Veterinary Medicines Directorate

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Veterinary Medicines Directorate
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NATIONAL PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Poulvac Procerta HVT-IBD Concentrate and Solvent for Suspension for Injection for Chickens

Date Created: March 2025

MODULE 1

PRODUCT SUMMARY

Name, strength and pharmaceutical form	Poulvac Procerta HVT-IBD Concentrate and Solvent for Suspension for Injection for Chickens, Concentrate and solvent for suspension for injection
Applicant	Zoetis UK Limited, 1st Floor, Birchwood Building, Springfield Drive, Leatherhead, Surrey, KT22 7LP
Active substance	Turkey herpes virus, strain HVT-IBD (cell-associated), expressing VP2 protein gene of infectious bursal disease virus, live: 3580 – 26500 PFU*. *PFU: plaque forming units.
ATC Vet code	QI01AD15
Target species	Chickens and embryonated chicken eggs
Indication for use	For active immunisation of one day old chickens and 18-19 day old embryonated chicken eggs to: - reduce mortality, clinical signs and lesions caused by Marek's disease (MD) virus and - prevent mortality and clinical signs and reduce lesions caused by infectious bursal disease (IBD) virus. Onset of immunity: - MD: 7 days post vaccination for in ovo and 9 days for subcutaneous use - IBD: 15 days post vaccination for in ovo and 12 days for subcutaneous use Duration of immunity: - MD: a single vaccination is sufficient to provide protection for the entire risk period - IBD: 64 days of age

MODULE 2

The Summary of Product Characteristics (SPC) for this product is available on the Product Information Database of the Veterinary Medicines Directorate.

(www.gov.uk/check-animal-medicine-licensed)

MODULE 3

PUBLIC ASSESSMENT REPORT

Legal basis of original application	Full application in accordance with Article 8 of Veterinary Medicine Regulations (VMRs) 2013 (Schedule 1, Part 1) as amended.
Date of conclusion of the procedure	16/01/2025

I. SCIENTIFIC OVERVIEW

This is a full application for Poulvac Procerta HVT-IBD Concentrate and Solvent for Suspension for Injection for Chickens, in accordance with Article 8 of VMRs 2013 (Schedule 1, Part 1) as amended.

Poulvac Procerta HVT-IBD is a live recombinant vector vaccine. The vaccine is indicated for active immunisation of one day old chickens and 18-19 day old embryonated chicken eggs to:

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

The product is intended for a single administration by either the subcutaneous (SC) route to chickens of at least 1 day of age (0.2 ml) or the in ovo (IO) route to embryonated eggs of between 18 to 19 days of embryonation (0.05 ml).

Poulvac Procerta HVT-IBD consists of a frozen cell associated viral suspension (concentrate) to be diluted in an aqueous diluent (Poulvac Solvent) to obtain the final suspension for injection. Each dose of vaccine contains 3,580 – 26,500 plaque forming units (PFU) per dose.

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, any reactions observed are indicated in the SPC[1]. 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[2] 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.

[1] SPC – Summary of product Characteristics.
[2] Efficacy – The production of a desired or intended result.

II. QUALITATIVE AND QUANTITATIVE PARTICULARS OF THE CONSTITUENTS

II.A. Composition

The product contains Turkey herpes virus, strain HVT-IBD (cell-associated), expressing VP2 protein gene of infectious bursal disease virus, live: 3580 – 26500 PFU. The concentrate contains the excipients dimethyl sulfoxide, bovine calf serum, L-glutamine and DMEM and the solvent contains the excipients sucrose, potassium dihydrogen phosphate, dipotassium phosphate, peptone (NZ Amine), phenol red and water for injection.

The container system consists of flame sealed hydrolytic type I glass ampoules containing 2,000 or 4,000 doses held in canes stored in liquid nitrogen. The diluent is presented in polyvinylchloride (PVC) or polypropylene plastic bags containing 200 ml, 400 ml, 800 ml, 1,000 ml. The particulars of the containers and controls performed are provided and conform to the regulation.

