Veterinary Medicines Directorate

United Kingdom
Veterinary Medicines Directorate
Woodham Lane
New Haw
Addlestone
Surrey KT15 3LS

DECENTRALISED PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Canishield 0.77 g Medicated Collar for Small and Medium Sized Dogs

Canishield 1.04 g Medicated Collar for Large Sized Dogs

Merlin 1.04 g Medicated Collar for Large Sized Dogs

Date Created: September 2018

MODULE 1

PRODUCT SUMMARY

EU Procedure numbers	UK/V/0657/001/DC UK/V/0606/001/DC UK/V/0656/001/DC
Name, strength and pharmaceutical form	Canishield 0.77 g Medicated Collar for Small and Medium Sized Dogs Canishield 1.04 g Medicated Collar for Large Sized Dogs Merlin 1.04 g Medicated Collar for Large Sized Dogs
Applicant	Beaphar B.V. Drostenkamp 3 8101 BX Raalte Netherlands
Active substance(s)	Deltamethrin
ATC Vetcode	QP53AC11
Target species	Dogs
Indication for use	The veterinary medicinal product provides: • Persistent flea (*Ctenocephalides felis*) killing activity for 16 weeks; • Persistent tick (*Ixodes ricinus*) killing activity for 6 months; • Sandfly (*Phlebotomus perniciosus*) anti-feeding and killing activity for 5.5 months.

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	Generic 'hybrid' applications in accordance with Article 13(3) of Directive 2001/82/EC as amended.
Date of conclusion of the decentralised procedures	09/08/2018 and 06/09/18
Concerned Member States for original procedure	Canishield 0.77 g Medicated Collar for Small and Medium Sized Dogs: Bulgaria, Croatia, Czech Republic, Finland, France, Germany, Hungary, Latvia, Lithuania, Netherlands, Norway, Poland, Romania, Slovakia and Slovenia. Canishield 1.04 g Medicated Collar for Large Sized Dogs: Belgium, Bulgaria, Croatia, Cyprus, Czech republic, Estonia, France, Germany, Greece, Hungary, Ireland, Italy, Latvia, Lithuania, Malta, Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia and Spain. Merlin 1.04 g Medicated Collar for Large Sized Dogs: France, Italy, Portugal and Spain.

I. SCIENTIFIC OVERVIEW

These applications were submitted in accordance with Article 13(3) of Directive 2001/82/EC, as amended by 2004/28/EC. The reference product is Scalibor Protectorband 4% w/w 65 cm Collar for Large Sized Dogs, which has been authorised in the UK since 21st March 2002.

These were determined generic 'hybrid' applications because as the products are locally acting, *in vivo* bioequivalence cannot be demonstrated. An *in vitro* dissolution study and *in vivo* comparative release study, to demonstrate a comparable release profile of the proposed products compared to the reference product were provided. The products contain either 0.77 g or 1.04 g of deltamethrin, depending on for which size of dog the products are intended.

The products are produced and controlled using validated methods and tests which ensure the consistency of the product released onto the market. It has been shown that the products can be safely used in the target species, any reactions observed are indicated in the SPC.[1] The products are safe for the user and for the environment, when used as recommended. Suitable warnings and precautions are indicated in the SPC. The efficacy [2] of the products was demonstrated according to the claims made in the SPC. The overall benefit/risk analysis is in favour of granting a marketing authorisation.

II. QUALITATIVE AND QUANTITATIVE PARTICULARS OF THE CONSTITUENTS

II.A. Composition

The products are medicated collars for dogs containing Deltamethrin as the active substance, in a coloured, plastic base. The base is formed from the excipients; Stearic Acid, Triphenyl Phosphate, Calcium Stearate, epoxidized soybean oil, diisononyl adipate, zinc stearate, polyvinyl chloride, with carbon black as colouring.

Collars are packed in a multi-layered polyethylene terephthalate (PET)/polyethylene (PE)/aluminium (AI) foil/surlyn sachet. The particulars of the containers and controls performed are provided and conform to the regulation.

