Veterinary Medicines Directorate

United Kingdom
Veterinary Medicines Directorate
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DECENTRALISED PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Avishield ND B1, Lyophilisate for Oculonasal Suspension/Use in Drinking Water for Chickens

Date Created: May 2018

PuAR correct as of 30/10/2018 when RMS was transferred to NL.
Please contact the RMS for future updates

MODULE 1

PRODUCT SUMMARY

EU Procedure number	UK/V/0646/001/DC
Name, strength and pharmaceutical form	Avishield ND B1, Lyophilisate for Oculonasal Suspension/Use in Drinking Water for Chickens
Applicant	Genera Inc. Svetonedeljska cesta 2, Kalinovica 10436 Rakov Potok Croatia
Active substance	Each dose contains Active substance: Live, lentogenic virus of Newcastle disease, strain Hitchner B1 $10^{6.0}$ to $10^{7.0}$ $TCID_{50}$ $TCID_{50}$ = Tissue Culture Infective Dose
ATC Vetcode	QI01AD06
Target species	Chickens (broilers and future layers/breeders)
Indication for use	For active immunisation of chickens (broilers and future layers/breeders) to reduce mortality and clinical signs due to infection with Newcastle disease virus. Onset of immunity: 3 weeks post vaccination. Duration of immunity: 5 weeks post vaccination.

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 12 (3) of Directive 2001/82/EC as amended.
Date of conclusion of the decentralised procedure	28th February 2018
Date product first authorised in the Reference Member State (MRP only)	Not applicable.
Concerned Member States for original procedure	Austria, Belgium, Croatia, Czech Republic, Denmark, Estonia, France, Germany, Greece, Hungary, Ireland, Italy, Latvia, Lithuania, The Netherlands, Poland, Portugal, Romania, Slovakia, Slovenia, Spain

I. SCIENTIFIC OVERVIEW

This was a full application, submitted in accordance with Article 12 (3) of Directive 2001/82/EC as amended, for Avishield ND B1, Lyophilisate for Oculonasal Suspension/Use in Drinking Water, for Chickens. The product is indicated for the active immunisation of chickens (broilers and future layers/breeders) to reduce mortality and clinical signs due to infection with Newcastle disease virus. The onset of immunity is 3 weeks after vaccination. Duration of immunity is 5 weeks after vaccination.

The product is used as a coarse spray administered via the oculonasal route and spray from one day of age, or via drinking water from 7 days of age.

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 live, attenuated and lentogenic virus of Newcastle disease, strain Hitchner B1 $10^{6.0}$ to $10^{7.0}$ $TCID_{50}$. The excipients are as follows: povidone K-25, bacto-peptone, monosodium glutamate, potassium dihydrogen phosphate, potassium hydroxide and dextran 40000.

The container/closure system consists of colourless glass vials (type I), which are closed with bromobutyl rubber stoppers and sealed with aluminium caps.

Carton box with 10 vials of 1000 doses of vaccine.
Carton box with 10 vials of 2500 doses of vaccine.
Carton box with 10 vials of 5000 doses of vaccine.

The particulars of the containers and controls performed are provided and conform to the regulation.

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

The product is an established pharmaceutical form and its development is adequately described in accordance with the relevant European 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 the following:

Phase I: Preparation of the virus for production, disinfection and loading of SPF eggs, embryo growth, inoculation of eggs with working dilution of seed strain, replication of Newcastle disease virus, harvesting of allantoic fluid, freezing and storage.

Phase II: Defrost of viral antigen, preparation and filling of lyophilisation mixture into vials, freeze-drying, capping, quality control testing, labelling and packaging of the product.

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

II.C. Control of Starting Materials

The active substance is a live, attenuated and lentogenic virus strain of Newcastle disease virus, Hitchner B1 strain, presented as a lyophilisate for oculonasal suspension/use in drinking water, for chickens. The active substance complies with an in-house specification. The active substance is manufactured in accordance with the principles of good manufacturing practice.

Starting materials of a non-biological origin used in production comply with the European Pharmacopoeia (Ph. Eur). Bacto-peptone is a product of biological origin, which complies with an in-house specification.

Biological starting materials used are in compliance with the relevant Ph. Eur. Monographs and guidelines. The master and working seeds have been produced according to the Seed Lot System as described in the relevant guideline. The packaging is appropriate for use and complies with specification.

II.C.4. Substances of Biological Origin

The applicant has provided a signed TSE/BSE declaration confirming that the peptone used in the product complies with current regulatory requirement described in Ph. Eur. 1483 Products with risk of transmitting agents of animal encephalopathies.

