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Institute for State Control of Veterinary Biologicals and Medicines
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BRNO
(Reference Member State)

MUTUAL RECOGNITION PROCEDURE

DRAFT PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

EquiShield EHV,
emulsion for injection for horses

MODULE 1

PRODUCT SUMMARY

EU Procedure number	CZ/V/0153/001/MR
Name, strength and pharmaceutical form	EquiShield EHV, emulsion for injection for horses
Applicant	Dechra Regulatory B.V. Handelsweg 25 5531 AE Bladel Netherlands
Active substance(s)	Inactivated equine herpes virus type 1 min. 2.1 $\log_{10}$ VNI[1] [1] Virus neutralization index determined in serum of hamsters
ATC Vetcode	QI05AA05
Target species	Horses
Indication for use	For active immunization of horses to reduce clinical signs and to reduce virus excretion during respiratory disease caused by equine herpesvirus type 1 (EHV-1) infections. Onset of immunity: 2 weeks after the second vaccine injection Duration of immunity has only been demonstrated after the administration of three vaccine injections (see section 4.9): 6 months after the 3rd vaccine injection. For active immunisation of pregnant mares to reduce the occurrence of abortions caused by equine herpesvirus type 1 (EHV-1) infections. Onset immunity: 3 weeks after the 3rd vaccine injection during gestation Duration of immunity: until the end of pregnancy.

MODULE 2

The Summary of Product Characteristics (SPC) for this product is available on the Heads of Veterinary Medicines Agencies website (http://www.HMA.eu).

MODULE 3

PUBLIC ASSESSMENT REPORT

Legal basis of original application	Mutual Recognition application in accordance with Article 32 of Directive 2001/82/EC as amended.
Date of completion of the original mutual recognition procedure	Day 90: 23/10/2018
Date product first authorised in the Reference Member State	13/06/2018
Concerned Member States for original procedure	AT, BE, DE, DK, ES, FI, FR, , IE, IS, IT, LU, NL, NO, PT, SE, UK

I. SCIENTIFIC OVERVIEW

The vaccine EquiShield EHV is produced and controlled using validated methods and tests, which ensure the consistency of the product released on the market.

It has been shown that the product can be safely used in the target species.

The product 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 product was demonstrated according to the claims made in the SPC.

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

II. QUALITY ASPECTS

A. Qualitative and quantitative particulars

The vaccine contains inactivated equine herpes virus type 1, the adjuvant is Montanide ISA 35 VG and excipients (thiomersal, sodium chloride, potassium chloride, potassium dihydrogen phosphate, disodium hydrogen phosphate dodecahydrate, water for injections and sodium hydroxide - for pH adjustment).

The choice of the adjuvant, vaccine strain, substrate for virus multiplication, antigen content in dose, inactivating agent and preservative are justified.

The inactivation process and the detection limit of the control of inactivation are correctly validated.

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

B. Method of Preparation of the Product

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

Process validation data on the product have been presented in accordance with the relevant European guidelines.

C. Control of Starting Materials

The active substance is inactivated equine herpes virus type 1 (EHV1) that is an established active substance. The active substance is manufactured in accordance with the principles of good manufacturing practice.

The active substance specification is considered adequate to control the quality of the material. Batch analytical data demonstrating compliance with this specification have been provided.

Starting materials of non-biological origin used in production comply with the European Pharmacopeia monographs or in-house specifications.

Biological starting materials used are in compliance with the relevant Ph. Eur. Monographs and guidelines and are appropriately screened for the absence of extraneous agents according to the Ph. Eur. and European guidelines, any deviation was adequately justified.

The master and working seeds have been produced according to the Seed Lot System as described in the relevant guideline.

Scientific data and/or certificates of suitability issued by the EDQM have been provided and compliance with the Note for Guidance on Minimising the Risk of Transmitting Animal Spongiform Encephalopathy Agents via Human and Veterinary Medicinal Products has been satisfactorily demonstrated.

