26 November 2020
EMA/193705/2019
Veterinary Medicines Division

Committee for Medicinal Products for Veterinary Use

CVMP assessment report for Innovax-ND-IBD (EMEA/V/C/004422/II/0004)

Vaccine common name: Newcastle disease, infectious bursal disease and Marek's disease vaccine (live recombinant)

To extend the duration of immunity for the protection against Newcastle disease (ND) and infectious bursal disease (IBD) from 8 weeks to the entire risk period. Additionally, following the update of the pharmaceutical form to the current standard term, MAH takes opportunity to correct the old term 'suspension' in a consistent way throughout the Product Information.

Assessment report as adopted by the CVMP with all information of a commercially confidential nature deleted.

Product profile

Invented name:	Innovax-ND-IBD
Active Substances:	Turkey herpes virus, strain hvp360, expressing Newcastle disease virus and infectious bursal disease virus, live
Target Species:	Chicken embryonated eggs and Chickens
Pharmaceutical Form:	Concentrate and solvent for suspension for injection
Strength:	--
Therapeutic Indication:	For active immunisation of one-day-old chicks or 18–19 day-old embryonated chicken eggs: - to reduce mortality and clinical signs caused by Newcastle disease (ND) virus, - to prevent mortality and to reduce clinical signs and lesions caused by infectious bursal disease (IBD) virus, - to reduce mortality, clinical signs and lesions caused by Marek's disease (MD) virus.
ATCvet code	QI01AD16
Pharmacotherapeutic group	IMMUNOLOGICALS
Applicant	Intervet International B.V.

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1. Introduction

On 7 October 2020, the CVMP adopted an opinion and CVMP assessment report.

On 20 November 2020, the European Commission adopted a Commission Decision granting the marketing authorisation for Innovax-ND-IBD.

1.1. Submission of the variation application

In accordance with Article 16 of Commission Regulation (EC) No 1234/2008, the marketing authorisation holder, Intervet International B.V. (the applicant), submitted to the European Medicines Agency (the Agency) on 30 March 2020 an application for a type II variation for Innovax-ND-IBD.

1.2. Scope of the variation

Variation(s) requested		**Type**
C.I.6.a	Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one	II

To extend the duration of immunity for the protection against Newcastle disease (ND) and infectious bursal disease (IBD) from 8 weeks to the entire risk period. Additionally, following the update of the pharmaceutical form to the current standard term, MAH takes opportunity to correct the old term 'suspension' in a consistent way throughout the Product Information.

1.3. Changes to the dossier held by the European Medicines Agency

This application relates to the following sections of the current dossier held by the Agency:

Part 1, Part 2 and Part 4

1.4. Scientific advice

Not applicable.

1.5. MUMS/limited market status

Not applicable.

2. Scientific overview

Innovax-ND-IBD is a cell-associated live recombinant turkey herpesvirus (strain HVP360), expressing the fusion protein of Newcastle disease virus and the VP2 protein of infectious bursal disease virus. The vaccine is indicated for active immunisation of one-day-old chicks and embryonated chicken eggs to reduce mortality and clinical signs caused by Newcastle disease (ND) virus, to prevent mortality and to reduce clinical signs and lesions caused by infectious bursal disease (IBD) virus and to reduce mortality, clinical signs and lesions caused by Marek’s disease (MD) virus. The MD duration of immunity (DOI) claim is for the entire risk period, and the DOI claim for the ND and IBD components is 8 weeks. This variation

application intends to extend the DOI claim for the NDV and IBDV components in Innovax-ND-IBD to the entire risk period.

In order to support the proposed variation to extend the DOI against ND and IBD from '8 weeks' to 'the entire risk period' the applicant provided new clinical data.

A vaccination-challenge study was performed in one-day-old SPF chicks. One group was vaccinated with Innovax-ND-IBD mixed with Nobilis Rismavac (both at minimum potency) via subcutaneous route, while the second group of hatch mates received solvent only. Challenge was performed via i.m. injection of NDV at 9, 50 and 60 weeks of age. The study was valid in accordance with 9CFR requirements and although it was not fully compliant with Ph. Eur. 0450 requirements, this is acceptable for a non-pivotal efficacy study. The Relative Protection Percentage in the vaccinates was 97, 94 and 100% at 9, 50 and 60 weeks of age respectively. Since no data (serological or challenge) beyond 60 weeks of age were provided and the economic life span of chickens (layers) can be considerably longer, the claimed DOI for NDV is restricted to 60 weeks.

