Institute for State Control of Veterinary Biologicals and Medicines
Hudcova 56a
621 00 Brno
Czech Republic
(Reference Member State)

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

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

PRODUCT SUMMARY

EU procedure number	CZ/V/0208/001/DC
Name, strength and pharmaceutical form	Nexpraz Duo 18.7 mg/g + 140.3 mg/g Oral Paste for Horses Nexpraz Vet 18.7 mg/g +140.3 mg/g Oral Paste for Horses (SE, NO, FI)
Applicant	Bioveta, a.s., Komenského 212 683 23 Ivanovice na Hané, Czech Republic
Active substance(s)	Ivermectin, Praziquantel
ATC vetcode	QP54AA51
Target species	Horses
Indication for use	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)

PRODUCT INFORMATION

The Summary of Product Characteristics (SPC), the labelling and package leaflet for this veterinary medicinal product (VMP) is available in the Union Product Database (UPD).

SUMMARY OF ASSESSMENT

Legal basis of original application*	Hybrid application in accordance with Article 19(1) of Regulation (EC) 2019/6 as amended.
Reference product (RP)	Equimax Oral gel for Horses
Marketing authorisation holder	Virbac
MS where the RP is or has been authorised	CZ
Marketing authorisation number EU procedure number	96/001/06-C IE/V/0501/001
Date of authorisation	26/01/2006
Date of completion of the original mutual recognition procedure	21/06/2004
Date veterinary medicinal product first authorised in the Reference Member State (MRP only)	N.A.
Concerned Member States for original procedure	AT, ES, FI, IE, IT, NO, SE, UK(NI).
Concerned Member States for subsequent recognition procedure	N.A.
Withdrawn CMS during original decentralised procedure	N.A:

*Please be aware that certain parts of the dossier may be varied and consequently be subject to protection of technical documentation – for these and other changes of referenceability to parts of the dossier, please see chapter POST-AUTHORISATION PROCEDURES

1. SCIENTIFIC OVERVIEW

The veterinary medicinal product (VMP) is produced and controlled using validated methods and tests, which ensure the consistency of the VMP released on the market.

It has been shown that the VMP can be safely used in the target species; the reactions observed are indicated in the SPC.

The VMP is safe for the user, the consumer of foodstuffs from treated animals and for the environment, when used as recommended. Suitable warnings and precautions are indicated in the SPC.

The efficacy of the VMP was demonstrated according to the claims made in the SPC.

The overall risk/benefit analysis is in favour of granting a marketing authorisation.

2. QUALITY DOCUMENTATION (physicochemical, biological or microbiological information)

A. Product description

The VMP contains ivermectin 18.7 mg/g and praziquantel 140.3 mg/g as the active substances and the excipients hydroxypropyl cellulose ELF, hydrogenated castor oil, sucralose, green apple flavour, Ceylon cinnamon bark essential oil, brilliant blue FCF, tartrazine, titanium dioxide and propylene glycol.

The container/closure system consists of a white HDPE multi-dose pre-filled oral syringe with scale printed HDPE piston, PP dosing ring and HDPE cap. The authorised package sizes are cardboard carton with 1 x 7.49 g or 10 x 7.49 g.

The VMP is an established pharmaceutical form and its development is adequately described in accordance with the relevant European guidelines.

B. Description of the manufacturing method

The VMP is manufactured fully in accordance with the principles of good manufacturing practice at a licensed manufacturing site.

The VMP is manufactured using conventional manufacturing techniques. Process validation for full-scale batches will be performed post-authorisation.

C. Production and control of starting materials

The active substances are ivermectin and praziquantel, established active substances described in the European Pharmacopeia. The active substances are manufactured in accordance with the principles of good manufacturing practice.

The specifications for active substances are considered adequate to control the quality of the material. Batch analytical data demonstrating compliance with these specifications have been provided.

Certificates of suitability issued by the EDQM have been provided for each active substance.

The excipients hydroxypropyl cellulose, hydrogenated castor oil, sucralose, Ceylon cinnamon bark essential oil, titanium dioxide and propylene glycol are described in the European Pharmacopeia monographs and they are controlled accordingly. The excipients green apple flavour, brilliant blue FCF and tartrazine are not listed in the European Pharmacopeia and are controlled according to in-house specifications.

Quality control of the container-closure system is described and considered adequate.

There are no substances within the scope of the TSE Guideline present or used in the manufacture of this VMP.

D. Control tests carried out on isolated intermediates during the manufacturing process

Not applicable.

E. Control tests on the finished product

The finished product specification controls the relevant parameters for the pharmaceutical form. The tests in the specification and their limits have been justified and are considered appropriate to adequately control the quality of the VMP.

