FRENCH AGENCY FOR VETERINARY MEDICINAL PRODUCTS
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MUTUAL RECOGNITION PROCEDURE

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Merlin 0.77 g medicated collar for small and medium sized dogs

DATE : 18/03/2021

MODULE 1

PRODUCT SUMMARY

EU Procedure number	FR/V/0432/001/MR
Name, strength and pharmaceutical form	Merlin 0.77 g medicated collar for small and medium 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 website
https://www.anses.fr/en/thematique/veterinary-medicine-anmv

MODULE 3

PUBLIC ASSESSMENT REPORT

Legal basis of original application	Hybrid application in accordance with Article 13 (3) of Directive 2001/82/EC as amended.
Date of completion of the original mutual recognition	10/02/2021
Date product first authorised in the Reference Member State (MRP only)	09/08/2019
Concerned Member States for original procedure	ES IT PT

I. SCIENTIFIC OVERVIEW

This application was 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, which has been authorised in Germany since the 06th of September 1999.
This is a hybrid application because as the products are locally acting, *in vivo* bioequivalence cannot be demonstrated. An *in vitro* dissolution study and *in vivo* release comparison and efficacy studies, to demonstrate a comparable release profile and efficacy of the proposed product compared to the reference product were provided.

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

II. QUALITY ASPECTS

A. Composition

The product contains 0,77 g of deltamethrinand carbon black, epoxidized soybean oil, diisononyl adipate, triphenyl phosphate, polyvinyl chloride, calcium stearate, zinc stearate, stearic acid as excipients.

The packaging of the finished product is as described on the SPC. The particulars of the containers and controls performed are provided and conform to the regulation.
The product is an established pharmaceutical form and its development is adequately described in accordance with the relevant European guidelines.

B. Method of Preparation of the Product

The product is manufactured fully in accordance with the principles of good manufacturing practice from a licensed manufacturing site.
Process validation data on the product have been presented in accordance with the relevant European guidelines.

C. Control of Starting Materials

The active substance is deltamethrin, an established active substance. 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.

D. Specific Measures concerning the Prevention of the Transmission of Animal Spongiform Encephalopathies

Scientific data have been provided and compliance with the Note for Guidance on Minimising the Risk of Transmitting Animal Spongiform Encephalopathy Agents via Human and Veterinary Medicinal Products has been satisfactorily demonstrated.

E. Control on intermediate products

Not applicable.

F. 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.

G. 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.
The shelf-life as detailed on the SPC has been supported by appropriate data.

H. Genetically Modified Organisms

Not applicable.

J. Other Information

Not applicable.

III. SAFETY AND RESIDUES ASSESSMENT (PHARMACO-TOXICOLOGICAL)

As this is a hybrid application according to Article 13 (3), and bioequivalence with a reference product cannot be demonstrated, results of toxicological and safety tests are not required.

The safety aspects of this product are identical to the reference product.

Warnings and precautions as listed on the product literature are the same as those of the reference product and are adequate to ensure safety of the product to users and the environment.

III.A Safety Testing

Pharmacological Studies

As this is a hybrid application according to Article 13 (3), no studies were required. Deltametrin acts through contact with insects and acarines and leads to a sustained increase in the sodium permeability of the insect’s nerve

membranes. This results in hyperactivity followed by paralysis (shock effect), tremor and death of the parasite.

Toxicological Studies

As this is a hybrid application according to Article 13 (3), no studies were required.

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 Risk Assessment

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 ASSESSMENT (EFFICACY)

This is a hybrid application according to Article 13 (3), and the reference product is Scalibor Protectorband 4% w/w 65 cm Collar for Large Sized Dogs, which has been authorised in Germany since the 06th of September 1999.

IV.A Pre-Clinical Studies

Pharmacology

Since the application is made in accordance with Article 13(3) of Directive 2004/28/EC, of a local action product the equivalence was demonstrated on the basis of essential similarity. A comparative dissolution and an *in vivo* release studies were performed to compare the release profile of the deltamethrin from the two products.

Tolerance in the Target Species of Animals

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.

Resistance

A literature review of resistance was made.

IV.B Clinical Studies

Five dose confirmation studies on artificially infested dogs and one clinical field study performed in Europe were provided to support the indications for use. Studies were designed according to the CVMP “Guideline for the testing and evaluation of the efficacy of antiparasitic substances for the treatment and prevention of tick and flea infestations in dogs and cats” (EMEA/CVMP/EWP/005/2000 - Rev.3) or “Demonstration of efficacy of ectoparasiticides » (7AE17a) depending on the relevant ectoparasites.

V. OVERALL CONCLUSION AND BENEFIT– RISK ASSESSMENT

The data submitted in the dossier demonstrate that when the product is used in accordance with the Summary of Product Characteristics, the risk benefit profile for the target species is favourable and the quality and safety of the product for humans and the environment is acceptable.

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 veterinary Heads of Agencies website (https://www.hma.eu/veterinarymedicines.html).

This section 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.

<None>