The choice of the formulation 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. Description of the Manufacturing Method

The product is manufactured fully in accordance with the principles of good manufacturing practice from a licensed manufacturing site. The manufacturing process is as follows:

- **Blank compound (compound without active substance) production**

PVC, calcium stearate and zinc stearate are accurately weighed and released into mixer 1. All the components are blended and the blank compound is unloaded into mixer 2.

- **Transport of blank compound to mixing device 3**

The blank compound is transported to mixer 3.

[1] SPC – Summary of product Characteristics.
[2] Efficacy – The production of a desired or intended result.

- **Add and homogenise Deltamethrin and excipients**

Deltamethrin, stearic acid and colour mixture are mixed with the blank compound. In the third mixer, this final compound is mixed thoroughly until homogeneous.

- **Transport to extruder**

After mixing, final compound is transported to the extruder.

- **Extrusion**

The final compound is extruded into a plastic strip.

Adjusting the strip to width and weight & cooling

The warm strip is automatically adjusted to a set width. The force of pulling determines the width of the strip. After pulling, the width and specific weight are fixed by cooling in a water tank.

- **Roll on reel**

The produced strip is transported onto a reel, which will contain batch size ±10 kg of strip.

- **Assembly to robot**

Based on specific weight, the strip is cut to an appropriate length. A buckle is attached, and the collar is rolled.

- **Packing in sachet**

The rolled collars are packed into a 12 µm PET/20 grams PE/9 µm aluminium foil/50 grams surlyn sachet, which is packed into a cardboard box. After extrusion, assembly and packaging is completed.

The product is manufactured using conventional manufacturing techniques. Process validation for full-scale batches will be performed post-authorisation.

II.C. Control of Starting Materials

The active substance is Deltamethrin, an established active substance described in the British Veterinary Pharmacopoeia. The active substance is manufactured in accordance with the principles of good manufacturing practice.

The active substance specification is considered adequate to control the quality of the material. Batch analytical data demonstrating compliance with this specification have been provided.

A certificate of analysis was provided for each of the three batches of Deltamethrin, demonstrating compliance with the proposed specification. Information on the active substance was provided in an ASMF.

Stearic Acid, Calcium Stearate and Zinc Stearate are controlled in accordance with their Ph. Eur. monographs.

The collar is provided in a sachet comprising (outer to inner) 12 µm PET/20 grams PE/9 µm aluminium foil/50 grams surlyn coating and the sachet is packed in cardboard box.

II.C.4. Substances of Biological Origin

The applicant states that no materials of animal origin are used in the manufacture of Deltamethrin, TPP, Epoxidized Soybean Oil, DINA, PVC and Carbon Black. For Stearic Acid and Calcium Stearate, certificates have been provided that declare that these materials are of non-animal origin. For zinc Stearate, a certificate has been provided that the raw material does not contain and is not derived from bovine, ovine or caprine materials other than those derived from animals born, continuously reared and slaughtered in a country or region classified in accordance with Article 5(2) of Regulation (EC) No 999/2001 as a country or region posing a negligible or controlled BSE risk.

II.D. Control Tests Carried Out at Intermediate Stages of the Manufacturing Process

Not applicable.

II.E. Control Tests on the Finished Product

The finished product specification controls the relevant parameters for the pharmaceutical form. The tests in the specification, and their limits, have been justified and are considered appropriate to adequately control the quality of the product. Satisfactory validation data for the analytical methods have been provided. Batch analytical data from the proposed production site have been provided demonstrating compliance with the specification. Control tests on the finished product are those for appearance, identification of Deltamethrin, identification of collar, identification of colour black, weight, length, width, thickness, and density of collar, uniformity of mass, assay Deltamethrin, assay triphenyl phosphate and tests for related substances.

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.