D. Control tests during production

The tests performed during production are described and the results of 3 consecutive runs, conforming to the specifications, are provided.

E. Control Tests on the Finished Product

The tests performed on the final product conform to the relevant requirements; any deviation from these requirements is justified.

The tests include in particular:
- appearance
- extractable volume
- sterility
- inactivation test (residual live virus)*****
- identity and potency******
- pH value
- content of thiomersal
- airtightness
- viscosity

* Performed as in-process control.

** Performed on bulk of vaccine

F. Batch to batch consistency

The demonstration of the batch to batch consistency is based on the results of 3 batches produced according to the method described in the dossier. Other supportive data provided confirm the consistency of the production process.

G. Stability

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

Stability data on the finished product have been provided in accordance with applicable European guidelines, demonstrating the stability of the product throughout its shelf life (18 months) when stored under the approved conditions (2-8 °C).

The in-use shelf-life of the broached vaccine (10 hours) is supported by the data provided.

H. Other Information

Non applicable

III. SAFETY ASSESSMENT

EquiShield EHV is an inactivated vaccine for active immunization against equine herpesvirus.

The vaccine is recommended for horses from the age of 6 months for 3 injections by intramuscular administration (the first injection from the age of 6 months; the second injection 4 weeks later, and the third injection 3 months after the second dose) and then revaccination every 6 months is recommended.

The vaccine is recommended for pregnant mares for 3 injections by intramuscular administration (one dose of the vaccine in the second month after mating, one dose in the fifth or sixth month of pregnancy and one dose in the ninth month of pregnancy). The three dose vaccination scheme should be repeated for subsequent pregnancies.

Safety studies have been performed with a vaccine batch with maximum antigen content produced according the described production process.

Field studies have been performed with three representative vaccine batches produced according the described production process.

Laboratory trials

The safety of the administration of one dose and the repeated administration of one dose in the target animal (foals, pregnant mares) is demonstrated. The investigation was performed according to the recommendations of Directive 2001/82/EC as amended and the relevant guidelines. No local reactions at the injection site and no clinical changes in the health status were found in foals and pregnant mares.

The following was reported based on post-marketing surveillance experience of an identical reference product:
Temporary temperature increases (at max. 40°C for 4 days) are very common after vaccination. The developments of local reactions that may reach up to 5x10 cm diameter are rare and persist for a maximum of 5 days. Anaphylactic reaction is very rare. Symptomatic treatment should be provided.

Effects on reproductive performance were examined. No influence on the process of gestation, birth or progeny was observed during the safety study performed in pregnant animals.

There are no data suggesting that this product might adversely affect the immune system of the vaccinated animal or its progeny therefore a specific study was not carried out.

The vaccine is inactivated and thus the specific tests to be performed for live vaccines are not applicable.

The adjuvant and excipients used do not create residues in vaccinated animals. Based on this information, no withdrawal period is proposed.

No specific assessment of the interaction of this product with other medicinal product was made. Therefore, an appropriate warning in the SPC is included.

Field studies

The applicant has performed a study to evaluate the efficacy and safety of the vaccine under field conditions, in compliance with the principles of Good laboratory Practice (GLP) and Good clinical Practice (GCP).

The safety of the vaccination following the recommended vaccination schedule was evaluated with foals and mares in six horse-breeding farms.
The study included safety assessment after administration of vaccine according vaccination schedule to foals and pregnant mares. The safety evaluation was based on: observation of local and systemic reactions, measurement of rectal temperatures and evaluation of possible influence of the vaccination on gestation, parturition and progeny.

The safety of the vaccine in foals and pregnant mares in the field has been demonstrated. The results from field trials reflect those observed in laboratory trials.

Environmental Risk Assessment

The applicant provided a first phase environmental risk assessment in compliance with the relevant guideline which showed that no further assessment is required.

The assessment concluded that there is a negligible risk to the environment associated with use of the vaccine. Warnings and precautions as listed on the product literature are adequate to ensure safety to the environment when the product is used as directed.

