## 1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Nexpraz Duo 18.7 mg/g + 140.3 mg/g Oral Paste for Horses

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each g contains:
**Active substances:**
Ivermectin 18.7 mg
Praziquantel 140.3 mg

**Excipients:**

| **Qualitative composition of excipients and other constituents** | **Quantitative composition if that information is essential for proper administration of the veterinary medicinal product** |
|---|---|
| Brilliant blue FCF | 0.005 mg |
| Tartrazine | 0.021 mg |
| Titanium dioxide | 20.0 mg |
| Castor oil, hydrogenated | |
| Hydroxypropylcellulose | |
| Propylene glycol | |
| Sucralose | |
| "Green Apple flavour" | |
| Cinnamon bark oil, Ceylon | |

Green paste.

## 3. CLINICAL INFORMATION

### 3.1 Target species

Horses

### 3.2 Indications for use for each target species

For the treatment of mixed cestode and nematode or arthropod infestations caused by adults or immature stages of nematodes, lungworms, botfly larvae and tapeworms in horses.
The veterinary medicinal product is only indicated when use against parasite groups targeted by each of the combined active substances is indicated at the same time.

♦ **Nematodes:**
Large strongyles:
*Strongylus vulgaris* (adults and L4 arterial larval stages)
*Strongylus edentatus* (adults and L4 tissue larval stages)
*Strongylus equinus* (adults)
*Triodontophorus* spp. (adults)

Small strongyles:
*Cyathostomum* spp., *Cylicocyclus* spp., *Cylicostephanus* spp., *Cylicodontophorus* spp., *Gyalocephalus* spp. (adults and uninhibited mucosal larvae)
*Parascaris*: *Parascaris equorum* (adults and larvae)
*Oxyuris*: *Oxyuris equi* (larvae)
*Trichostrongylus*: *Trichostrongylus axei* (adults)
*Strongyloides*: *Strongyloides westeri* (adults)
*Habronema*: *Habronema* spp. (adults)
*Onchocerca*: *Onchocerca* spp.microfilariae i.e. cutaneous onchocerciasis
Lungworms: *Dictyocaulus arnfieldi* (adults and larvae)

- **Cestodes:** *Anoplocephala perfoliata* (adults) **Botflies:** *Gasterophilus* spp. (larvae)

### 3.3 Contraindications

Do not use in foals under 2 weeks of age.
Do not use in case of hypersensitivity to the active substances or to any of the excipients.

### 3.4 Special warnings

Unnecessary use of antiparasitics or use deviating from the instructions given in the SPC 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 group of animals.

Repeated use for an extended period, particularly when using the same class of substances, increases the risk of resistance development. Within a herd, maintenance 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.

In the absence of risk of co-infection, a narrow spectrum product should be used.

Partial cross-resistance between ivermectin and moxidectin has been reported. Furthermore, resistance to ivermectin (an avermectin) has been reported in *Parascaris equorum* in horses in a number of countries including the EU. Therefore, the use of this 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). Confirmed resistance should be reported to the marketing authorisation holder or to the competent authorities."

Tapeworm infestations are rare in foals before 2 months of age, therefore treatment of foals younger than 2 months of age is not considered necessary.

Confirmed cases of praziquantel resistance in tapeworms infecting horses have been reported in the USA, and the first isolated cases of ivermectin resistance in cythostomins have been reported in the USA from horses imported from the EU. Given the global horse trade, the risk of resistance emerging in Europe is significant.

It is recommended to further investigate suspected resistance cases using an appropriate diagnostic method (e.g., Faecal Egg Count Reduction Test), especially in imported animals or those without a known history of origin.

Tapeworm speciation was not performed in the efficacy study of the veterinary medicinal product. The indication for *A. perfoliata* is based on the typical pathoanatomical finding observed during the efficacy study and its predominant prevalence among equine tapeworms.

### 3.5 Special precautions for use

Special precautions for safe use in the target species:
Not applicable.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
People with known hypersensitivity to ivermectin, praziquantel, tartrazine, or cinnamon should avoid contact with the veterinary medicinal product.
This veterinary medicinal product may cause skin and eye irritation. Avoid contact with skin and eyes. Personal protective equipment consisting of gloves should be worn when handling the veterinary medicinal product.
In the case of accidental contact with skin or eyes wash the affected area immediately with plenty of water. If skin or eye irritation persist, seek medical advice.
In the case of accidental ingestion, especially by a child, seek medical advice immediately and show the package leaflet or label to the physician.
Do not eat, drink or smoke while handling the veterinary medicinal product.
Wash hands after use.

Special precautions for the protection of the environment:
Not applicable.

Other precautions:
Avermectins may not be well tolerated in all non-target species. Cases of intolerance have been reported in dogs, especially collies, Old English Shepherd dogs and related breeds or their crossbreds, as well as in turtles and tortoises.
Dogs and cats should not have access to paste residues or used applicators due to the possibility of side effects associated with ivermectin toxicity.

### 3.6 Adverse events

Horses:

| | |
|---|---|
| Very rare<br>(< 1 animal / 10,000 animals treated, including isolated reports): | Colic [1,3], Loose Stool [2], Diarrhoea [3]<br>Anorexia [3]<br>Allergic reaction (such as hypersalivation, lingual oedema, urticaria, tachycardia, congested mucous membrane, Allergic oedema) |
| Undetermined frequency (cannot be estimated from the available data) | Swelling [4]<br>Itching [4] |

[1] Mild transient in case of very high levels of infestation, caused by destruction of the parasites
[2] In case of very high levels of infestation, caused by destruction of the parasites
[3] In particular when there is heavy worm burden.
[4] For horses carrying heavy infection of Onchocerca microfilariae. It is assumed that these reactions are the result of the destruction of large numbers of microfilariae.