A valid EDQM certificate of suitability has been provided for peptone used in the vaccine. The country of origin of source materials (porcine and bovine) is the USA. Confirmation has been provided by the manufacturer that the base powder for MEM contains no substances of animal 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

A variety of control tests are performed during production of the product.

II.E. Control Tests on the Finished Product

The tests performed on the final product conform to the relevant requirements. Tests include those for appearance, identification of the vaccine virus, virus titre, bacterial and fungal contamination, absence of extraneous agents, residual humidity, intact vacuum of the product and batch to batch consistency.

II.F. Stability

Stability data on the active substance have been provided in accordance with applicable European guidelines, demonstrating the stability of the active substance when stored under the approved conditions.

G. Other Information

Shelf life of the veterinary medicinal product as packaged for sale: 2 years.
Shelf life after reconstitution according to directions: 3 hours.
Store and transport refrigerated (2°C – 8°C).
Protect from light.

Do not freeze.

III. SAFETY ASSESSMENT

Laboratory trials

A single safety study of the administration of one dose was not investigated. The safety of an overdose (x 10, GLP[3] study) and the repeated administration of one dose in the target animal were demonstrated. It was concluded that the product had an acceptable safety profile based on these results.

Three non-GLP studies supported the following conclusions: a) the oculonasal route is the least safe route of vaccinations with regard to demonstrating clinical signs of disease. b) Most spread of the vaccine is observed when it is administered by spray or oculonasal route. c) Peak of viral replication in the upper respiratory tract is approximately 3-5 days post-vaccination for all three routes of administration.

No investigation of effect on reproductive performance was conducted because the vaccine is not intended for this category of animals. Safety of the vaccine on immunological function was addressed by analysis of the data provided from several laboratory and field trials.

A study was conducted to assess the impact of the vaccine in the trachea, spleen, kidneys, lung, caecal tonsils, duodenum and brain. The study was combined with analysis of dissemination of the vaccine to unvaccinated control animals. The study was performed only by oculo-nasal route in one day old chicks at a suitable passage level of virus. The vaccine virus was at a suitable passage level for the study. No adverse effects were noted from spread of the vaccine to tissues.

Six studies were presented for analysis of reversion to virulence. Reversion to virulence was not detected.

Published data on the biological properties of the Newcastle disease virus, strain Hitchner B1 and on genetic reassortment were provided. On analysis of the data, it was concluded that the risk of genetic reassortment with field or other strains is low.

A user safety risk assessment was provided. Newcastle disease virus can infect humans, the key symptom being conjunctivitis, with associated reddening and lachrymation of the eye. Infections are usually transient and are not passed from human to human. The SPC and product literature carry suitable warnings. Neither the vaccine not the excipients are thought to pose a risk to the user when used as recommended:

- Care should be taken when handling and administering the vaccine.
- Newcastle disease virus can cause a mild transient conjunctivitis in the person administering the vaccine.
- Personal protective equipment consisting of well-fitting masks and eye protection to European standards should be worn when handling the veterinary medicinal product. Personnel involved in attending vaccinated

[3] GLP – Good laboratory practice.

chickens should follow general hygiene principles (washing/disinfecting hands, changing clothes, wearing gloves, cleaning and disinfection of boots) and take particular care in handling animal waste and bedding materials litter from recently vaccinated chickens.

Field studies

Five field trials were carried out to assess the safety of the product. Data from the first two trials were considered as supportive only, as these were not performed strictly to specification. No adverse reactions were noted that are not cited in 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, Warnings and precautions as listed on the product literature are adequate to ensure safety to the environment when the product is used as directed.

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.

Two laboratory studies were performed. Studies were performed with vaccine containing the minimum amount of antigen $10^{6.0}$ $TCID_{50}$ or $10^{6.1}$ $TCID_{50}$.

The first immunogenicity study was carried out to demonstrate the efficacy of the vaccine in one-day-old SPF-chickens by spray or oculonasal route, or 7-day old chickens orally with $10^{6.0}$ EID_{50} (egg infectious dose) per bird. The vaccine prevented 90% of birds succumbing to infection via spray from a virulent challenge, compared to all non-vaccinated birds. 100% protection was achieved via the oculonasal route and via spraying.

The second study used a challenge model, and investigated the onset and duration of immunity of the vaccine as administered by orally or by spray in broiler chickens having maternally-derived antibody (MDA). MDA+ chickens were used in order to determine the impact of MDA on the efficacy of the vaccine. The protection level was 70% using spray and 100% via drinking water 35 days post-vaccination.

