EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Veterinary Medicines Division

Committee for Medicinal Products for Veterinary Use

CVMP assessment report for Nobilis IB Primo QX (EMEA/V/C/002802/II/0008)

Vaccine common name: Avian infectious bronchitis vaccine (live)

to present new data on the safe use of Nobilis IB Primo QX during the laying period with the purpose to remove the warning in the relevant sections of the SPC and package leaflet. Furthermore, there is a minor editorial change.

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

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1. Introduction

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 6 February 2020 an application for a type II variation for Nobilis IB Primo QX.

1.2. Scope of the variation

Variation(s) requested		**Type**
C.I.4	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	II

to present new data on the safe use of Nobilis IB Primo QX during the laying period with the purpose to remove the warning in the relevant sections of the SPC and package leaflet. Furthermore, there is a minor editorial change.

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 3.

1.4. Scientific advice

Not applicable.

1.5. MUMS/limited market status

Not applicable.

2. Assessment

Nobilis IB Primo QX is intended for active immunisation of chickens in order to reduce respiratory signs of avian infectious bronchitis caused by QX-like variants of IB virus. The vaccine contains live attenuated IB virus strain D388 in stabilizer for intranasal/ocular and spray administration to chickens.

During initial registration safety during lay was not investigated and SPC contains a warning not to use the product in birds in lay or within 4 weeks before the onset of laying period.

A field study was performed to assess the safety of the vaccine in chickens when revaccinated during the period of lay:

Safety of vaccination of chickens with Nobilis IB Primo QX during the laying period.

Healthy laying hens from 2 different farms in Germany (about 62000 birds) were used in the study. Birds were at least 20 weeks old and in production at time of first vaccination. Nobilis IB Primo QX was administered at maximum dose by coarse spray (≥250 microns) twice during lay. Controls received a standard dose of Nobilis IB Ma5 (22/23 weeks) and Nobilis IB 4/91 (32/33 weeks) by drinking water. Close monitoring for general health, feed intake and respiratory signs during 14 days after each vaccination (with scoring) was carried out. Also, monitoring of egg production and mortality until 36-38 weeks of age where the study ended. Blood sampling was done for serology.

The results from the study showed absence of any general reactions nor any respiratory signs in all groups. Decreased feed intake was observed at one farm for day 11 to 14 after first vaccination but in both vaccine and control groups (may be linked to the fact that birds had access to the outdoor area).

After the 2nd vaccination, decreased feed intake was only recorded at one farm from day 14 to 18 in vaccinated group and from D8 to D18 in control group.

Mortality remained within normal range throughout the study. It was slightly lower in the vaccinated group (1.26%) than in control group (1.45%). Minor increases in mortality were observed due to crowding in farm 2.

Overall daily egg production was slightly higher in the vaccinated group (91.2%) compared to the control group (90.0%) without any abnormalities.

Infection with IBV strain D181 was identified in farm 1 leading to reduction of feed intake and drop in egg production (study week 12 – 1 to 2 weeks after the 2nd vaccination). This event was not considered to be related to vaccination. At the end of the study, feed intake and egg production improved but infection was still ongoing.

Groups of farm 2 were medicated with neomycin sulfate on week 13 (enteritis due to E. coli). All chickens were treated with flubendazole for helminthiases caused by Ascardia galli and Heterakis gallinarum.

The safe use of the vaccine during the laying period was confirmed following vaccination of chickens at 22/23 and 32/33 weeks of age with maximal dose of vaccine when administered by coarse spray. No impact of vaccination on birds and egg production was observed. The applicant did not discuss the safe use of the vaccine during lay after an oculo-nasal administration. Considering that safety of the vaccination via both administration routes (coarse spray and oculonasal route) has been investigated in the initial dossier for MA and that laying chickens will more probably be vaccinated by coarse spray, no question on this point was raised.

Overall assessment of the proposed variation

This variation raised some issues which needed to be addressed.

