Eqvalan & Eqvalan Duo Oral Paste for Horses Annual Wormer Pack

	Revised	AN
Eqvalan Oral Paste	May 2019	01364/2018
Eqvalan Duo Oral Paste	November 2018	01034/2018

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Eqvalan Oral Paste for Horses (Ivermectin 18.7 mg/g)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each gram contains:

Active substance
Ivermectin 18.7 mg

Excipients
Titanium Dioxide (E171) 20.0 mg

For the full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Oral paste.
Clean, white, homogeneous paste

4. CLINICAL PARTICULARS

4.1 Target species

Horses and donkeys.

4.2 Indications for use, specifying the target species

The product is indicated for the treatment of parasitic infestations in horses and donkeys due to:

Large strongyles
Strongylus vulgaris (adults and arterial larval stages)
S. edentatus (adults & tissue larval stages)
S. equinus (adults)
Triodontophorus spp. (adults)
Triodontophorus brevicauda
Triodontophorus serratus
Craterostomum acuticaudatum (adults)

Small Strongyles
Adult and immature (fourth stage larvae) small strongyles or cyathostomes, including benzimidazole-resistant strains:
Coronocyclus spp.
Coronocyclus coronatus
Coronocyclus labiatus
Coronocyclus labratus

Cyathostomum spp.
Cyathostomum catinatum
Cyathostomum pateratum
Cylicocyclus spp.
Cylicocyclus ashworthi
Cylicocyclus elongatus
Cylicocyclus insigne
Cylicocyclus leptostomum
Cylicocyclus nassatus
Cylicocyclus radiatus
Cylicostephanus spp.
Cylicostephanus asymetricus
Cylicostephanus bidentatus
Cylicostephanus calicatus
Cylicostephanus goldi
Cylicostephanus longibursatus
Cylicostephanus minutus
Cylicodontophorus spp.
Cylicodontophorus bicornatus
Gyalocephalus capitatus
Parapoteriostomum spp.
Parapoteriostomum euproctus
Parapoteriostomum mettami
Petrovinema spp.
Petrovinema poculatum
Poteriostomum spp.
Poteriostomum imparidentatum

Lungworms (adult and immatures)
Dictyocaulus arnfieldi

Pinworms (adult and immatures)
Oxyuris equi

Ascarids (adults and third & fourth stage larvae)
Parascaris equorum

Hairworms (adults)
Trichostrongylus axei

Large-mouth stomach worms (adults)
Habronema muscae

Neck threadworms (microfilariae)
Onchocerca spp.

4.3 Contra-indications

The product has been formulated specifically for use in horses and donkeys only. Dogs and cats may be adversely affected by the concentration of ivermectin in this product if they are allowed to ingest spilled paste or have access to used syringes.

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.

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.

Resistance to macrocyclic lactones (which includes ivermectin) has been reported in *Parascaris equorum* in horses in a number of countries within the EU. Therefore, the use of this product should be based on local (regional, farm) epidemiological information about susceptibility of gastro-intestinal 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:

No special precautions are required.

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

Do not smoke, eat or drink while handling the product.
Wash hands after use.
This product may cause skin and eye irritation. Therefore, the user should avoid contact of the product with the skin and the eyes. In the case of contact, rinse immediately with plenty of water.
In the case of accidental ingestion or eye irritation after contact seek medical advice immediately and show the package insert or the label to the physician.

4.6 Adverse reactions (frequency and seriousness)

Some horses carrying heavy infection of *Onchocerca* microfilariae have experienced oedema and pruritus following dosing, assumed to be the result of death of large numbers of microfilariae. These signs resolve within a few days but symptomatic treatment may be advisable.

4.7 Use during pregnancy, lactation or lay

Horses and donkeys of all ages, including pregnant mares and breeding stallions, have been treated with no adverse effect.

4.8 Interaction with other medicinal products and other forms of interaction

The product has been used in conjunction with other equine health care products and no interactions have been identified.

4.9 Amounts to be administered and administration route

Administer orally to both horses and donkeys at the recommended dose level of 0.2 mg ivermectin per kilogram of bodyweight. Each syringe delivers 120 mg ivermectin, sufficient to treat 600 kg of bodyweight.

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

Dosing instructions
Each weight marking on the syringe plunger will deliver sufficient paste to treat 100 kg bodyweight. Unlock the knurled ring by making 1/4 turn and slide the knurled ring up the plunger shaft so that the side nearest the barrel is at the prescribed weight marking. Turn the knurled ring 1/4 turn to lock in place. Remove the plastic cap from the tip of the nozzle. Make sure the horse's mouth contains no feed. Insert the syringe into the horse's mouth at the interdental space. Advance the plunger as far as it will go, depositing the medication on the base of the tongue.

