SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Oriverm 10 mg/mL solution for injection for cattle, sheep and pigs.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1 mL contains:
Active substance:

Ivermectin 10 mg

For the full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Solution for injection.
A clear colourless to off-white liquid, free from visible particles.

4. CLINICAL PARTICULARS

4.1 Target species

Cattle, sheep and pigs.

4.2 Indications for use, specifying the target species

The product is indicated for the effective treatment and control of the spread of parasitic disease of the following parasites:

CATTLE

Parasite	Adult	L4	L4 (inhibited)
Gastrointestinal Roundworms			
Ostertagia lyrata	•	•	
Ostertagia ostertagi	•	•	•
Cooperia oncophora	•	•	
Cooperia pectinata	•	•	
Cooperia punctata	•	•	
Haemonchus placei	•	•	
Trichostrongylus axei	•	•	
Trichostrongylus colubriformis	•	•	
Bunostomum phlebotomum	•	•	
Oesophagostomum radiatum	•	•	
Strongyloides papillosus	•		
Nematodirus helvetianus	•		
Nematodirus spathiger	•		
Toxocara vitulorum	•		
Trichuris spp.	•		

Lungworms			
Dictyocaulus viviparus	•	•	•
Eye Worms			
Thelazia spp.	•		
Parasites			
Warbles (all parasitic stages)			
Hypoderma bovis			
H. lineatum			
Mange Mites (scabies)			
Psoroptes bovis			
Sarcoptes scabei var. *bovis*			
Sucking Lice			
Linognathus vituli			
Haematopinus eurysternus			
Solenopotes capillatus			

The product may also be used as an aid in the control of the mange mite *Chorioptes bovis,* but complete elimination may not occur.

Persistent Activity

Given at the recommended dosage of 1 mL per 50 kg bodyweight., the product controls re-infection with the following nematodes up to the duration shown:

Parasite	No. of Days After Treatment
Haemonchus placei	14
Cooperia spp.	14
Trichostrongylus axei	14
Ostertagia ostertagi	21
Oesophagostomum radiatum	21
Dictyocaulus viviparus	28

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 a qualified professional person.

SHEEP

Parasite	Adult	L4	L4 (inhibited)
Gastrointestinal Roundworms			
Teladorsagia (Ostertagia) circumcincta	•	•	•
Haemonchus contortus	•	•	•
Trichostrongylus axei	•		
T. colubriformis	•	•	
T. vitrinus	•		
Cooperia curticei	•	•	

Oesophagostomum columbianum	•	•
O. venulosum	•	
Nematodirus filicollis	•	•
Chabertia ovina	•	•
Trichuris ovis	•	
Lungworms		
Dictyocaulus filaria	•	•
Protostrongylus rufescens	•	
Nasal Bots (all larval stages)		
Oestrus ovis		
Mange Mites		
Psoroptes communis var. ovis[*]		
Sarcoptes scabiei[*] *Psorergates (Psorobia) ovis*		

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

PIG

Parasite	**Adult**	**L4**	**Somatic larval stages**
Gastrointestinal Roundworms			
Ascaris suum	•	•	
Hyostrongylus rubidus	•	•	
Oesophagostomum spp	•	•	
*Strongyloides ransomi**	•		•
Lungworms			
Metastrongylus spp	•		
Kidney Worms			
Stephanurus dentatus	•	•	•
Lice			
*Haematopinus suis***			
Mange Mites			
Sarcoptes scabei var. *suis*			

*) Product given to sows 7 to 14 days before farrowing effectively controls transmission via the milk of *Strongyloides ransomi* infections to piglets.
**) Louse eggs are unaffected by ivermectin and may require up to 3 weeks to hatch. Louse infestations developing form hatching eggs may require re-treatment.

4.3 Contraindications

The product should be administered only by the subcutaneous route and other routes are not authorised.
Do not use in animals with known hypersensitivity to ivermectin or to any of the excipients.
Do not use in other species as severe adverse reactions, including fatalities in dogs, may occur.

