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SCIENCE MEDICINES HEALTH

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Veterinary Medicines Division

Committee for Veterinary Medicinal Products (CVMP)

CVMP assessment report for a grouped variation requiring assessment for Bluevac BTV (EMEA/V/C/000156, EMA/VRA/0000293372)

Common name: Bluetongue virus vaccine (inactivated)

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

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Table of contents

Introduction

Submission of the variation application

In accordance with Article 64 of Regulation (EU) 2019/6, the marketing authorisation holder, CZ Vaccines S.A.U. (the applicant), submitted to the European Medicines Agency (the Agency) on 22 August 2025 an application for a group of variations requiring assessment for Bluevac BTV.

Scope of the variation

Variation(s) requested	
G.I.18	G.I.18 One-off alignment of the product information with version 9.0 of the QRD templates i.e. major update of the QRD templates in accordance with Regulation (EU) 2019/6, for veterinary medicinal products placed on the market in accordance with Directive 2001/82/EC or Regulation (EC) No 726/2004
G.I.13	G.I.13 Variations concerning the replacement or addition of a serotype, strain, antigen or combination of serotypes, strains or antigens for a veterinary vaccine based on a multistrain dossier

The aim of this grouped variation is to allow up to three different inactivated bluetongue virus serotypes to be included in the final vaccine for sheep, and to align the product information with the latest version of the QRD available (version 9.1).

Changes to the dossier held by the European Medicines Agency

This application relates to the following sections of the current dossier held by the Agency:

Part 1, Part 2, Part 3

Scientific advice

Not applicable.

Limited market status

Not applicable.

Scientific Overview

With this grouped variation, the applicant intends

1. to allow up to three different inactivated bluetongue virus serotypes to be included in the final vaccine for sheep, and

2. to align the product information with the latest version of the QRD available (version 9.1).

In order to fulfil the requirements of 'Guideline on data requirements for multi-strain dossiers for inactivated veterinary vaccines' (EMA/CVMP/IWP/105506/2007 Rev. 2), and to accept the new combination of serotypes as part of the multi-strain dossier, complementary information regarding quality and new studies regarding safety have been provided.

For the first variation (combination of three serotypes), it is considered not necessary to perform any further study or to submit any additional documentation to demonstrate that up to now three different inactivated bluetongue virus serotypes in the final product are efficacious for sheep as it is assumed that the combination of three serotypes will be at least as efficacious as the monovalent vaccines.

Based on the new safety study provided, it can furthermore be concluded, that the trivalent combination of BTV-1, BTV-4 and BTV-8 antigens will be safe in sheep.

Concerning quality, an updated version of the qualitative and quantitative composition, flow chart for the production and controls as well as the description of the manufacturing process of Bluevac BTV were provided to include monovalent/bivalent/trivalent vaccines. The same control tests on the finished product as those already authorised for Bluevac BTV are proposed and considered adequate.

Potency of the vaccine is currently determined on monovalent and bivalent finished product, i.e. on the filled vaccine, by an *in vivo* potency test in sheep. For trivalent vaccines, the potency test is now proposed based on the same potency test as for monovalent and bivalent vaccines. However, considering the 3Rs principle, as well as the European directives and regulations on animal welfare, the replacement of this in vivo method for potency testing with an adequately validated in vitro test and any effort in this regard concerning the development of an in vitro potency test is strongly encouraged.

The documentation submitted for this variation is generally acceptable to sustain the proposed trivalent vaccine for sheep.

For the second variation concerning the alignment of the product information with version 9.1 of the QRD templates, the information has been updated or transcribed directly from the relevant sections of the previously approved product information to the relevant sections of the newly proposed product information presented with this application.

Benefit-risk assessment of the proposed change

Bluevac BTV is a suspension for injection for cattle and sheep. This product is authorised for:

Sheep

For active immunisation of sheep to prevent the viraemia* caused by bluetongue virus serotype 1 and/or 4 and/or 8 and to reduce clinical signs caused by bluetongue virus serotype 8 (combination of maximum 2 serotypes).

