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AGENCE NATIONALE DU
MEDICAMENT VETERINAIRE

FRENCH AGENCY FOR FOOD, ENVIRONNEMENTAL AND OCCUPATIONAL HEALTH SAFETY

FRENCH AGENCY FOR VETERINARY MEDICINAL PRODUCTS

14 RUE CLAUDE BOURGELAT – PARC D'ACTIVITES DE LA GRANDE MARCHE JAVENE – CS 70611 – 35306 FOUGERES

PUBLICLY AVAILABLE ASSESSMENT REPORT FOR A VETERINARY MEDICINAL PRODUCT

Vitakraft 1.25 g + 0.56 g medicated collar for cats (FR)
REMUVET PRO 1.25 g + 0.56 g medicated collar for cats (ES, IT, PT)

Vitakraft 1.25 g + 0.56 g medicated collar for dogs up to 8 kg (FR)
REMUVET PRO 1.25 g + 0.56 g medicated collar for dogs up to 8 kg (ES, IT, PT)

Vitakraft 4.50 g + 2.03 g medicated collar for dogs over 8 kg (FR)
REMUVET PRO 4.50 g + 2.03 g medicated collar for dogs over 8 kg (ES, IT, PT)

PRODUCT SUMMARY

EU procedure number	FR/V/0513/001-003/DC
Name, strength and pharmaceutical form	Vitakraft 1.25 g + 0.56 g medicated collar for cats (FR) REMUVET PRO 1.25 g + 0.56 g medicated collar for cats (ES, IT, PT) Vitakraft 1.25 g + 0.56 g medicated collar for dogs up to 8 kg (FR) REMUVET PRO 1.25 g + 0.56 g medicated collar for dogs up to 8 kg (ES, IT, PT) Vitakraft 4.50 g + 2.03 g medicated collar for dogs over 8 kg (FR) REMUVET PRO 4.50 g + 2.03 g medicated collar for dogs over 8 kg (ES, IT, PT)
Applicant	BEAPHAR B.V. DROSTENKAMP 3 8101BX RAALTE NETHERLANDS
Active substance(s)	Imidacloprid Flumethrin
ATC vetcode	QP53AC55
Target species	Cats Dogs (≤ 8 kg) Dogs (> 8 kg)
Indication for use	One collar per animal to be fastened around the neck. Cat : For cats with, or at risk from, mixed parasitic infestations by ticks and fleas. The veterinary medicinal product is only indicated when use against ticks and fleas is indicated at the same time. Treatment and prevention of flea re-infestations (*Ctenocephalides felis*) due to insecticidal activity for 5.5 months. Protects the animal's immediate surroundings against flea larvae development for 10 weeks. The veterinary medicinal product can be used as part of a treatment strategy for the control of Flea Allergy Dermatitis (FAD). Prevention of re-infestation with ticks (*Ixodes ricinus*) through acaricidal (killing) effect from 9 days to 8

	months and through repellent (anti-feeding) effect from 2 days to 8 months. It is effective against larvae, nymphs and adult ticks. Dogs: For dogs with, or at risk from, mixed parasitic infestations by ticks or fleas and / or sand flies. The veterinary medicinal product is only indicated when use against ticks or fleas and / or sand flies is indicated at the same time. Treatment and prevention of flea re-infestations (*Ctenocephalides canis, Ctenocephalides feli*s) due to insecticidal activity for 6 months. Protects the animal's immediate surroundings against flea larvae development for 3 months. The veterinary medicinal product can be used as part of a treatment strategy for the control of Flea Allergy Dermatitis (FAD). Prevention of re-infestation with ticks (*Dermacentor reticulatus*) through acaricidal (killing) effect and through repellent (anti-feeding) effect from 2 days to 8 months. Prevention of re-infestation with ticks (*Ixodes ricinus*) through acaricidal (killing) effect from 5 days to 8 months, and through repellent (anti-feeding) effect from 2 days to 8 months. Prevention of re-infestation with ticks (*Rhipicephalus sanguineus*) through acaricidal (killing) effect from 16 days to 8 months, and through repellent (anti-feeding) effect from 14 days to 8 months. It is effective against larvae, nymphs and adult ticks. Reduction of the risk of infection with *Leishmania infantum* via transmission by sand flies for 8 months. The effect is indirect due to the veterinary medicinal product's activity against the vector.