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, 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 antihelmintic belonging to another pharmacological class and having a different mode of action should be used.

Resistance to macrocyclic lactones (which includes ivermectin) has been reported in *Teladorsagia* spp. in sheep and in *Cooperia* spp. in cattle within the EU. Therefore, the use of this product should be based on local (regional, farm) epidemiological information about susceptibility of nematodes and recommendations on how to limit further selection for resistance to anthelmintics.

4.5 Special precautions for use

Special precautions for use in animals

When treating groups of animals use of an automatic dosing device (with vented draw off apparatus) is recommended when using the 100 mL vial.
Syringes must be filled from the vial through a dry sterile draw-off needle that has been placed in the vial stopper.

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. Contact between treated, infected and untreated flocks must be avoided until at least seven days after treatment. In sheep, 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.

Swab septum before removing each dose. Use a sterile needle and syringe.

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

- People with known hypersensitivity to the active substance or any of the excipients should avoid contact with the veterinary medicinal product.
- The veterinary medicinal product should not be administered by pregnant women.
- Avoid contact with the skin and eyes. In case of skin or eye contact, immediately rinse affected area with water.
- Take care to avoid self-injection: the product may cause local irritation and/or pain at the site of injection.
- In case of accidental self-injection, seek medical advice and show the label or package leaflet to the physician.
- Do not smoke, drink or eat while handling the product.
- Wash hands after use.

Other precautions

The product is very toxic to aquatic organisms and dung insects. Treated animals should not have direct access to ponds, streams or ditches for 14 days after treatment. 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/flock health, as advised by a veterinarian.

4.6 Adverse reactions (frequency and seriousness)

The frequency of adverse reactions has not been defined, however the following have been observed.

Cattle

Mild and transient discomfort has occasionally been observed in cattle following subcutaneous administration. A low incidence of soft tissue swelling at the injection site has been observed.

Sheep

Discomfort, sometimes intense but usually transient, has been observed in some sheep following subcutaneous administration.

In both species these reactions disappear without treatment.

Pigs

Mild and transient pain reactions may be seen in some pigs following subcutaneous administration.

4.7 Use during pregnancy, lactation or lay

Pregnancy and lactation

Product can be administered to cows and ewes at any stage of pregnancy or lactation provided that the milk is not intended for human consumption.

Product can be administered to sows at any stage of pregnancy or lactation, when used at the recommended dose levels.

Fertility

It can be used in breeding ewes, rams, sows, boars, bulls and cows without affecting fertility. Product can be given to all ages of animals including young calves, lambs and piglets.

4.8 Interaction with other medicinal products and other forms of interaction

No data available.

4.9 Amounts to be administered and administration route

Syringes must be filled from the vial through a dry, sterile draw-off needle that has been placed in the vial stopper. Vial stoppers must not be broached more than 20 times.

Cattle and Sheep

Product should be given only by subcutaneous injection, using aseptic precautions, at the recommended dosage level of 200 µg of ivermectin/kg b.w. under the loose skin in front of, or behind, the shoulder in cattle and in the neck of the sheep**.**

To ensure administration of a correct dose, bodyweight should be determined as accurately as possible; accuracy of the dosing device should be checked.

Use this chart as a guide in working out the appropriate dose rate:

CATTLE (1 mL/50 kg)		**SHEEP** (0.5 mL/25 kg)	
Bodyweight (kg)	**Dose Volume (mL)**	**Bodyweight (kg)**	**Dose Volume (mL)**
Up to 50	1.0	Up to 5	0.1
51 – 100	2.0	5.1 – 10	0.2
101 – 150	3.0	10.1 – 15	0.3
151 – 200	4.0	15.1 – 25	0.5
201 – 250	5.0	25.1 – 50	1.0
251 – 300	6.0	50.1 – 75	1.5
301 – 350	7.0	75.1 - 100	2.0
351 – 400	8.0		
For cattle weighing over 400 kg calculate the dose at the rate of 1 mL/50 kg b.w.		For sheep weighing over 100 kg calculate the dose at the rate of 0.5 mL/25 kg b.w.	