*Below the level of detection by the validated RT-PCR method at 1 log10 TCID50/ml for serotypes 8 and 4, and 1.3 log10 TCID50/ml for serotype 1.

Cattle

For active immunisation of cattle to prevent viraemia* caused by bluetongue virus serotype 1 and/or 4 and/or 8 (combination of maximum 2 serotypes).

*Below the level of detection by the validated RT-PCR method at 1 log10 TCID50/ml for serotypes 8 and 4, and 1.3 log10 TCID50/ml for serotype 1.

The active substance is an inactivated bluetongue virus (BTV). Currently, a maximum of two of the following inactivated serotypes could be added:

Inactivated bluetongue virus, serotype 1 (BTV-1), strain BTV-1/ALG/2006/01, ≥ 9.06 µg/ml
Inactivated bluetongue virus, serotype 4 (BTV-4), strain BTV-4/SPA-1/2004, ≥ 22.06 µg/ml
Inactivated bluetongue virus, serotype 8 (BTV-8), strain BTV8/BEL/2006/01, ≥ 245.67 µg/ml

The proposed variation is to allow up to three different inactivated bluetongue virus serotypes to be included in the final vaccine for sheep. At present, only two inactivated bluetongue virus serotypes can be included; consequently, changes in the SPC, Labelling and Package Leaflet are needed. Additionally, the product information is also updated with the latest version of the QRD template (version 9.1).

Benefit assessment

Direct therapeutic benefit

The benefits of the product remain unaffected by this variation.

Additional benefits

A change of the multi-strain dossier to allow up to three different inactivated bluetongue virus serotypes in the final product (trivalent vaccine) for sheep means that corresponding vaccines that contain this/these strain(s) can quickly be produced in the event of an outbreak of bluetongue disease in the EU caused by the specific BTV serotype(s). This may be considered an additional benefit. Furthermore, the ability to mix different combinations of strains may increase the flexibility to react to respective emergency situations.

Risk assessment

Quality:

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

Safety:

Safety (user, consumer, environmental) remains unaffected by this variation.

According to the assessment of the target animal safety and taking into account the same safety profile of the vaccine, no significant risks have been identified when the product is used as indicated in SPC and under common veterinary practice conditions.

Risk management or mitigation measures

Risk management or mitigation measures remain unaffected by this variation.

Evaluation of the benefit-risk balance

Based on the data presented, the overall benefit-risk remains unchanged and, thus, is deemed positive.

Conclusion

Based on the original and complementary data presented on quality, safety and efficacy the Committee for Veterinary Medicinal Products (CVMP) concluded that the application for variation to the terms of

the marketing authorisation for Bluevac BTV can be approved, since the data satisfy the requirements as set out in the legislation (Regulation (EU) 2019/6), as follows:

G.I.13 Variations concerning the replacement or addition of a serotype, strain, antigen or combination of serotypes, strains or antigens for a veterinary vaccine based on a multistrain dossier

- to allow up to three different inactivated bluetongue virus serotypes to be included in the final vaccine, and

G.I.18 One-off alignment of the product information with version 9.0 of the QRD templates i.e. major update of the QRD templates in accordance with Regulation (EU) 2019/6, for veterinary medicinal products placed on the market in accordance with Directive 2001/82/EC or Regulation (EC) No 726/2004

- to align the product information with the latest version of the QRD available (version 9.1).

Based on the original data presented on quality, safety and efficacy the Committee for Veterinary Medicinal Products (CVMP) concluded that the application for variation to the terms of the marketing authorisation for Bluevac BTV can be approved.

Changes are required in the following Annexes to the Union marketing authorisation.

I, II, IIIA and IIIB

As a consequence of this variation, the SPC is updated. The Package Leaflet is updated accordingly.