Stability data on the finished product have been provided in accordance with applicable European guidelines, demonstrating the stability of the product throughout its shelf life when stored under the approved conditions.

G. Other Information

Shelf life of the veterinary medicinal product as packaged for sale: 30 months.
Shelf life after first opening the sachet: use immediately.
This veterinary medicinal product does not require any special temperature storage conditions.
Keep the sachets in the outer carton.

III. SAFETY AND RESIDUES DOCUMENTATION (PHARMACO-TOXICOLOGICAL)

III.A Safety Documentation

Pharmacological & Toxicological Studies

These applications are generic 'hybrid' products and were submitted in accordance with Article 13(3) of Directive 2001/82/EC, as amended, since bioequivalence cannot be demonstrated. The applications were submitted on the basis that the formulation is qualitatively the same as the reference product in regard to active substance and pharmaceutical form, pharmacological and toxicological studies were not required for these applications.

User Safety

A user risk assessment was provided in compliance with the relevant guideline which shows that the likely routes of dermal exposure through handling the collar and having contact with the treated animal and subsequent oral exposure through hand to mouth contact have been identified. In addition, accidental oral exposure through a child chewing or sucking the collar has been considered. Deltamethrin and triphenyl phosphate (TPP) were identified as substances of concern and exposure calculations were considered for both.

Warnings and precautions as listed on the product literature are adequate to ensure safety to users of the product. Therefore the following applicant's user recommendations are appropriate:

- Accidental ingestion of this product may cause adverse reactions, including neurotoxic effects.

- Keep the product in the original carton. Keep the collar in the sachet until use.
- Do not smoke, eat or drink while handling the collar.
- Do not allow children to play with the collar or to put it into their mouths. Immediately dispose of any remnants or cut-offs of the collar.

- Wash hands with cold water after fitting the collar.
- Avoid prolonged contact with the collar or dog wearing the collar. This includes sharing a bed with dogs wearing the collar; this is particularly important for children.
- In case of accidental oral exposure or ingestion, seek medical advice and show the package leaflet or the label to the doctor.

Deltamethrin may cause hypersensitivity (allergic) reactions in sensitive people. People with known hypersensitivity to Deltamethrin should avoid contact with the veterinary medicinal product and the treated animal. Seek medical advice in case of hypersensitivity reactions.

Environmental Safety

The Environmental Risk Assessment (ERA) was carried out in accordance with VICH and CVMP guidelines.

Phase I:
The applicant provided a Phase I ERA and has correctly shown that the assessment should conclude at question 3 of the decision tree, based on use in non-food producing animals only. However, since the products are ectoparasiticides for topical use, an additional risk mitigation measure has been added as follows: Deltamethrin is toxic for aquatic organisms. Dogs wearing the collar are not allowed to enter waterways.
The disposal advice also includes the wording: This product should not enter water courses as this may be dangerous for fish and other aquatic organisms.

The product will only be used in non-food animals and as a result environmental exposure will be low. A Phase II ERA was not required.

IV CLINICAL DOCUMENTATION

IV.I. Pre-Clinical Studies

Since the application is made in accordance with Article 13(3) of Directive 2004/28/EC, on the basis of essential similarity, data on this section of the dossier were not provided.

Tolerance in the Target Species

Since the application is made in accordance with Article 13(3) of Directive 2004/28/EC, on the basis of essential similarity, target animal safety studies were not required. Local tolerance was provided by five dose confirmation studies and one clinical field study. The applicant submitted literature to support safety of excipients and the active substance. An *in vitro* dissolution study and *in vivo* comparative release study, to demonstrate a comparable release profile of the proposed products compared to the reference product was also provided.

IV.I. Clinical Studies

Five dose confirmation studies and one clinical field study were provided to support the indications for use.

V OVERALL CONCLUSION AND BENEFIT– RISK ASSESSMENT

The data submitted in the dossier demonstrate that when the products are used in accordance with the Summary of Product Characteristics the benefit/risk profile of the products 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)