Field Trials

Four field studies were conducted. Two field safety/efficacy studies were performed on commercial broilers, with a laboratory efficacy challenge phase included, and two comparative field safety/efficacy studies were performed on commercial broilers and layers.

Study	Field trial to evaluate the safety and efficacy of Avishield ND B1 (Strain Hitchner B1), in commercial broilers in field conditions The first day of housing is defined as day 1 of the study (SD 1), the actual age of birds at SD1 is 0 day. This trial was conducted in Slovenia.
Animals	Commercial broilers One Group of 8,900 birds Chickens were housed in one location
Vaccine	Investigational Veterinary Product (IVP): Avishield ND B1 Potency: $10^{6.0}$ to $10^{7.0}$ $TCID_{50}$ live lentogenic Newcastle disease virus (strain Hitchner B1) per dose.
Vaccine scheme and Administration route	Newcastle disease: Avishield ND B1 (Genera) at the age of 7 days (on SD 8) via drinking water. Additionally, Infectious bronchitis: Bronhikal I SPF, (Genera) at the age of 14 days (on SD 15) and Infectious bursal disease: Gumbokal IM forte, (Genera) at the age 18 days (on SD 19).
Follow-up	Cloacal and tracheal swabs suitable for PCR were taken from 10 birds and tested for the presence of NDV before the vaccination (SD 8) and before slaughter (SD 39). Samples were examined by real-time RT-PCR detection systems. Efficacy of Avishield ND B1 was performed in the laboratory test, which was separated from this trial. For the laboratory phase altogether 160 chickens were removed from this flock on specific days. From this study only serological response to vaccination was measured. Blood samples were taken before the vaccination and at the end of the fattening period, before the slaughter. To establish the level of maternal antibodies against NDV, blood samples were taken from 20 animals on SD1 and on SD8, i.e. before vaccination. To determine the level of antibody response to vaccination 20 blood samples were taken on SD39. Serological response against NDV was performed by inhibition haemagglutination (HAI) method according to standard procedure, using 4 HA units of antigen and 1% chicken red blood cells (OIE Terrestrial Manual 2013).
Statistical analysis	N/A
Results	Clinical signs, mortality, body weight and feed conversion results were discussed in Part III Safety. Before the vaccination, at hatching and on the day of vaccination the level of maternal derived antibodies (MDA) was relatively high (on SD1 AMT was 5.40, on SD8 AMT was 3.60). After vaccination, on SD39 specific antibodies to NDV was

	detected only in one sera sample and the AMT was 0.15.
Conclusions	Antibody response to vaccination was measured as secondary variable. The results showed that vaccine Avishield ND B1 did not induce specific antibody response in HAI test probably due to presence of high level of MDA on vaccination day. It was noted however that immunity lasted (at least partially), to 35 days in MDA+ birds, in drinking water, after vaccination on day 7.

Study	Field trial was carried out to evaluate Avishield ND B1 in commercial broilers in field conditions This trial was conducted in several sites in Slovenia. The first day of housing is defined as day 1 of the study (SD 1), the actual age of birds at SD1 is 0 day.
Animals	Commercial broilers One Group of 26,000 birds
Vaccine	Investigational Veterinary Product (IVP): Avishield ND B1 Potency: $10^{6.0}$ to $10^{7.0}$ $TCID_{50}$ live lentogenic Newcastle disease virus (strain Hitchner B1) per dose.
Vaccine scheme and Administration route	Vaccination of day-old broiler chickens was performed with the vaccine Avishield ND B1 in the hatchery (SD 1) by coarse spray. The nozzle was set to produce a coarse spray (nozzles of 1 mm at pressure of 4 bars). Additionally, Infectious bronchitis: Bronhikal I SPF, (Genera) at the age of 14 days and Infectious bursal disease: Gumbokal IM forte, (Genera) at the age 18 days.
Follow-up	Efficacy of Avishield ND B1 was performed in the laboratory test, which was separated from this trial. For the laboratory phase a total of 160 chickens were removed from this flock. To establish the level of maternally derived antibodies against NDV, blood samples were taken from 20 animals on SD1, i.e. before vaccination. To determine the level of antibody response to vaccination 20 blood samples were taken on SD39. Detection of antibodies against NDV was performed by inhibition haem-agglutination test (HAI) using 4 HAU and 1% chicken red blood cells (OIE Terrestrial Manual 2013, Newcastle disease, Chapter 2.3.14).
Statistical analysis	N/A
Results	Before the vaccination, at hatching and on the day of vaccination the level of maternally derived antibodies was relatively high (on SD1 arithmetic mean titre was 4.80). After vaccination, on SD39 low titres of specific antibodies to NDV was detected in 10 sera samples.
Conclusions	In this trial antibody response to vaccination was measured as secondary variable. The results showed that vaccine

	Avishield ND B1 induced very low specific antibody response in HAI test probably due to the presence of high level of MDA on vaccination day. A conclusion on efficacy was not reached on the basis of this study alone.

