College ter Beoordeling van Geneesmiddelen / Medicines Evaluation Board

Graadt van Roggenweg 500
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DECENTRALISED PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Avishield IBD INT

NL/V/0244/001/DC

January 2019

MODULE 1

PRODUCT SUMMARY

EU Procedure number	NL/V/0244/001/DC
Name, strength and pharmaceutical form	Avishield IBD INT
Applicant	Genera Inc. Svetonedeljska cesta 2, Kalinovica Rakov Potok 10436, Croatia.
Active substance(s)	Live attenuated Avian infectious bursal disease virus, IM strain VMG 91
ATC Vetcode	QI01AD09
Target species	Chickens
Indication for use	For active immunisation of chickens (broilers, future layers and breeders), with maternally derived antibodies, to prevent mortality and clinical disease, due to infection caused by Avian Infectious Bursal Disease viruses.

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	Full application in accordance with Article 12 (3) of Directive 2001/82/EC as amended.
Date of completion of the original decentralised procedure	21 November 2018
Concerned Member States for original procedure	AT, BE, CZ, DE, EL, ES, HU, IE, IT, PL, PT, RO, SK

I. SCIENTIFIC OVERVIEW

The product 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; no adverse reactions were observed.

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

II. QUALITY ASPECTS

A. Composition

The product contains live attenuated avian Infectious Bursal Disease virus, strain VMG 91 min. 4.0 log10 TCID50 and max. 5.0 log10 TCID50, and excipients povidone K25, bacto peptone, monosodium glutamate, potassium dihydrogen phosphate and potassium hydroxide.
The container consists of a clear glass vial of hydrolytic glass type I, closed with bromobutyl stoppers and sealed with aluminium caps. The particulars of the containers and controls performed are provided and conform to the regulation.
The choice of vaccine strain is justified.

B. Method of Preparation of the Product

The product is manufactured fully in accordance with the principles of good manufacturing practice from 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 a live avian infectious bursal disease virus, an established active substance. The active substance is manufactured in accordance with the principles of good manufacturing practice.
Starting materials of non-biological origin used in production comply with the European Pharmacopoeial (Ph. Eur.) monographs where these exist. For the substances where there is no such requirement the company has identified the source of the substance, explained how its quality is controlled and provided relevant certificates of analysis.
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. 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.

D. Specific Measures concerning the Prevention of the Transmission of Animal Spongiform Encephalopathies

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.

E. Control on intermediate product

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

F. 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, vacuum, residual moisture, identity, potency, purity (microbial limit), mycoplasmas and extraneous agents.
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.

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 when stored under the approved conditions.
The claim of a 3-hour in-use stability is based on the demonstration of stability for three batches reconstituted in drinking water and stored for 3 hours at room temperature.

H. Genetically Modified Organisms

Not applicable.

J. Other Information

None.

III. SAFETY ASSESSMENT

Laboratory trials

The safety of the administration of one dose, an overdose and the repeated administration of one dose in the target animal were demonstrated in 8-day old SPF chickens. The investigation was performed according to the recommendations of Directive 2001/82/EC as amended and the relevant guidelines. No adverse reactions attributable to the vaccine were seen.

No studies have been performed in birds during lay, this was appropriately justified, a relevant warning is included in the SPC.

Immunosuppression by the virus was studied in accordance with the relevant Ph.Eur. monograph. The Master seed virus complied with the test, no immunosuppression was observed.

Reversion to virulence was studied largely in accordance with the relevant monograph, where the method differed from the one described this was adequately justified. The fifth passage of the virus was tested for its ability to cause damage to the bursa of Fabricius and for immunosuppressive properties. An increase in virulence was observed, evidenced by increased bursal lesion scores. No clinical signs or gross lesions were observed. The passaged virus did not induce overt immunosuppression since adequate protection against Newcastle Disease Virus was induced in vaccinated animals by concurrent vaccination with ND vaccine. However, lower ND antibody titres were induced in chicks infected with the passaged strain compared to chicks infected with the master seed virus. It was concluded an increase in virulence occurred but the virus did not revert to full virulence. Warning sentences regarding measures to prevent circulation of the vaccine strain are included in the SPC.

Spread of the vaccine strain was examined, the vaccine strain spreads to unvaccinated birds. Spread to non-target species was not examined. Appropriate warnings regarding spread as well as measures to limit spread of the vaccine strain are included in the SPC, these precautionary measures are considered to sufficiently reduce the risk of recirculation and thus reversion to virulence.

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

Recombination and/or reassortment of IBDV virus strains likely occurs in the field, leading to the appearance of new variants. However, the VMG 91 strain strongly resembles other vaccine strains already on the market and is not considered to pose an additional threat regarding the possible occurrence of new variant strains.

Field studies

Two combined safety and efficacy field trails were performed. One study in commercial broilers and one study in commercial layer pullets. Both studies were positively controlled, one group was vaccinated with the investigational veterinary medicinal product a second group with a control veterinary medicinal product.