When treating sheep of less than 16 kg, seek veterinary advice regarding the use of 1 mL disposable syringes graduated in increments of 0.1 mL. For the treatment of individual sheep, a syringe not exceeding 2.0 mL and calibrated in increments of 0.1 mL should be used.

Each mL contains 10 mg of ivermectin sufficient to treat 50 kg of bodyweight of cattle and sheep. The injection may be given with any standard automatic or single-dose or hypodermic syringe. Replace with a fresh sterile needle after every 10 to 12 animals. Injection of wet or dirty animals is not recommended.

For the treatment and control of sheep scab, two injections with a seven day interval are required to treat clinical signs of scab and to eliminate mites.

Pigs

At the recommended dosage level of 300 µg of ivermectin/kg b.w., administer only subcutaneously in the neck in pigs.

Each mL contains 10 mg of ivermectin sufficient to treat 33 kg of bodyweight of pigs.

Use the following dosage table:

Bodyweight (kg)	**Dose Volume (mL)**
<= 3	0.1
>3-6	0.2
>6-10	0.3
>10-13	0.4
>13-16	0.5
17-33	1.0
34-50	1.5

51-66	2.0
67-99	3.0
100-133	4.0
134-166	5.0
167-200	6.0

Over 200 kg bodyweight, give 1.0 mL/33 kg b.w.

The injection may be given with any standard automatic or single-dose or hypodermic syringe. Replace with a fresh sterile needle after every 10 to 12 animals. Injection of wet or dirty animals is not recommended.

In young pigs, especially those weighing under 16 kg for which less than 0.5 mL of the product is indicated, dosing accuracy is important. The use of a syringe that can accurately deliver increments of 0.1 mL is recommended. For piglets weighing less than 16 kg give 0.1 mL/3 kg.

When treating pigs of less than 16 kg seek veterinary advice regarding the use of 1 mL disposable syringes graduated in increments of 0.1 mL.

Recommended treatment programme

Young animals and adults

Sows:
Treat prior to farrowing, preferably 7-14 days before, to minimize infection of piglets.

Gilts:
Treat 7-14 days prior to breeding. Treat 7-14 days prior to farrowing.

Boars:
Frequency of and need for treatments are dependent upon exposure.

To ensure the correct dose, determine the live weight of each animal as accurately as possible.

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

Cattle
Single doses of 4.0 mg ivermectin/kg b.w. (equal to 20 times the recommended dose) given subcutaneously resulted in ataxia and depression.

Sheep
Ivermectin administered subcutaneously has demonstrated adequate safety at the recommended dose level. At the oral dose of a commercial formulation an oral administration of up to 4mg ivermectin per kg (20 times the recommended dose) administered by a gastric tube did not cause undesirable toxic reactions.

Pigs
A dose of 30 mg ivermectin/kg b.w. (equal to 100 times the recommended dose) injected subcutaneously to pigs caused lethargy, ataxia, bilateral mydriasis, intermittent tremors, laboured breathing and lateral recumbency.
No antidote has been identified; however, symptomatic therapy may be beneficial.

4.11 Withdrawal period(s)

Cattle:
Meat and offal: 49 days.
Milk: Do not use in cattle producing milk for human consumption.

Sheep:
Meat and offal: 28 days.
Milk: Do not use in sheep producing milk for human consumption.

Pigs
Meat and offal: 28 days.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: endectocides, macrocyclic lactones, avermectins, ivermectin.
ATCvet code: QP54AA01.

5.1 Pharmacodynamic properties

Ivermectin is a member of the macrocyclic lactone class of endectocides which have a unique mode of action. 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 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.

5.2 Pharmacokinetic particulars

Maximum plasma concentration

Cattle
At a dose level of 0.2 mg ivermectin/kg b.w. a maximum plasma concentration of 35-50 ng/mL is reached in about 2 days and the half-life in plasma is 2.8 days. It is also established that ivermectin is carried mainly in the plasma (80%). This distribution between plasma and blood cells remains relatively constant.