The choice of the vaccine strain and absence of preservative are justified.

The product is an established pharmaceutical form, and its development is adequately described in accordance with the relevant regulatory guidelines.

II.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. The manufacturing method consists of:

- Virus propagation
- Harvest, formulation and filling
- Diluent production

Process validation data on the product have been presented in accordance with the relevant regulatory guidelines.

II.C. Control of Starting Materials

The active substance is Turkey herpes virus, strain HVT-IBD (cell-associated), expressing VP2 protein gene of infectious bursal disease virus, live: 3580 – 26500 PFU, a novel 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 relevant Ph. Eur. monographs or American Chemical Society (ACS) and United States Pharmacopeia (USP).

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.

The master and working seeds have been produced according to the Seed Lot System as described in the relevant guidelines.

The packaging materials comply with Ph. Eur.

II.C.4. Substances of Biological Origin

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.

II.D. Control Tests Carried Out at Intermediate Stages of the Manufacturing Process

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

II.E. Control Tests on the Finished Product

The tests performed on the final product conform to the relevant requirements and any deviation from these requirements is justified. The tests are visual appearance, identity, potency, fill volume, sterility and absence of mycoplasma.
The demonstration of the batch-to-batch consistency is based on the results of six consecutive batches, produced according to the method described in the dossier. Other supportive data provided confirm the consistency of the production process.

II.F. Stability

The active substance is fully tested to ensure compliance with its specification immediately prior to its use in manufacture of the product.

Stability data on the finished product have been provided in accordance with applicable regulatory 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

The shelf life of both the vaccine and the solvent (Poulvac Solvent) as packaged for sale is two years. The shelf life after dilution according to directions is two hours.

The vaccine concentrate should be stored and transported frozen in liquid nitrogen (or vapour phase) at or below -150 °C. The Poulvac Solvent should be stored at or below 25 °C and protected from light.

III. SAFETY ASSESSMENT

The vaccine batches used in the EU pre-clinical studies supplied by the applicant were manufactured according to approved specifications.

Laboratory trials

The safety of the administration of an overdose in the target animal is demonstrated in a study giving 10x overdose of the HVT-IBD vaccine to a total of 240 SPF (specific pathogen free), 1-day-old chicks and in 18-day embryonated chicken eggs. The investigation was performed according to the recommendations of VMRs 2013 as amended and the relevant Ph. Eur. No symptoms were observed after the administration of this overdose which demonstrated that an administration of a 10x maximum dose of the vaccine by the two routes, to 18-day embryonated eggs or 1-day-old chicks, can be considered safe.

No investigation of effect on reproductive performance was conducted. Therefore, it is detailed in the Summary of Product Characteristics that the safety of the veterinary medicinal product has not been established during lay.

Studies supplied by the applicant provided sufficient information to conclude that there are no evident risks of immunosuppression following the administration of the vaccine.

Specific studies were carried out to describe the spread, dissemination, reversion to virulence, biological properties, recombination or genetic reassortment of the vaccine strain. The vaccine strain may be excreted by vaccinated chickens for a maximum of six weeks post-vaccination and has the potential to spread to turkeys and to a very limited extent to chickens. Safety trials (including reversion to virulence studies in chickens) have shown that the strain is safe for turkeys and chickens. However, precautionary measures, including following general hygiene principles, and taking particular care in handling animal waste and bedding materials from recently vaccinated chickens, should be taken to avoid spreading of the vaccine strain.

The excipients used are commonly used in other vaccines and do not raise any safety concerns. Based on this information, no withdrawal period is proposed.

No information is available on the safety and efficacy of this vaccine when used with any other veterinary medicinal product. Therefore, a decision to use this vaccine before or after any other veterinary medicinal product needs to be made on a case-by-case basis.

Field studies

Three GCP compliant clinical studies were performed to assess the field safety and efficacy of the vaccine. All three studies followed the same study protocol and were controlled with a similar commercially available comparator product. All three studies were performed in commercial broiler farms with field conditions similar to those of farms in the UK.

