7 September 2017
EMA/602841/2017
Veterinary Medicines Division

Committee for Medicinal Products for Veterinary Use

CVMP assessment report for Bovilis Blue-8 (EMEA/V/C/004776/0000)

Common name: bluetongue virus vaccine (inactivated), serotype 8

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

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
Send a question via our website www.ema.europa.eu/contact

Introduction

On 20 June 2017 the applicant INTERVET INTERNATIONAL B.V. submitted an application for a marketing authorisation to the European Medicines Agency (the Agency) for Bovilis Blue-8 through the centralised procedure.

The eligibility to the centralised procedure was agreed upon by the CVMP on 14-16 March 2017 under Article 3(2) of regulation (EC) no 726/2004.

The applicant applied for the following indication:

Sheep

For the active immunisation of sheep from 2.5 months of age to prevent viraemia* and to reduce clinical signs caused by bluetongue virus serotype 8.

*(Cycling value (Ct) ≥ 36 by a validated RT-PCR method, indicating no presence of viral genome)

Onset of immunity: 20 days after the second dose.

Duration of immunity: 1 year after the second dose.

Cattle

For the active immunisation of cattle from 2.5 months of age to prevent viraemia* caused by bluetongue virus serotype 8.

*(Cycling value (Ct) ≥ 36 by a validated RT-PCR method, indicating no presence of viral genome)

Onset of immunity: 31 days after the second dose.

Duration of immunity: 1 year after the second dose.

The active substance of Bovilis Blue-8 is an inactivated serotype 8 bluetongue virus for the active immunisation of sheep and cattle. The product is intended for administration by subcutaneous use.

One dose for sheep contains 2 ml of vaccine and one dose for cattle contains 4 ml.

Bovilis Blue-8 is presented in high density polyethylene (HDPE) bottles of 52 ml, 100 ml or 252 ml with bromobutyl stoppers and aluminium seals containing either 26 sheep doses or 13 cattle doses (52 ml), either 50 sheep doses or 25 cattle doses (100 ml), either 126 sheep doses or 63 cattle doses (252 ml) respectively of inactivated serotype 8 virus of $10^{6.5}$ $CCID_{50}$* (* equivalent to titre prior to inactivation per ml.

The rapporteur appointed is Esther Werner and the co-rapporteur is Paolo Pasquali.

This legal basis for this application refers to Article 13(c) of Directive 2001/82/EC, relating to informed consent from a marketing authorisation holder for an authorised veterinary medicinal product: BLUEVAC BTV8 authorised in the Community on 14 April 2011 (EU/2/11/122/001-003).

On 7 September 2017, the CVMP adopted an opinion and CVMP assessment report.

On 21 November 2017, the European Commission adopted a Commission Decision granting the marketing authorisation for Bovilis Blue-8.

Marketing authorisation under exceptional circumstances

Not applicable.

Scientific advice

Not applicable.

MUMS/limited market status

Not applicable.

Part 1 - Administrative particulars

Detailed description of the pharmacovigilance system

A detailed description of the pharmacovigilance system which fulfils the requirements of Directive 2001/82/EC was provided. Based on the information provided the applicant has the services of a qualified person responsible for pharmacovigilance and the necessary means for the notification of any adverse reaction occurring either in the Community or in a third country. The pharmacovigilance system is considered acceptable.

Manufacturing authorisations and inspection status

Manufacture of the final product takes place at CZ VETERINARIA, S.A., Spain. The site has a manufacturing authorisation issued on 9 May 2017 by the competent national authority of Spain (Agencia Española de Medicamentos y Productos Sanitarios, AEMPS). Good Manufacturing Practice (GMP) certification, which confirms the date of the last inspection and shows that the site is authorised for the manufacture, packaging and batch release/quality control testing of such veterinary dosage forms has been provided issued on 19 July 2016. The site was considered appropriately certified as complying with GMP requirements.

The site for batch release is at INTERVET UK LIMITED, United Kingdom, for which a GMP certificate of compliance was issued on 24 July 2017 by the competent national authority of the United Kingdom (Veterinary Medicines Directorate, VMD).

A GMP declaration for the active substance manufacturing site was provided from the Qualified Person (QP) at CZ VETERINARIA, S.A., Spain. The declaration was based on an on-site audit by the manufacturing site responsible for batch release which has taken into consideration the GMP certificate available for the active substance site issued by competent authority of the Autonomous Community of Galicia in Spain on behalf of AEMPS following inspection.

Overall conclusions on administrative particulars

The detailed description of the pharmacovigilance system and the GMP certification of the manufacturing sites are considered in line with legal requirements.

All sites are appropriately authorised/certified as complying with GMP requirements.

Part 2 – Quality

This application is an informed consent of BLUEVAC BTV8. The quality data in support of the application for Bovilis Blue-8 are identical to the up-to-date quality data of the BLUEVAC BTV 8 dossier, which has been assessed and approved (including all post-marketing procedures). Therefore, no quality data have been submitted. This is considered acceptable.

Part 3 – Safety

This application is an informed consent of BLUEVAC BTV8. The safety data in support of the application for Bovilis Blue-8 are identical to the up-to-date safety data of the BLUEVAC BTV8 dossier, which has been assessed and approved (including all post-marketing procedures).
Therefore, no safety data have been submitted. This is considered acceptable.

