7 May 2015
EMA/310242/2015
Veterinary Medicines Division

Committee for Medicinal Products for Veterinary Use (CVMP)

CVMP assessment report for Canigen L4 (EMEA/V/C/004079/0000)

Common name: Canine leptospirosis vaccine (inactivated)

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 8 December 2014 Intervet International B.V. submitted an application for a marketing authorisation to the European Medicines Agency (the Agency) for Canigen L4 in accordance with Article 82(1) of Regulation (EC) No 726/2004 (duplicate application).

The eligibility to the centralised procedure was agreed upon by the CVMP on 11 September 2014. Canigen L4 is a duplicate application of Nobivac L4 which has been authorised in the Community since 16 July 2012. The rapporteur appointed was B. Urbain and the co-rapporteur R. Breathnach.

The applicant applied for the following indication: For active immunisation of dogs against *Leptospira interrogans* serogroup Canicola serovar Canicola, *Leptospira interrogans* serogroup Icterohaemorrhagiae serovar Copenhageni and *Leptospira kirschneri* serogroup Grippotyphosa serovar Bananal/Lianguang to reduce infection and urinary excretion and against *Leptospira interrogans* serogroup Australis serovar Bratislava to reduce infection.

Canigen L4 is a suspension for injection that contains inactivated *L. interrogans* serogroup Canicola serovar Portland-vere (strain Ca-12-000), inactivated *L. interrogans* serogroup Icterohaemorragiae serovar Copenhageni (strain Ic-02-001), inactivated *L. interrogans* serogroup Australis serovar Bratislava (strain As-05-073) and inactivated *L. kirschneri* serogroup Grippotyphosa serovar Dadas (strain Gr-01-005). It is presented in packs containing 10 or 50 vials of 1 ml (1 dose) or 1 vial of 10 ml (10 doses). The route of administration is subcutaneous use.

The dossier has been submitted in line with the requirements for submissions under Article 13c of Directive 2001/82/EC (informed consent).

On 7 May 2015 the CVMP adopted an opinion and CVMP assessment report.

On 3 July 2015, the European Commission adopted a Commission Decision granting the marketing authorisation for Canigen L4.

Part 1 - Administrative particulars

Detailed description of the pharmacovigilance system

The applicant has provided a detailed description of the pharmacovigilance system (dated 1 April 2014) which fulfils the requirements of Directive 2001/82/EC. 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. There are no outstanding issues.

Manufacturing authorisations and inspection status

Canigen L4 is manufactured by Intervet International B.V., Boxmeer, The Netherlands. Secondary packaging and batch release for the European Union (EU) will be also carried out by Intervet International B.V., Boxmeer, The Netherlands.

A valid manufacturing authorisation and a valid good manufacturing practice (GMP) certificate have been provided for Intervet International B.V. in Boxmeer, The Netherlands.

Qualified person (QP) declarations in line with the current guidance concerning GMP compliance of active

substance manufacture (EMA/196292/2014) have been provided for each active substance.

Summary of product characteristics (SPC), labelling and package leaflet

The reference product, Nobivac L4, is authorised to be mixed with other specified Nobivac vaccines containing canine distemper virus, canine adenovirus type 2 and/or canine parvovirus and to be used on the same day with Nobivac vaccines against *Bordetella bronchiseptica* and/or parainfluenza virus.

The CVMP considered that the applicant has adequately justified the deviation from the SPC of Nobivac L4 in support of the mixing of Canigen L4 with other Canigen vaccines containing canine distemper virus, canine adenovirus type 2 and/or canine parvovirus authorised to the same marketing authorisation holder and to be used on the same day with Canigen vaccines against *Bordetella bronchiseptica* and/or parainfluenza virus authorised to the same marketing authorisation holder.

Overall conclusions on administrative particulars

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

Part 2 - Quality

This application is a duplicate application of Nobivac L4 by informed consent. The quality data in support of the application for Canigen L4 are therefore considered identical to the up-to-date quality data contained on the dossier for Nobivac L4 at the time of submission of the application for Canigen L4.

Therefore, no quality data have been submitted which is acceptable.

