

DATA SHEET

Closamectin Solution for Injection for Sheep

Region: UK and Republic of Ireland

Presentation

Closamectin Solution for Injection for Sheep is a clear amber solution for injection containing:

Ivermectin 5 mg/ml
Closantel (as closantel sodium dihydrate) 125 mg/ml

Other Substances

Contains sodium formaldehyde sulphonylate 5 mg/ml (as antioxidant)

Uses

For the treatment of mixed trematode (flake) and nematode or arthropod infestations due to gastrointestinal roundworms, trematodes, lungworms, nasal bots and mites of sheep.

Gastrointestinal roundworms

Ostertagia circumcincta (including inhibited L4), *Ostertagia trifurcata* (adult and L4), *Haemonchus contortus* (including inhibited L4), *Trichostrongylus axei* (adult), *Trichostrongylus colubriformis* (adult and L4), *T. vitrinus* (adult), *Cooperia curticei* (adult and L4), *Oesophagostomum columbianum* (adult and L4), *O. venulosum* (adult), *Chabertia ovina* (adult and L4), *Nematodirus filicollis* (adult and L4), *Trichuris ovis* (adult).

[L4 = fourth stage larvae]

Lungworms

Dictyocaulus filaria (adult and 4th stage larvae)
Protostrongylus rufescens (adult)

Liver Fluke (trematodes)

Fasciola gigantica, *Fasciola hepatica*

Treatment of fluke at 12 weeks (mature) >95% efficacy.

Treatment of fluke at 7 weeks (late immature) 100% efficacy.

Nasal Bots

Oestrus ovis

Mange Mites

Psoroptes ovis

In sheep, treatment of psoroptic mange (sheep scab) with one injection of this product will not be effective in eliminating all the mites. A suitable ivermectin-only injectable product must be administered seven days after the treatment with this product to treat clinical signs and to eliminate the mites.

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 with an appropriate product. Contact between treated, infected and untreated flocks must be avoided until at least seven days after treatment.

Benzimidazole resistant strains of *Haemonchus contortus* and *Ostertagia circumcincta* are also controlled.

Dosage and Administration:

Closamectin Injection should be administered at a dosage rate of 200 µg ivermectin per kg bodyweight and 5 mg closantel per kg bodyweight (1 ml per 25 kg). It should only be injected subcutaneously into the neck. A sterile 16-gauge, one-inch needle is recommended.

For the treatment and control of sheep scab an injection of Closamectin Injection for Sheep may be administered but must be followed with a second injection of an ivermectin only product seven days after the initial injection to treat clinical signs of scab and to eliminate mites. This injection should be administered at the other side of the neck.

This product does not contain an antimicrobial preservative. Swab septum before removing each dose. Use a dry sterile needle and syringe. 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 40 broachings per vial. If more than 40 broachings are required, use of a draw off needle is recommended.

The timing for treatment should be based on epidemiological factors and should be customised for each individual farm. As with other anthelmintics, veterinary advice should be sought on appropriate dosing programmes and stock management to achieve adequate parasite control and reduce the likelihood of resistance developing.

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 under- or over-dosing.

Mode of Action:

Ivermectin is an endectocide with activity against a wide range of internal and external parasites. Ivermectin is a macrocyclic lactone and acts by inhibiting nerve impulses. It binds 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 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.

Closantel is a member of the salicylanilide class of anthelmintics. Salicylanilides are hydrogen (proton) ionophores (referred to as oxidative phosphorylase uncouplers).

The chemical structure of salicylanilides illustrates the possession of a detachable proton. This type of molecule is lipophilic and is known to shuttle protons across membranes, in particular the inner mitochondrial membrane. Closantel acts by uncoupling oxidative phosphorylation.

Closantel is a parasiticide with flukicide activity and efficacy against certain other helminths and arthropods. In cattle, treatment with Closamectin Solution for Injection when fluke are five weeks and greater has been shown to reduce subsequent reproductive capacity and egg shedding.

Contraindications, Warnings, etc:

Meat and offal withdrawal period: 28 days

Milk withdrawal period: Not permitted for use in animals producing milk for human consumption, including pregnant animals intended to produce milk for human consumption.

Do not use intravenously or intramuscularly.

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 or crosses, and also in turtles/tortoises).

Do not use in cases of known hypersensitivity to the active substances or to any of the excipients.

Transitory swelling has occasionally been observed at the injection site. Occasionally this swelling is accompanied by pain and discomfort. This swelling completely resolves within 14 days of treatment.

Closamectin Injection can be administered to sheep at any stage of pregnancy or lactation provided that the milk is not intended for human consumption.

Do not administer concomitantly with chlorinated compounds. The effect of GABA agonists is increased by ivermectin. In the absence of compatibility studies, this veterinary medicinal product must not be mixed with other veterinary medicinal products.

Dose levels up to 4.0 mg/kg ivermectin (20 times the recommended dosage) administered subcutaneously, result in ataxia and depression in sheep.

Closantel like other salicylanilides is a potent uncoupler of oxidative phosphorylation and the safety index is not as high as is the case of many other anthelmintics. However where used as directed there are unlikely to be any untoward effects. Signs of overdosage can include loss of appetite, decreased vision, loose faeces and increased frequency of defaecation. High doses may cause blindness, hyperventilation, hyperthermia, general weakness, inco-ordination, convulsions, tachycardia and in extreme cases death. Treatment of overdosage is symptomatic as no antidote has been identified.

Pharmaceutical Precautions:

EXTREMELY DANGEROUS TO FISH AND AQUATIC LIFE. Do not contaminate surface waters or ditches with the product or used container. Any unused product or waste materials derived from such veterinary medicinal products should be disposed of in accordance with local requirements.

Do not smoke, eat or drink 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.

Do not store above 25°C.

Protect from light.

Discard unused material.

Shelf-life of the veterinary product as packaged for sale: 18 months.
Shelf-life after first opening of immediate packaging: 28 days.

Legal Category: UK: POM-VPS. ROI: LM.

Package Quantities:

100 ml, 250 ml and 500 ml Type I glass multidose vials and aluminium caps complete with bromobutyl bungs and aluminium seals.

Not all pack sizes may be marketed.

Further Information:

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 and closantel has been reported in *Haemonchus contortus* in sheep. Therefore the use of this product should be based on local epidemiological information about the susceptibility of the *Haemonchus contortus* and recommendations on how to limit further selection for resistance to anthelmintics.

Pharmacokinetic Properties:

After subcutaneous administration of Closamectin Injection to sheep at a dose rate of 200µg ivermectin per kg and 5mg closantel per kg the following parameters were observed:

Ivermectin C_{max} of 24.52ng/ml and AUC of 2082.93ng.h/ml;
Closantel C_{max} of 70.4µg/ml and AUC of 41043µg.h/ml.

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 metabolised. 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.

Salicylanilides are poorly metabolised and are excreted mainly unchanged. The main excretion route is the faeces via the bile. Closantel is extensively bound to plasma proteins, almost exclusively to albumin. The distribution to tissues is poor. Closantel has a long elimination half life.

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For Animal Treatment Only

Keep out of reach and sight of Children