IV. EFFICACY

All experiments conducted with EquiShield EHV in laboratory and field conditions were designed to meet the requirements of the relevant veterinary legislation, including European Directive 2001/82/EC, as amended (2009/9/ES) and relevant European Pharmacopoeia monographs in force. The efficacy of the product has been demonstrated in laboratory challenge studies on the target species in animals at the minimum age recommended for vaccination (6 months) and in pregnant mares. The vaccine batches with minimum or subminimum antigen content used in the laboratory trials were manufactured using the procedure described in the marketing authorisation documentation.

Field studies have been performed with three representative vaccine batches produced according the described production process.

Laboratory Trials

The efficacy of the product has been demonstrated in laboratory studies in accordance with the relevant requirements which show that the vaccine reduce clinical signs and to reduce virus excretion during respiratory disease caused by equine herpesvirus type 1 (EHV-1) infections in horses and that the vaccine reduce the occurrence of abortions caused by equine herpesvirus type 1 (EHV-1) infections in pregnant mares.

The laboratory efficacy study included the following evaluation:

a) Verification of efficacy against equine herpesvirus 1 (EHV-1) in laboratory animals
b) Onset of immunity against equine herpesvirus EHV-1
c) Duration of immunity against equine herpesvirus EHV-1

d) Immunity against equine herpesvirus EHV-1 in pregnant mares

e) Efficacy of the vaccine with a sublimit antigen content against equine herpesvirus EHV-1

Onset of immunity is established at 2 weeks after the second vaccine injection.

Duration of immunity has only been demonstrated after the administration of three vaccine injections (see section 4.9 of the SPC): 6 months after the 3rd vaccine injection.

In the case of vaccinations of pregnant mares onset immunity is established at 3 weeks after the 3rd vaccine injection during gestation and duration of immunity is until the end of pregnancy.

Efficacy of vaccination was demonstrated in controlled laboratory challenge studies by challenge each horse by nasal instillation with a quantity of equid herpesvirus 1 , sufficient to produce in a susceptible horse characteristic signs of the disease or with quantity of equid herpesvirus 1 sufficient to produce abortion in susceptible horses.

Vaccinated animals showed slight sign of respiratory infection with comparison characteristic signs of control animals. The average number of days on which virus is excreted and the respective virus titres are significantly statistically lower in vaccinated horses than in control horses.
Abortions did not occur in the vaccinated mares compared with the control group.

The results of the laboratory studies demonstrate full protection for the vaccinated animal against equine herpesvirus as required by the European Pharmacopoeia monograph 1613.

Field Trials

The applicant has performed a study to evaluate the efficacy and safety of the vaccine under field conditions, in compliance with the principles of Good laboratory Practice (GLP) and Good clinical Practice (GCP).

The efficacy of the vaccination following the recommended vaccination schedule was evaluated with foals and mares under field condition in six horse-breeding farms.

Efficacy of vaccination in foals was demonstrated including 36 vaccinated foals and 10 controls vaccinated with comparator vaccine. Efficacy of vaccination in mares was demonstrated including 26 vaccinated pregnant mares and 7 unvaccinated controls.

The efficacy evaluation was based on serological profile of antibodies against equine herpes virus and health status of new-born foals.
The field testing demonstrated the satisfactory safety and efficacy of the vaccine. The results obtained in field studies confirm laboratory trials findings.

V. OVERALL CONCLUSION AND BENEFIT– RISK ASSESSMENT

The data submitted in the dossier demonstrate that when the product 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 product for humans and the environment is acceptable.

MODULE 4

POST-AUTHORISATION ASSESSMENTS

The SPC and package leaflet may be updated to include new information on the quality, safety and efficacy of the veterinary medicinal product. The current SPC is available on the Heads of Veterinary Medicines Agencies website (www.HMA.eu).

This section contains information on significant changes which have been made after the original procedure which are important for the quality, safety or efficacy of the product.

None.