Study	Field trial to evaluate the safety and efficacy of Avishield ND B1 in commercial broilers. This trial was conducted in a farm located in Slovenia. The evaluation of the tested vaccine in commercial broilers was conducted by serological response, clinical signs, mortality, body weight and feed conversion.
Animals	Group 1 (two flocks, houses 1 and 3) contained 38,240 birds and was assigned randomly to Avishield ND B1 (IVP). Group 2 (two flocks, houses 2 and 4) contained 38,260 birds and was assigned randomly to Nobilis ND C2 (CVP).
Vaccine	Investigational Veterinary Product (IVP): Avishield ND B1 Potency: $10^{6.0}$ to $10^{7.0}$ EID_{50} live lentogenic live Newcastle disease virus (strain Hitchner B1) per dose. Control Veterinary Products (CVP): Nobilis ND C2 Potency: $10^{5.7}$ to $10^{7.5}$ EID_{50} of live attenuated Newcastle disease virus (NDV) strain C2 per dose
Vaccine scheme and Administration route	Birds were vaccinated at the age of 17 days either with Avishield ND B1 or Nobilis ND C2 by oral administration of one dose per bird via drinking water. In addition to vaccination against NDV, birds from all flocks were vaccinated against infectious bronchitis by spray in the hatchery and on SD 15 by drinking water. Also, birds were vaccinated against infectious bursal disease on SD 11 or SD 12 by drinking water. Farming practices and management were comparable in all flocks.
Follow-up	To determine the level of specific antibodies at the day of vaccination and antibody response after vaccination, blood samples were taken by wing vein puncture from 20 chickens per flock. The samples were tested by standard haemagglutination inhibition (HAI) test using 4 HA unit. Blood samples were taken before the vaccination (SD 17) and at the end of the fattening period, before the slaughter, to establish the efficacy of the test vaccine. Cloacal and tracheal swabs suitable for PCR were taken from 10 birds from each flock and tested for the presence of NDV before the vaccination (SD 17) and before slaughter.
Statistical analysis	General linear model (GLM) was used to analyse data on body weight, total animal loss and antibody titres according to tested vaccines and flocks. Data were analysed using software IBM SPSS Statistics 17.0; values of $P<0.05$ were considered significant for all analyses.
Results	Results on Adverse Events, mortality and other losses (culling) were assessed under the safety section of the

	assessment report. Statistical analysis showed that the level of antibodies against NDV before vaccination (SD 17) was significantly higher in flock 3 than in flock 2 ($P<0.05$), whereas no other significant differences in the level of antibodies among flocks was observed ($P>0.05$). In all flocks, the antibody titres significantly increased after vaccination; titre on SD 39 was significantly higher than on SD 17 in all flocks ($P<0.05$). Antibody titre was significantly higher in flocks 1 and 4 than in flocks 2 and 3 ($P<0.05$). Vaccination with both vaccines induced significant increase of antibody response in all flocks; and no significant difference in antibody titre was observed at the end of the trial between the tested vaccines ($P>0.05$). In all flocks tracheal and cloacal swabs were taken on the day of vaccination and on the end of the fattening period for molecular detection of NDV and results were negative. Also, the production parameters for the IVP group were numerically similar to licensed alternative when administered by drinking water to 17 day-old chicks.
Conclusion	The level of maternal derived antibodies against NDV before vaccination (SD 17) was significantly higher in house 3 than in house 2 ($P<0.05$), whereas no other significant differences in the level of antibodies among houses was observed ($P>0.05$). In all flocks antibody titres significantly increased after vaccination; titre on SD 39 was significantly higher than on SD 17 in all flocks ($P<0.05$). At the end of the trial no difference in antibody titres was observed between the tested vaccines ($P>0.05$). However, the differences were near the limit of significance ($P=0.047$ and $P=0.052$ for SD 17 and SD 39, respectively). As there was no sign of natural infection and the vaccination schedule differed to that of the SPC, only the similarity between the proposed vaccine and the authorised vaccine could be determined.