PRODUCT INFORMATION

The Summary of Product Characteristics (SPC), the labelling and package leaflet for this veterinary medicinal product (VMP) is available in the Union Product Database (UPD).

SUMMARY OF ASSESSMENT

Legal basis of original application*	Hybrid application in accordance with Article 19 of Regulation (EC) 2019/6 as amended.
Reference product (RP)	Seresto 1.25 g + 0.56 g collar for cats, Seresto 1.25 g + 0.56 g collar for dogs ≤ 8 kg, Seresto 4.50 g + 2.03 g for dogs > 8 kg
Marketing authorisation holder	ELANCO GmbH
MS where the RP is or has been authorised	AT, BE, BG, CY, CZ, DE, DK, EE, EL, ES, FI, FR, HU, IE, IS, IT, LT, LU, LV, NL, NO, PL, PT, RO, SE, SI, SK, UK(NI)
Marketing authorisation number EU procedure number	DE/V/0143/001/DC, DE/V/0143/002/DC, DE/V/0143/004/DC
Date of authorisation	27 July 2011
Date of completion of the original decentralised procedure	29 October 2025
Concerned Member States for original procedure	AT, BE, BG, CY, CZ, DE, EL, ES, FI, HR, HU, IT, MT, NL, PL, PT, RO, SE, SI
Concerned Member States for subsequent recognition procedure	Not Applicable

*Please be aware that certain parts of the dossier may be varied and consequently be subject to protection of technical documentation – for these and other changes of reference ability to parts of the dossier, please see chapter POST-AUTHORISATION PROCEDURES

1. SCIENTIFIC OVERVIEW

The veterinary medicinal product (VMP) is produced and controlled using validated methods and tests, which ensure the consistency of the VMP released on the market.

It has been shown that the VMP can be safely used in the target species; the reactions observed are indicated in the SPC.

The VMP 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 VMP was demonstrated according to the claims made in the SPC.

The overall risk/benefit analysis is in favour of granting a marketing authorisation.

2. QUALITY DOCUMENTATION (physicochemical, biological or microbiological information)

A. Product description

The veterinary medicinal products are medicated collars containing imidacloprid and flumethrin as active substances. The medicated collars for cats or dogs up to 8 kg contain 1.25 g imidacloprid and 0.56 g flumethrin and the excipients di-n-butyl adipate, epoxidized soybean oil, stearic acid, titanium dioxide, iron oxide black and polyvinyl chloride. The medicated collars for dogs above 8 kg contain 4.50 g imidacloprid and 2.03 g flumethrin and the excipients di-n-butyl adipate, epoxidized soybean oil, stearic acid, titanium dioxide, iron oxide black and polyvinyl chloride.

The collars are individually packed in surlyn/aluminium/PE/PET sachet placed in an outer carton box.

The choice of the formulation is justified.

The VMP is an established pharmaceutical form and its development is adequately described in accordance with the relevant European guidelines.

B. Description of the manufacturing method

The VMP is manufactured fully in accordance with the principles of good manufacturing practice at a licensed manufacturing site.

Process validation data on the VMP have been presented in accordance with the relevant European guidelines.

C. Production and control of starting materials

The active substances are imidacloprid and flumethrin, two established active substances. Imidacloprid is an established substance described in the European Pharmacopeia. Both active substances are manufactured in accordance with the principles of good manufacturing practice.

The active substances specifications are considered adequate to control the quality of the material. Batch analytical data demonstrating compliance with these specifications have been provided.

Scientific data and certificates of suitability issued by the EDQM have been provided.

There are no substances within the scope of the TSE Guideline present or used in the manufacture of this VMP.

D. Control tests carried out on isolated intermediates during the manufacturing process

Not Applicable.

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 VMP.

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.

F. Stability tests

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

G. Other information

Not Applicable.