The same batch of vaccine was used in these trials and vaccine was administered as a standard dose of 5,673 PFU/dose. In two of the studies, one day old chicks were vaccinated with a standard dose subcutaneously and in the

other study chickens were vaccinated in ovo. Clinical signs and mortality were monitored daily until the end of each study along with the Feed Conversion Ratio (FCR) and EPEF (European production efficiency factor). The studies were divided in two phases: rearing until early slaughter (thinning) and rearing until the final processing.

Total mortality figures in all three studies were not different between birds vaccinated with Poulvac Procerta HVT-IBD and those vaccinated with the comparator vaccine, and, in each study, it was in line with historical mortality data at each specific farm. Dead birds were necropsied and showed no signs of IBD or MD lesions in either the gross pathology or the histopathology assessment of all treatment groups.

In each trial no significant difference in body weight was detected between the two treatment groups.

In conclusion, the data from the three field studies provided support the results of the pre-clinical safety studies and show that the product is safe when used at the recommended dose in commercial broiler chickens when administered either subcutaneously or in ovo according to the SPC.

Ecotoxicity

The applicant provided a Phase 1 environmental risk assessment in compliance with the relevant guideline, which showed that no further assessment is required. The assessment concluded that the overall risk to the environment was low. Additionally, information concerning the release of genetically modified organisms was provided in the form of appropriate studies and literature and showed that any risk emerging from the use of the attenuated vaccine is expected to be low for the environment. Therefore, no warnings regarding protection of the environment are required.

IV. CLINICAL ASSESSMENT (EFFICACY)

Clinical Studies

Laboratory Trials

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

In total, 22 laboratory studies were performed to demonstrate the efficacy of the vaccine. In all studies, chickens were vaccinated at the proposed minimum age via the in ovo route at day 18 of embryonation or via the subcutaneous route on the day of hatch. Validated analytical methods were used in the trials.

Validated challenge models were conducted and used to assess onset and duration of immunity against Marek’s Disease and Infectious Bursal Disease.

Onset of Immunity

Marek's Disease

Seven studies were performed to determine the efficacy and onset of immunity for Marek's Disease in SPF (specific pathogen free) chickens. Two of the studies included animals vaccinated by the in ovo route, and five of the studies used animals vaccinated by the subcutaneous route.

Challenge was performed at seven days post vaccination for the in ovo route, and 9 days post vaccination for the subcutaneous route, using an appropriate dose of Marek's Disease material given by subcutaneous administration.

In the pivotal in ovo route study, 140 SPF eggs, at day 18 of embryonation, were vaccinated. A further 140 eggs remained unvaccinated as controls. At day four (seven days post vaccination) birds in the vaccinated and control groups were challenged, and a sufficient level of protection was reached in vaccinated birds compared to the controls. Therefore, the onset of immunity of seven days post vaccination is demonstrated for in ovo use.

In the pivotal subcutaneous study, 187 SPF chicks at hatch were vaccinated and compared to a group of unvaccinated control chicks. At day nine post vaccination, birds in the vaccinated and control groups were challenged and a sufficient level of protection was reached in vaccinated birds compared to the controls. Therefore, the onset of immunity nine days post vaccination is demonstrated for subcutaneous use.

Infectious Bursal Disease

Eight studies were performed to determine the effiacy and onset of immunity for Infectious Bursal Disease in SPF chickens. Three of the studies included animals vaccinated by the in ovo route, and five used animals vaccinated by the subcutaneous route.

Challenge was performed 12 or 14 days post vaccination for the subcutaneous route and 15 or 17 days post vaccination for the in ovo route using an appropriate dose of Infectious Bursal Disease virus given by eye drop.

In the pivotal in ovo study, 108 SPF eggs at day 18 of embryonation were vaccinated. A further 108 eggs remained unvaccinated as controls. At day 15 post vaccination birds in the vaccinated and control groups were challenged with very virulent Infectious Bursal Disease virus and a sufficient level of protection was reached in vaccinated birds, compared to the controls. Therefore, the onset of immunity is demonstrated for in ovo use of the vaccine 15 days post vaccination.