Regarding the safety of vaccination during lay, an initial question was raised, on the absence of transmission of the vaccine strain in eggs for breeders and layers and possible adverse effects of vaccination on egg quality (shell pigmentation, texture and shape, albumen cleanliness or viscosity).

The applicant provided further clarification and it was considered that sufficient data were available (studies performed with the vaccine or scientific knowledge on infectious bronchitis virus) to support safety of vaccination with Nobilis IB Primo QX during the laying period.

An additional point was raised on the efficacy of the vaccine when re-administered to breeders or layers during laying period, as linked to the removal of the contra-indication, positioning of the vaccine and vaccine

scheme needed to be revised and justified. Furthermore, as long as no additional efficacy data are available, it was proposed to amend section 4.7 of the SPC as follows: "the efficacy of Nobilis IB Primo QX has not been demonstrated when administered during lay. A decision to use this vaccine during lay should be made on a case by case basis." The applicant included the proposed statement as required and this point was resolved.

3. Scientific Overview

Nobilis IB Primo QX is indicated in young birds from 1 day of age to reduce respiratory signs of avian infectious bronchitis caused by QX-like variants. During initial assessment, studies were mostly conducted in one day old SPF chicks or commercial broilers. No data were provided in birds during lay as vaccine was not indicated during this period. The applicant has now performed a field safety study to demonstrate safety of the vaccination during laying period. The vaccine was administered by coarse spray in 62000 birds vaccinated 2 times and no adverse effects on birds and egg production was observed.

Based on this study, the applicant proposes to remove a contra-indication in the SPC (section 4.3) and to state the safe use of the vaccine during lay (section 4.7) in the product literature for Nobilis IB Primo QX.

Data in the study is acceptable to ensure safety of the vaccination when administered during the laying period by coarse spray with regard to production parameters. Although the safe use of the vaccine during lay after oculo-nasal administration was not investigated, considering that safety of the vaccination via both administration routes was investigated in the initial dossier for MA (and that laying chickens will more probably be vaccinated by coarse spray), this is consider acceptable.

No data have been provided to support efficacy of the vaccination during laying period. A relevant statement has been included in section 4.7. of the SPC to specify that vaccination during lay should be conducted on a case by base basis taking into account that efficacy of the vaccine when used in birds during lay has not been demonstrated.

4. Benefit-risk assessment of the proposed change

This product is authorised for the active immunisation of chickens from one day-old onwards in order to reduce respiratory signs of Infectious Bronchitis caused by QX-like variants of Infectious Bronchitis Virus.

The benefits of Nobilis IB Primo QX are the active immunisation of chickens in order to reduce respiratory signs of infectious bronchitis caused by QX-like variants of infectious bronchitis virus. The most common side effects are a mild transient respiratory reaction (including nasal exudates) which may occur for at least 10 days, however these reactions are very rare.

The proposed variation is to remove contra-indication in chickens during lay.

4.1. Benefit assessment

Benefit of the vaccination as currently indicated – vaccination of young birds to reduce respiratory signs – remain unchanged following the variation.

Benefits of the product when administered during the laying period has not been investigated. A statement on this point has been included in the SPC.

4.2. Risk assessment

Quality:

Quality remains unaffected by this variation.

Safety:

Safety data have been provided that support safety of the vaccination when layers are vaccinated during the laying period.

4.3. Evaluation of the benefit-risk balance

The product has been shown to be safe when administered during the laying period with regard to production parameters.

The overall benefit-risk is deemed positive.

5. Conclusion

Based on the original data presented on safety and answers provided by the applicant to the identified objections, the Committee for Medicinal Products for Veterinary Use (CVMP) concluded that the application for variation to the terms of the marketing authorisation of Nobilis IB Primo QX is approvable.

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, sections 4.3 and 4.7 of the SPC are updated. The corresponding sections of the package leaflet are updated accordingly.