Study	Field trial to evaluate the safety and efficacy of Avishield ND B1 in commercial layers. This trial was conducted in several sites in Slovenia. Efficacy of the test vaccine was evaluated by measuring serological response to vaccination.
Animals	Commercial layers Group 1 (Flock 1) contained 11,220 birds and was assigned randomly to Avishield ND B1 (IVP). Group 2 (Flock 1) contained 9,860 birds and was assigned randomly to Nobilis ND C2 and Pestikal LaSota SPF, Genera (CVP).
Vaccine	Investigational Veterinary Product (IVP): Avishield ND B1 Potency: $10^{6.0}$ to $10^{7.0}$ EID_{50} live lentogenic Newcastle disease virus (strain Hitchner B1) per dose.

	Control Veterinary Products (CVP): Nobilis ND C2 Potency: $10^{5.7}$ to $10^{7.5}$ EID_{50} of live attenuated Newcastle disease virus (NDV) strain C2 per dose Control Veterinary Products (CVP): Potency: $\geq 10^{6.0}$ EID_{50} live lentogenic Newcastle disease virus (strain La Sota) per dose.
Vaccine scheme and Administration route	Commercial layers were vaccinated with vaccine Avishield ND B1 and with comparator vaccines Nobilis ND C2, MSD and Pestikal LaSota SPF, Genera. Vaccines were applied by spray administration. Birds of both groups were vaccinated via spray administration against NDV four times; three vaccinations were performed in the rearing period and one in the production period. Birds were vaccinated at the age of 3 weeks, and then revaccinated at 8, 16 (during rearing period). Last revaccination was performed in production period, at the age of 24 weeks. See below; **Group 1:** Vaccine Avishield ND B1, Genera (1^{st} , 2^{nd} , 3^{rd} and 4^{th} vaccination) **Group 2:** Vaccine Nobilis ND C2 (1^{st} and 2^{nd} vaccination), Vaccine Pestikal La Sota SPF (3^{rd} and 4^{th} vaccination) In addition to vaccination against NDV, birds from both flocks were vaccinated against Marek's disease, infectious bronchitis, infectious bursal disease, *Salmonella* Enteritidis, fowl pox and avian encephalomyelitis according to the regular vaccination program. Farming practices and management were comparable in both groups. Each group was housed on the same farm till the age of approximately 18 weeks. After that birds (150 from group 1 and 550 from group 2) were moved into production farms.
Follow-up	Before each vaccination and at the end of observation period, birds from both groups were checked for the presence of NDV virus by molecular methods. Efficacy of the test vaccine was evaluated by measuring serological response to vaccination. Blood samples were taken before the first vaccination against NDV and three weeks after each vaccination. Sera samples were examined for specific antibodies against NDV by standard haemagglutination inhibition test (HAI) using 4 HA units.
Statistical analysis	General linear model (GLM) and t-test was used to analyse data on body weight, total animal loss and antibody titres

	according to tested vaccines. Data were analysed using software IBM SPSS Statistics 17.0; values of P<0.05 were considered significant for all analyses.
Results	Efficacy of the test vaccine was conducted by measuring the serological response to vaccination. The level of maternally derived antibodies against NDV before vaccination was significantly higher in a group vaccinated with vaccine Avishield ND B1 (group 1) than in the control group. Vaccination with vaccine Avishield ND B1 induced specific antibody response. Antibody titres after all four vaccinations were significantly higher than before the first vaccination at age of 21 days (P<0.05). In the group vaccinated with vaccine Nobilis ND C2 no increase of antibody response was observed after the 1st and the 2nd vaccination. Antibody titres significantly decreased (P>0.05). After the 3rd and 4th vaccination performed with vaccine Pestikal La Sota SPF, antibody titres in the comparison group significantly increased (P<0.05). After the 3rd vaccination antibody titre was significantly higher in a group vaccinated with Pestikal La Sota SPF than in a group vaccinated with vaccine Avishield ND B1, Genera (P<0.05), whereas after the 4th vaccination no significant difference in antibody titre between tested vaccines was observed (P>0.05).
Conclusions	The applicant concluded that live, lentogenic, attenuated vaccine Avishield ND B1 administered by spray induced an increase of specific antibodies to NDV in layers and did not cause negative adverse effect on production parameters. Only the similarity between the proposed vaccine and the authorised vaccine could be determined.

Interference on efficacy was seen from MDA during relevant studies. Because of possible interference from MDA on the development of active immunity, the SPC carries a suitable warning:

Maternally Derived Antibodies (MDA) can interfere with the development of active immunity. In flocks where high levels of MDAs are expected, vaccination programme should be planned accordingly.

Results from all studies contributed to the final refinement of the time to onset of immunity and duration of immunity, as cited in the SPC:

Onset of immunity: 3 weeks post vaccination.
Duration of immunity: 5 weeks post vaccination.

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.

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

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.

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