7 September 2017
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Veterinary Medicines Division

Committee for Medicinal Products for Veterinary Use

CVMP assessment report for Nobivac LeuFel (EMEA/V/C/004778/0000)

Common name: Feline leukaemia vaccine (inactivated)

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

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Introduction

On 20 June 2017 the applicant Virbac submitted an application for a marketing authorisation to the European Medicines Agency (the Agency) for Nobivac LeuFel through the centralised procedure.

The eligibility to the centralised procedure was agreed upon by the CVMP on 12 April 2017 under Article 3(1) of Regulation (EC) no 726/2004 as Nobivac LeuFel has been developed by recombinant DNA technology. This application is also a multiple application of the centrally authorised product Leucogen (EU/2/09/096/001–002) as it falls within the scope of Article 82(1) of Regulation (EC) No 726/2004.

The applicant applied for the following indication: Active immunisation of cats from eight weeks of age against feline leukaemia for the prevention of persistent viraemia and clinical signs of the related disease. Onset of immunity: 3 weeks after the primary vaccination. The duration of immunity is one year after the primary vaccination.

The active substance of Nobivac LeuFel is feline leukaemia purified p45 FeLV-envelope antigen with a minimum quantity of 102 µg per 1 ml dose. The target species is cats. The product is intended for use by subcutaneous administration.

Nobivac LeuFel is a suspension for injection presented in a glass vial of 3 ml with a 13 mm-diameter butyl elastomer stopper and set with an aluminium capsule. The vaccine is presented in boxes of 10 or 50 vials.

The rapporteur appointed is Esther Werner and the co-rapporteur is Noemi Garcia del Blanco.

The 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: Leucogen authorised in the Community on 17 June 2009 (EU/2/09/096/001-002).

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

On 6 November 2017, the European Commission adopted a Commission Decision granting the marketing authorisation for Nobivac LeuFel.

Part 1 - Administrative particulars

Detailed description of the pharmacovigilance system

A detailed description of the pharmacovigilance system (dated September 2014), 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 and batch release take place at

Virbac.
06516 Carros Cedex
France

The site has a manufacturing authorisation issued by the French National Agency for Veterinary Medicinal Products on 25 August 2015. A Good Manufacturing Practice (GMP) certificate of compliance issued on 5 April 2016 by Anses ANMV/France has been provided, 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.

Manufacturing of the active substance (p45 FeLV-envelope antigen) including quality control testing takes place at:

PP Manufacturing Corporation
01702 Framingham, Massachusetts
United States

A GMP certificate of compliance issued on 23 May 2016 by Anses ANMV/France for PP Manufacturing Corporation, Framingham, USA was provided.

A GMP declaration for the active substance manufacturing site was provided by the Qualified Person (QP) at Virbac Carros, France. The declaration is based on an on-site audit by the manufacturing site responsible for batch release taking into consideration the GMP certificate available for the active substance site issued by the French National Agency for Veterinary Medicinal Products.

Overall conclusions on administrative particulars

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

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

Part 2 – Quality

This application is a multiple application of Leucogen by informed consent. The quality data in support of the application for Nobivac LeuFel are identical to the up-to-date quality data of the Leucogen 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 a multiple application of Leucogen by informed consent. The safety data in support of the application for Nobivac LeuFel are identical to the up-to-date safety data of the Leucogen 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 duplicate products, Nobivac LeuFel and

Leucogen, which is currently on a three-yearly cycle. Common PSURs should be submitted and the next data lock point (DLP) should therefore be 30 June 2020.

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 a multiple application of Leucogen by informed consent. The efficacy data in support of the application for Nobivac LeuFel are identical to the up-to-date efficacy data of the Leucogen 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

Nobivac LeuFel is a suspension for injection containing the purified recombinant p45 FeLV-envelope antigen that was derived from the gp70 surface glycoprotein of the FeLV subgroup A and is expressed in *Escherichia coli*. The active substance is known.

The product is intended to be used for the active immunisation of cats from eight weeks of age against feline leukaemia for the prevention of persistent viraemia and clinical signs of the related disease.

The application for Nobivac LeuFel has been submitted as a multiple application of the centrally authorised product Leucogen (EU/2/09/096/001–002) in accordance with Article 82(1) of Regulation (EC) No 726/2004. The dossier has been submitted in line with the requirements for submissions under Article 13c of Directive 2001/82/EC. As this application is an informed consent of Leucogen no new quality, safety and efficacy data have been submitted. Therefore, this section refers to the Leucogen dossier, which has been assessed and approved (including all post-marketing procedures).

Benefit assessment

1.1.1. Direct therapeutic benefit

The benefit of Nobivac LeuFel is its efficacy concerning the active immunisation of cats from eight weeks of age against feline leukaemia for the prevention of persistent viraemia and clinical signs of the related disease. The onset of immunity is 3 weeks after the primary vaccination and the duration of immunity is one year after the primary vaccination.

1.1.2. Additional benefits

Nobivac LeuFel increases the number of available vaccines (prophylaxis possibilities) for the active immunisation of cats against feline leukaemia. Safety and efficacy data are available which

demonstrate that this vaccine can be mixed with Feligen CRP or Feligen RCP and administered at one injection site.

1.1.3. 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, which 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 Nobivac LeuFel in accordance with SPC recommendations is generally well tolerated.

For cats, there is a risk of local and systemic reactions after vaccination. The local reactions could be swellings, oedemas or nodules (≤ 2 cm), which resolve spontaneously within 3 to 4 weeks at the most. The following signs can also be observed: pain at palpation, sneezing, conjunctivitis, hyperthermia (lasting 1 to 4 days), apathy and digestive disturbances. The wording in the SPC and package leaflet is adequate in this matter.

The vaccine should not be used in pregnant cats or during lactation. A corresponding warning is included in the SPC and package leaflet.

Only feline leukaemia virus (FeLV) negative cats should be vaccinated. Therefore, a test for the presence of FeLV before vaccination is recommended.

Risk for the user:

It is 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:

Nobivac LeuFel 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.

Efficacy:

Maternally derived antibodies in cats may have an impact on the protection induced by the vaccine.

Risk management or mitigation measures

Appropriate information has been included in the SPC to inform about the potential risks of this product relevant to the target animal, user and environment 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 duplicate product, Leucogen.

1.1.4. Evaluation of the benefit-risk balance

This product has been shown to be efficacious for the active immunisation of cats from eight weeks of age against feline leukaemia for the prevention of persistent viraemia and clinical signs of the related disease.

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 and the environment when used as recommended. Appropriate precautionary measures 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 Nobivac LeuFel 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.