Sheep
At a dose level of 0.3 mg ivermectin/kg b.w. an average peak of 16 ng/mL is reached one day after injection.

Pigs
During trials carried out at a dose rate of 0.2 mg/kg b.w. ivermectin, a plasma concentration of 10-20 ng/mL was reached in about 2 days and half-life in plasma was 0.5 days.

Excretion: length of time and route

Cattle
A liquid chromatographic method with fluorescence detection allows the determination of ivermectin residues in tissues. After an injection of 0.3 mg ivermectin/kg b.w., the liver (target tissue) had residues

ranging from 454 ppb at 2 days post treatment to 11 ppb at 28 days post treatment. All other tissues had lower residues at all time periods: fat > kidney > muscle. The injection site had residues shortly after treatment, ranging up to 69 ppm at 2 days withdrawal, but by 28 days the average residue was negligible (< 2 ppb). Cattle receiving a single dose of tritium-labelled ivermectin (0.2 - 0.3 mg/ kg b.w.) were slaughtered at 7, 14, 21 and 28 days after dosing. Composites of faeces collected during the first 7 days after dosing contained almost all the dosed radioactivity. Only about 1-2% of the dosed radioactivity was excreted in the urine.
Analyses of the faeces showed that about 40-50% of the excreted radioactivity was present as unaltered drug. The remaining 50-60% was present as metabolites or degradation products almost all which were more polar than the ivermectin.

Sheep
A liquid chromatographic method with fluorescence detection allows the determination of ivermectin residues in tissues. After an injection of 0.3 mg ivermectin/kg b.w., the liver (target tissue) had residues ranging from 160 ppb at 3 days post treatment to 7.2 ppb at 28 days post treatment. The highest residue levels were recovered in fat (from 230 ppb at 3 days post treatment to 13 ppb at 28 days post treatment). Residues in all tissues were below 30 ppb at 28 days post treatment. Radioactive ivermectin was administered to sheep at a dose rate of 0.3 mg/kg. Analyses of the faeces showed that about 99% of the drug and its metabolites are excreted in the faeces, about 1% being excreted in the urine.

Pigs
A liquid chromatographic method with fluorescence detection allows the determination of ivermectin residues in tissues. After an injection of 0.4 mg/kg ivermectin the liver (target tissue) contained average residues ranging from 69 ppb at 3 days post dose to 13 ppb at 14 days post dose. No liver residue (< 2 ppb) was found at 28 days post dose. Swine receiving a single dose of tritium-labelled ivermectin (0.3-0.4 mg/kg) were slaughtered at 1, 7, 14 and 28 days after dosing. Composites of faeces collected during the first 7 days after dosing contained only about 36% of the dosed radioactivity. Less than 1% of the dosed radioactivity was found in the urine. Analysis of the faeces showed that about 40% of the excreted radioactivity was unaltered drug.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Propylene glycol (E 1520)
Glycerol formal

6.2 Major incompatibilities

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

6.3 Shelf life

100 ml vials: Shelf life of the veterinary medicinal product as packaged for sale: 3 years.
50 ml vials: Shelf life of the veterinary medicinal product as packaged for sale: 2 years.
Shelf life after first opening the immediate packaging: 28 days.

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and composition of immediate packaging

50 ml or 100 ml amber glass vials (Type II) closed with chlorobutyl rubber stoppers and aluminium caps in carton box.
Pack sizes:

Carton box with 1 glass vial of 50 ml
Carton box with 1 glass vial of 100 ml

Not all pack sizes may be marketed.

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

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

7. MARKETING AUTHORISATION HOLDER

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Fax: + 49 40 2286 481 99
E-mail: info@actrevo.com

8. MARKETING AUTHORISATION NUMBER(S)

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation:

10 DATE OF REVISION OF THE TEXT

PROHIBITION OF SALE, SUPPLY AND/OR USE

To be supplied only on veterinary prescription.