IPAR

Publicly Available Assessment Report for a
Veterinary Medicinal Product

PRODUCT SUMMARY

Name, strength and pharmaceutical form	Gallivac IBD S706 NEO effervescent tablet for use in drinking water for chickens = $10^{4.0}$ to $10^{5.3}$ CCID50
Active substance(s)	Infectious Bursal Disease virus, attenuated strain S706
Applicant	Boehringer Ingelheim Vetmedica GmbH Binger Strasse 173 55216 Ingelheim am Rhein Germany
Legal basis of application	Application in accordance with Article 12(3) of Directive 2001/82/EC as amended.
Date of completion of procedure	27/09/2020
Target species	Chickens
Indication for use	Active immunisation of chickens to protect against mortality and to reduce lesions associated with Infectious Bursal (Gumboro) Disease. Onset of immunity: 2 weeks after the first administration. Duration of immunity: immunity has been shown under field conditions to persist throughout the rearing period.
ATC vet code	QI01AD09

PUBLIC ASSESSMENT REPORT

The public assessment report reflects the scientific conclusion reached by the Health Products Regulatory Authority (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 Infectious Bursal Disease virus, attenuated strain S706 at 4.0 – 5.3 log 10 $CCID_{50}$ / dose, with the excipients sucrose, sodium glutamate, lactalbumin hydrolysate and purified water. The tableting excipients are citric acid, sodium bicarbonate, magnesium stearate, sunset yellow FCF and water for injection.

The container/closure system consists of a blister 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 in the form of a lyophilisate (Gallivac IBD freeze-dried vaccine). The Gallivac IBD S706 NEO effervescent tablet formulation incorporates the exact same active ingredient at the same infective titre as already used in the freeze-dried Gallivac IBD vaccine. Acceptable equivalence studies have been performed using the reconstituted vaccine suspension from the effervescent tablet and the reconstituted freeze-dried forms. The excipients have been satisfactorily shown not to 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 Infectious Bursal Disease virus, attenuated strain S706. 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 relevant Ph. Eur. 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 master and working seeds have been produced according to the Seed Lot System as described in the relevant guideline.

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 IBD S706 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 IBD S706 NEO effervescent tablet for suspension for chickens is a new formulation of the nationally authorised Gallivac IBD freeze-dried pellet vaccine (VPA 10454/057/001). Gallivac IBD S706 NEO contains the same active ingredient as Gallivac IBD (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 IBD.
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 IBD. Therefore, the new pharmaceutical form has the same indications for use in the same species, the same category of animals, and the same safety profile.

Gallivac IBD S706 NEO is administered via drinking water to chickens from 8 days of age. Gallivac IBD is authorised for use via coarse spray or via drinking water, however only the coarse spray method is indicated for use in chickens below 8 days of age. The recommendations for use for Gallivac IBD S706 are the same as the recommendations for use for the drinking water route for Gallivac IBD, with amendments where necessary with respect to the resuspension of the effervescent tablet (compared to that of a lyophilised vaccine), and the minimum age of vaccination is increased to 8 days of age.

The safety data for Gallivac IBD S706 NEO therefore reflects that of Gallivac IBD. The Summary of Product Characteristics (SPC) for Gallivac IBD is available on the HPRA's website.

Laboratory Trials

Cross-reference is made to the safety data of Gallivac IBD to support the safety of Gallivac IBD S706 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 the 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 IBD S706 NEO. This GLP-standard study was performed in the target species, chickens, vaccinated at 7 days old and included a group of chickens vaccinated with a 10x overdose of the currently authorised Gallivac IBD vaccine. The study demonstrated that vaccination of 7 day old chickens with an overdose of the proposed new formulation is as safe as vaccination with an overdose of the currently authorised formulation.
There were no vaccine-related adverse reactions observed after vaccination in any of the vaccinated groups. No differences in the safety profile were observed in the groups vaccinated with Gallivac IBD S706 NEO compared to Gallivac IBD. The current information in section 4.6 (adverse reactions) of the SPC of Gallivac IBD is therefore considered appropriate for inclusion in the SPC of Gallivac IBD S706 NEO ('*Laboratory studies have shown that when the vaccine virus was experimentally passed from bird to bird, damage to the bursa increased. This was detected by histological examination of the bursae. However, this is not considered to result in an immunosuppressive effect.*')

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

Withdrawal Period

A withdrawal period of zero days is proposed based upon the withdrawal period of zero days of Gallivac IBD. There are no additional components in the formulation of Gallivac IBD S706 NEO that impact on the withdrawal period.