An out-of-specification result has been reported in the reference product, Nobivac L4. The CVMP cannot conclude at this stage that the out-of-specification result is not batch specific, and awaits future stability testing data that will allow it to conclude on this point.

The CVMP considered that any issues relating to the quality of Nobivac L4 would be equally applicable to Canigen L4 once authorised.

Part 3 – Safety

This application is a duplicate application of Nobivac L4 by informed consent. The safety data in support of the application for Canigen L4 are therefore considered identical to the up-to-date safety data contained on the dossier for Nobivac L4 at the time of submission of the application for Canigen L4.

Therefore, no safety data have been submitted which is acceptable.

Part 4 – Efficacy

This application is a duplicate application of Nobivac L4 by informed consent. The efficacy data in support of the application for Canigen L4 are therefore considered identical to the up-to-date efficacy data contained on the dossier for Nobivac L4 at the time of submission of the application for Canigen L4.

Therefore, no efficacy data have been submitted which is acceptable.

The out of specification result reported for Nobivac L4 does not represent at present a concern for efficacy over the duration of immunity of the vaccine. Batches will be monitored to ensure that they remain above the required efficacy.

The CVMP considered that any issues relating to the efficacy of Nobivac L4 would be equally applicable to Canigen L4.

Part 5 – Benefit-risk assessment

Introduction

Canigen L4 is a tetravalent inactivated vaccine that contains *L. interrogans* serogroup Canicola serovar Portland-Vere, *L. interrogans* serogroup Icterohaemorrhagiae serovar Copenhageni, *L. interrogans* serogroup Australis serovar Bratislava and *L. kirschneri* serogroup Grippotyphosa serovar Dadas. The proposed indication is "For active immunisation of dogs against:

- *Leptospira interrogans* serogroup Canicola serovar Canicola to reduce infection and urinary excretion;
- *Leptospira interrogans* serogroup Icterohaemorrhagiae serovar Copenhageni to reduce infection and urinary excretion;
- *Leptospira interrogans* serogroup Australis serovar Bratislava to reduce infection;
- *Leptospira kirschneri* serogroup Grippotyphosa serovar Bananal/Liangguang to reduce infection and urinary excretion."

One dose of vaccine is administered twice subcutaneously with a 4 week interval. Onset of immunity is 3 weeks after the last injection. Annual booster vaccination is recommended.

The application has been submitted in accordance with Article 13c of Directive 2001/82/EC (informed consent).

Benefit assessment

Direct therapeutic benefit

The benefit of Canigen L4 is the same as that for Nobivac L4, i.e. its efficacy in the active immunisation of dogs against:

- *L. interrogans* serogroup Canicola serovar Canicola to reduce infection and urinary excretion;
- *L. interrogans* serogroup Icterohaemorrhagiae serovar Copenhageni to reduce infection and urinary excretion;
- *L. interrogans* serogroup Australis serovar Bratislava to reduce infection;
- *L. kirschneri* serogroup Grippotyphosa serovar Bananal/Lianguang to reduce infection and urinary excretion.

Additional benefits

Canigen L4 increases the range of available treatment possibilities against leptospirosis in dogs.

Risk assessment

The risks of Canigen L4 are the same as those identified for Nobivac L4 including the uncertainty arising from the out of specification result reported for Nobivac L4.

Risk management or mitigation measures

The risk mitigation measures are the same as those for Nobivac L4. Appropriate information has been included in the SPC to inform on the potential risks of this product relevant to the target animal, user and the environment and to provide advice on how to prevent or reduce these risks.

Evaluation of the benefit-risk balance

This application is a duplicate application of Nobivac L4 by informed consent. The quality, safety and efficacy data in support of the application for Canigen L4 are therefore considered identical to the up-to-date data contained on the dossier for Nobivac L4 at the time of submission of the application for Canigen L4.

Canigen L4 has been shown to have a positive benefit-risk balance overall.

Conclusion on benefit-risk balance

The overall benefit-risk evaluation is deemed positive with a sufficient clear and complete product information.

Conclusion

Based on the original and complementary data presented the CVMP concluded that the application for Canigen L4 is approvable since the data presented 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.