Parasite control program
Veterinary advice should be given on appropriate dosing programs and stock management to achieve adequate parasite control for both tapeworm and roundworm infestations. Foals may be treated initially at 6-8 weeks of age if indicated. Discard any unused material.

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

Mild transitory signs (slowed pupillary light response and depression) have been seen at a dose of 1.8 mg/kg (9 times the recommended dose level). Other signs seen at higher doses include mydriasis, ataxia, tremors, stupor, coma and death. The less severe signs have been transitory. No antidote has been identified; however, symptomatic therapy may be beneficial.

4.11 Withdrawal periods

Donkeys - meat: 21 days
Horses - meat: 21 days

Do not use in mares producing milk for human consumption.

5. PHARMACOLOGICAL or IMMUNOLOGICAL PROPERTIES

ATC Vet 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-gates 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 properties

Maximum plasma concentration
In the horse the maximum plasma concentration (average of 32 ng/ml) is reached 6 hours after administration of a dose rate of 0.3 mg ivermectin per kg bodyweight. This peak falls off gradually to an average level of 2 ng/ml at 10 days.

Excretion: length of time and route
Ivermectin residues (expressed as dihydro B_{1a}) in the liver, muscle, kidney, fat and blood were determined with a liquid chromatographic method with fluorescence detection. No residue (except one 28 day fat sample) reached the limit of detection of > 2 ppb 21, 28 and 42 days post dose.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Titanium dioxide (E171)
Hyprolose
Hydrogenated Castor Oil
Propylene Glycol

6.2 Major Incompatibilities

None known.

6.3 Shelf-life

Shelf life of the veterinary medicinal product as packaged for sale: 3 years.

6.4 Special precautions for storage

Do not store above 25ºC.
Protect from light.

6.5 Nature and composition of immediate packaging

Disposable white, opaque, polypropylene syringe barrel and plunger with a white, opaque, low density polyethylene cap. Each syringe contains 6.42 g paste.

Each carton contains 1 syringe.

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

EXTREMELY DANGEROUS TO FISH AND AQUATIC LIFE. Do not contaminate ponds, waterways or ditches with the 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

Boehringer Ingelheim Animal Health UK Ltd
Ellesfield Avenue
Bracknell
Berkshire
RG12 8YS

8. MARKETING AUTHORISATION NUMBER

Vm 08327/4177

9. DATE OF FIRST AUTHORISATION

18 April 1994

10. DATE OF REVISION OF THE TEXT

May 2019

Approved: 10 May 2019

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

EQVALAN DUO, oral paste
IVOMEC COMP, oral paste (Denmark, Finland, Norway, Sweden)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each syringe contains 7.74 g of paste and delivers:

Active substances:

Ivermectin	0.120 g (15.5 mg/g)
Praziquantel	**0.600 g (77.5 mg/g)**

Excipients:

Butylhydroxyanisole (E320):	0.002 g
Sunset Yellow (E110):	0.003 g
Titanium dioxide (E171):	0.155 g

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Oral paste.
Smooth, homogeneous orange paste.

4. CLINICAL PARTICULARS

4.1 Target species

Horses

4.2 Indications for use, specifying the target species

FOR THE TREATMENT OF MIXED CESTODE AND NEMATODE OR ARTHROPOD INFESTATIONS IN HORSES. THE FOLLOWING PARASITES OF HORSES ARE SENSITIVE TO THE ANTIPARASITIC EFFECTS OF EQVALAN DUO, ORAL PASTE:

Adult Tapeworms:
Anoplocephala perfoliata
Anoplocephala magna

Large strongyles:
Strongylus vulgaris (adults and arterial larval stages)
Strongylus edentatus (adults and tissue larval stages)
Strongylus equinus (adults)
Triodontophorus spp (adults)
Triodontophorus brevicauda
Triodontophorus serratus

Craterostomum acuticaudatum (adults)
Adult and immature (intraluminal fourth-stage larvae) of small strongyles or cyathostomes, including benzimidazole-resistant strains:

Coronocyclus spp
Coronocyclus coronatus
Coronocyclus labiatus
Coronocyclus labratus
Cyathostomum spp
Cyathostomum catinatum
Cyathostomum pateratum
Cylicocyclus spp
Cylicocyclus ashworthi
Cylicocyclus elongatus
Cylicocyclus insigne
Cylicocyclus leptostomum
Cylicocyclus nassatus
Cylicodontophorus spp
Cylicodontophorus bicornatus
Cylicostephanus spp
Cylicostephanus calicatus
Cylicostephanus goldi
Cylicostephanus longibursatus
Cylicostephanus minutus
Parapoteriostomum spp
Parapoteriostomum mettami
Petrovinema spp
Petrovinema poculatum
Poteriostomum spp

Adult hairworms: *Trichostrongylus axei*
Adult and immature (fourth stage Larvae) pinworms: *Oxyuris equi*
Adult, third- and fourth-stage larvae of roundworms (ascarids): *Parascaris equorum*
Microfilariae of neck threadworms: *Onchocerca* spp
Adult intestinal threadworms: *Strongyloides westeri*
Adult large-mouth stomach worms: *Habronema muscae*
Oral and, gastric stages of bots: *Gasterophilus* spp
Adult and immature (inhibited fourth stage larvae) lungworms: *Dictyocaulus arnfieldi*

4.3 Contraindications

Do not use in mares producing milk for human consumption.
The product has been formulated for use in horses only. Cats, Dogs, especially Collies, Old English Sheepdogs and related breeds or crosses, and also turtles and tortoises may be adversely affected by the concentration of ivermectin in this product if they are allowed to ingest spilled paste or have access to used syringes

4.4 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 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 anthelmintic 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 *Parascaris equorum* in horses in the EU. Therefore the use of this product should be based on local (regional, farm) epidemiological information about susceptibility of gastro-intestinal nematodes and recommendations on how to limit further selection for resistance to anthelmintics

4.5 Special precautions for use

i. Special precautions for use in animals

Safety studies were not conducted in foals younger than 2 months of age, or in stallions, the use of Eqvalan Duo, oral paste is not recommended in these categories of animals.

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

Wash hands after use.

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

This product may cause skin and eye irritation. Therefore, the user should avoid contact of the product with the skin and the eyes. In case of contact, rinse immediately with plenty of water.

In the case of accidental ingestion or eye irritation after contact seek medical advice immediately and show the package insert or the label to the physician.

4.6 Adverse reactions (frequency and seriousness)

Some horses with heavy infections of *Onchocerca* spp. microfilariae have experienced oedema and pruritis following treatment; such reactions were assumed to be the result of the death of large numbers of microfilariae. These signs resolve within a few days but symptomatic treatment may be advisable.
In cases of heavy infestations with tapeworms, signs of mild, transient colic and loose stool may be observed.
Following administration of Eqvalan Duo, there have been rare reports of inflammation of the mouth, lip and tongue, which results in various clinical signs such as oedema, hypersalivation, erythema, tongue disorder and stomatitis. These reactions have been transitory in nature, appearing within 1 hour and abating within 24 to 48 hours following administration. In case of severe oral reactions symptomatic treatment is recommended

4.7 Use during pregnancy, lactation or lay

Studies performed in laboratory animals showed no teratogenic or embryotoxic effect of either ivermectin or praziquantel at the recommended doses during therapy.

Ivermectin-Praziquantel combination can be used after the first three months of gestation and during lactation. In the absence of clinical data in early pregnancy EQVALAN DUO can only be used in the first three months of gestation according to a risk benefit analysis by the veterinarian.

4.8 Interaction with other medicinal products and other forms of interaction

No data available.

4.9 Amounts to be administered and administration route

The recommended dosage is 200 mcg ivermectin per kilogram of bodyweight and 1mg praziquantel per kilogram of bodyweight corresponding to 1.29 g of paste per 100 kg bodyweight in a single administration.
Bodyweight and dosage should be accurately determined prior to treatment. The contents of one syringe will treat horses up to 600 kg. Calibrated markings are provided at 100 kg bodyweight intervals. The syringe should be adjusted to the calculated dosage by setting the ring on the appropriate place on the plunger.

Directions for use

EQVALAN DUO, oral paste is for oral administration only. While holding the plunger, turn the knurled ring on the plunger ¼ turn to the left and slide it so the stop ring is at the prescribed weight marking. Lock the ring in place by turning it ¼ turn to the right in order to bring the two arrows, the one visible on the ring and the one on the plunger rod, into alignment. Make sure the horse's mouth contains no feed. Remove the cover from the tip of the syringe. Insert the syringe tip into the horse's mouth at the interdental space and deposit the paste on the base of the tongue. Immediately raise the horse's head for a few seconds after dosing and ensure that the paste is consumed.