Satisfactory validation data for the analytical methods have been provided.

Batch analytical data from the proposed production site have been provided demonstrating compliance with the specification.

F. Stability tests

Stability data on the active substance praziquantel have been provided in accordance with applicable European guidelines, demonstrating the stability of the active substance when stored under the approved conditions.

The active substance ivermectin is completely tested to ensure compliance with its specification immediately prior to its use in manufacture of the VMP.

Stability data on the finished product have been provided in accordance with applicable European guidelines, demonstrating the stability of the VMP throughout its shelf life when stored under the approved conditions.

3. SAFETY DOCUMENTATION (safety and residues tests)

As this is a hybrid application according to Article 19 of Regulation (EC) 2019/6 and essential similarity to a reference VMP has been demonstrated, results of pharmacological and toxicological tests are not required.

User safety

The applicant has provided a user safety assessment in compliance with the relevant guideline and warnings and precautions as listed on the product literature are adequate to ensure safety to users of the VMP.

Environmental Risk Assessment

This application has been submitted in accordance with Article 19 of Regulation (EU) 2019/6 as a hybrid application. An environmental risk assessment (ERA) has not been provided. This approach was accepted, because according to the Reflection paper on the interpretation of Article 18(7) of Regulation (EU) 2019/6 (EMA/CVMP/ERA/622045/2020), no ERA is required as the reference product has been authorized after October 2005. In line with similar products on the market, the toxicity of ivermectin to dung organisms and aquatic species has been addressed in the product literature.

B. Residues documentation

The application for the product has been made in accordance with Article 19 of Regulation (EU) 2019/6, as amended. The reference and hybrid products have the same pharmaceutical forms, the same qualitative and quantitative composition in terms of active substances. The applicant has not submitted residue data based on demonstration of bioequivalence of ivermectin with the reference product. The demonstration of bioequivalence for praziquantel is not applied due to the nature of the substance.

Residue tests

No own residue depletion studies have been submitted.

Maximum Residue Limits

The active substances ivermectin and praziquantel are allowed substances as described in Table 1 of the Annex to Commission Regulation (EU) No 37/2010:

Pharmacologically active substance(s)	**Marker residue**	**Animal species**	**MRLs (µg/kg)**	**Target tissues**	**Other provisions**
Ivermectin	22, 23-Dihydroavermectin B 1a	All mammalian food producing species	30 µg/kg 100 µg/kg 100 µg/kg 30 µg/kg	Muscle Fat Liver Kidney	For porcine species the fat MRL relates to 'skin and fat in natural proportions' Not for use in animals from which milk is produced for human consumption
Praziquantel	NOT APPLICABLE	Ovine, Equidae	No MRL required	NOT APPLICABLE	NO ENTRY

Excipients (hydrogenated castor oil, propylene glycol, Ceylon cinnamon essential oil, brilliant blue, tartrazine, sucralose, hydroxypropyl cellulose, titanium dioxide, "Green apple" flavour) are included in Table 1 of the Annex to Commission Regulation (EU) No 37/2010, or fall within the category of substances intended for human consumption.

Withdrawal Periods

The following withdrawal periods have been established for horses for the hybrid product, based on the reference product:
Meat and offal: 35 days.
Not authorised for use in animals producing milk for human consumption.

4. EFFICACY DOCUMENTATION (preclinical studies and clinical trials)

This is a hybrid application according to Article 19 of Regulation (EC) 2019/6 and bioequivalence with a reference VMP has been demonstrated, as well as efficacy study (dose confirmation study).

A. Pre-Clinical Studies

Pharmacology

Development of resistance and related risk in animals

Based on the provided information on the resistance of parasites to the medicinal substances contained in the veterinary medicinal product, adequate warnings and precautions appear on the product literature.

Dose determination and confirmation

The applicant has conducted dose confirmation study on support of the efficacy of the praziquantel against adult *Anoplocephala perfoliata* following administration of the veterinary medicinal product.

Tolerance in the target species of animals

The applicant evaluated the tolerance in target animals as the second goal of the bioequivalence study as well as the dose confirmation study. The product literature accurately reflects the type and incidence of adverse effects, which might be expected.

B. Clinical trials

No clinical trials were performed.

5. OVERALL CONCLUSION AND BENEFIT-RISK ASSESSMENT

The data submitted in the dossier demonstrate that when the VMP is used in accordance with the Summary of Product Characteristics, the risk benefit profile for the target species is favourable and the quality and safety of the VMP for humans and the environment is acceptable.

POST-AUTHORISATION PROCEDURES

The SPC and package leaflet may be updated to include new information on the quality, safety and efficacy of the VMP. The current SPC is available in the Union Product Database (UPD).

None