Four flocks of approximately 20.000 broiler chicks originating from the same hatchery but kept in separate houses on the same farm were included in the study. Animals were vaccinated on D18 via drinking water, after calculation of the appropriate age for vaccination using the Deventer formula. There was no difference in mortality or bodyweight at slaughter between the groups. Overall production results were good and comparable between the groups.

Four flocks of approximately 20.000 layer pullets originating from the same producer and the same hatchery but kept in separate houses on the same farm were included in the study. Animals were vaccinated on D23/24 and D56/57 via drinking water. The first day of vaccination was calculated using the Deventer formula. No adverse events were recorded during the study, mortality was low with no significant difference between the groups. Feed intake and bodyweight were similar in both groups, production parameters were normal.
The data from the field studies supports the safety of the vaccine as determined in the laboratory studies.

User Safety

A user safety risk assessment was conducted in accordance with the appropriate Guideline. The overall risk associated with exposure of users to the product is considered negligible.
Warnings and precautions as listed on the product literature are adequate to ensure safety of the product to users.

Ecotoxicity

The applicant provided a first phase environmental risk assessment in compliance with the relevant guideline which showed that no further assessment was required.
Warnings and precautions as listed on the product literature are adequate to ensure safety to the environment when the product is used as directed.

Residue Studies

No withdrawal period is required.

IV. CLINICAL ASSESSMENT (EFFICACY)

Laboratory Trials

The efficacy of the product has been demonstrated in laboratory studies in accordance with the relevant requirements.

Three vaccine batches were used in efficacy studies, these batches were manufactured in accordance with the method detailed in the dossier.

The onset of immunity was evaluated in 8 day-old SPF chicks, three groups of 20 animals were vaccinated by eye-drop, coarse spray or orally. An unvaccinated control group was included in the study. All animals were challenged with IBD virus 2 weeks after vaccination. The animals were monitored for clinical signs daily and bursa lesions were determined at necropsy ten days post challenge. The efficacy of the vaccine was demonstrated by prevention of mortality and clinical signs and reduction of bursal lesion scores.

The onset of immunity was further evaluated in MDA+ layer chicks, two groups of 40 animals were vaccinated with the product or a control VMP by oral administration. One group of 30 animals remained as unvaccinated controls. The time of vaccination was determined by serology, using the Deventer formula and was predicted to be 38 days of age. Serum samples taken at Day 38 confirmed that MDA-levels had decreased sufficiently. Twenty animals in each group were challenged with vvIBD virus 2 weeks after vaccination. Ten days after challenge 10 chicks per group were necropsied and bursa lesion scores were determined. Morbidity and mortality was prevented by the vaccine as well as the control VMP, confirming efficacy (onset of immunity) in MDA+ animals.

Duration of immunity was evaluated in 8-day-old SPF chicks, 20 animals vaccinated orally and 10 animals remaining unvaccinated. All animals were challenged with vvIBD virus 28 days after vaccination. Animals were monitored for clinical signs and bursa lesions were determined at necropsy ten days post challenge. The efficacy of the vaccine at 28 days was demonstrated by prevention of clinical signs and mortality and reduction of bursal lesion scores.

The duration of immunity was further evaluated in MDA+ commercial broiler chicks, two groups of 8 chicks were used in the study. One group was vaccinated in the field via drinking water at 13 days of age (calculated using the Deventer formula) while a second group remained unvaccinated. Challenge was performed 28 days after vaccination. Mortality or clinical signs were not observed in any of the animals. The efficacy of the vaccine was demonstrated by reduction of bursal lesion scores.

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 Trials

Two combined safety and efficacy field trails were performed. One study in commercial broilers and one study in commercial layer pullets. Both studies were positively controlled, one group was vaccinated with the investigational veterinary medicinal product a second group with a control veterinary medicinal product.

Four flocks of approximately 20.000 broiler chicks originating from the same hatchery but kept in separate houses on the same farm were included in the study. Animals were vaccinated on D18 via drinking water, after calculation of the appropriate age for vaccination using the Deventer formula. There was no difference in mortality or bodyweight at slaughter between the groups. Overall production results were good and comparable between the groups. Antibody levels after vaccination were comparable between the groups.

Four flocks of approximately 20.000 layer pullets originating from the same producer and the same hatchery but kept in separate houses on the same farm were included in the study. Animals were vaccinated on D23/24 and D56/57 via drinking water. The first day of vaccination was calculated using the Deventer formula. No adverse events were recorded during the study, mortality was low with no significant difference between the groups. Feed intake and bodyweight were similar in both groups, production parameters were normal. Vaccination induced a serological response that was comparable between the groups.

The data from the field studies generally support the efficacy of the vaccine as determined in the laboratory studies.

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 benefit/risk 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 Vetrinary 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.