The applicant provided five studies to investigate onset of immunity following vaccination of one day old chickens by the subcutaneous route. In two of the studies animals were challenged 12 days post vaccination and in three of the studies challenge was done 14 days post vaccination. One of the studies where chickens were challenged at day 12, demonstrated sufficient levels of protection but the second study provided 87.5% protection, which is below the Ph. Eur. monograph requirement.

In a subcutaneous study that included a day 14 challenge, 175 day-old SPF chicks were vaccinated at hatch and compared to a group of unvaccinated control chicks. At day 14 post vaccination, birds in both vaccinated and control groups were challenged with very virulent Infectious Bursal Disease virus and a sufficient level of protection was reached in vaccinated birds compared to the control. Therefore, the onset of immunity is demonstrated for subcutaneous use of the vaccine 14 days after vaccination.

Duration of Immunity

Marek's Disease

One study was conducted to show the duration of immunity and efficacy of the vaccine against Marek's Disease. This was performed by monitoring the presence of vaccine virus and serology to determine antibody levels to Marek's Disease, following vaccination by either the in ovo or subcutaneous routes.

120 embryonated SPF chicken eggs were used and divided into three groups, where one group was vaccinated in ovo, one group was vaccinated by the subcutaneous route, and one group remained unvaccinated as controls.

Blood samples were taken for serology on Days 21, 42, 49, 56, and 63 and tested for Marek's Disease virus antibody levels. Feather pulp samples were collected on Days 21, 42, 49, 56 and 63, and tested for the presence of the vaccine strain.

Both vaccinated groups showed the production of antibodies at the last observation point (Day 63) following vaccination by either in ovo or subcutaneous administration. The Marek's Disease antibody levels for both vaccinated groups were statistically significantly different from the unvaccinated controls at all timepoints.

Alongside published support for lifelong persistence, the applicant's data are adequate to support duration of immunity to cover the entire risk period for Marek's Disease, following administration of the vaccine by either route of administration.

Infectious Bursal Disease

Two studies were conducted to investigate the duration for immunity for Infectious Bursal Disease in SPF chickens. One study involved animals vaccinated by the in ovo route and the other involved animals vaccinated by the subcutaneous route.

In the subcutaneous study, 216 SPF chickens were either vaccinated or left unvaccinated as controls. They were challenged with very virulent Infectious Bursal Disease virus at an age of 64 days, and a sufficient level of protection was reached in the vaccinated group. Therefore, the study supported a duration of immunity of 64 days for this disease, when the vaccine is administered via subcutaneous route.

In the in ovo study, 270 SPF eggs, were either vaccinated or left unvaccinated as controls. They were challenged with very virulent Infectious Bursal Disease

virus at 64 days of age (67 days post in ovo vaccination), and a sufficient level of protection was reached in the vaccinated group. Therefore, the study supported a duration of immunity of 64 days for this disease when the vaccine is administered via the in ovo route.

Influence of maternally derived antibodies vaccine efficacy

In addition to the data on onset of immunity and duration of immunity, the applicant also provided data to show that the presence of maternally derived antibodies does not have a significant effect on efficacy of the vaccine.

Field Trials

Three field studies were carried out in commercial broiler chickens in three different EU countries (Spain, Hungary and Italy), using both the in ovo and subcutaneous routes of administration. The trials compared commercial batches of the Poulvac vaccine to a similar vaccine available on the market.

Antibody levels tested demonstrated the efficacy of the vaccine for when given via both routes of administration.

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 of the product is favourable.

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 Product Information Database of the Veterinary Medicines Directorate website.

(www.gov.uk/check-animal-medicine-licensed)

The post-authorisation assessment (PAA) 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.

The PAA for this product is available on the Product Information Database of the Veterinary Medicines Directorate website.

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