To ensure comprehensive adverse event surveillance and to benefit from the possibility of aligning periodic safety update report (PSUR) submissions for informed consent products as foreseen in the legislation, PSUR submissions should be synchronised for the informed consent products, Bovilis Blue-8 and BLUEVAC BTV8, which is currently on a yearly cycle. The next data lock point (DLP) is expected to be 30 June 2018. In addition, surveillance of the data in EudraVigilance Veterinary (EVVet) will also be synchronised for signal detection of the two products.

Part 4 – Efficacy

This application is an informed consent of BLUEVAC BTV8. The efficacy data in support of the application for Bovilis Blue-8 are identical to the up-to-date efficacy data of the BLUEVAC BTV8 dossier, which has been assessed and approved (including all post-marketing procedures). Therefore, no efficacy data have been submitted. This is considered acceptable.

Part 5 – Benefit-risk assessment

Introduction

Bovilis Blue-8 is a suspension for injection containing bluetongue virus (inactivated) serotype 8. The active substance is known.

The product is intended for use in sheep and cattle to induce sufficient immunity to prevent viraemia in both sheep and cattle and to decrease the impact of clinical signs for sheep.

The application for Bovilis Blue-8 has been submitted as an informed consent application of the centrally authorised product BLUEVAC BTV8 (EU/2/11/122/001-003) in line with the requirements for submissions under Article 13c of Directive 2001/82/EC. As this application is an informed consent of BLUEVAC BTV8 no new quality, safety and efficacy data has been submitted. Therefore, this section refers to the BLUEVAC BTV8 dossier, which has been assessed and approved (including all post-marketing procedures).

Benefit assessment

Direct therapeutic benefit

The benefit of Bovilis Blue-8 is its efficacy concerning the active immunisation of sheep from 2.5 months of age to prevent viraemia and to reduce clinical signs caused by bluetongue virus serotype 8 and the active immunisation of cattle from 2.5 months of age to prevent viraemia caused by bluetongue virus serotype 8.

The onset of immunity is 20 days after the second dose in sheep and 31 days after the second dose in cattle. The duration of protection is one year after the second dose in both sheep and cattle.

Additional benefits

Bovilis Blue-8 increases the number of available vaccines (prophylaxis possibilities) for the active immunisation of sheep and cattle against bluetongue virus serotype 8. As a standard inactivated vaccine it fits in with accepted vaccination practice in the field.

In addition, vaccination has been shown to be safe for use during pregnancy in sheep and cattle, which is valuable during a widespread vaccination program usually necessary to control the spread of disease. Vaccination was also shown to be safe for use during lactation in ewes and cows, as the milk yield was not negatively impacted.

Risk assessment

Quality:

Information on development, manufacture and control of the active substance and finished product has been presented in a satisfactory manner. The results of tests carried out indicate consistency and uniformity of important product quality characteristics, and these in turn lead to the conclusion that the product should have a satisfactory and uniform performance in clinical use.

Safety:

Measures to manage the risks identified below are included in the risk management section.

Risks for the target animal:

Administration of Bovilis Blue-8 in accordance with SPC recommendations is generally well tolerated.

For sheep and cattle there is a risk of a slight rise in temperature (between 0.5 and 1.0 °C) which lasts no longer than 24-48 hours. Temporary swellings at the injection site may occur following vaccination. These swellings may last for over 14 days in sheep and cattle. The SPC wording is adequate to this matter.

Risk for the user:

It concluded that user safety for this product is acceptable when used according to the SPC recommendations. Standard safety advice is included in the SPC.

Risk for the environment:

Bovilis Blue-8 is not expected to pose a risk for the environment when used according to the SPC

recommendations. Standard advice on waste disposal is included in the SPC.

Risk for the consumer:

There are no components which require an MRL; therefore there are no concerns over failure to observe an MRL. The product contains components found in other marketed products and therefore the risk is no greater than already exists. A withdrawal time of zero days is justified.

Risk management or mitigation measures

Appropriate information has been included in the SPC to inform on the potential risks of this product relevant to the target animal, user, environment and consumer and to provide advice on how to prevent or reduce these risks.

To ensure comprehensive adverse event surveillance, signal detection and PSUR submissions will be synchronised with those for the informed consent product, BLUEVAC BTV8.

Evaluation of the benefit-risk balance

The product has been shown to be efficacious to induce sufficient immunity to prevent viraemia in both sheep and cattle and to decrease the impact of clinical signs for sheep.

Information on development, manufacture and control of the active substance and finished product has been presented and lead to the conclusion that the product should have a satisfactory and uniform performance in clinical use. It is well tolerated by the target animals and presents an acceptable risk for users, the environment and consumers, when used as recommended. Appropriate precautionary measures, including withdrawal period, have been included in the SPC and other product information.

Conclusion

Based on the original and complementary data presented on quality, safety and efficacy, the Committee for Medicinal Products for Veterinary Use (CVMP) concluded that the application for Bovilis Blue-8 is approvable since these data satisfy the requirements for an authorisation set out in the legislation (Regulation (EC) No 726/2004 in conjunction with Directive 2001/82/EC).

The CVMP considers that the benefit-risk balance is positive and, therefore, recommends the granting of the marketing authorisation for the above mentioned medicinal product.