IPAR

Publicly Available Assessment Report for a Veterinary Medicinal Product

GALLIVAC IB88 NEO effervescent tablet for suspension for nebulisation for chickens

PRODUCT SUMMARY

Name, strength and pharmaceutical form	Gallivac IB88 NEO effervescent tablet for suspension for nebulisation for chickens = 4.0 log 10 EID_{50}/dose Effervescent tablet for suspension for nebulisation
Active substance(s)	Attenuated Infectious Bronchitis coronavirus, CR88121 strain
Applicant	Boehringer Ingelheim Vetmedica GmbH Binger Strasse 173 55216 Ingelheim am Rhein Germany
Legal basis of application	Application in accordance with Article 1 (3) of Directive 2001/82/EC as amended.
Date of completion of procedure	8th October 2015
Target species	Chickens
Indication for use	Reduces clinical signs and lesions of respiratory disease caused by the coronavirus variant, strain CR88 (793B) in broiler chickens. Immunity has been demonstrated 21 days after vaccination, and the duration of immunity is 6 weeks after vaccination.
ATCvet code	QI01AD07

PUBLIC ASSESSMENT REPORT

The public assessment report reflects the scientific conclusion reached by the HPRA at the end of the evaluation process and provides a summary of the grounds for approval of the marketing authorisation for the specific veterinary medicinal product. It is made available by the HPRA for information to the public, after the deletion of commercially confidential information. The legal basis for its creation and availability is contained in Article 25.4 of EC Directive 2001/82/EC as amended by Directive 2004/28/EC for veterinary medicinal products. It is a concise document which highlights the main parts of the documentation submitted by the applicant and the scientific evaluation carried out by the HPRA leading to the approval of the product for marketing in Ireland.

The Summary of Product Characteristics (SPC) for this product is available on the HPRA's website.

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; the slight reactions observed are indicated in the SPC.

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 product contains live attenuated infectious bronchitis virus (CR88121 strain) at = 4.0 log 10 EID_{50}/dosein a freeze-drying protective substrate, containing tableting excipients (citric acid, sodium hydrogen carbonate, magnesium sterate, casein hydrolysate, D-mannitol, sodium hydroxide, water for injection).

The container/closure system consists of ablister of two heat-sealed aluminium foils, one foil is laminated against a PVC layer.

The choice of the vaccine strain is acceptable as it is already available on the market under the form of a lyophilisate in Gallivac IB88 freeze-dried vaccine.The Gallivac IB88 effervescent tablet formulation incorporates the exact same active ingredient at the same infective titre as already used in freeze-dried Gallivac IB88 vaccine. Acceptable equivalence studies have been performed of the reconstituted vaccine suspension with effervescent tablet and the reconstittued freeze-dried forms. Safety and efficacy of the vaccine suspension prepared using either the effervescent tablet or lyophilized formulations are the same as the excipients do not play a role in the immune response.

The product is a novel pharmaceutical form for a vaccine 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 for the manufacturing process has been presented in accordance with the relevant European guidelines.

C. Control of Starting Materials

The active substance is live attenuated infectious bronchitis coronavirus strain CR88121. 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 pharmacopoeia monographs and 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. Any deviation was adequately justified.

The active substance is produced by a classical manufacturing process for live virus in SPF embryonated eggs. Quantification is based on the determination of the infective titre (50% egg infective dose) on SPF eggs in accordance with Ph. Eur. 0442.

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

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 (immunologicals)

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 titration of the active ingredient, viral purity and sterility.

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.

F. Stability

Stability data on the finished product has 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 in-use shelf-life of the reconstituted vaccine is supported by the data provided.

G. Other Information

Not applicable.

III. SAFETY ASSESSMENT

The application for Gallivac IB88 NEO was submitted in accordance with Article 12(3), of Directive 2001/82/EC, as amended, i.e. a full application. The application concerns a change to an existing marketing authorisation for a national product leading to an extension as referred to in Annex I of Commission Regulation (EC) no 1234/2008 – change or addition of a new pharmaceutical form.

Gallivac IB88 NEO effervescent tablets in blisters is a new formulation of the nationally authorised Gallivac IB88 freeze-dried pellet vaccine (VPA 10857/051/001). Gallivac IB88 NEO contains the same active ingredient as Gallivac IB88 (freeze-dried), however for the effervescent tablet presentation the active ingredient is blended with tableting excipients. The new pharmaceutical form was developed in order that the

dissolved tablets provide a vaccine suspension of the same potency (same infective titre) as obtained with the freeze-dried Gallivac IB88. Studies were presented in Part 2 of the dossier which demonstrated the equivalence of the reconstituted vaccine suspension obtained with the effervescent tablet and reconstituted freeze-dried forms of the vaccine (comparative *in vitro*and *in vivo*studies). As equivalency of the reconstituted vaccine suspension between both formulations has been demonstrated, the safety of the effervescent tablet is supported by the original studies conducted with Gallivac IB88. Therefore, the new pharmaceutical form has the same indications for use in the same species and category of animals, the same recommended administration method as Gallivac IB88, and the same safety profile.

The safety data for Gallivac IB88 NEO therefore reflects that of Gallivac IB88. The Summary of Product Characteristics (SPC) for Gallivac IB88 is available on the HPRA's website.

