routes and method of administration

For subcutaneous use.

Cattle:
0.2 mg ivermectin/kg b.w. (i.e., 1 ml of product/50 kg b.w.), subcutaneously into loose skin in front of or behind the shoulder blade.

The veterinary medicinal product is effective against all stages of subcutaneous warbles in cattle, but the time of treatment is important. Consult your veterinarian on the correct timing of treatment. Please also see *Special precautions for safe use in the target species*:

Sheep:
0.2 mg ivermectin/kg b.w. (i.e. 0.5 ml of product/25 kg b.w.) subcutaneously into the loose skin between the shoulders. .

In unshorn sheep, before directly applying the dose, make sure that the needle has penetrated the wool and through the skin.

When treated against Psoroptes, treatment should be repeated after 7 days.

For infestations with *Psoroptes ovis*, the need for and frequency of re-treatment(s) should be based on professional advice and should take into account the local epidemiological situation and the animal's lifestyle.

Pigs:
0.3 mg ivermectin/kg b.w. (i.e., 1 ml of product/33 kg b.w.) to be administered subcutaneously, in the neck area behind the ear.

9. Advice on correct administration

Underdosing could result in ineffective use and may favour resistance development.

To ensure a correct dosage, body weight (b.w.)should be determined as accurately as possible. If animals are to be treated collectively, reasonably homogeneous groups should be set up, and all animals of a group should be dosed at the rate corresponding to the heaviest one.

Accuracy of the dosing device should be thoroughly checked.

A sterile 18-gauge or 21-gauge, needle is recommended. Use a dry sterile needle and syringe.

The injection can be administered with a standard automatic dispenser or syringe under aseptic conditions. For 250 ml and 500 ml pack sizes, use of a multiple dose syringe is recommended. To refill the syringe, use of a draw-off needle is recommended to avoid excessive broaching of the stopper.

Do not exceed 30 broachings per stopper.

10. Withdrawal periods

Meat and offal
Cattle: 49 days.
Pigs and sheep: 28 days.

Milk
Not authorised for use in animals producing milk for human consumption. Do not use in pregnant animals which are intended to produce milk for human consumption within 60 days of expected parturition.

11. Special storage precautions

Keep out of the sight and reach of children.

Store below 25°C.

Do not use this veterinary medicinal product after the expiry date which is stated on carton and bottle after Exp. The expiry date refers to the last day of that month.

Shelf life after first opening the immediate packaging: 28 days.
After the first opening of the container, calculate the discard date of the remaining product in the container based on the shelf-life after the first opening as stated in this package leaflet. Write this date in the space provided on the label.

12. Special precautions for disposal

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

This veterinary medicinal product should not enter water courses as ivermectin is very toxic for fish and other aquatic organisms.

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 applicable national collection systems. These measures should help to protect the environment.

Ask your veterinary surgeon or pharmacist how to dispose of medicines no longer required.

13. Classification of veterinary medicinal products

Veterinary medicinal product subject to prescription

14. Marketing authorisation numbers and pack sizes

Brown glass bottles (type II) closed with a chlorobutyl rubber stopper (type I) and sealed with an aluminium and flip off polypropylene cap packed into an outer cardboard box.

Pack sizes:
Cardboard box with one vial with 50 ml solution for injection.
Cardboard box with one vial with 100 ml solution for injection.
Cardboard box with one vial with 250 ml solution for injection.
Cardboard box with one vial with 500 ml solution for injection.

Not all pack sizes may be marketed.

15. Date on which the package leaflet was last revised

{MM/YYYY}
{MM/YYYY}
{DD month YYYY}

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

16. Contact details

Marketing authorisation holder:
ADOH B.V.
Godfried Bomansstraat 31
6543 JA Nijmegen
The Netherlands
+31 24 379 2936

Manufacturer responsible for batch release:
PASTEUR FILIALA FILIPESTI S.A.
Principală Street, no. 944
Filipeştii de Pădure, Prahova County
Romania

Local representatives and contact details to report suspected adverse reactions:

17. Other information

Environmental properties: Ivermectin is very toxic to aquatic organisms and dung fauna and can accumulate in soil and sediment. 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.