Serum samples were taken from the same vaccination challenge study and antibody titres against NDV and IBD VP2 antigens were quantified.Generally, the results support a continued serological response against NDV and the IBD VP2 antigen over the 58-week follow-up period. From available literature, it is known that VP2 is a major capsid protein of IBD and a major immunogen that can induce virus-neutralising antibodies (conferring clinical protection). Based on the results of a previous study, birds with average Log2 antibody titres of 14.14-14.53 may be expected to be fully protected. Since the average titres in the DOI study were well above these values (15.12, 15.62 and 15.90 at 9, 27 and 58 weeks of age respectively) and do not show any evidence of waning, the study results are considered to support the continued protection against IBDV for at least 58 weeks post vaccination. Based on these data and the data provided on protection against NDV (since both genes are expressed by the same vector) a DOI of 60 weeks for IBDV can be accepted.

3. Benefit-risk assessment of the proposed change

Innovax-ND-IBD is a suspension and solvent for suspension for injection for chickens, containing cell-associated live recombinant turkey herpesvirus (strain HVP360) expressing the fusion protein of Newcastle disease virus and the VP2 protein of infectious bursal disease virus in the quantity of $10^{3.3}$ – $10^{4.6}$ plaque-forming units. This product is authorised for active immunisation of one-day-old chicks or 18-19-day-old embryonated chicken eggs to reduce mortality and clinical signs caused by Newcastle disease (ND) virus, to prevent mortality and to reduce clinical signs and lesions caused by infectious bursal disease (IBD) virus, and to reduce mortality, clinical signs and lesions caused by Marek's disease (MD) virus. The vaccine is given subcutaneously as one single injection of 0.2 ml per chick, or *in ovo* as one single injection of 0.05 ml per chicken egg. The withdrawal period is zero days.

The proposed variation is to extend the duration of immunity for the protection against Newcastle disease (ND) and infectious bursal disease (IBD) from 8 weeks to the entire risk period. Additionally, following the update of the pharmaceutical form to the current standard term, MAH takes opportunity to correct the old term 'suspension' in a consistent way throughout the Product Information.

3.1. Benefit assessment

Direct therapeutic benefit

The direct therapeutic benefit of Innovax-ND-IBD is slightly changed as consequence of this variation (DOI for ND and IBD).

The proposed benefit of Innovax-ND-IBD is its efficacy in active immunisation of one-day-old chicks:

- to reduce mortality and clinical signs caused by Newcastle disease (ND) virus,
- to prevent mortality and to reduce clinical signs and lesions caused by infectious bursal disease (IBD) virus,
- to reduce mortality, clinical signs and lesions caused by Marek's disease (MD) virus.

The benefit was demonstrated in a large number of well-designed laboratory and field studies conducted to an acceptable standard.

OOI was established against NDV infection at 4 weeks post vaccination, against MDV at 9 days post vaccination and against IBDV at 3 weeks post vaccination.

DOI of 8 weeks was established for NDV and IBDV. With this variation, data were provided with the aim to support a DOI for NDV and IBDV for the entire risk period. Based on the data provided, a DoI of 60 weeks can be accepted for both NDV and IBDV. No data are provided for the DOI against MDV infection and this is acceptable as the HVT virus produces a persistent infection providing a lifelong immunity.

Vaccination against the three target diseases was found to be efficacious in MDA-positive chickens.

Additional benefits

The additional benefits of Innovax-ND-IBD do not change as consequence of this variation.

3.2. Risk assessment

The potential risks do not change as a consequence of this variation.

3.3. Risk management or mitigation measures

There is no change to the risk mitigation measures as a consequence of this variation.

3.4. Evaluation of the benefit-risk balance

A DOI of 60 weeks can be accepted for NDV and IBDV, which enhances the benefit of the product. The overall benefit-risk balance for the product remains unchanged.

4. Conclusion

Based on the original and complementary data presented on efficacy, the Committee for Medicinal Products for Veterinary Use (CVMP) concluded that the application for variation to the terms of the marketing authorisation for Innovax-ND-IBD can be approved, since the data satisfy the requirements as set out in the legislation (Commission Regulation (EC) no. 1234/2008), as follows:

The duration of immunity for NDV and IBDV is changed from 8 weeks to 60 weeks.

The CVMP considers that the benefit-risk balance remains positive and, therefore, recommends the approval of the variation to the terms of the marketing authorisation for the above-mentioned medicinal product.

Changes are required in the following Annexes to the Community marketing authorisation:

I and IIIB

Please refer to the separate product information showing the tracked changes.

As a consequence of this variation, section 4.2 of the SPC is updated. The corresponding section of the Package Leaflet is updated accordingly.