Laboratory Trials

Cross-reference is made to the safety data of Gallivac IB88 to support the safety of Gallivac IB88 NEO. As discussed in the introduction to safety assessment, this approach was considered acceptable.
Additionally, in order to verify that the safety of the overdose of the effervescent tablet is similar to the safety of the overdose of live freeze-dried vaccine, the applicant conducted one laboratory study to assess the safety of a high dose (maximum release dose) and of an overdose (equivalent to 10 maximum release doses) of Gallivac IB88 NEO. This GLP-standard study was performed in the target species, chickens, vaccinated at one day old and included a group of chickens vaccinated with a 10x overdose of the currently authorised Gallivac IB88 vaccine. The study demonstrated that vaccination of one day old chicks with an overdose of the proposed new formulation is as safe as vaccination with an overdose of the currently authorised formulation.
The adverse reactions observed after vaccination (in all vaccinated groups) at overdose were limited to mild upper respiratory signs that may persist for up to 17 days and/or a transient reduced weight gain and are described in section 4.10 of the SPC. Following vaccination at the recommended dose, mild respiratory signs have been reportedvery commonly in studies and signs may persist for up to 23 days and are described in section 4.6 of tghe SPC.

User Safety

Cross-reference is made to the user safety data of Gallivac IB88 to support the user safety of Gallivac IB88 NEO. As discussed in the introduction to safety assessment, this approach was considered acceptable in principle.

However, due to the differences in pharmaceutical form, exposure to the veterinary medicinal product is slightly different to that of Gallivac IB88 and therefore the user safety warnings were updated to take this into account.
Warnings and precautions as listed on the product literature are adequate to ensure safety to users of the product.

Field Trials

Cross-reference is made to the safety data of Gallivac IB88 to support the safety in the field of Gallivac IB88 NEO. As discussed in the introduction to safety assessment, this approach was considered acceptable.

Environmental Risk Assessment

Cross-reference is made to the safety data of Gallivac IB88 to support the safety of Gallivac IB88 NEO for the environment. As discussed in the introduction to safety assessment, this approach was considered acceptable.
In conclusion, extrapolation of the safety data of the currently authorised Gallivac IB88 freeze-dried vaccine to that of Gallivac IB88 NEO effervescent tablets was considered acceptable. Therefore it was concluded that the use of Gallivac IB88 NEO is safe for the target species, the consumer of foodstuffs from treated animals, the person administering the veterinary medicinal product to animals and for the environment, when used as recommended.

IV. CLINICAL ASSESSMENT

As discussed under Part III Safety, the application for Gallivac IB88 NEO was submitted in accordance with Article 12(3), of Directive 2001/82/EC, as amended, i.e. a full application. The application concerns a change to an existing marketing authorisation for a national product leading to an extension as referred to in Annex I of Commission Regulation (EC) no 1234/2008 – change or addition of a new pharmaceutical form.

Gallivac IB88 NEO effervescent tablets in blisters is a new formulation of the nationally authorised Gallivac IB88 freeze-dried pellet vaccine (VPA 10857/051/001). Gallivac IB88 NEO contains the same active ingredient as Gallivac IB88 (freeze-dried), however for the effervescent tablet presentation the active ingredient is blended with tableting excipients. The new pharmaceutical form was developed in order that the dissolved tablets provide a vaccine suspension of the same potency (same infective titre) as obtained with the freeze-dried Gallivac IB88. Studies were presented in Part 2 of the dossier which demonstrated the equivalence of the reconstituted vaccine suspension obtained with the effervescent tablet and reconstituted freeze-dried forms of the vaccine (comparative *in vitro*and *in vivo*studies). As equivalency of the

reconstituted vaccine suspension between both formulations has been demonstrated, the efficacy of the effervescent tablet is supported by the original studies conducted with Gallivac IB88. Therefore, the new pharmaceutical form has the same indications for use in the same species and category of animals and the same recommended administration method as Gallivac IB88.

Cross-reference is made to the efficacy data of the currently authorised Gallivac IB88 freeze-dried vaccine to support the efficacy of Gallivac IB88 NEO. As discussed above, because equivalent potency of the two formulations was demonstrated, this approach was considered acceptable.

The Summary of Product Characteristics (SPC) for Gallivac IB88 is available on the HPRA's website. Gallivac IB88 is indicated for use in broiler chickens from 14 days of age as follows; '*Reduces clinical signs and lesions of respiratory disease caused by the coronavirus variant, strain CR88 (793B) in broiler chickens. Immunity has been demonstrated 17 days after vaccination, and the duration of immunity is at least 5 weeks*.'

- Identical claims are considered acceptable for Gallivac IB88 NEO. However, following submission of a type II variation, it was accepted that the product may be administered to broiler chicks from 1 day of age and that immunity has been demonstrated 21 days after vaccination and the duration of immunity is for 6 weeks afetr vaccination.
- Apart from the above, Section 4.9 differs only with respect to the instructions for reconstituting the effervescent tablet in water prior to diluting in a volume of water appropriate for the type of spraying equipment to be used and the number of doses to be administered.
- The minimum and maximum titre of the viral strain included in the vaccine is identical to that of Gallivac IB88.
- The shelf life of the vaccine once reconstituted is identical for both formulations (2 hours).

In conclusion, extrapolation of the efficacy data of the currently authorised Gallivac IB88 freeze-dried vaccine to that of Gallivac IB88 NEO effervescent tablets was considered acceptable. Therefore it was concluded that the efficacy of Gallivac IB88 NEO has been demonstrated, when used in accordance with recommendations.

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.

VI. 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 HPRA website.

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.

Safety/Efficacy Changes

Type II (C.I.6.a) Addition of a new therapeutic indication or modification of an approved one	**Approval date**
To reduce the minimum age of vaccination from 14 days to 1 day of age	16/07/2018