User Safety

Cross-reference is made to the user safety data of Gallivac IBD to support the user safety of Gallivac IBD S706 NEO. As discussed in the introduction to safety assessment, this approach was considered acceptable. The applicant considered the implications of the new pharmaceutical form on user safety and it was concluded that there were no additional risks to the user arising from the new pharmaceutical form.
Warnings and precautions as listed on the product literature are adequate to ensure safety to users of the product.

Field Studies

Cross-reference is made to the safety data of Gallivac IBD to support the safety in the field of Gallivac IBD S706 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 IBD to support the safety of Gallivac IBD S706 NEO for the environment. As discussed in the introduction to safety assessment, this approach was considered acceptable.
Warnings and precautions as listed on the product literature are adequate to ensure safety to the environment when the product is used as directed.

In conclusion, extrapolation of the safety data of the currently authorised Gallivac IBD freeze-dried vaccine to that of Gallivac IBD S706 NEO effervescent tablets was considered acceptable. Therefore it was concluded that the use of Gallivac IBD S706 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 IBD S706 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 IBD S706 NEO effervescent tablet for suspension for chickens is a new formulation of the nationally authorised Gallivac IBD freeze-dried pellet vaccine (VPA 10454/057/001). Gallivac IBD S706 NEO contains the same active ingredient as Gallivac IBD (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 IBD.

Equivalency of the reconstituted vaccine suspension between both formulations has been supported by data provided in Part 2 of the dossier, in addition to an *in vivo* immunogenicity study provided in Part 4 (see below). 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 IBD. Therefore, the new pharmaceutical form has the same indications for use in the same species and in the same category of animals.

Gallivac IBD S706 NEO is administered via the drinking water to chickens from 8 days of age. Gallivac IBD is authorised for use via coarse spray or via drinking water, and may be used from 1 day of age. The recommendations for use for Gallivac IBD S706 NEO are therefore in accordance with the recommendations for use for the drinking water route for Gallivac IBD, with amendments where necessary with respect to the resuspension of the effervescent tablet (compared to that of a lyophilised vaccine), and the minimum age of vaccination for the new pharmaceutical formulation is increased to 8 days of age.

Cross-reference is made to the efficacy data of the currently authorised Gallivac IBD freeze-dried vaccine to support the efficacy of Gallivac IBD S706 NEO. As discussed above, because equivalent potency of the two formulations was demonstrated, this approach was considered acceptable.

In addition, the applicant has provided one *in vivo* immunogenicity study (laboratory challenge study) to support the efficacy of the new pharmaceutical form. In this study, following vaccination of 7 day old seronegative chickens, the results showed that the indications for use (protection against mortality and reduction of bursal lesions caused by virulent IBD challenge) were supported in the vaccinated chickens, compared to a non-vaccinated control group, in groups of chickens challenged with virulent IBD virus 2 weeks (onset of immunity) and in groups of chickens challenged at 7 weeks after vaccination (relevant to duration of immunity). Thus, because it has been shown that the potency and stability of the vaccine is not different depending on whether the vaccine is prepared from the lyophilised vaccine (Gallivac IBD) or from the effervescent tablet (Gallivac IBD S706 NEO), and that a new laboratory efficacy study is also provided to support the efficacy of the new pharmaceutical form, it is considered an acceptable approach to extrapolate the efficacy claims authorised for Gallivac IBD to that of Gallivac IBD S706 NEO.

The Summary of Product Characteristics (SPC) for Gallivac IBD is available on the HPRA's website. Gallivac IBD S706 NEO is indicated for use in chickens (broilers, future layers and broiler breeders as follows; '*Active immunisation of chickens to protect against mortality and to reduce lesions associated with Infectious Bursal (Gumboro) Disease. Onset of immunity: 2 weeks after the first administration. Duration of immunity: immunity has been shown under field conditions to persist throughout the rearing period*.'

- Identical claims are considered acceptable for Gallivac IBD S706 NEO.
- Section 4.9 of the SPC differs with respect to the omission of the coarse spray route, and differences to the vaccination schedule and minimum age of vaccination. The changes to the vaccination schedule mean that only the drinking water route is used for this vaccine, and the vaccination schedule is a two dose scheme (not the possible three doses as in the case of Gallivac IBD). As a consequence of removing the coarse spray route (for younger chickens), and to update the vaccination schedule in line with current practices, the age of vaccination for Gallivac IBD S706 NEO is established at 8 days of age.
- The minimum and maximum titre of the viral strain included in the vaccine is identical to that of Gallivac IBD.

In conclusion, based on some extrapolation of the efficacy data of the currently authorised Gallivac IBD freeze-dried vaccine to that of Gallivac IBD S706 NEO effervescent tablets, in addition to a new laboratory efficacy study with the new formulation, it was concluded that the efficacy of Gallivac IBD S706 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.

Changes:
None.