3. SAFETY DOCUMENTATION (safety and residues tests)

As this is a hybrid application according to Article 19 of Regulation (EC) 2019/6 and equivalence with the reference VMP has been demonstrated, results of toxicological tests are not required. The toxicological aspects of this VMP are identical to the reference VMP. Warnings and precautions as listed on the product literature are adequate to ensure safety of the product to users and the environment.

A. Safety tests

Pharmacological studies

See part 4

Toxicological studies

As this is a hybrid application according to Article 19 of Regulation (EC) 2019/6 and equivalence with a reference VMP has been demonstrated, results of toxicological tests are not required. However, toxicological data are presented which are mainly taken from the European MRL assessment reports.

Other studies

As this is a hybrid application according to Article 19 of Regulation (EC) 2019/6 and equivalence with the reference VMP has been demonstrated, results of safety tests are not required. However, toxicological data are presented which are mainly taken from the European MRL assessment and JECFA reports.

Observations in humans

As this is a hybrid application according to Article 19 of Regulation (EC) 2019/6 and equivalence with the reference VMP has been demonstrated, results of safety tests are not required. However, information on human clinical case reports and reviews were reported.

User safety

The applicant has provided a user safety assessment in compliance with the relevant guideline, which shows that a risk is identified during the application, and for a child, in case of an accidental oral exposure and during the post-application phase.

For the post-application phase, in order to characterise the exposure during animal's petting, a GLP wipe test has been conducted with the final formulation of the proposed VMP.

Warnings and precautions as listed on the product literature are adequate to ensure safety to users of the VMP.

Environmental Risk Assessment

The environmental risk assessment can stop in Phase I and no Phase II assessment is required because the VMP will only be used in non-food animals.

B. Residues documentation

Not applicable, as the test product is intended for non-food producing species.

4. EFFICACY DOCUMENTATION (preclinical studies and clinical trials)

As this is a hybrid application according to Article 19 of Regulation (EC) 2019/6 equivalence to the reference VMP has been demonstrated, and data to support efficacy have been evaluated as the efficacy claims for this VMP are not strictly similar to those of the reference VMP.

A. Pre-Clinical Studies

Pharmacology

Given the legal basis of this application and the claim of equivalence between the candidate and reference products, no pharmacodynamic and pharmacokinetic data were provided.

Pharmaceutical form

The test and the reference products have the same pharmaceutical form, i.e. medicated collar. There are two sizes of collar: 38 and 70 cm, same as the reference products.

Active substance qualitative and quantitative composition

The test and reference products have the same qualitative and quantitative composition in active substances:
1.25 g of imidacloprid and 0.56 g of flumethrin per collar of 38 cm (12.5 g)
and
4.50 g of imidacloprid and 2.03 g of flumethrin per collar of 70 cm (45.0 g)

Bioequivalence studies

No bioequivalence study was provided as this is not relevant according to the non-systemic action of the two active substances.

According to the GL EMEA/CVMP/EWP/005/2000 “for the testing and evaluation of the efficacy of antiparasitic substances for the treatment and prevention of tick and flea infestation in dogs and cats” the requirements of section 7 are applied.

In vivo comparative release studies, conducted with candidate and reference collars, were performed in dogs and in cats. The objective of these studies was to investigate the release of the two active substances, flumethrin and imidacloprid from the candidate and reference collars over time, when worn by dogs or cats for a period of 254 days (8 months), according to the Guideline “The quality of modified release dosage forms for veterinary use (EMA/CVMP/680/02)”.

Equivalence between the products has been concluded according to section 7 of the Guideline for testing and evaluation of the efficacy of antiparasitic substances for the treatment and prevention of tick and flea infestation in dogs and cats (EMEA/CVMP/EWP/005/2000).

Development of resistance and related risk in animals

The bibliographic search on possible resistance of claimed target parasites to imidacloprid or/and flumethrin conducted by the applicant did not identify specific emergence of resistance. Adequate warnings as recommended in the Guideline on the summary of product characteristics for antiparasitic veterinary (EMA/CVMP/EWP/170208/2005) appear in the product literature.

The efficacy of the collar against fleas is insufficient after 5,5 months of collar application in cats and 6 months in dogs. As a risk of development / emergence of resistance of fleas to imidacloprid cannot be excluded, a reasonable use after 5,5 months in cats and 6 months in dogs should be considered by the veterinarian and the pet owner. Beyond this period, in case of continuing flea infestation, the collar should be removed and an adequate treatment may be necessary.