Parasite control Program

Veterinary advice should be given on appropriate dosing programs and stock management to achieve adequate parasite control for both tapeworm and roundworm infestations.

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

No undesirable effects related to treatment were observed in 2 month old horses treated with EQVALAN DUO, oral paste at up to three times the recommended dose and in adult horses treated at ten times the recommended dose.

Transient decreased food consumption, increased body temperature, salivation and impairment of vision were noticed in horses treated twice with an ivermectin oral paste or once with EQVALAN DUO, oral paste at ten times the recommended dose (i.e., 2 mg/kg b.w.). All changes disappeared within five days.

No antidote has been identified; however, symptomatic therapy may be beneficial.

4.11 Withdrawal period(s)

Meat: 30 days.
Do not use in mares producing milk for human consumption.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group:	Anthelmintics
ATCvet code:	QP54AA51 ivermectin, combinations.

EQVALAN DUO, oral paste is an endectocide containing an association of an anthelmintic active ingredient, ivermectin, and a cestocide active ingredient, praziquantel.

5.1 Pharmacodynamic properties

Ivermectin is a member of the macrocyclic lactone class of endectocides. 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, which results 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 macrocyclic lactones do not readily cross the blood-brain barrier.

Praziquantel is a synthetic isoquinoline-pyrazine derivative with activity against several trematode and cestode parasites. *In vitro* and *in vivo* studies have found that trematodes and cestodes rapidly take up praziquantel within minutes; praziquantel causes tetanic contraction of the parasites' musculature and a rapid vacuolisation of their tegument. The net effect is that the parasite detaches from the host. Praziquantel affects membrane permeability in trematodes and cestodes, and influences divalent cation fluxes, particularly calcium ion homeostasis, which is thought to contribute to the rapid muscle contraction and vacuolisation. The margin of safety for the praziquantel is due to its rapid metabolism and excretion as well as its selective effect on susceptible parasites.

5.2 Pharmacokinetic particulars

After oral administration to horses of the recommended dose of EQVALAN DUO oral paste, praziquantel is rapidly absorbed and excreted, whereas ivermectin is more slowly absorbed and persists during a longer period in the body. Praziquantel maximum plasma concentrations (of the order of 1 µg/ml) are reached rapidly (approximately in the hour following treatment). The praziquantel plasma residue depletes rapidly to non-quantifiable levels by 7.5 hours post dose. Praziquantel is excreted as metabolites in the urine and faeces and the total amount excreted accounts for 31% and 24%, respectively of the administered dose within 24 hours.

Ivermectin maximum plasma concentrations (Cmax: 37.9 ng/ml) are reached in a longer period (tmax: approximately 9 hours after treatment) and levels fell to non detectable / no quantifiable values on or before 28 days after administration.

Faecal excretion is the major pathway of ivermectin elimination in all species studied.

NO PHARMACOLOGICAL INTERFERENCE BETWEEN IVERMECTIN AND PRAZIQUANTEL WAS NOTED.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

SUNSET YELLOW FCF (E110)
TITANIUM OXIDE (E171),
BUTYLHYDROXYANISOLE (E320)
HYDROXYPROPYLCELLULOSE
HYDROGENATED CASTOR OIL
GLYCEROL FORMAL

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 3 years
Shelf life after first opening the immediate packaging: 2 years

6.4 Special precautions for storage

Store in the original container. Replace the cap after use.

6.5 Nature and composition of immediate packaging

Immediate package

EQVALAN DUO, oral paste is available in syringes containing 7.74 g of paste: White polypropylene syringes barrel with a white LDPE cap, a rubber rod tip and a white polypropylene plunger rod, with dose divisions calibrated by body weight.

Outer package and sales presentations

Each syringe is sealed in a transparent polypropylene bag.

Carton box of 1 individual syringe.
Carton box of 50 individual syringes.

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 product or used syringes. Any unused product or waste material should be disposed of in accordance with national requirements.

7. MARKETING AUTHORISATION HOLDER

Boehringer Ingelheim Animal Health UK Limited
Ellesfield Avenue
Bracknell
Berkshire
RG12 8YS
United Kingdom

8. MARKETING AUTHORISATION NUMBER

Vm 08327/4206

9. DATE OF FIRST AUTHORISATION

05 September 2003

10. DATE OF REVISION OF THE TEXT

November 2018

Approved: 16 November 2018

D Austin