A veterinarian should be consulted if these signs persist.

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 its local representative 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:
Can be used during pregnancy and lactation.
Fertility:
The veterinary medicinal product can be used safely in stallions.

### 3.8 Interaction with other medicinal products and other forms of interaction

None known.

### 3.9 Administration routes and dosage

Oral use.
Single administration of 200 µg of ivermectin and 1.5 mg of praziquantel per kg bw, equivalent to 1.07 g of the paste per 100 kg of body weight.
To ensure correct dosing, it is necessary to determine the most accurate weight possible and to measure the appropriate dose to prevent underdosing which may increase the risk of developing anthelmintic resistance.

| Horse weight | Paste dose | Horse weight | Paste dose |
|---|---|---|---|
| Up to 100 kg | 1.070 g | 401–450 kg | 4.815 g |
| 101-150 kg | 1.605 g | 451-500 kg | 5.350 g |
| 151-200 kg | 2.140 g | 501-550 kg | 5.885 g |
| 201-250 kg | 2.675 g | 551-600 kg | 6.420 g |
| 251-300 kg | 3.210 g | 601-650 kg | 6.955 g |
| 301-350 kg | 3.745 g | 651-700 kg | 7.490 g |
| 351-400 kg | 4.280 g | | |

The first division of the applicator is sufficient to treat animals weighing 100 kg bw.
Each additional division of the applicator will provide a sufficient volume of paste for 50 kg bw. Set the applicator according to the calculated dose by moving the ring to the corresponding mark.

An applicator containing 7.49 g of paste will provide enough paste to treat a horse weighing 700 kg at the recommended dosage.

Instructions for use
Before administration, set the applicator according to the calculated dose by moving the ring to the corresponding mark. The paste is administered orally through the interdental space to the root of the tongue. The animal's mouth should not contain any food residue. Immediately after administration, raise the horse's head for a few seconds to ensure that the dose is swallowed properly.

In order to achieve an adequate level of prevention against infection with tapeworms and roundworms, it is necessary to provide veterinary consultancy on appropriate dosing and stock management.

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

A tolerance study performed in foals over 2 weeks of age at 5 times the recommended doses did not show any side effects.
Safety studies performed at 3 times the recommended doses of the veterinary medicinal product in mares at 14-day intervals throughout pregnancy and lactation did not reveal miscarriages, any adverse effects on pregnancy, parturition and general health of the mares, nor any abnormalities on the foals.
Safety studies performed at 3 times the recommended doses of the veterinary medicinal product in stallions did not show any adverse effects, especially on reproductive performance.

### 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

Meat and offal: 35 days.
Not authorised for use in animals producing milk for human consumption.

## 4. PHARMACOLOGICAL INFORMATION

### 4.1 ATCvet code: QP54AA51

### 4.2 Pharmacodynamics

Ivermectin is a macrocyclic lactone that has a broad antiparasitic effect against nematodes and arthropods. It works by inhibiting nerve impulses. The mode of action involves glutamate gates of chloride channels. Ivermectin binds selectively with high affinity to the glutamate gates of chloride channels that occur in nerve fibres and muscle cells of invertebrates. This leads to an elevation of permeability of the cell membrane for chloride ions with hyperpolarisation of nerve fibres or muscle cells, the result of which is paralysis and death of the parasite. Substances in this group may also affect other chloride channel ligands, such as the neurotransmitter gamma-aminobutyric acid (GABA). The safety of substances of this group is given by the fact that mammals do not have glutamate-chloride channels.
Praziquantel is a pyrazinoquinoline derivative that acts against many species of tapeworms and trematodes. It primarily acts by impairing the motility and the suction function of tapeworm. Its action includes impaired neuromuscular coordination, but also affects the permeability of the parasite's surface, leading to excessive calcium and glucose losses. This causes spastic paralysis of the parasite's muscle.
One of the hypothesized mechanisms of resistance to ivermectin is its metabolism by p-glycoproteins and washing out of cells by ABC transporters. Parasites resistant to ivermectin are known to show partial but not complete cross-resistance to moxidectin.

### 4.3 Pharmacokinetics

Following administration of the recommended dose to horses, peak plasma concentrations of ivermectin were reached in 24 hours. Ivermectin concentrations were still above 2 ng/ml 14 days after administration. The elimination half-life of ivermectin was 90 hours. Praziquantel peak plasma concentrations was reached within 1 hour. Praziquantel was rapidly eliminated and was not detected 8 hours after treatment. The praziquantel elimination half life is 40 minutes.

**Environmental properties**

Ivermectin is very toxic to aquatic organisms and dung fauna and can accumuate 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.

## 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: 18 months
Shelf life after first opening the immediate packaging: 6 months

### 5.3 Special precautions for storage

Store below 25 °C.
Keep the applicator tightly closed. Replace the cap after use.

### 5.4 Nature and composition of immediate packaging

White HDPE multi-dose pre-filled oral syringe with scale printed HDPE piston, PP dosing ring and HDPE cap.
Pack sizes:
Cardboard carton with 1 x 7.49 g oral syringe.
Cardboard carton with 10 x 7.49 g oral syringes.

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.
The veterinary medicinal product should not enter water courses as ivermectin is extremely dangerous to 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 national collection systems applicable to the veterinary medicinal product concerned.

## 6. NAME OF THE MARKETING AUTHORISATION HOLDER

Bioveta, a.s.

## 7. MARKETING AUTHORISATION NUMBER(S)

VPA22028/011/001

## 8. DATE OF FIRST AUTHORISATION

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

## 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).