Tolerance in the target species of animals

As this is a hybrid application according to Article 19 of Regulation (EC) 2019/6 and equivalence with the reference VMPs has been demonstrated, results of tolerance tests are not required. However, toxicological data are presented which are mainly taken from the European MRL assessment reports.

The product literature accurately reflects the type and incidence of adverse effects, which might be expected.

B. Clinical trials

Laboratory studies

The procedure is presented as a hybrid application according to Article 19 of Regulation (EC) 2019/6.

As this is an ectoparasiticidal product for external topical use, its efficacy of a proposed generic product has been confirmed under laboratory conditions in at least one controlled dose confirmation study (GCP) for each parasite species proposed for the generic product, on the target animal.

The applicant has conducted 9 dose confirmation studies according to both GCP and 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.

- *Ctenocephalides felis in cats and dogs*

From the study results submitted it can be concluded that the veterinary medicinal product provided immediate and long term insecticidal efficacy against the cat flea *Ct. felis* for 5.5 and 6 months in cats and dogs, respectively.

The larvicidal activity of the debris/hair coat obtained from treated cats and dogs during the course of long term studies have also been tested. A larvicidal blanket test revealed efficacy of 10 weeks and 3 months in the surroundings of treated cats and dogs, respectively. The proven long-term protection periods are adequately considered in the SPC.

For dogs, the applicant has provided relevant data to extrapolate efficacy against *Ctenocephalides felis* to *Ctenicephalides canis.*

- *Flea allergy dermatitis in cats and dogs*

No extra study for flea allergy dermatitis (FAD) has been requested as suitable persistence of efficacy against fleas was confirmed.

<u>Dose confirmation studies in ticks</u>

Dose confirmation studies (2 in cats, 5 in dogs) have been performed to confirm the acaridicidal efficacy of the collar against the main cat ticks i.e. *Ixodes ricinus*, and dog ticks i.e. *Ixodes ricinus, Dermacentor reticulatus* and *Rhipicephalus sanguineus*.

- *Ixodes ricinus* ticks in cats

The acaricidal and repellent efficacies of the collar against *Ixodes ricinus* were studied in two dose confirmation studies and were demonstrated from 9 days and 2 days, respectively, over a period of 11.6 months.

However, due to the absence of adequate clinical data, the same duration for the duration of the efficacy as for the reference product has been retained (8 months).

- *Ixodes ricinus* ticks in dogs

The acaricidal and repellent efficacies of the collar against *Ixodes ricinus* were studied in two dose confirmation studies and were demonstrated from 5 days and 2 days, respectively, over a period of 10.4 months.

However, due to the absence of adequate clinical data, the same duration for the duration of the efficacy as for the reference product has been retained (8 months).

- *Dermacentor reticulatus* ticks in dogs

The acaricidal and repellent efficacies of the collar against *Dermacentor reticulatus* were studied in one dose confirmation study and were demonstrated from 2 days, respectively, over a period of 10.5 months.

However, due to the absence of a second dose confirmation study and of adequate clinical data, the same duration for the duration of the efficacy as for the reference product has been retained (8 months).

- *Rhipicephalus reticulatus* ticks in dogs

The acaricidal and repellent efficacies of the collar against *Rhipicephalus reticulatus* were studied in two dose confirmation studies and were demonstrated from 16 days and 14 days, respectively, over a period of 8 months.

The product is effective against larvae, nymphs and adult ticks.

Clinical trial

- Reduction of the risk of infection with *Leishmania infantum*

The applicant has conducted a clinical trial to assess blocking efficacy of the candidate product in preventing Leishmaniosis caused by *Leishmania infantum* infection. A reduction of the risk of infection with *Leishmania infantum* via transmission by sand flies has been evidenced for 8 months. The effect is indirect due to the veterinary medicinal product's activity against the vector.

5. OVERALL CONCLUSION AND BENEFIT-RISK ASSESSMENT

The data submitted in the dossier demonstrate that when the VMPs are 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 VMP for humans and the environment is acceptable.